Society
for
Neuroscience

PROGRAM and ABSTRACTS

Third Annual Meeting

November 7-10, 1973
San Diego, California

Contents

General Information

REGISTRATION

Convention Center Foyer, Town and Country Hotel

Hours

Wednesday, November 7	10:00 AM– 6:00 PM
Thursday, November 8	7:30 AM– 5:00 PM
Friday, November 9	8:00 AM– 5:00 PM
Saturday, November 10	8:00 AM–11:00 AM

Fees

	In Advance	*At the Meeting*
Members	$25.00	$30.00
Nonmembers	$35.00	$40.00
Graduate Students	$ 5.00	$ 5.00
(Any student working toward a degree in neuroscience or an allied field)		
Social Registrants	$ 3.00	$ 3.00
(Nonscientist family members of registrants)		

Advance registration will be accepted until October 10. Mail appropriate fee to: Neuroscience Annual Meeting Office, 9650 Rockville Pike, Bethesda, Maryland 20014.

The official badge must be worn at all times for admission to scientific sessions, exhibits and social events.

INFORMATION/TICKET DESK AND MESSAGE CENTER

Convention Center Foyer, Town and Country Hotel

Open during registration hours. For information of any kind, consult the Information Desk in the registration area. Important notices about Annual Meeting events will be posted on bulletin boards near the Information/Ticket Desk.

Message boxes will be located adjacent to the registration area for delivery of messages to other registrants. Message boxes should be checked daily for mail, notes and telephone messages. Please suggest that callers who wish to reach you during the day ask the hotel operator (714 291-7131) for the Neuroscience Information Desk.

VISIBLE DIRECTORY OF REGISTRANTS

Convention Center Foyer, Town and Country Hotel

Registration cards are filed in the Visible Directory, located in the registration area. The Directory may be consulted for the hotel address of any registrant. Each advance registrant should check his convention address for accuracy.

PROGRAM AND ABSTRACT VOLUME

The Program/Abstract volume was mailed to each Society member and nonmember advance registrant. An advance registrant or a member registering at the meeting, who does not bring his copy of the Program/Abstract volume, may purchase another copy for $5.00 at the Annual Meeting Office.

TICKETS/SIGN-UP SHEETS

Tickets for the Wild Animal Park Tour/Wine and Cheese Party will be on sale at the Information/Ticket Desk located in the registration area, Convention Center Foyer, Town and Country Hotel. Tickets are $12.00 per person, which includes transportation to and from the Town and Country Hotel, Park admission, tour and monorail, and wine and cheese party at the Inn at Rancho Bernardo. *Tickets must be purchased by 3:00* PM *on Friday.* Tickets for events planned primarily for social registrants will be sold in the Guest Hospitality Room, Town and Country Hotel, Aqua Room.

Individuals interested in attending one of the informal discussion group dinners on Friday (see page 10 for further details) must indicate their attendance by signing the appropriate Special Interest Dinner sheet located at the Information/Ticket Desk, by *5:00* PM *on Thursday.*

ANNUAL MEETING AND SOCIETY OFFICES

Convention Center Foyer, Town and Country Hotel

The office of the Annual Meeting staff is located at the north end of the Convention Center Foyer; the Society office is located at the south end of the Foyer. Offices will be open on Wednesday, November 7, from 9 AM to 6:30 PM, and daily thereafter from 8 AM to 5:30 PM. Registrants requiring assistance with housing, presentation of papers, etc., should consult the Annual Meeting Office. Membership inquiries should be made to the Society office.

LOST AND FOUND

Inquiries concerning lost articles should be made to the Annual Meeting Office. Slides left in session rooms will be delivered by projection operators to this office.

PRESS ROOM

Conventioneer's Office, Convention Center Mezzanine, Town and Country Hotel. Members of the press should register in the Conventioneer's Office.

EXHIBITS

Golden West and California Rooms, Convention Center, Town and Country Hotel

Exhibits of pertinent laboratory equipment, books, and journals will be on display in the Convention Center during the following hours:

Thursday, November 8	8:00 AM– 5:00 PM
Friday, November 9	8:30 AM– 5:00 PM
Saturday, November 10	8:30 AM– 12 NOON

A coffee–discussion lounge will be located in the exhibit area. For exhibit floor plan and alphabetical list of exhibitors, see pages 453–458.

AIRLINES RESERVATIONS AND TICKETS

A Travel Desk operated by American Airlines will be available in the registration area to assist travelers in arranging or confirming reservations with all airlines. The desk will be open on Thursday, 12 NOON–5 PM; Friday, 9 AM–5 PM; and Saturday, 9 AM–11 AM.

COFFEE AND DISCUSSION LOUNGES

Golden West and California Rooms, Convention Center, and the Tiki Hut, Poolside, Town and Country Hotel

The Coffee and Discussion Lounges will be open during exhibit hours. Information about San Diego area attractions will be available.

INFORMAL GROUP DISCUSSIONS

In addition to the Special Interest Dinners on Friday (see page 10 for schedule), limited space is available on a first-come, first-served basis for informal discussions by small groups. Apply for room assignment to the Annual Meeting Office, Convention Center Foyer, Town and Country Hotel.

SOCIAL REGISTRANTS

The Guest Hospitality Room, for family members and guests of scientists, is located in the Aqua Room of the Town and Country Hotel, and is open to all social registrants from 1:00 to 5:00 PM on Wednesday, November 7; 9:00 AM to 5:00 PM on Thursday and Friday; and 9:00 AM until noon on Saturday. Complimentary coffee will be provided. Hostesses will be on hand to greet guests and offer assistance as needed. *All tickets to social registrant events will be sold in the Aqua Room and will not be available in the registration area.* Badges for social registrants who registered prior to October 10 have been placed in the registration packet of the sponsoring scientist. In addition to the Opening Reception on Wednesday and the Wild Animal Park Tour/Wine and Cheese Party on Saturday, social registrants are invited to participate in the following activities:

La Jolla and Salk Institute Tour—Thursday, 1:00–5:00 PM.
Appropriately called "The Jewel of the Pacific," La Jolla has the charm of a quiet Mediterranean Isle, with small shops and beautiful homes. Opportunity for shopping and a guided tour of the Salk Institute for Biological Studies. Transportation $6. Tickets must be purchased by 5:00 PM on Wednesday.

Brunch at Hotel Del Coronado and Shopping in "Old Mexico"—Friday, 9:30 AM–3:00 PM.

The hotel has stood as the city's official landmark since 1888, and because of its beauty is one of the most photographed subjects in the San Diego area.

After brunch, an opportunity to shop in Tijuana, Mexico, for curios and a variety of items imported duty-free from Europe, on the Avenida Revolucion. Transportation and Brunch $11.50. Tickets must be purchased by 2:00 PM on Thursday.

Further details, including bus departure hours, are included in the social registrant Program, available in the Guest Hospitality Room.

HOTEL CHECK-OUT HOUR AND LUGGAGE STORAGE

The check-out hour is 12 noon. Registrants with early afternoon flights on Saturday may wish to check out that morning and store their luggage in the Annual Meeting Office, located in the Convention Center Foyer. Baggage must be claimed by 1:00 PM.

Program Information

SCIENTIFIC SESSIONS

The scientific program begins at 1:30 PM on Wednesday, November 7, and continues through noon on Saturday, November 10.

Morning sessions begin at 8:30 AM; afternoon sessions begin at 1:30 PM and 3:30 PM. Sessions are scheduled in both the Town and Country Hotel and the adjacent LeBaron Hotel. See the Town and Country map, inside front cover, for the location of the gate and walk-through to the LeBaron.

A chart showing the four-day schedule is on pages 12 and 13.

DEMONSTRATIONS: VIDEO TAPE CASSETTES

Video Tape cassettes, demonstrating audio-visual approaches to teaching and innovative techniques and results, are available for viewing during exhibit hours in the Coffee/Discussion Lounge located in the exhibit area, Golden West and California Rooms, Town and Country Hotel. Titles of films submitted to date are as follows:

Wave properties of neural masses. **W. J. FREEMAN.** *Univ. of California, Berkeley, CA.*

Miniature eye movement. **R. M. STEINMAN.** *Univ. of Maryland, College Park, MD.*

Audio-visual approaches to teaching neuroscience. **T. W. SCHOULTZ.** *Univ. of Arkansas Med. Ctr., Little Rock, AR.*

Visual discrimination and reversal training of psychotic children: effect of the addition of verbal cues. **M. H. BAGSHAW.** *Stanford Univ. Sch. of Med., Stanford, CA.*

Basic signals of the nervous system as measured intracellularly in *Aplysia.* **R. P. GRUENER.** *Univ. of Arizona, Tucson, AZ.*

Characteristics of the resting potential as demonstrated by intracellular measurements in frog muscle. **R. P. GRUENER.** *Univ. of Arizona, Tucson, AZ.*

Introduction to the human brain (dissection and description). **J. B. ANGEVINE.** *Univ. of Arizona, Tucson, AZ.*

Experimental control of hyperkinetic and violent behavior in dogs. **S. A. CORSON, E. O'L. CORSON, V. KIRILCUK, J. KIRILCUK, L. E. ARNOLD** and **W. KNOPP.** *Ohio State Univ. Col. of Med., Columbus, OH.*

PANEL DISCUSSIONS

Two panel discussion sessions are scheduled during each afternoon period, 1:30 PM and 3:30 PM, on Thursday and Friday. One of these sessions is a review panel, three are State of the Art discussions, and four are "feedback commentaries." The commentary panels are for the purpose of extended discussion of interesting new research lines derived from abstracts presented at this meeting.

PRESIDENTIAL SYMPOSIUM

Wednesday, 4:00 PM–6:30 PM, Town and Country Room,
Town and Country Hotel

Topic: Brain Surgery and Human Behavior

Speakers: W. J. Nauta, President, Society for Neuroscience; E. Valenstein, University of Michigan; P. Crandall, UCLA; G. Quarton, University of Michigan; and L. Lasagna, University of Rochester.

SOCIETY BUSINESS MEETING

Thursday, 5:00 PM–6:30 PM, Town and Country Room,
Town and Country Hotel

Open to all members of the Society for Neuroscience.

GRASS FOUNDATION LECTURE

Thursday, 8:30 PM, Town and Country Room, Town and Country Hotel

Topic: Biochemical and Physiological Aspects of Dopamine in the Nervous System

Speaker: Arvid E. Carlsson, University of Göteborg, Sweden

PUBLIC LECTURE

Friday, 5:00 PM–6:30 PM, Town and Country Room,
Town and Country Hotel

Topic: Current Status of Research on Transmissible Virus Dementias

Speaker: D. Carleton Gajdusek, NINDS, National Institutes of Health, Bethesda

SOCIAL EVENTS AND SPECIAL FUNCTIONS

Tuesday, November 6

International Society for Developmental Psychobiology

9:00 AM–5:30 PM, *Sunset Room, Town and Country Hotel.* Papers will deal with the behavioral, biochemical and physiological aspects of development both in man and in experimental animals. Luncheon at 12:30 PM, followed by the Presidential Address, "Critical Periods in the Organization of Systems." Society business meeting follows the afternoon session. Further information is available from Dr. Williamina Himwich, Nebraska Psychiatric Institute, University of Nebraska College of Medicine, Omaha, NB 68105.

Society for Neuroscience Committee on Communication

2:00 PM–9:00 PM, *Room 1108, Town and Country Hotel.* To discuss all aspects of the Society's potential contribution to scientist-to-scientist communication. Chapter representatives are welcome.

Wednesday, November 7

International Society for Developmental Psychobiology

9:00 AM–12 NOON, *Sunset Room, Town and Country Hotel.* Continuation of Tuesday meeting.

Society for Neuroscience Chapters Officers and Representatives

9:00 AM–11:30 AM, *Committee Room, Town and Country Hotel.* To encourage participation of the chapters in society activities and provide a direct means of obtaining expressions of chapter opinions and needs.

Opening Reception

6:30 PM–8:00 PM, on the *Patio by the Tiki Hut, Poolside, Town and Country Hotel.* No-host cocktails. All registrants and their guests are cordially invited to attend. In case of inclement weather, the reception will be held in the nearby Meeting House.

Society for Neuroscience Committee on Social Issues Dinner Workshops

Three dinner discussion groups have been planned for consideration of major problem areas and to discuss the possibility of setting up long-term working groups and ways in which the Society might make its best contributions:

1. Psychosurgery. *Chairman:* Dr. Karl Frank, NINDS, NIH, Bethesda, MD 20014.

2. Drug abuse: prescription and non-prescription drugs and problems associated with development of new drugs that promise low economic return. *Chairman:* Dr. Peter Gessner, Dept. of Pharmacology, SUNY, Buffalo, NY 14214.

3. Preventable brain damage: mental retardation in children due to environmental insults, malnutrition or genetic deficiencies; dementia in adults from trauma or alcoholism. *Chairman:* Dr. Max Snodderly, Retina Fndn., 20 Staniford St., Boston, MA 02114.

Society members and Chapter Representatives who wish to reserve a place at a workshop and suggest specific topics for consideration should write to the appropriate chairman by *October 15*. Dinner and discussion will begin at 7:30 PM; the place of each workshop will be posted on the bulletin board located in the registration area.

Chemical Senses Informal Discussion Group

8:00 PM–10:00 PM, *Senate Room, Town and Country Hotel.* An informal meeting of neuroscientists interested in the chemical senses. Anyone who wishes to speak briefly about his or her current research should send an abstract of one or two sentences to Dr. Robert P. Erickson, Department of Psychology, Duke University, Durham, NC 27706, *by September 26.*

Friday, November 9

Special Interest Dinners

Following the Public Lecture, dinner meetings of groups sharing common scientific interests will be held at reasonably priced local restaurants. To date, twelve such dinners have been planned:

Groups	*Coordinators*
1. Biophysics and Neural Modeling	Donald Perkel*
2. Brain Stimulation and Motivation	James Olds
3. EEG and Clinical Neuroscience	Enoch Callaway
4. Memory, Learning and Neural Plasticity	Richard Thompson*
5. Neurochemistry	Eugene Roberts
6. Neuroendocrinology	Charles Sawyer and Anna Taylor
7. Neurotransmitters	Donald Jenden
8. Psychopharmacology	William Clark
9. Sensorimotor Integration and Motor Control	Earl Eldred
10. Tissue Culture	Stanley Crain
11. Ultrastructure and Morphology	The Scheibels
12. Vision	Donald Lindsley

Individuals interested in a particular group are urged to write to the Coordinator prior to November 1. Addresses may be found in the Program and/or Society Directory. *Regardless of prior communication with the Coordinator, individuals planning to attend a particular dinner must sign up on sheets which will be available in the registration area, Town and Country Hotel, by 5:00 PM on Thursday.*

* New addresses: Dr. Donald Perkel, Dept. of Biological Sciences, Stanford University, Stanford, CA 94305; Dr. Richard Thompson, Dept. of Psychology, Harvard University, Cambridge, MA 02138.

Sheets will list the time and place of each dinner.

In addition to the twelve groups listed above, additional groups may be formed by contacting Mrs. Barbara Nichols, Annual Meeting Office, 9650 Rockville Pike, Bethesda, MD 20014 (after November 5, the Town and Country Convention Center).

Saturday, November 10

Wild Animal Park Tour/Wine and Cheese Party

1:30 PM–6:00 PM *Buses will depart from the Fashion Valley Road entrance of the Town and Country Convention Center. Loading begins at 1:15* PM. A special tour of San Diego Zoo's renowned San Pasqual Wild Animal Park, followed by a wine and cheese tasting party, has been planned for registrants and their guests. The Park is an 1800-acre preserve where many exotic species (over 1000 animals) can be observed in surroundings like those of their native homelands. Following a five mile, 50-minute guide-narrated monorail tour, registrants will have the special privilege of touring a major animal research center—The Jerene Appleby Harnish Wild Animal Station for Medical Care and Research, dedicated to the maintenance of health and scientific observation of Park animals. After the "safari" buses will transport registrants to the nearby Inn at Rancho Bernardo for a party featuring California wines with varieties of cheese and breads.

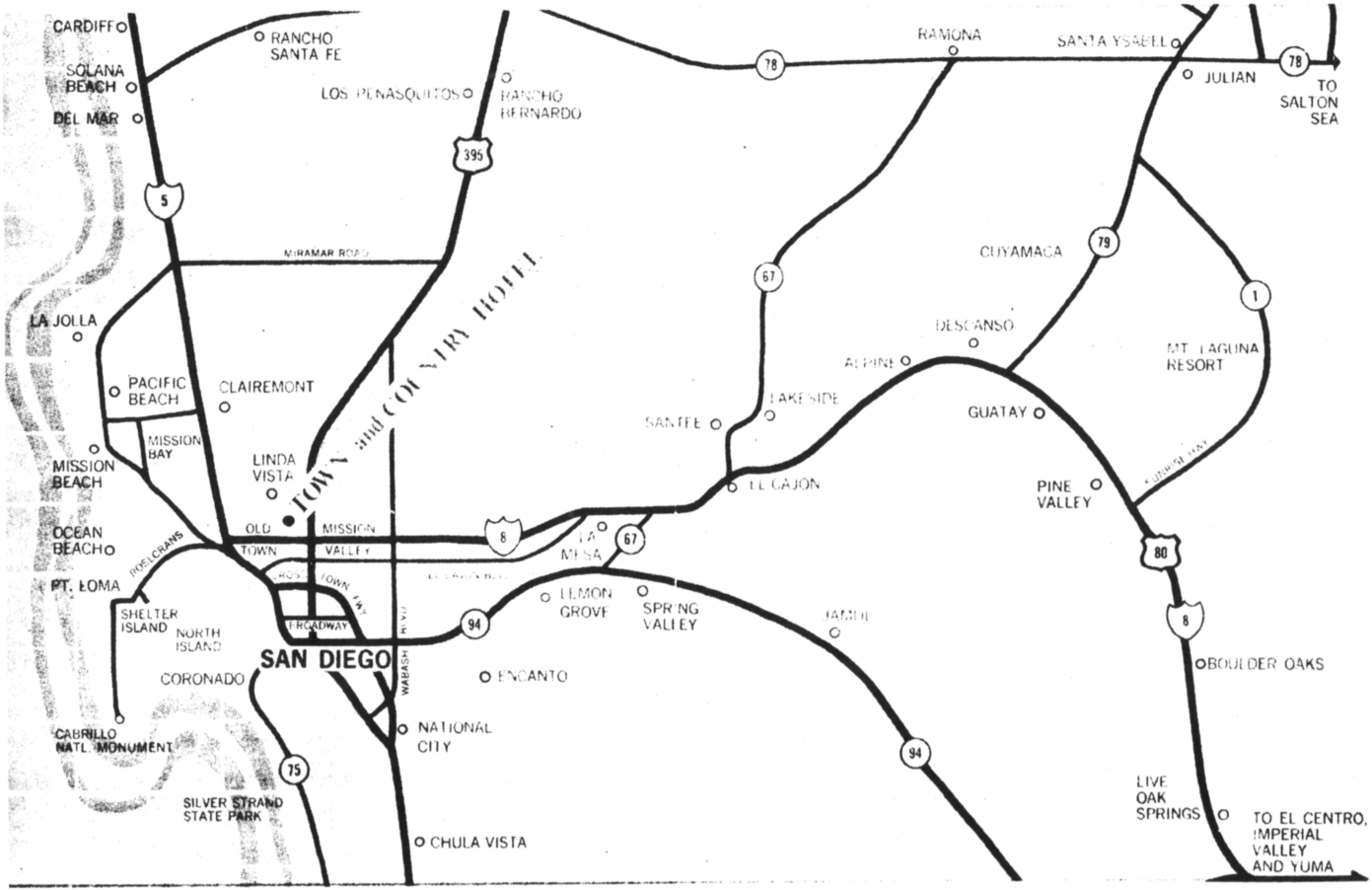
The cost, which includes transportation to and from the Town and Country Hotel, Park admission, monorail, special tour, and wine and cheese party, is $12 per person. Tickets are available at the Information/Ticket Desk in the registration area of the Town and Country Convention Center, and *must be purchased by 3:00* PM *on Friday, November 9.*

* Events planned primarily for Social Registrants

	WEDNESDAY NOVEMBER 7	THURSDAY NOVEMBER 8
MORNING	10 AM–6 PM Registration and Information	7:30 AM–5 PM Registration and Information
		8 AM–5 PM Exhibits
		8:30–11:30 AM Symposia and Volunteer Paper Sessions
AFTERNOON	1:30–4 PM Volunteer Paper Sessions	*1–5 PM La Jolla and Salk Institute Tour
	4–6:30 PM Presidential Symposium	1:30–3 PM Panel Discussions and Volunteer Paper Sessions
		3:30–5 PM Panel Discussions and Volunteer Paper Sessions
EVENING	6:30–8 PM Opening Reception	5–6:30 PM Society Business Meeting
	7:30 PM Committee on Social Issues Dinner Workshops	
	8–10 PM Chemical Senses Discussion Group	8:30 PM Grass Foundation Lecture

CALENDAR

FRIDAY NOVEMBER 9	SATURDAY NOVEMBER 10
8 AM–5 PM Registration and Information	8 AM–11:00 AM Registration and Information
8:30 AM–5 PM Exhibits	8:30 AM–12 NOON Exhibits
8:30–11:30 AM Symposia and Volunteer Paper Sessions	8:30–11:30 AM Symposia and Volunteer Paper Sessions
*9:30 AM–3 PM Hotel Del Coronado Brunch and Tijuana Tour	
1:30–3 PM Panel Discussions and Volunteer Paper Sessions	1:30–6 PM Wild Animal Park Tour and Wine and Cheese Party
3:30–5 PM Panel Discussions and Volunteer Paper Sessions	
5–6:30 PM Public Lecture	
After 6:30 PM Special Interest Group Dinners	



MAP OF SAN DIEGO AREA

VOLUNTEER PAPERS

1. Spinal Reflex Control of Movement

1:30 PM—*Sunrise Room, Town and Country Hotel*

Chairman: **E. ELDRED**

1:30 1.1 Post-contractile changes in static discharge of muscle spindles. **R. S. HUTTON, E. ELDRED** and **J. L. SMITH.** *Univ. of Washington, Seattle, WA, and Univ. of California, Los Angeles, CA.*

1:45 1.2 Fusimotor innervation and response characteristics of the primate muscle spindle. **P. D. CHENEY** and **J. B. PRESTON.** *SUNY Upstate Med. Ctr., Syracuse, N.Y.*

2:00 1.3 On the origin of primary afferent depolarization in the frog cord. **S. GLUSMAN, E. RIVAUD** and **P. RUDOMIN.** *Ctr. Invest. IPN, Mexico 14, DF.*

2:15 1.4 Primary afferent hyperpolarization and presynaptic disinhibition of Ia fiber terminals produced by large cutaneous fibers in the cat cord. **P. RUDOMIN, R. NUNEZ, J. MADRID** and **R. E. BURKE.** *Ctr. Invest. IPN Mexico 14, DF, and NIH, Bethesda, MD.*

2:30 1.5 Analysis of spike activity of the dorsal root reflex. **G. K. MATHESON** and **R. D. WURSTER.** *Stritch Sch. of Med., Loyola Univ., Maywood, IL.*

2:45 1.6 Effects of secondary muscle spindle afferent discharge on extensor motoneurones in the decerebrate cat. **W. Z. RYMER** and **J. V. WALSH.** *NIH, Bethesda, MD.*

3:00 1.7 The identification of group Ib interneurons. **M. E. LUCAS** and **W. D. WILLIS, JR.** *US Army, Office of Surgeon General and Marine Biomed. Inst., Univ. of Texas Med. Branch, Galveston, TX.*

3:15 1.8 Segmental reflexes mediated by joint afferent neurons. **P. GRIGG.** *Univ. of Massachusetts Med. Sch., Worcester, MA.*

3:30 1.9 The involvement of gamma motoneurons in the audiospinal reflex. **G-M. MOOLENAAR** and **C. D. BARNES.** *Howard Univ. Med. Sch., Washington, DC, and Indiana State Univ., Terra Haute, IN.*

3:45 1.10 An electrophysiological study of the spinal cords of deafferented monkeys. **R. M. WYLIE, G. BARRO, P. N. PERRELLA, S. G. WEINBERG** and **E. TAUB.** *Walter Reed Army Med. Ctr., Washington, DC, and Inst. for Behavioral Res., Silver Spring, MD.*

VOLUNTEER PAPERS

2. Synaptic Ultrastructure

1:30 PM—*Council Room, Town and Country Hotel*

Chairman: **T. S. REESE**

1:30 **2.1** Freeze-fracture study of excitatory and inhibitory synapses. **D. M. D. LANDIS** and **T. S. REESE.** *NIH, Bethesda, MD.*

1:45 **2.2** Effects of osmolarity of fixatives on fine structure of synaptic vesicles of nerve terminals in the crayfish stretch receptor. **A. D. TISDALE** and **Y. NAKAJIMA.** *Purdue Univ., W. Lafayette, IN.*

2:00 **2.3** Effects of osmolarity of fixatives on the fine structure of synaptic vesicles in the neuromuscular junctions of the frog. **Y. NAKAJIMA** and **T. NAAB.** *Purdue Univ., W. Lafayette, IN.*

2:15 **2.4** Cytochemical studies of synaptic vesicles and related structures in frog retinal photoreceptor cells. **S. SCHACHER** and **E. HOLTZMAN.** *Columbia Univ., New York, NY.*

2:30 **2.5** An electron microscopic study of alterations in hippocampal dentate gyrus synaptic morphology and associated electron densities: immediate postmortem effects. **A. ROUTTENBERG** and **S. TARRANT.** *Northwestern Univ., Evanston, IL.*

2:45 **2.6** Synaptic profiles on somata and dendrites of the tuberoinfundibular nucleus of the mouse. **N. LEMKEY-JOHNSTON** and **V. BUTLER.** *Illinois State Pediatric Inst. and Univ. of Illinois at the Med. Ctr., Chicago, IL.*

3:00 **2.7** The development of synapses in the cerebellum of the chick embryo. **R. F. FOELIX** and **R. W. OPPENHEIM.** *North Carolina Dept. of Mental Health, Raleigh, NC.*

3:15 **2.8** The anteroventral nucleus of the thalamus: synaptic organization in the albino rat. **N. J. LENN.** *Univ. of Chicago, Chicago, IL.*

3:30 **2.9** A quantitative ultrastructural analysis of the sacral parasympathetic nucleus of the rabbit. **R. W. SOLLER** and **L. L. ROSS.** *Cornell Univ. Med. Col., New York, NY.*

3:45 **2.10** Ultrastructure of ependymal cells and tanycytes of the hypothalamic third ventricle. **R. BLEIER** and **G. SCOTT.** *Univ. of Wisconsin Med. Sch., Madison, WI.*

VOLUNTEER PAPERS

3. Plasticity I

1:30 PM—*Chamber Room, Town and Country Hotel*

Chairman: **J. V. NADLER**

1:30 **3.1** Hemispherectomy and functional plasticity of the human brain. **A. SMITH.** *Univ. of Michigan Med. Sch., Ann Arbor, MI.*

1:45 **3.2** Recovery of structure in injured mammalian brain. **A. F. MARKS.** *Johns Hopkins Univ., Baltimore, MD.*

2:00 **3.3** Axon sprouting in the hippocampal formation and behavioral recovery following unilateral entorhinal cortex lesions. **R. L. SMITH, O. STEWARD, C. COTMAN** and **G. LYNCH.** *Univ. of California, Irvine, CA.*

2:15 **3.4** Sprouting of noradrenergic nerve terminals subsequent to freeze lesions of rabbit cerebral cortex. **F. P. BOWEN, C. DEMIRJIAN, S. E. KARPIAK** and **R. KATZMAN.** *Columbia Univ., Col. of Phys. and Surg., New York, NY, and Albert Einstein Med. Ctr., New York, NY.*

2:30 **3.5** A reversible reduction in accumulation of tyrosine hydroxylase enzyme protein in locus coeruleus after hypothalamic lesions. **R. A. ROSS, T. H. JOH** and **D. J. REIS.** *Cornell Univ. Med. Col., New York, NY.*

2:45 **3.6** Enzymatic development and biochemical plasticity within a developing cholinergic projection in the CNS. **J. V. NADLER, D. A. MATTHEWS, C. W. COTMAN** and **G. S. LYNCH.** *Univ. of California, Irvine, CA.*

3:00 **3.7** Site specific regeneration of type I cutaneous receptors in the cat. **K. W. HORCH, K. B. ENGLISH, L. J. STENSAAS** and **P. R. BURGESS.** *Univ. of Utah Col. of Med., Salt Lake City, UT.*

3:15 **3.8** Precision and plasticity in a regenerating sensory system. **J. PALKA** and **J. S. EDWARDS.** *Univ. of Washington, Seattle, WA.*

VOLUNTEER PAPERS

4. Habituation and Conditioning

1:30 PM—*Cabinet Room, Town and Country Hotel*

Chairman: **J. OLDS**

1:30 **4.1** Conditioned responses in the reticular formation. **J. MONTPLAISIR** and **J. OLDS.** *California Inst. of Tech., Pasadena, CA.*

1:45 **4.2** Habituation and modification of reticular formation neuron responses in cats. **D. F. LINDSLEY, S. K. RANF, M. J. SHERWOOD** and **W. G. PRESTON.** *USC Sch. of Med., Los Angeles, CA.*

2:00 **4.3** Effects of repeated presentation of acoustic stimulation upon evoked potentials in the auditory cortex of the cat. **N. M. WEINBERGER, I. S. WESTENBERG, G. PAIGE, B. GOLUB** and **M. ESPOSITO.** *Univ. of California, Irvine, CA.*

2:15 **4.4** Slow positive potentials in nucleus reticularis thalami during conditioned expectancy in chronic cats. **J. E. SKINNER** and **C. D. YINGLING.** *Methodist Hosp., Baylor Col. of Med., and Rice Univ., Houston, TX.*

2:30 **4.5** Cortical steady potential shift and integrated mass unit activity in forms of temporal conditioning. **P. SHEAFOR** and **V. ROWLAND.** *Case Western Reserve Sch. of Med., Cleveland, OH.*

2:45 **4.6** Differential conditioning of eye blink in cats following bilateral decortication or removal of caudate nucleus. **R. J. NORMAN, J. A. SCHWAFEL, K. A. BROWN, J. R. VILLABLANCA** and **J. S. BUCHWALD.** *Mental Retardation Ctr., UCLA, Los Angeles, CA.*

3:00 **4.7** Acquisition of a classically conditioned eyeblink by pairing click conditioned stimulus with electrical stimulation of facial nerve. **P. BLACK-CLEWORTH, C. D. WOODY** and **J. NIEMANN.** *Mental Retardation Ctr., UCLA, Los Angeles, CA.*

3:15 **4.8** Hyperthermia and operant responding for heat evoked in the monkey by intrahypothalamic prostaglandin. **M. B. WALLER** and **R. D. MYERS.** *Purdue Univ., Lafayette, IN.*

3:30 **4.9** Operant conditioning of cortical steady potential shifts in monkeys. **S. C. ROSEN, D. L. LOISELLE** and **J. S. STAMM.** *SUNY, Stony Brook, NY.*

VOLUNTEER PAPERS

5. Neurohormones

1:30 PM—*Forum Room, Town and Country Hotel*

Chairman: **K. KOIZUMI**

1:30 **5.1** Some electrical and chemical properties of arcuate neurons antidromically identified by stimulation of the median eminence. **R. L. MOSS** and **P. RISKIND.** *Univ. of Texas Southwestern Med. Sch. Dallas, TX.*

1:45 **5.2** Sensory input and firing patterns of antidromically identified supraoptic neurons in unanesthetized monkey. **J. N. HAYWARD** and **K. MURGAS.** *Reed Neurol. Res. Ctr., Sch. of Med., UCLA, Los Angeles, CA.*

2:00 **5.3** Study of neurosecretory cells in vitro: their facilitation and inhibition through axon collaterals. **K. KOIZUMI** and **T. ISHIKAWA.** *SUNY Downstate Med. Ctr., Brooklyn, NY.*

2:15 **5.4** Blockade of angiotensin-induced thirst by 1-Sar-8-Ala angiotensin II analog. **A. N. EPSTEIN, S. HSIAO** and **A. K. JOHNSON.** *Inst. of Neurol. Sci., Univ. of Pennsylvania, Philadelphia, PA.*

2:30 **5.5** Hormonal modulation of aggressive behavior in female hamsters. **O. R. FLOODY** and **D. W. PFAFF.** *Rockefeller Univ., New York, NY.*

2:45 **5.6** Suppression of sexual receptivity in the hormone-primed female hamster by electrical stimulation of the medial preoptic area. **C. W. MALSBURY** and **D. W. PFAFF.** *Rockefeller Univ., New York, NY.*

3:00 **5.7** Strain differences in behavioral sensitivity to testosterone and its neural metabolites in mice. **W. G. LUTTGE** and **N. R. HALL.** *Univ. of Florida Col. of Med., Gainesville, FL.*

3:15 **5.8** Sex differences in the effects of dexamethasone phosphate on behavior in rats. **J. A. MULICK, J. M. JOFFE** and **J. M. PETERSON.** *Univ. of Vermont, Burlington, VT.*

3:30 **5.9** Weanling rat ventromedial versus dorsomedial hypothalamic syndrome. **L. L. BERNARDIS, J. K. GOLDMAN, L. A. FROHMAN** and **J. D. SCHNATZ.** *SUNY at Buffalo, and VA Hosp., Buffalo, NY.*

VOLUNTEER PAPERS

6. Vision: Extraocular Movements

1:30 PM—*Senate Room, Town and Country Hotel*

Chairman: J. SCHLAG

1:30 **6.1** Monkey superior colliculus and eye–head movements. **DAVID LEE ROBINSON** and **C. D. JARVIS.** *NIMH, Bethesda, MD.*

1:45 **6.2** Programming of saccadic eye movements as function of stimulus eccentricity. **D. O. FROST** and **E. O. E. POEPPEL.** *MIT, Cambridge, MA.*

2:00 **6.3** Thalamic involvement in initiation of eye movements. **J. SCHLAG, I. LEHTINEN** and **M. SCHLAG-REY.** *UCLA Sch. of Med., Los Angeles, CA.*

2:15 **6.4** Differentiation of dorsal and ventral abducens neurons by means of motor unit responses. **S. J. GOLDBERG, G. LENNERSTRAND** and **C. D. HULL.** *Mental Retardation Res. Ctr., NPI, UCLA, Los Angeles, CA.*

2:30 **6.5** Brainstem neurons associated with vertical eye movements. **W. M. DAVIS-KING** and **A. F. FUCHS.** *Univ. of Washington, Seattle, WA.*

2:45 **6.6** The response of frontal eye field neurons to visual stimuli and saccadic eye movements in monkey. **C. W. MOHLER, M. E. GOLDBERG** and **R. H. WURTZ.** *NIMH, Bethesda, MD.*

3:00 **6.7** Visual inhibition of nystagmus by the flocculus. **B. COHEN** and **S. TAKEMORI.** *Mt. Sinai Sch. of Med., New York, NY.*

3:15 **6.8** Regulation of extraocular motoneuron discharge at low frequencies. **N. H. BARMACK** and **M. L. DALEY.** *Good Samaritan Hosp. and Med. Ctr., Portland, OR.*

3:30 **6.9** Eye movement potentials following visual deafferentation in cats. **J. B. MUNSON.** *Univ. of Florida Col. of Med., Gainesville, FL.*

3:45 **6.10** Neuronal control of eye movements. **A. T. BAHILL** and **L. STARK.** *Univ. of California, Berkeley, CA.*

PRESIDENTIAL SYMPOSIUM

7. Brain Surgery and Human Behavior

4:00 PM—*Town and Country Room, Town and Country Hotel*

Chairman: **F. PLUM**

Introductory remarks: **W. J. NAUTA**, President, Society for Neuroscience. *MIT, Cambridge, MA.*

The evidence: Can behavior be modified by selective tissue destruction or removal? **E. VALENSTEIN.** *Univ. of Michigan, Ann Arbor, MI.*

Predictability in the operative approach to the brain of man. **P. CRANDALL.** *Univ. of California, Los Angeles, CA.*

Present evidence on the effects of brain surgery on human behavior. **G. QUARTON.** *Univ. of Michigan, Ann Arbor, MI.*

How can one evaluate new treatments that produce irreversible effects? **L. LASAGNA.** *Univ. of Rochester, Rochester, NY.*

SYMPOSIUM

8. The Release of Biologically Active Substances

8:30 AM—*Town and Country Room, Town and Country Hotel*

Chairman: **J. AXELROD**

Excitation secretion coupling mechanisms in secretory cells. **W. W. DOUGLAS.** *Yale Univ., New Haven, CT.*

Adrenal medullary exocytosis. **N. KIRSHNER.** *Duke Univ. Med. Ctr., Durham, NC.*

Mechanisms of exocytosis in sympathetic nerve terminals. **I. J. KOPIN.** *NIMH, Bethesda, MD.*

Actin-like proteins in the release of central transmitters. **S. BERL.** *Columbia Univ., Col. of Phys. and Surg., New York, NY.*

SYMPOSIUM

9. Brain Mechanisms of Social Behavior

8:30 AM—*San Diego Room, Town and Country Hotel*

Chairman: **P. D. MacLEAN**

Role of striatal complex in species-typical behavior of the squirrel monkey (*Saimiri sciureus*). **P. D. MacLEAN.** *NIMH, Bethesda, MD.*

Changes in social behavior evoked by hypothalamic stimulation in rhesus monkeys. **A. A. PERACHIO.** *Yerkes Regional Primate Res. Ctr., Atlanta, GA.*

Limbic lesions and the agonistic and gamopractic behavior of the golden hamster. **B. N. BUNNELL.** *Univ. of Georgia, Athens, GA.*

Amygdalectomy, testosterone, and social behavior in the macaque. **A. KLING.** *Rutgers Med. Sch., Piscataway, NJ.*

VOLUNTEER PAPERS

10. Memory: Transfer, Discrimination

8:30 AM—*Sunrise Room, Town and Country Hotel*

Chairman: **J. M. FUSTER**

8:30 **10.1** Synthetic scotophobin: analysis of effects on mice. **D. H. MALIN** and **G. J. RADCLIFFE, JR.** *Mental Health Res. Inst., Univ. of Michigan, Ann Arbor, MI, and Baylor Col. of Med., Houston, TX.*

8:45 **10.2** Dark-avoidance factor from trained fish brain. **J. L. WARREN, R. C. BRYANT, F. PETTY** and **W. L. BYRNE.** *Brain Res. Inst. and Univ. of Tennessee Med. Units, Memphis, TN.*

9:00 **10.3** Isolation from goldfish brain of two peptides coding for color discrimination-based avoidance behavior. **L. GALVAN** and **G. UNGAR.** *Baylor Col. of Med., Houston, TX.*

9:15 **10.4** Purification from goldfish brain of a peptide facilitating a learned motor adaptation. **J. A. HELTZEL** and **G. UNGAR.** *Baylor Col. of Med., Houston, TX.*

9:30 **10.5** Comparison of direct vs. indirect assessments of biochemically transferred classical conditioning effects in goldfish. **W. G. BRAUD** and **P. V. LAIRD.** *Univ. of Houston, Houston, TX.*

9:45 **10.6** Biochemical transfer of a classical conditioning effect in goldfish with nonreinforced preference testing of recipients. **P. V. LAIRD** and **W. G. BRAUD.** *Univ. of Houston, Houston, TX.*

10:00 **10.7** Enhanced acquisition and the effects of UCB 6215 on the electroretinogram and the evoked potential. **O. L. WOLTHUIS** and **H. de VROOME.** *Med. Biol. Lab. TNO, Rijswijk Z.H., The Netherlands.*

10.15 **10.8** Effects of motivational changes on multiple unit correlates of discrimination training. **S. I. SIDEROFF** and **D. BINDRA.** *McGill Univ., Montreal, Canada.*

10:30 **10.9** Discrete lesions in the area dentata of the mouse hippocampus: memory deficits for an inhibitory avoidance response. **C. A. BOAST** and **S. F. ZORNETZER.** *Univ. of Florida Col. of Med., Gainesville, FL.*

10:45 **10.10** Deficit of delayed color matching by localized cortical cooling. **R. H. BAUER** and **J. M. FUSTER.** *Brain Res. Inst., Sch. of Med., Univ. of California, Los Angeles, CA.*

11.00 **10.11** Detailed analysis of the development and decline of human memory and learning by selective reminding. **H. BUSCHKE.** *Albert Einstein Col. of Med., Bronx, NY.*

11:15 **10.12** A thirty-year retrograde amnesia following electroconvulsive therapy in depressed patients. **L. R. SQUIRE.** *Univ. of California, San Diego Sch. of Med., La Jolla, CA.*

VOLUNTEER PAPERS

11. Neurochemistry: Brain Proteins

8:30 AM—*Council Room, Town and Country Hotel*

Chairman: **C. F. BAXTER**

8:30 **11.1** The uptake and incorporation of amino acids into subcellular brain proteins of trained mice. **M. HERSHKOWITZ.** *Univ. of North Carolina Sch. of Med., Chapel Hill, NC.*

8:45 **11.2** The contribution of plasma glucose carbon to proteins and lipids of brain in fed and fasted rats. **A. BARKAI, S. MAHADIK** and **M. M. RAPPORT.** *New York State Psychiat. Inst. and Columbia Univ., Col. of Phys. and Surg., New York, NY.*

9:00 **11.3** Binding of vinblastine and colchicine to macromolecular components in a soluble fraction from immature rat brain. **S. L. TWOMEY, S. RAEBURN** and **C. F. BAXTER.** *VA Hosp., Sepulveda, CA, City of Hope Natl. Med. Ctr., Duarte, CA, and UCLA Sch. of Med., Los Angeles, CA.*

9:15 **11.4** The circadian rhythm of protein synthesis in a molluscan neuron R15 of *Aplysia.* **Y. P. LOH** and **R. P. PETERSON.** *Univ. of Pennsylvania Sch. of Med., Philadelphia, PA.*

9:30 **11.5** Synaptic regulation of specific protein synthesis in an identified neuron. **H. GAINER** and **J. L. BARKER.** *NIH, Bethesda, MD.*

9:45 **11.6** Electrophoresis of human glia-specific proteins. **E. G. BRUNNGRABER, J. P. SUSZ** and **K. WARECKA.** *Illinois State Psychiat. Inst., Chicago, IL, and Neurochem. Lab. der Psychiat.-Neurol. Klin., Lubeck, Germany.*

10:00 **11.7** Immunofluorescent localization of brain-specific proteins S-100 and 14-3-2. **K. L. SIMS** and **B. W. MOORE.** *NIMH, Washington, DC, and Washington Univ. Sch. of Med., St. Louis, MO.*

10:15 **11.8** Genetic transcription in the cerebrum and cerebellum of the primate brain. **W. E. HAHN.** *Univ. of Colorado Sch. of Med., Denver, CO.*

10:30 **11.9** Protein composition of bovine myelin-free axons. **G. H. De VRIES, M. G. HADFIELD, L. F. ENG** and **B. H. LIWNICZ.** *Virginia Commonwealth Univ., Richmond, VA, VA Hosp., Palo Alto, CA, and Albert Einstein Col. of Med., Bronx, NY.*

10:45 **11.10** The effects of Wallerian degeneration on the proteins and lipids of rat sciatic nerve. **J. G. WOOD** and **R. M. C. DAWSON.** *Inst. of Animal Physiol. Babraham, Cambridge, England.*

11:00 **11.11** Alteration of brain proteinase activities with hypercapnic hypoxia, acute asphyxia, anesthesia, and confinement according to time of day. **G. F. BULETZA, JR.** and **W. B. QUAY.** *Univ. of California, Berkeley, CA.*

VOLUNTEER PAPERS

12. Vestibular System

8:30 AM—*Chamber Room, Town and Country Hotel*

Chairman: **V. J. WILSON**

8:30 **12.1** Intracellular recordings from *Aplysia* statocyst receptor cells. **M. L. WIEDERHOLD.** *Armed Forces Radiobiol. Res. Inst., Bethesda, MD.*

8:45 **12.2** The functional allometry of the semicircular canals of fishes. **H. C. HOWLAND.** *Cornell Univ., Ithaca, NY, and MPIV 8131, Seewiesen, Germany.*

9:00 **12.3** Scanning electron microscopy of the neuromorphology of the peripheral vestibular system in the pigeon and its functional implications. **M. J. CORREIA, E. R. YOUNG** and **J. P. LANDOLT.** *Univ. of Texas Med. Branch, Galveston, TX, and DCIEM, Downsview, Canada.*

9:15 **12.4** Dynamic response characteristics of pigeon primary vestibular neurons. **J. P. LANDOLT** and **M. J. CORREIA.** *DCIEM, Downsview, Canada, and Univ. of Texas Med. Branch, Galveston, TX.*

9:30 **12.5** Branching of vestibulospinal axons. **B. W. PETERSON, C. ABZUG, M. MAEDA** and **V. J. WILSON.** *Rockefeller Univ., New York, NY.*

9:45 **12.6** Dynamic response of brainstem vestibular neurons. **R. H. SCHOR.** *Rockefeller Univ., New York, NY.*

10:00 **12.7** Semicircular canal input to cat neck motoneurons. **V. J. WILSON** and **M. MAEDA.** *Rockefeller Univ., New York, NY.*

10:15 **12.8** Intracellular responses of spinal motoneurons in the pigeon to stimulation of the vestibular system. **A. RABIN.** *Rockefeller Univ., New York, NY.*

10:30 **12.9** Cervical effects on abducens motoneurons and their interaction with vestibulo-ocular reflex. **M. MAEDA** and **O. HIKOSAKA.** *Inst. of Brain Res., Univ. of Tokyo, Japan.*

10:45 **12.10** Projections from specific labyrinthine receptors to trochlear motoneurons. **R. BAKER, W. PRECHT** and **A. BERTHOZ.** *Univ. of Iowa, Iowa City, IA, Max-Planck Inst. for Brain Res., Frankfurt, Germany, and Lab. de Physiol. du Travail, Paris, France.*

11:00 **12.11** Postural responses to galvanic stimuli, modulation by head position and by proprioceptive cues from the feet. **L. M. NASHER.** *Good Samaritan Hosp. and Med. Ctr., Portland, OR.*

THURSDAY MORNING

VOLUNTEER PAPERS

13. Axoplasmic Transport: Experimental Applications

8:30 AM—*Cabinet Room, Town and Country Hotel*

Chairman: **S. OCHS**

8:30 **13.1** Rapid intracellular movements of particles in cultured cerebellar neurons. **D. S. FORMAN, G. R. SIGGINS** and **R. S. LASHER.** *NIMH, St. Elizabeths Hosp., Washington, DC, and Univ. of Colorado Sch. of Med., Denver, CO.*

8:45 **13.2** Cold block of fast axoplasmic transport: reversibility and effects of colchicine and vinblastine. **S. OCHS.** *Indiana Univ. Med. Ctr., Indianapolis, IN.*

9:00 **13.3** Reversibility of fast axoplasmic transport following differing durations of anoxic block in vitro and in vivo. **J. LEONE** and **S. OCHS.** *Indiana Univ. Med. Ctr., Indianapolis, IN.*

9:15 **13.4** Interaction of local anesthetics with microtubules during in vitro repolymerization. **R. H. HASCHKE, M. R. BYERS** and **B. R. FINK.** *Univ. of Washington Sch. of Med., Seattle, WA.*

9:30 **13.5** Dynamics of axoplasmic transport in the optic system of the rat. **D. J. SCHLICHTER** and **W. O. McCLURE.** *Univ. of Illinois, Urbana, IL.*

9:45 **13.6** Projection of noradrenergic neurons of locus coeruleus to telencephalon. **R. Y. MOORE, B. E. JONES** and **A. E. HALARIS.** *Univ. of Chicago, Chicago, IL.*

10:00 **13.7** Tracing of the nigro-striatal projection by electron microscopic autoradiography. **T. HATTORI, H. C. FIBIGER** and **P. L. McGEER.** *Univ. of British Columbia, Vancouver, Canada.*

10:15 **13.8** Connections of the mammillary body in the rat. **J. A. F. CRUCE** and **R. BLEIER.** *Univ. of Wisconsin Med. Sch., Madison, WI.*

10:30 **13.9** Efferent connections of the ventral lateral geniculate nucleus. **L. W. SWANSON** and **W. M. COWAN.** *Washington Univ. Sch. of Med., St. Louis, MO.*

10:45 **13.10** An autoradiographic study of the thalamic and cortical projections of the amygdala in the rat. **J. E. KRETTEK** and **J. L. PRICE.** *Washington Univ. Sch. of Med., St. Louis, MO.*

11:00 **13.11** Mediodorsal nucleus projection to macaque prefrontal cortex: an orthograde study. **T. J. TOBIAS.** *Univ. of Pennsylvania Sch. of Med., Philadelphia, PA.*

VOLUNTEER PAPERS

14. Cerebellum

8:30 AM—*Forum Room, Town and Country Hotel*

Chairman: **R. LLINAS**

8:30 **14.1** Comparison of cerebellar unit and focal activity elicited by graded intensity sound. **R. J. SHOFER** and **A. NEWMAN.** *Albert Einstein Col. of Med., Bronx, NY.*

8:45 **14.2** Trigger features for the visual climbing fiber input to rabbit vestibulo-cerebellum. **J. I. SIMPSON** and **K. E. ALLEY.** *Univ. of Iowa, Iowa City, IA.*

9:00 **14.3** Responses of dentate neurons to inputs from cerebral cortex. **G. I. ALLEN** and **T. OHNO.** *SUNY, Buffalo, NY.*

9:15 **14.4** Muscle afferent pathways to the interpositus nucleus. **W. A. MacKAY** and **J. T. MURPHY.** *Univ. of Toronto, Toronto, Canada.*

9:30 **14.5** Possible sources of preferred centripetal conduction of dendritic spikes in alligator Purkinje cells: a compartmental neuron model. **J. A. MORTIMER** and **E. W. POTTALA.** *NIH, Bethesda, MD.*

9:45 **14.6** Modulation of primary spindle afferents from the region of the red nucleus. **H. B. NUDELMAN, G. AGARWAL** and **J. BRODKEY.** *Univ. of Texas Med. Sch., Houston, TX.*

10:00 **14.7** The spinal action of the dendate output projecting via the "extra-pyramidal" nuclei. **J. R. BLOEDEL.** *Univ. of Minnesota Sch. of Med., Minneapolis, MN.*

10:15 **14.8** Cerebellar dentate nucleus precedes motor cortex in the initiation of a prompt volitional movement. **W. T. THACH.** *Yale Med. Sch., New Haven, CT.*

10:30 **14.9** Electrical transmission between cells in the inferior olive of the cat. **R. LLINAS, R. BAKER** and **C. SOTELO.** *Univ. of Iowa, Iowa City, IA, and Hopital de Port-Royal, Paris, France.*

10:45 **14.10** Two prenatally induced cerebellar malformations in the cat with contrasting symptomatology. **R. K. HADDAD, W. E. LAWSON, R. M. DUMAS** and **A. RABE.** *New York Inst. for Basic Res. in Mental Retardation, New York, NY.*

11:00 **14.11** Predatory attack, grooming and consummatory behaviors evoked by electrical stimulation of cerebellar nuclei in cat. **D. J. REIS, N. DOBA** and **M. A. NATHAN.** *Cornell Univ. Med. Col., New York, NY.*

THURSDAY MORNING

VOLUNTEER PAPERS

15. Developmental Neurobiology: Structure and Function

8:30 AM—*Senate Room, Town and Country Hotel*

Chairman: **B. UZMAN**

8:30 **15.1** Invertebrate synapse: postsynaptic morphology following degeneration of presynaptic structures. **J. J. WINE.** *Stanford Univ., Stanford, CA.*

8:45 **15.2** Renewal and regeneration of olfactory neurons in adult mice. **J. F. METCALF.** *Florida State Univ., Tallahassee, FL.*

9:00 **15.3** Myelin formation: effect of vinblastine sulfate on sciatic nerve development in chick embryos. **B. G. UZMAN, G. M. VILLEGAS** and **F. A. RAWLINS.** *Sparks Regional Med. Ctr., Fort Smith, AR, and Inst. Venezolano de Investigaciones Cientificas, Caracas, Venezuela.*

9:15 **15.4** Synaptogenesis in rat cerebellum. **M. J. WEST** and **M. del CERRO.** *Univ. of Rochester Sch. of Med. and Dent., Rochester, NY.*

9:30 **15.5** Methylazoxymethanol-induced ultrastructural lesions in the postnatal mouse cerebellum. **M. Z. JONES, E. GARDNER** and **M. YANG.** *Michigan State Univ., East Lansing, MI.*

9:45 **15.6** Fine structure of a developing lepidopteran nervous system and its accessibility to lanthanum and horseradish peroxidase. **B. J. McLAUGHLIN.** *Univ. of Cambridge, Cambridge, England.*

10:00 **15.7** The influence of estrogen administered during various times of prepuberal life on the sexual behavior of rats. **S. E. HENDRICKS** and **M. WELTIN.** *Univ. of Nebraska, Omaha, NB.*

10:15 **15.8** Enhanced avoidance conditioning in rats after neonatal injection of testosterone. **A. G. PHILLIPS** and **G. DEOL.** *Univ. of British Columbia, Vancouver, Canada.*

10:30 **15.9** Dendritic branching: attempt to mimic complex environment effects by long-term training. **W. T. GREENOUGH, J. M. JURASKA, D. FLOOD, F. R. VOLKMAR** and **T. DeVOOGD.** *Univ. of Illinois, Urbana-Champaign, IL, and Stanford Univ. Sch. of Med., Stanford, CA.*

10:45 **15.10** Genetic variation in the status of postnatal development of brain and behavior of the mouse. **D. WAHLSTEN.** *Univ. of Waterloo, Waterloo, Canada.*

11:00 **15.11** The neonatal split-brain kitten as an animal model for minimal brain dysfunction. **J. A. SECHZER.** *Cornell Med. Col., White Plains, NY.*

11:15 **15.12** Neural lateralization of vocal control in songbirds. I. Hypoglossal role. **F. NOTTEBOHM.** *Rockefeller Univ., New York, NY.*

VOLUNTEER PAPERS

16. Neural Nets

8:30 AM—*Sunset Room, Town and Country Hotel*

Chairman: **J. A. FREEMAN**

8:30 **16.1** Current source density analysis in the central nervous system: theoretical considerations. **C. NICHOLSON** and **J. A. FREEMAN.** *Univ. of Iowa, Iowa City, IA, and Vanderbilt Univ. Med. Sch., Nashville, TN.*

8:45 **16.2** Optimization of experimental technique for current source density analysis in the central nervous system: application to amphibian cerebellum. **J. A. FREEMAN** and **C. NICHOLSON.** *Vanderbilt Univ. Med. Sch., Nashville, TN, and Univ. of Iowa, Iowa City, IA.*

9:00 **16.3** Reverberations of pulses in real and simulated neuron pools. **R. J. MacGREGOR** and **R. L. PALASEK.** *Univ. of Colorado, Boulder, CO.*

9:15 **16.4** Stochastic properties of an intensity continuum in two neuronal models. **R. J. SCLABASSI, E. LABOS, B. MAGALHAES-CASTRO, B. E. STEIN** and **L. KRUGER.** *UCLA Sch. of Med., Los Angeles, CA.*

9:30 **16.5** Diffusion processes modeling single neuron's activity. **L. M. RICCIARDI.** *Univ. of Chicago, Chicago, IL.*

9:45 **16.6** Theoretical and computer simulation studies of rhythmic activity in the hippocampus. **T. W. CALVERT** and **K-C. YANG.** *Simon Fraser Univ., Burnaby, Canada.*

10:00 **16.7** Spatial filtering properties predicted for cortical neuron populations. **S. M. AHN** and **W. J. FREEMAN.** *Univ. of California, Berkeley, CA.*

10:15 **16.8** An EEG model from randomly connected neural nets. **P. A. ANNINOS** and **V. K. MURTHY.** *UCLA Sch. of Med., Los Angeles, CA.*

VOLUNTEER PAPERS

17. Membranes: Structure and Function

8:30 AM—*Windsor Court Room, Le Baron Hotel*

Chairman: **S. H. BARONDES**

8:30 **17.1** Differential development of tetrodotoxin binding in regions of chick and mouse brain. **D. R. HAFEMANN** and **B. R. UNSWORTH.** *Marquette Univ., Milwaukee, WI.*

8:45 **17.2** Muscle plasma membranes: an in vitro approach to evaluation of their general functions and junctional receptor properties. **B. W. FESTOFF, J. SCIABBARRASI** and **W. K. ENGEL.** *NIH, Bethesda, MD.*

9:00 **17.3** Developmentally regulated agglutinins of formalinized erythrocytes: potential role in intercellular interactions. **S. D. ROSEN, D. L. SIMPSON, J. KAFKA** and **S. H. BARONDES.** *Univ. of California, San Diego Sch. of Med., La Jolla, CA.*

9:15 **17.4** The role of membrane lipids in neuroblastoma differentiation. **R. M. ARNESON, W. G. STRUVE, C. K. CARTWRIGHT** and **P. D. JONES.** *Univ. of Tennessee Med. Units, Memphis, TN.*

9:30 **17.5** Regulation of brain membrane lipids by dietary deficiency. **G. Y. SUN, J. GO, H. WINNICZEK** and **T. M. YAU,** *Cleveland Psychiat. Inst., Cleveland, OH.*

9:45 **17.6** Nodal, paranodal and internodal membranes of cerebellar myelinated fibers visualized by freeze-etching and electron microscopy. **B. SCHNAPP** and **E. MUGNAINI.** *Univ. of Connecticut, Storrs, CT.*

10:00 **17.7** Changes of surface charge on the axon membrane during the development of nervous tissue. **R. C. YU** and **W. HILD.** *Univ. of Texas Med. Branch, Galveston, TX.*

10:15 **17.8** Synaptosome membrane potential changes monitored with a fluorescent probe. **J. M. GOLDRING** and **M. P. BLAUSTEIN.** *Washington Univ. Sch. of Med., St. Louis, MO.*

10:30 **17.9** Threshold changes in single fibers of frog sciatic nerve following nerve impulse discharges. **S. A. RAYMOND.** *MIT, Cambridge, MA.*

10:45 **17.10** Excitabilities in membranous microspheres produced from proteinoid and phospholipid. **Y. ISHIMA** and **S. W. FOX.** *Univ. of Miami, Coral Gables, FL.*

11:00 **17.11** Binding of spin labeled local anesthetics to biological membranes. **H. H. WANG, G. J. GIOTTA, D. D. KOBLIN** and **R. J. GARGIULO.** *Univ. of California, Santa Cruz, CA.*

THURSDAY MORNING

VOLUNTEER PAPERS

18. Chemical Senses

8:30 AM—*Hampton Court Room, Le Baron Hotel*

Chairman: **B. M. WENZEL**

8:30 **18.1** A method to prepare suspensions of taste bud cells. **J. G. BRAND** and **R. H. CAGAN.** *Univ. of Pennsylvania and VA Hosp., Philadelphia, PA.*

8:45 **18.2** Spatial, qualitative, and quantitative integration in rat chorda tympani taste fibers. **I. J. MILLER, JR.** *Bowman Gray Sch. of Med., Wake Forest Univ., Winston-Salem, NC.*

9:00 **18.3** Time course of the rat chorda tympani response to constant depolarizing current. **D. V. SMITH** and **S. L. BEALER.** *Univ. of Wyoming, Laramie, WY.*

9:15 **18.4** Distention-evoked differential modulation of membrane depolarization characteristics of lingual chemoreceptors. **K. N. SHARMA, S. DUA-SHARMA, M. J. K. DOSS** and **H. L. JACOBS.** *St. John's Med. Col., Bangalore, India, and US Army Labs., Natick, MA.*

9:30 **18.5** Response of cat geniculate ganglion tongue units to amino acids, nucleotides and other biochemical substances. **J. C. BOUDREAU.** *Univ. of Texas Grad. Sch. Biomed. Sci., Houston, TX.*

9:45 **18.6** Taste responses of gerbils to inorganic salts. **W. JAKINOVICH, JR.** and **B. OAKLEY.** *Univ. of Michigan, Ann Arbor, MI.*

10:00 **18.7** Multiple sensitivity to chemical stimuli in single human taste papillae. **S. L. BEALER.** *University of Wyoming, Laramie, WY.*

10:15 **18.8** Odor evoked slow potentials in the turtle olfactory bulb. **R. W. BEUERMAN.** *Univ. of Washington Sch. of Med., Seattle, WA.*

10:30 **18.9** Single unit discrimination of fish odors released by salmon populations. **B. OAKLEY, K. B. DOVING** and **H. NORDENG.** *Univ. of Michigan, Ann Arbor, MI, and Univ. of Oslo, Blindern, Norway.*

10:45 **18.10** A neuroanatomical investigation of the olfactory projection field in the pigeon (*Columba livia*). **G. K. RIEKE** and **B. M. WENZEL.** *UCLA Sch. of Med., Los Angeles, CA.*

11:00 **18.11** Odor detection curves for α-ionone in dog and man. **D. A. MARSHALL** and **D. G. MOULTON.** *Univ. of Pennsylvania and VA Hosp., Philadelphia, PA.*

11:15 **18.12** Olfactory continuous recognition task in the assessment of functional brain deficits. **R. G. DAVIS.** *VA Hosp., Knoxville, IA.*

VOLUNTEER PAPERS

19. Visual Cortex

8:30 AM—*Sheffield Court Room, Le Baron Hotel*

Chairman: **J. M. SPRAGUE**

8:30 **19.1** Synaptic and neuroependymal contacts in "visual" cortex of the turtle. **F. F. EBNER** and **M. COLONNIER.** *Brown Univ., Providence, RI, and Univ. of Ottawa, Ottawa, Canada.*

8:45 **19.2** Receptive field properties of visual cortical neurons in the tree shrew (*Tupaia glis*). **P. KAUFMAN, E. WALLINGFORD, R. OSTDAHL** and **G. SOMJEN.** *Duke Univ., Durham, NC.*

9:00 **19.3** Cortical visual areas of the rabbit. **C. N. WOOLSEY, C. SITTHIAMORN, U. T. KEESEY** and **R. A. HOLUB.** *Univ. of Wisconsin Sch. of Med., Madison, WI.*

9:15 **19.4** Effect of interaction of two moving lines on the responses of single units in the cat's visual cortex. **R. W. PHELPS.** *Stanford Med. Sch., Stanford, CA.*

9:30 **19.5** Analysis of motion selectivity in visual cortex neurons of the cat. **L. GANZ** and **A. F. LANGE.** *Stanford Univ., Stanford, CA.*

9:45 **19.6** Structural and functional properties of individual neurons in the striate cortex of the cat. **J. P. KELLY** and **D. C. VAN ESSEN.** *Harvard Med. Sch., Boston, MA.*

10:00 **19.7** Neuronal variability: population responses of visual cortical neurons in normal cat. **G. J. TOMKO** and **D. R. CRAPPER.** *Univ. of Toronto, Toronto, Canada.*

10:15 **19.8** Effect of striate and extra striate visual cortical lesions on learning and retention of form discriminations. **J. M. SPRAGUE, J. LEVY, A. Di BERARDINO** and **J. CONOMY.** *Univ. of Pennsylvania Sch. of Med., Philadelphia, PA.*

10:30 **19.9** Visual perimetry of cats with visual cortex ablations. **S. M. SHERMAN.** *Univ. of Virginia Sch. of Med., Charlottesville, VA.*

10:45 **19.10** Parallel processing of color, shape, and directional information by cells in rhesus monkey foveal striate cortex. **B. M. DOW.** *NIH, Bethesda, MD.*

11:00 **19.11** Extrageniculostriate vision in the monkey: effect of optic chiasm section and accessory optic system lesions. **T. PASIK** and **P. PASIK.** *Mt. Sinai Sch. of Med. and CUNY, New York, NY.*

11:15 **19.12** Psychophysics of electrical stimulation of striate cortex in macaques. **B. B. LEE, R. W. DOTY, J. R. BARTLETT** and **N. NEGRAO.** *Univ. of Rochester, Rochester, NY.*

THURSDAY AFTERNOON

FEEDBACK COMMENTARY PANEL

Extended discussion of new research lines derived from abstracts presented at this meeting.

20. How Are Neuronal Circuits Specified?

1:30 PM—*Town and Country Room, Town and Country Hotel*

Chairman: **M. JACOBSON**

M. JACOBSON. *Univ. of Miami, Miami, FL.*

M. YOON. *Univ. of Dalhousie, Halifax, N.S., Canada.*

H. V. B. HIRSCH. *SUNY, Albany, NY.*

STATE OF THE ART PANEL

21. Hair Cells: A Most Stimulating and Exciting State

1:30 PM—*San Diego Room, Town and Country Hotel*

Chairman: **W. D. NEFF** (Organized by **H. J. KARTEN** and **B. SZAMIER**)

A tale on a tail: transduction in hair cells. **A. FLOCK.** *Konung Gustaf V:s forskninginstitut.*

From herring to hearing: the organ of Corti. **C. SMITH.** *Univ. of Oregon Med. Sch., Portland, OR.*

Electroreceptors: the potency of bald hair cells. **M. V. L. BENNETT.** *Albert Einstein Col. of Med., Bronx, NY.*

How to get out of a shocking jam. **T. H. BULLOCK.** *Univ. of California, San Diego, La Jolla, CA.*

Round Table Discussion
J. FEX. *Indiana Univ., Bloomington, IN.*
L. FRISHKOPF. *MIT, Cambridge, MA.*
A. KALMIJN. *Univ. of California, San Diego, La Jolla, CA.*
B. SZAMIER. *Univ. of Texas, Houston, TX.*

THURSDAY AFTERNOON

VOLUNTEER PAPERS

22. Basal Ganglia

1:30 PM—*Sunrise Room, Town and Country Hotel*

Chairman: **M. R. DeLONG**

1:30 **22.1** Afferent connections of the substantia nigra in the rat. **R. L. SMITH, E. H. STRAYHORN** and **W. R. MEHLER.** *Univ. of California Sch. of Med., San Francisco, CA, and NASA Ames Res. Ctr., Moffett Field, GA.*

1:45 **22.2** Striato-nigral and sensory interactions in centrum medianum. **G. KRAUTHAMER** and **M. DALSASS.** *CMDNJ-Rutgers Med. Sch., Piscataway, NJ.*

2:00 **22.3** Striatal inputs to pallidal neurons. **N. A. BUCHWALD, C. D. HULL, M. S. LEVINE** and **D. R. G. FULLER.** *UCLA, Los Angeles, CA.*

2:15 **22.4** Alterations in spontaneous firing rates of caudate neurons. **M. S. LEVINE, N. A. BUCHWALD** and **J. R. VILLABLANCA.** *UCLA, Los Angeles, CA.*

2:30 **22.5** The interrelationship of dopaminergic and cholinergic influences in the extrapyramidal system of the squirrel monkey. **H. W. GOLDMAN, D. LEHR, E. FRANK** and **P. CASNER.** *New York Med. Col., Valhalla, NY.*

2:45 **22.6** Activity of basal ganglia, motor cortex, and cerebellar neurons during slow and rapid limb movements. **M. R. DeLONG** and **P. L. STRICK.** *NIMH, Bethesda, MD.*

THURSDAY AFTERNOON

VOLUNTEER PAPERS

23. Neurochemistry: Behavioral Correlates

1:30 PM—*Council Room, Town and Country Hotel*

Chairman: **G. P. SMITH**

1:30 **23.1** Phentolamine—an antagonist of cyclic AMP regulation of narcosis. **M. L. COHN** and **M. COHN.** *Univ. of Pittsburgh Sch. of Med., Pittsburgh, PA.*

1:45 **23.2** Opposite effects of intraventricularly infused dopamine and norepinephrine on shock-induced fighting. **M. A. GEYER** and **D. S. SEGAL.** *Univ. of California, San Diego Sch. of Med., La Jolla, CA.*

2:00 **23.3** Direct role of dopa in the central nervous system. **A. J. VAZQUEZ, W. J. GIARDINA, L. MADRID-PEDEMONTE, A. D. MOSNAIM** and **H. C. SABELLI.** *Chicago Med. Sch., Chicago, IL.*

2:15 **23.4** Rats do not explore an open field but are active in home cages after hypothalamic injections of 6-hydroxydopamine. **R. C. YOUNG** and **G. P. SMITH.** *New York Hosp.-Cornell Med. Ctr., White Plains, NY.*

2:30 **23.5** Survival of free-ranging primates after 6-hydroxydopamine. **D. E. REDMOND, JR.** and **J. W. MAAS.** *NIMH, Bethesda, MD, and Yale Col. of Med., New Haven, CT.*

2:45 **23.6** Eating induced by diazepam in rats. **R. A. WISE** and **V. DAWSON.** *Sir George Williams Univ., Montreal, Canada.*

3:00 **23.7** Temporal summation and the neuropharmacology of the reward effect in self-stimulating rats. **C. R. GALLISTEL** and **D. EDMONDS.** *Univ. of Pennsylvania, Philadelphia, PA.*

3:15 **23.8** Effect of serotonin manipulations on activity of rats. **B. L. JACOBS, E. E. EUBANKS** and **W. D. WISE.** *Princeton Univ., Princeton, NJ.*

3:30 **23.9** Effects of Δ^9-tetrahydrocannabinol on social behavior of group-caged macaques. **E. N. SASSENRATH, J. D. COWAN** and **G. P. GOO.** *Univ. of California, Davis Sch. of Med., Davis, CA.*

3:45 **23.10** Muricidal block produced by delta-9-tetrahydrocannabinol. **P. D'ENCARNACAO** and **R. BOWERS.** *Memphis State Univ., Memphis, TN.*

4:00 **23.11** Behavioral and neurophysiological effects of methionine and its metabolites. **J. M. BEATON, G. V. PEGRAM, R. J. BRADLEY** and **J. R. SMYTHIES.** *Univ. of Alabama, Birmingham, AL.*

4:15 **23.12** Rat scotophobin causes temporary dark avoidance in roaches. **H. N. GUTTMAN** and **M. HOFFMAN.** *Univ. of Illinois, Chicago Circle, Chicago, IL.*

4:30 **23.13** Effect of behavioral training on transfer RNAs of goldfish brain. **B. B. KAPLAN, J. C. DYER** and **J. L. SIRLIN.** *Cornell Univ. Med. Col., New York, NY.*

4:45 **23.14** Neural processes involved in the alteration of brain composition by environmental sensory stimulation. **R. N. WALSH, R. A. CUMMINS** and **O. BUDTZ-OLSEN.** *Stanford Univ. Med. Sch., Stanford, CA, and Queensland Univ., Australia.*

VOLUNTEER PAPERS

24. Epilepsy

1:30 PM—*Chamber Room, Town and Country Hotel*

Chairman: **M. A. B. BRAZIER**

1:30 **24.1** Effects of pentylenetetrazol on *Aplysia* neurons: induced oscillations and altered current-voltage relation under voltage clamp. **R. J. DAVID** and **W. A. WILSON.** *Epilepsy Ctr., VA Hosp., Durham, NC.*

1:45 **24.2** Voltage clamp analysis of pentylenetetrazol effects upon excitability in molluskan neurons. **T. L. WILLIAMSON** and **W. E. CRILL.** *Univ. of Washington, Seattle, WA.*

2:00 **24.3** Effect of diphenylhydantoin on the activity of selected enzymes in chronic isolated cerebral cortex of cat and enzyme activities and hyperexcitability in the chronic isolated cerebral cortex monkey. **J. R. GREEN, L. M. HALPERN** and **J. A. AMICK-CORKILL.** *Univ. of Washington Sch. of Med., Seattle, WA.*

2:15 **24.4** Astroglia in alumina epileptic foci. **A. B. HARRIS.** *Univ. of Washington Sch. of Med., Seattle, WA.*

2:30 **24.5** Cortical effects of discrete extradural cobalt implantations in the cat. **G. R. HANNA** and **L. F. STEWART.** *Univ. of Virginia Sch. of Med., Charlottesville, VA.*

2:45 **24.6** Spontaneous seizures produced by long-term repetitive amygdaloid stimulation in rats. **J. P. J. PINEL, A. G. PHILLIPS, R. F. MUCHA** and **G. DEOL.** *Univ. of British Columbia, Vancouver, Canada.*

3:00 **24.7** Determination of critical mass for acetylcholine induced seizure activity. **J. H. FERGUSON, D. R. CORNBLATH** and **P. A. HAVRE.** *Case Western Reserve Univ. Sch. of Med., Cleveland, OH.*

3:15 **24.8** Cholinergic mechanisms of hippocampal epilepsy in cats. **T. L. BABB, C. A. OTTINO** and **P. H. CRANDALL.** *UCLA Sch. of Med., Los Angeles, CA.*

3:30 **24.9** The role of cholinergic pathways in petit mal epilepsy. **J. D. GLASS** and **G. H. FROMM.** *Univ. of Pittsburgh Sch. of Med., Pittsburgh, PA.*

3:45 **24.10** Uridine control of nucleoside incorporation in penicillin-induced experimental epilepsy (*Rana catesbeiana*). **C. A. ROBERTS, N. R. KREISMAN** and **M. WALTMAN.** *Tulane Univ. Sch. of Med., New Orleans, LA.*

4:00 **24.11** Can localized seizure activity be a conditioned signal? An experimental study of epileptic aura. **E. C. ZUCKERMANN** and **M. E. WOLSKI.** *Yale Univ. Sch. of Med., New Haven, CT.*

4:15 **24.12** Immunologically induced effects on EEG and conditioned behavior in rats. **S. E. KARPIAK, F. P. BOWEN** and **M. M. RAPPORT.** *Columbia Univ., Col. of Phys. and Surg., and New York State Psychiat. Inst., New York, NY.*

4:30 **24.13** The anticonvulsant carbamazepine (Tegretol®)—a pilot study. **A. S. TROUPIN** and **J. R. GREEN.** *Univ. of Washington, Seattle, WA.*

4:45 **24.14** Effects of diazepam and phenobarbital on spontaneous electrical activity of the limbic system and cortex in man. **J. P. LIEB, M. A. B. BRAZIER** and **P. H. CRANDALL.** *UCLA Sch. of Med., Los Angeles, CA.*

VOLUNTEER PAPERS

25. Cutaneous Sensation

1:30 PM—*Cabinet Room, Town and Country Hotel*

Chairman: **C. J. VIERCK**

1:30 **25.1** Responses of slowly and rapidly adapting mechanosensitive afferents associated with stiff hairs on the monkey's face. **S. STARKMAN, R. SUMINO, B. MUNGER** and **R. DUBNER.** *NIH, Bethesda, MD, and M. S. Hershey Med. Ctr., Hershey, PA.*

1:45 **25.2** Discharge variability of slowly adapting mechanoreceptive afferent fibers innervating glabrous skin of squirrel monkey and raccoon hand. **L. M. PUBOLS** and **B. H. PUBOLS, JR.** *Hershey Med. Ctr., Pennsylvania State Univ., Hershey, PA.*

2:00 **25.3** Coding of mechanical stimulus velocity and indentation depth during static displacement of squirrel monkey and raccoon slowly adapting mechanoreceptors in glabrous skin. **B. H. PUBOLS, JR.** and **L. M. PUBOLS.** *Hershey Med. Ctr., Pennsylvania State Univ., Hershey, PA.*

2:15 **25.4** Capacity of humans and monkeys for discrimination and identification of vibratory stimuli delivered to the hand. **R. H. LaMOTTE.** *Johns Hopkins Univ., Baltimore, MD.*

2:30 **25.5** Responses of facial cutaneous thermosensitive afferents in the monkey to noxious heat stimulation. **R. SUMINO, S. STARKMAN** and **R. DUBNER.** *NIH, Bethesda, MD.*

2:45 **25.6** Depression of Na^+-K^+ pump as a transduction mechanism of thermoreceptors. **D. C. SPRAY.** *University of Florida Col. of Med., Gainesville, FL.*

3:00 **25.7** Different effects of ouabain on rat cutaneous mechano- and thermoreceptors. **FR.-K. PIERAU** and **D. CARPENTER.** *Armed Forces Radiobiol. Res. Inst., Bethesda, MD.*

3:15 **25.8** Spinal cord dorsal horn cells subserving peripheral nerve stimulation in *Gallus domesticus.* **J. A. HOLLOWAY.** *Howard Univ. Sch. of Med., Washington, DC.*

3:30 **25.9** Organization of the dorsal spinal gray of cat as studied by quantitative stimulation of the type I receptor system. **D. N. TAPPER** and **P. B. BROWN.** *Cornell Univ., Ithaca, NY.*

3:45 **25.10** Responses of dorsal horn cells to graded noxious and non-noxious stimuli. **A. C. BROWE** and **D. D. PRICE.** *Med. Col. of Virginia, Virginia Commonwealth Univ., Richmond, VA.*

4:00 **25.11** Somatotopic representation of hindlimb skin in dorsal horn of cat. **P. B. BROWN** and **J. L. FUCHS.** *Boston State Hosp., Boston, MA.*

4:15 **25.12** Somatotopic organization of external cuneate nucleus in albino rats. **T. D. PARKER, S. R. CAMPBELL** and **W. I. WELKER.** *Univ. of Wisconsin, Madison, WI.*

4:30 **25.13** Response properties of neurons in the trigeminal nucleus excited by the lingual nerve. **M. A. BIEDENBACH.** *Univ. of Washington, Seattle, WA.*

4:45 **25.14** Absolute and differential sensitivities to touch stimuli after spinal cord lesions in monkeys. **C. J. VIERCK, JR.** *Univ. of Florida Col. of Med. and VA Hosp., Gainesville, FL.*

VOLUNTEER PAPERS

26. Adrenergic Mechanisms

1:30 PM—*Forum Room, Town and Country Hotel*

Chairman: **E. COSTA**

1:30 **26.1** Fluorometric assay of dopamine with fluorescamine. **K. IMAI, S. STEIN, P. BOHLEN** and **S. UDENFRIEND.** *Roche Inst. of Molec. Biol., Nutley, NJ.*

1:45 **26.2** Regulation of catecholamine synthesis in rat brain synaptosomes **R. L. PATRICK** and **J. BARCHAS.** *Stanford Univ. Sch. of Med., Stanford, CA.*

2:00 **26.3** CNS inhibitors of dopamine-β-hydroxylase. **F. C. BROWN** and **M. DeFOOR.** *Univ. of Tennessee, Memphis, TN.*

2:15 **26.4** Dopamine-β-hydroxylase from adrenal chromaffin granules: evidence for a common glycoprotein subunit structure for soluble and membrane-bound forms. **H. B. POLLARD, N. M. CHASE** and **J. T. COYLE.** *NIH, Bethesda, MD.*

2:30 **26.5** The relationship among multiple forms of monoamine oxidase. **J. C. SHIH** and **S. EIDUSON.** *UCLA, Los Angeles, CA.*

2:45 **26.6** Effect of amantadine on the stimulation induced release of ^{3}H-norepinephrine by the sympathetic nerve terminals of the rat iris. **C. MYTILINEOU** and **R. E. BARRETT.** *Columbia Univ., New York, NY.*

3:00 **26.7** Exocytosis and endocytosis in the isolated adrenal perfused with horseradish peroxidase. **J. A. THOMAS, N. B. THOA, J. L. COSTA** and **I. J. KOPIN.** *NIMH, Bethesda, MD.*

3:15 **26.8** Norepinephrine turnover in the central nervous system—estimated in the rat from urinary 3-methoxy-4-hydroxyphenylglycol excretion. **F. KAROUM, R. WYATT** and **E. COSTA.** *NIMH, St. Elizabeths Hosp., Washington, DC.*

3:30 **26.9** Effect of trypsin on norepinephrine uptake in cortical homogenates and nerve ending particles. **B. A. HITZEMANN, R. J. HITZEMANN** and **H. H. LOH.** *Univ. of California, San Francisco, CA.*

3:45 **26.10** Ontogeny of catecholamine receptors in the brain. **C. KELLOGG** and **G. WENNERSTROM.** *Univ. of Rochester, Rochester, NY.*

4:00 **26.11** Cyclic adenosine 3',5'-monophosphate: selective increase in the rat striatum following the administration of L-dopa. **E. GARELIS** and **N. H. NEFF.** *NIMH, St. Elizabeths Hosp., Washington, DC.*

4:15 **26.12** Phenylethylamine and phenylethanolamine in rat brain. **J. WILLNER, H. LeFEVRE** and **E. COSTA.** *NIMH, St. Elizabeths Hosp., Washington, DC.*

4:30 **26.13** Differential effects of two putative neuromodulators: 2-phenylethylamine and phenylethanolamine. **H. C. SABELLI, A. J. VAZQUEZ** and **D. F. FLAVIN.** *Chicago Med. Sch., Chicago, IL.*

4:45 **26.14** Further evidence for a role of 2-phenylethylamine as a mediator for the stimulant action of Δ^9-tetrahydrocannabinol. **A. D. MOSNAIM, C. WHALLEY, W. A. PEDEMONTE, A. J. VAZQUEZ** and **H. C. SABELLI.** *Chicago Med. Sch. and Univ. of Chicago, Chicago, IL.*

THURSDAY AFTERNOON

VOLUNTEER PAPERS

27. Audition

1:30 PM—*Senate Room, Town and Country Hotel*

Chairman: **J. ROSE**

1:30 **27.1** Responses of neurons in nucleus angularis in the domestic chicken to pure tone stimuli. **R.E. BEITEL, M. M. GIBSON** and **M. C. VIVION.** *Univ. of Wisconsin, Madison, WI.*

1:45 **27.2** First spike latency in the anteroventral and posteroventral nuclei of the cat in response to pure tones. **L. KITZES, M. M. GIBSON, J. ROSE** and **J. E. HIND.** *Univ. of Wisconsin Med. Sch., Madison, WI.*

2:00 **27.3** Discharge pattern of cat lateral superior olivary neurons to tone burst stimuli. **C. TSUCHITANI.** *Univ. of Texas, Houston, TX.*

2:15 **27.4** Plastic properties of vocalization detector cells in monkey auditory cortex: arousal level and reticular stimulation. **J. D. NEWMAN** and **D. SYMMES.** *NIH, Bethesda, MD.*

2:30 **27.5** Electrophysiological evidence of pattern reversals during auditory perception. **L. T. ANDREWS** and **M. L. PINHEIRO.** *Med. Col. of Ohio, Toledo, OH.*

2:45 **27.6** Distribution of volume-conducted auditory-evoked far field potentials on the heads of man, cat, and rat. **J. S. WILLISTON, R. J. PLANTZ** and **D. L. JEWETT.** *Univ. of California, San Francisco, CA.*

VOLUNTEER PAPERS

28. Alcohol

1:30 PM—*Sunset Room, Town and Country Hotel*

Chairman: **E. NOBLE**

1:30 **28.1** Adrenocortical hormone as a mediating factor in ethanol-induced increase of brain ribosomal protein synthesis. **P. Y. SZE** and **J. L. HESS.** *Univ. of Connecticut, Storrs, CT.*

1:45 **28.2** Stimulatory effect of ethanol on in vitro preparation of rat brain choline acetyltransferase activity. **R. B. REISBERG** and **J. J. NOVAL.** *Bureau of Res., New Jersey Neuropsychiat. Inst., Princeton, NJ, and Temple Med. Sch., Philadelphia, PA.*

2:00 **28.3** Increased dopamine level of caudate nucleus associated with chronic alcohol administration. **A. Y. SUN.** *Cleveland Psychiat. Inst., Cleveland, OH.*

2:15 **28.4** Regional differences in nerve impulse activity in response to alcohol. **W. R. KLEMM** and **R. E. STEVENS III.** *Texas A & M Univ., College Station, TX.*

2:30 **28.5** Ethanol withdrawal syndrome in rats: behavioral and electrographic correlates. **B. E. HUNTER, D. W. WALKER, C. A. BOAST** and **S. F. ZORNETZER.** *Univ. of Florida Col. of Med. and VA Hosp., Gainesville, FL.*

2:45 **28.6** Alcohol effects on acquisition, retention, and spontaneous locomotor activity in the common goldfish. **R. C. BRYANT, F. PETTY, J. WARREN** and **W. L. BYRNE.** *Univ. of Tennessee Med. Units, Memphis, TN.*

VOLUNTEER PAPERS

29. Developmental Neurobiology: Visual System

1:30 PM—*Windsor Court Room, Le Baron Hotel*

Chairman: **D. N. SPINELLI**

1:30 **29.1** Development of retinal receptive fields in the neonatal rabbit. **R. H. MASLAND.** *Massachusetts Gen. Hosp., Boston, MA.*

1:45 **29.2** Development of receptive field characteristics of neurons in the dorsal lateral geniculate nucleus of rabbits. **S. C. RAPISARDI, L. H. MATHERS** and **K. L. CHOW.** *Stanford Univ., Stanford, CA.*

2:00 **29.3** Specificity of retino-tectal projection in the chick as studied by partial lesions of the optic cup. **W. J. CROSSLAND, W. M. COWAN, L. A. ROGERS** and **J. P. KELLY.** *Washington Univ. Sch. of Med., St. Louis, MO, and Harvard Med. Sch., Boston, MA.*

2:15 **29.4** Postnatal development of visual acuity, cytoarchitectural and chemical organization of the striate cortex and growth of the brain, pituitary and adrenals in the squirrel monkey (*Saimiri sciureus*). **J. M. ORDY, K. R. BRIZZEE** and **T. SAMORAJSKI.** *Tulane Univ., New Orleans, LA, and Cleveland Psychiat. Inst., Cleveland, OH.*

2:30 **29.5** Visual system in early and late infancy. **D. N. SPINELLI, J. METZLER** and **R. W. PHELPS.** *Stanford Univ. Sch. of Med., Stanford, CA.*

2:45 **29.6** A developmental model for striate cortex. **B. KRIPKE.** *Univ. of Utah Col. of Med., Salt Lake City, UT.*

VOLUNTEER PAPERS

30. Morphine and Addiction I

1:30 PM—*Hampton Court Room, Le Baron Hotel*

Chairman: **H. H. LOH**

1:30 **30.1** Effects of prior morphine dependence on single alternation learning. **K. A. KHAVARI** and **T. C. PETERS.** *Univ. of Wisconsin, Milwaukee, WI.*

1:45 **30.2** Effect of repeated heroin administration on ad lib self-stimulation, eating, and drinking. **G. F. KOOB, N. H. SPECTOR** and **J. L. MEYERHOFF.** *Walter Reed Inst. of Res., Washington, DC.*

2:00 **30.3** Evoked EEG response characteristics of infants born to methadone-treated mothers. **A. LODGE** and **M. M. MARCUS.** *Children's Hosp., San Francisco, CA, and Sonoma State Hosp., Eldridge, CA.*

2:15 **30.4** Period analytic descriptors of the effects of psychotropic drugs in the subhuman primate. **L. P. GONZALEZ, H. L. ALTSHULER** and **N. R. BURCH.** *Texas Res. Inst. of Mental Sci., Houston, TX.*

2:30 **30.5** Pupillary responsivity during acute heroin withdrawal in Viet Nam. **M. G. ROBINSON, J. G. VARNI, R. C. HOWE** and **F. W. HEGGE.** *Walter Reed Army Inst. of Res., Washington, DC.*

2:45 **30.6** The rapid development of tolerance to barbiturates by pellet implantation. **I. K. HO, V. C. SUTHERLAND** and **H. H. LOH.** *Langley Porter Neuropsychiat. Inst. and Univ. of California, San Francisco, CA.*

VOLUNTEER PAPERS

31. Nerve–Muscle Interaction

1:30 PM—*Sheffield Court Room, Le Baron Hotel*

Chairman: **P. G. NELSON**

1:30 **31.1** Fluorescent staining of acetylcholine receptors at vertebrate neuromuscular junctions. **M. J. ANDERSON** and **M. W. COHEN.** *McGill Univ., Montreal, Canada.*

1:45 **31.2** The effects of long-term administration of cholinesterase inhibitors on neuromuscular transmission and morphology in rats. **M. D. WARD, M. S. FORBES** and **T. R. JOHNS.** *Univ. of Virginia Sch. of Med., Charlottesville, VA.*

2:00 **31.3** Acetylcholine receptors in normal and denervated muscle. **D. K. BERG** and **Z. HALL.** *Harvard Med. Sch., Boston, MA.*

2:15 **31.4** Enzyme activity changes related to formation of neuromuscular junctions in cell culture. **B. K. SCHRIER, E. L. GILLER, JR., A. SHAINBERG, H. R. FISK** and **P. G. NELSON.** *NIH, Bethesda, MD.*

2:30 **31.5** A comparison of α-bungarotoxin binding in fast and slow muscle. **R. R. ALMON, C. G. ANDREW** and **S. H. APPEL.** *Duke Med. Ctr., Durham, NC.*

2:45 **31.6** Effect of prednisolone on neuromuscular transmission. **R. W. WILSON, M. D. WARD** and **T. R. JOHNS.** *Univ. of Virginia Sch. of Med., Charlottesville, VA.*

3:00 **31.7** Conductance of single acetylcholine receptors in electroplaques from *Electrophorus electricus.* **H. A. LESTER** and **J-P. CHANGEUX.** *Inst. Pasteur, Paris, France.*

3:15 **31.8** Neuromuscular transmission of the frog during random and regular stimulation. **A. C. SANDERSON** and **D. L. IJPEIJ.** *Delft Univ. of Tech., Delft, and State Univ. of Leiden, Leiden, The Netherlands.*

3:30 **31.9** Lithium and sodium movements in short-term denervated muscle. **N. ROBBINS.** *Case Western Reserve Sch. of Med., Cleveland, OH.*

3:45 **31.10** Histochemical profiles of intrafusal fibers in normal, denervated, cordotomized and denervated guinea pig muscles. **A. MAIER.** *UCLA, Los Angeles, CA.*

4:00 **31.11** Effects of use and disuse on skeletal muscle metabolism. **D. H. RIFENBERICK, J. CARLO** and **S. R. MAX.** *Univ. of Maryland Sch. of Med., Baltimore, MD.*

4:15 **31.12** Dynamic and metabolic properties of slow-twitch muscle as influenced by hyperinnervation and synergist-denervation. **J. LEE** and **V. R. EDGERTON.** *UCLA, Los Angeles, CA.*

4:30 **31.13** Contractile properties of dog gastrocnemius muscle during reflex recruitment of motor units. **D. J. REED.** *Univ. of Oregon Med. Sch., Portland, OR.*

4:45 **31.14** Effects of inactivity and programmed stimulation on the physiology of a cat tail muscle. **D. A. RILEY.** *NIH, Bethesda, MD.*

STATE OF THE ART PANEL

32. Cell Marker Techniques for Neuroanatomical Investigations

3:30 PM—*Town and Country Room, Town and Country Hotel*

Chairman: **R. J. LASEK**

The cellular basis of the movement of markers within neurons. **R. J. LASEK.** *Case Western Res. Univ., Cleveland, OH.*

Tracing neuronal connections with radioisotopes applied extracellularly. **A. HENDRICKSON.** *Univ. of Washington Sch. of Med., Seattle, WA.*

Intracellular injection of ^{3}H-amino acids in studies of vertebrate neurons. **A. GLOBUS.** *Univ. of California, Irvine, CA.*

Iontophoresis of dyes and heavy metals in studies of neuronal geometry. **C. TWEEDLE.** *Michigan State Univ., East Lansing, MI.*

A method based on retrograde intra-axonal transport of proteins to identify cell bodies which give rise to specific axon terminals. **J. LaVAIL.** *Children's Hospital Med. Ctr., Boston, MA.*

Discussion

REVIEW PANEL DISCUSSION

33. Physiology and Pharmacology of Choroid Plexus and Blood–Brain Barrier

3:30 PM—*San Diego Room, Town and Country Hotel*

Chairman: **E. A. BERING**

Cerebrospinal fluid formation, circulation, and absorption. **E. A. BERING, JR.** *NIH, Bethesda, MD.*

Transport mechanisms in the choroid plexus. **M. POLLAY.** *Univ. of New Mexico, Albuquerque, NM.*

Transport mechanisms between brain and CSF. **J. D. FENSTERMACHER.** *NIH, Bethesda, MD.*

Relationships between extracellular fluid of the brain and CSF with evidence for a bulk flow of brain extracellular fluid. **H. CSERR.** *Brown Univ., Providence, RI.*

Amino acid transport in cerebrospinal fluid and brain. **A. LORENZO.** *Children's Hospital Med. Ctr., Boston, MA.*

Discussion

VOLUNTEER PAPERS

34. Neurotransmitters: Acetylcholine

3:30 PM—*Sunrise Room, Town and Country Hotel*

Chairman: **D. J. JENDEN**

3:30 **34.1** Demonstration of adenosine triphosphate and an electron dense particle in cholinergic synaptic vesicles. **A. F. BOYNE, T. P. BOHAN** and **T. H. WILLIAMS.** *Tulane Med. Sch., New Orleans, LA.*

3:45 **34.2** The effect on in vivo ACh release from cat caudate nucleus of surgical and pharmacological manipulation of dopaminergic nigrostriatal neurons. **B. E. JONES, P. GUYUNET, A. CHERAMY, C. GAUCHY** and **J. GLOWINSKI.** *Col. de France, Paris, France.*

4:00 **34.3** Specific choline accumulating synaptosomes in rat brain. **H. I. YAMAMURA** and **S. H. SNYDER.** *Johns Hopkins Univ. Sch. of Med., Baltimore, MD.*

4:15 **34.4** Kinetic study of choline in plasma and brain. **J. J. FREEMAN, R. L. CHOI** and **D. J. JENDEN.** *UCLA Sch. of Med., Los Angeles, CA.*

4:30 **34.5** Kinetic properties of the imidazole catalyzed synthesis of acetylcholine. **A. M. BURT.** *Agricultural Res. Council, Babraham, England.*

4:45 **34.6** Effect of preganglionic denervation on enzymes of acetylcholine metabolism in the ciliary ganglion. **J. B. SUSZKIW, H. UCHIMURA, E. GIACOBINI** and **G. PILAR.** *Univ. of Connecticut, Storrs, CT.*

5:00 **34.7** Total brain choline changes during the development of tolerance to DFP. **V. G. CARSON** and **D. J. JENDEN.** *UCLA Sch. of Med., Los Angeles, CA.*

VOLUNTEER PAPERS

35. Mechanisms of Cellular Habituation

3:30 PM—*Senate Room, Town and Country Hotel*

Chairman: G. HOYLE

3:30 **35.1** Automatic entrainment for a cellular learning study. T. TOSNEY and G. HOYLE. *Univ. of Oregon, Eugene, OR.*

3:45 **35.2** Bulk as a signal regulating feeding behavior in *Aplysia californica.* A. J. SUSSWEIN and I. KUPFERMANN. *New York Univ. Med. Sch. and Public Health Res. Inst., New York, NY.*

4:00 **35.3** Classical conditioning, sensitization and pseudoconditioning in *Aplysia.* B. JAHAN-PARWAR. *Clark Univ., Worcester, MA.*

4:15 **35.4** Firing pattern changes induced by low intensity microwave radiation of isolated neurons from *Aplysia californica.* H. WACHTEL, W. JOINES, R. SEAMAN and C. WALKER. *Duke Univ., Durham, NC.*

4:30 **35.5** Operant modification of unit responses in visual cortex. P. G. SHINKMAN. *Univ. of North Carolina, Chapel Hill, NC.*

4:45 **35.6** Conditioning, extinction, and habituation in the spinal rat. S. F. CHOPIN, M. H. BENNETT and J. M. KERRIGAN. *Louisiana State Univ. Med. Ctr., New Orleans, LA, and Univ. of Pittsburgh Sch. of Med., Pittsburgh, PA.*

5:00 **35.7** Habituation of the flexor reflex in adrenalectomized rats. J. A. PEARSON and R. A. VICKARS. *Univ. of British Columbia, Vancouver, Canada.*

VOLUNTEER PAPERS

36. Cortex: Higher Functions

3:30 PM—*Sunset Room, Town and Country Hotel*

Chairman: **A. L. TOWE**

3:30 **36.1** Size, number and spatial distribution of neurons in layer IV of mouse S I cortex. **J. F. PASTERNAK** and **T. A. WOOLSEY.** *Washington Univ. Sch. of Med., St. Louis, MO.*

3:45 **36.2** Action of topical strychnine on evoked potentials and single neurons of postcruciate cortex of cats. **M. D. MANN** and **A. L. TOWE.** *Univ. of Washington Sch. of Med., Seattle, WA.*

4:00 **36.3** Termination of thalamic afferents in the cat motor cortex. **P. L. STRICK.** *NIMH, Bethesda, MD.*

4:15 **36.4** Simultaneous and independent IPSPs in nearby neurons in cat motor cortex. **W. RAABE.** *St. Paul-Ramsey Hosp., St. Paul, MN.*

4:30 **36.5** Intracellular recording during focal cooling of glia and neurons in cat pericruciate cortex. **A. F. REYNOLDS, JR., G. A. OJEMANN** and **A. A. WARD, JR.** *Univ. of Washington, Seattle, WA.*

4:45 **36.6** The parietal association areas and immediate extrapersonal space. **J. C. LYNCH, C. ACUNA, H. SAKATA, A. GEORGOPOULOS** and **V. B. MOUNTCASTLE.** *Johns Hopkins Univ. Sch. of Med., Baltimore, MD.*

5:00 **36.7** Scanning of cortical neurons in the EEG: a possible mechanism of attention and consciousness. **R. ELUL.** *UCLA Sch. of Med., Los Angeles, CA.*

VOLUNTEER PAPERS

37. Sleep

3:30 PM—*Windsor Court Room, Le Baron Hotel*

Chairman: C. E. SPOONER

3:30 **37.1** Different physiological properties of neurons in the rostral and ventral part of nucleus reticularis thalami. **M. WASZAK.** *VA Hosp. and SUNY, Upstate Med. Ctr., Syracuse, NY.*

3:45 **37.2** Effects of locus coeruleus stimulation on raphe unit activity. **E. BERMAN, W. STERN** and **P. MORGANE.** *Worcester Fndn. for Exp. Biol., Shrewsbury, MA.*

4:00 **37.3** Role of biorhythm of sleep and paradoxical sleep in the periodicity of gonadotrophin secretion in rats. **N. HAGINO** and **S. YAMAOKA.** *Southwest Fndn. for Res. and Educ. and Univ. of Texas Health Sci. Ctr., San Antonio, TX.*

4:15 **37.4** Induction of REM sleep in cats by growth hormone. **W. C. STERN, J. E. JALOWIEC, W. B. FORBES** and **P. J. MORGANE.** *Worcester Fndn. for Exp. Biol., Shrewsbury, MA.*

4:30 **37.5** Ontogeny and character of paradoxical sleep in the chick. **C. J. SCHLEHUBER, D. G. FLAMING, C. E. SPOONER** and **G. D. LANGE.** *Univ. of California, San Diego Sch. of Med., La Jolla, CA.*

4:45 **37.6** Possible direct modulator role of serotonin precursors and metabolites on sleep mechanisms in newly hatched chicks. **W. PEDEMONTE** and **H. C. SABELLI.** *Chicago Med. Sch., Chicago, IL.*

5:00 **37.7** Arousal in the female rat: the effect of stimulus relevance and motivational state. **S. R. ZOLOTH** and **N. T. ADLER.** *Univ. of Pennsylvania, Philadelphia, PA.*

VOLUNTEER PAPERS

38. Hallucinogenic Drugs

3:30 PM—*Hampton Court Room, Le Baron Hotel*

Chairman: **W. H. BRIDGER**

3:30 **38.1** LSD-25 induced "hallucinatory" behavior in cats: relationship to PGO waves. **S. HENRIKSEN, B. JACOBS** and **W. C. DEMENT.** *Stanford Univ. Sch. of Med., Stanford, CA.*

3:45 **38.2** Effect of lysergic acid diethylamide on serotonin content and turnover in six discrete areas of rat brain. **R. D. HUFFMAN** and **W. W. MORGAN.** *Univ. of Texas Med. Sch., San Antonio, TX.*

4:00 **38.3** The role of serotonin in the action of psychotomimetic drugs. **D. X. FREEDMAN** and **A. E. HALARIS.** *Pritzker Sch. of Med., Univ. of Chicago, Chicago, IL.*

4:15 **38.4** Is 3,4-dimethoxyphenylethylamine hallucinogenic? **W. H. BRIDGER, D. M. STOFF** and **I. J. MANDEL.** *Albert Einstein Col. of Med., Bronx, NY.*

4:30 **38.5** CNS stimulus properties of mescaline: lack of generalization by 3,4,5-trimethoxyphenylethanol. **R. G. BROWNE** and **B. T. HO.** *Texas Res. Inst. of Mental Sci., Houston, TX.*

4:45 **38.6** *N*-Methylation of tryptamine and β-phenylethylamine in brain in vitro with *N*-methyltetrahydrofolic acid or *S*-adenosyl-L-methionine as the methyl donor. **L. L. HSU** and **A. J. MANDELL.** *Univ. of California, San Diego Sch. of Med., La Jolla, CA.*

5:00 **38.7** Electroencephalographic alterations produced by kryptopyrrole. **J. L. WALKER.** *Brandon Univ., Brandon, Canada.*

SYMPOSIUM

39. Sex Hormones in Brain Development

8:30 AM—*Town and Country Room, Town and Country Hotel*

Chairman: **R. W. GOY**

Effects of hormones on development of brain-pituitary interrelationships. **R. A. GORSKI.** *Univ. of California Med. Sch., Los Angeles, CA.*

Hormonal determinants of female behavior in the male and female. **A. GERALL** and **J. L. DUNLAP.** *Tulane Univ., New Orleans, LA.*

Hormonal influences on development of sexual behavior: comparative aspects. **R. W. GOY.** *Univ. of Wisconsin, Madison, WI.*

Physiological studies of steroid hormone actions on reproductive behavior. **D. PFAFF.** *Rockefeller Univ., New York, NY.*

Mechanism of hormone action: biotransformation of androgens to estrogens in brain. **F. NAFTOLIN.** *Harvard Univ., Boston, MA.*

SYMPOSIUM

40. Effects of Viruses on Nerve Cells

8:30 AM—*San Diego Room, Town and Country Hotel*

Chairman: **R. T. JOHNSON**

The diversity of pathological reactions to viral infections of the nervous system. **R. T. JOHNSON.** *Johns Hopkins Univ. Sch. of Med., Baltimore, MD.*

Ultrastructural studies of viral infections of neural cells in vitro and in vivo. **C. S. RAINE.** *Albert Einstein Col. of Med., New York, NY.*

Latency of virus in neurons. **J. G. STEVENS.** *Univ. of California, Los Angeles, CA.*

Biochemical correlates of tumorigenic virus transformation. **R. BRADY.** *NIH, Bethesda, MD.*

VOLUNTEER PAPERS

41. Plasticity II

8:30 AM—*Sunrise Room, Town and Country Hotel*

Chairman: **J. J. BERNSTEIN**

8:30 **41.1** Quantitative analysis of the regenerative process following spinal core transection in the nurse shark (*Ginglymostoma cirratum*). **J. B. GELDERD.** *Louisiana State Univ. Med. Ctr., New Orleans, LA.*

8:45 **41.2** Persistent increases in synaptic efficacy following brief tetanic stimulation in isolated frog spinal cord. **P. B. FAREL.** *Univ. of North Carolina Sch. of Med., Chapel Hill, NC.*

9:00 **41.3** Spinal cord regeneration in rats. **E. FERINGA, R. JOHNSON** and **J. WENDT.** *VA Hosp. and Univ. of Michigan, Ann Arbor, MI.*

9:15 **41.4** Alteration in synaptic compliment on neurons proximal to the site of spinal cord hemisection in the rat: a model in neuronal plasticity. **J. J. BERNSTEIN, J. B. GELDERD** and **M. E. BERNSTEIN.** *Univ. of Florida Col. of Med., Gainesville, FL.*

9:30 **41.5** An analysis of pyramidal tract section in trained primates. **R. J. SCHWARTZMAN.** *Univ. of Miami Sch. of Med., Miami, FL.*

9:45 **41.6** Effects of ablation of motor-sensory cortex are different in newborn and mature rats. **S. P. HICKS** and **C. J. D'AMATO.** *Univ. of Michigan, Ann Arbor, MI.*

10:00 **41.7** Structural changes in neurons of the mammalian cerebral cortex associated with increased "use." **L. T. RUTLEDGE, C. WRIGHT** and **J. DUNCAN.** *Univ. of Michigan Med. Sch., Ann Arbor, MI.*

10:15 **41.8** Sensitization and habituation of the plantar cushion reflex in cats. **M. D. EGGER, N. R. ADAMS, J. W. BISHOP** and **C. H. CONE.** *Yale Univ. Sch. of Med., New Haven, CT.*

10:30 **41.9** Selective action of factors controlling post-lesion axonal growth. **G. LYNCH** and **C. W. COTMAN.** *Univ. of California, Irvine, CA.*

10:45 **41.10** Translaminar growth of axons in the kitten LGND following removal of one eye. **T. L. HICKEY** and **R. W. GUILLERY.** *Univ. of Wisconsin, Madison, WI.*

11:00 **41.11** Some cortical synaptic effects of visual deprivation depend on the complexity of the rearing environment. **T. B. FLEISCHMANN.** *Harvard Univ., Cambridge, MA.*

11:15 **41.12** Formation of retinotectal projections during light or dark deprivations in goldfish. **M. G. YOON.** *Dalhousie Univ., Halifax, Canada.*

VOLUNTEER PAPERS

42. Synaptic Transmission: Central

8:30 AM—*Council Room, Town and Country Hotel*

Chairman: J. G. NICHOLLS

8:30 **42.1** Characteristics of evoked potentials from isolated olfactory cortex. C. N. SCHOLFIELD and J. A. HARVEY. *Univ. of Iowa, Iowa City, IA.*

8:45 **42.2** Differences in facilitation and depression at synapses of a sensory cell upon two motoneurons in the leech CNS. K. J. MULLER and J. G. NICHOLLS. *Harvard Med. Sch., Boston, MA.*

9:00 **42.3** Effect of excess K^+ on synaptic transmission through the cuneate nucleus. M. E. MORRIS and K. KRNJEVIC. *McGill Univ., Montreal, Canada.*

9:15 **42.4** α-Bungarotoxin and acetylcholine receptor in brain. V. A. ETEROVIC and E. L. BENNETT. *Univ. of California, Berkeley, CA.*

9:30 **42.5** Two types of inhibition activated by physostigmine in the lateral geniculate nucleus of the cat. N. IWATA, K. HATADA and E. F. DOMINO. *Lafayette Clin., Detroit, and Univ. of Michigan, Ann Arbor, MI.*

9:45 **42.6** Noradrenergic synapses and the effects of microelectrophoretically applied noradrenaline in the ventral horn of the cat spinal cord. L. M. JORDAN. *Univ. of Manitoba, Manitoba, Canada.*

10:00 **42.7** Scorpion toxin-induced catecholamine release from synaptosomes. J. MOSS, R. W. COLBURN and I. J. KOPIN. *NIMH, Bethesda, MD.*

10:15 **42.8** Mechanism of action of a sympathomimetic drug, *para*-methoxyphenylethylamine, in the vertebrate CNS. R. ASHKENAZI, B. HABER, J. D. COULTER and W. D. WILLIS, JR. *Marine Biomed. Inst., Univ. of Texas Med. Branch, Galveston, TX.*

10:30 **42.9** A cyclic AMP-dependent repolarization of neurons (short latency): isolation of a new receptor for cyclic AMP. C. TORDA. *Mt. Sinai Sch. of Med. and Downstate Med. Col., New York, NY.*

10:45 **42.10** Effects of glutamate and glutamate diethylester on natural cutaneous activation of cat spinal cord interneurones. **J. O. DOSTROVSKY** and **B. H. POMERANZ.** *Univ. of Toronto, Toronto, Canada.*

11:00 **42.11** Evidence for a recurrent collateral inhibitory system in the septum. **J. J. MILLER** and **H. McLENNAN.** *Univ. of British Columbia, Vancouver, Canada.*

11:15 **42.12** Prolonged inhibition of pyramidal tract neurons by visceral afferent stimulation. **F. ROSENTHAL, H. COLERIDGE** and **J. C. G. COLERIDGE.** *Univ. of California, San Francisco, CA.*

FRIDAY MORNING

VOLUNTEER PAPERS

43. Memory: Neurochemical and Electrophysiological Manipulations

8:30 AM—*Chamber Room, Town and Country Hotel*

Chairman: **A. CHERKIN**

8:30 **43.1** Memory in the context of the optomotor behavior of crustaceans. **R. HIRSH** and **C. A. G. WIERSMA.** *California Inst. of Tech., Pasadena, CA.*

8:45 **43.2** Cue-dependent amnesia: effects of cycloheximide and the training/reinstatement interval. **E. E. QUINTON.** *Univ. of Louisville, Louisville, KY.*

9:00 **43.3** α-Amanitin, a potent inhibitor of form II DNA-dependent RNA polymerase, and its effects upon active and passive avoidance retention in mice. **P. D. THUT, R. E. HRUSKA, A. KELTER, J. MIZNE** and **T. J. LINDELL.** *Arizona Med. Ctr., Tucson, AZ.*

9:15 **43.4** In vitro RNA polymerase in brain cell nuclei after various types of in vivo stimulation. **P. A. FERCHMIN, J. F. FLOOD** and **E. L. BENNETT.** *Univ. of California, Berkeley, CA.*

9:30 **43.5** Temperature shift or flurothyl attenuate retrograde amnesia in goldfish. **W. H. RIEGE** and **A. CHERKIN.** *VA Hosp., Sepulveda, and UCLA Sch. of Med., Los Angeles, CA.*

9:45 **43.6** Retrograde enhancement of memory by mild flurothyl treatment in the chick. **A. CHERKIN.** *VA Hosp., Sepulveda, and UCLA Sch. of Med., Los Angeles, CA.*

10:00 **43.7** Retrograde amnesia produced by unilateral and bilateral subseizure stimulation of the amygdala. **P. E. GOLD** and **J. L. McGAUGH.** *Sch. of Biol. Sci., Univ. of California, Irvine, CA.*

10:15 **43.8** Amnesic and electrographic effects of an intracranial electroshock in neonatal chicks. **L. K. GERBRANDT, S. E. HERZOG** and **A. CHERKIN.** *California State Univ., Northridge, and VA Hosp., Sepulveda, CA.*

10:30 **43.9** Combined electroconvulsive shock and cycloheximide effects on protein synthesis and memory in mice. **P. T. KELLY, M. L. ANDRY, D. K. ANDRY** and **M. W. LUTTGES.** *Univ. of Colorado, Boulder, CO.*

10:45 **43.10** Memory deficits following inhibition of catecholamine biosynthesis in mice. **R. VAN BUSKIRK, J. W. HAYCOCK** and **J. L. McGAUGH.** *Sch. of Biol. Sci., Univ. of California, Irvine, CA.*

11:00 **43.11** Effects of L-dopa and adenosine 3',5'-cyclic monophosphate on learned behavior in goldfish. **J. C. DYER, B. B. KAPLAN** and **J. L. SIRLIN.** *Cornell Univ. Med. Col., New York, NY.*

11:15 **43.12** Effects of electroconvulsive shock on conditioned autonomic and skeletal responses in rats. **R. R. MILLER** and **A. D. SPRINGER.** *Brooklyn Col., CUNY, Brooklyn, NY.*

FRIDAY MORNING

VOLUNTEER PAPERS

44. Axoplasmic Transport: General

8:30 AM—*Cabinet Room, Town and Country Hotel*

Chairman: **E. G. McGEER**

8:30 **44.1** Profile analysis of isotope distributions established by rapid axoplasmic transport in C-fibers. **G. W. GROSS** and **L. M. BEIDLER.** *Florida State Univ., Tallahassee, FL.*

8:45 **44.2** Analysis of proteins undergoing axonal transport in nigrostriatal neurons. **V. K. SINGH, H. C. FIBIGER, E. G. McGEER** and **P. L. McGEER.** *Univ. of British Columbia, Vancouver, Canada.*

9:00 **44.3** Changes in axoplasmic transport of dopamine in nigrostriatal neurons after reserpine. **H. C. FIBIGER** and **E. G. McGEER.** *Univ. of British Columbia, Vancouver, Canada.*

9:15 **44.4** Effects of corticosterone and protein synthesis inhibitor on brain tryptophan hydroxylase activity. **E. C. AZMITIA, JR.** and **B. S. McEWEN.** *Rockefeller Univ., New York, NY.*

9:30 **44.5** Colchicine blockage of a synaptic modification induced by hyperactivity. **H. L. FERNANDEZ** and **A. L. DONOSO.** *Catholic Univ. of Chile, Santiago, Chile.*

9:45 **44.6** Olfactory mechanisms mediating pheromone responses in cockroaches. **E. F. BLOCK, IV.** *Univ. of Kansas, Lawrence, KS.*

10:00 **44.7** Axonal transport of phospholipid in the goldfish visual system. **S. C. SPECHT, J. A. MILLER** and **B. GRAFSTEIN.** *Cornell Univ. Med. Col., New York, NY.*

10:15 **44.8** Distribution of labeled RNA in the optic nerve of the rabbit after intraocular injection of ^{3}H uridine. **P. GAMBETTI, L. AUTILIO-GAMBETTI** and **B. SHAFER.** *Univ. of Pennsylvania, Philadelphia, PA.*

10:30 **44.9** RNA transport in regenerating optic nerves of goldfish. **N. A. INGOGLIA** and **J. MYCEK.** *New Jersey Med. Sch., Newark, NJ.*

10:45 **44.10** The extent of axoplasmic migration of materials synthesized in the nerve cell body. **C. J. MADSEN** and **S. C. BONDY.** *Univ. of Colorado Med. Ctr., Denver, CO.*

11:00 **44.11** Projections of serotonin neurons of the midbrain raphe. **A. E. HALARIS, B. E. JONES** and **R. Y. MOORE.** *Univ. of Chicago, Chicago, IL.*

FRIDAY MORNING

VOLUNTEER PAPERS

45. Motor Neurons

8:30 AM—*Forum Room, Town and Country Hotel*

Chairman: **E. HENNEMAN**

8:30 **45.1** Glycogen histochemistry in spinal motor neurons of vertebrates. **J. F. CAMPA, H. B. SARNAT** and **J. M. LLOYD.** *Univ. of Virginia Sch. of Med., Charlottesville, VA.*

8:45 **45.2** Motoneuron excitability during sinusoidal foot oscillation. **W. FREEDMAN** and **R. HERMAN.** *Temple Univ. Health Sci. Ctr., Philadelphia, PA.*

9:00 **45.3** Effects of inhibitory inputs on the rank-order of motoneurons. **H. P. CLAMANN** and **E. HENNEMAN.** *Harvard Med. Sch., Boston, MA.*

9:15 **45.4** Spatial and dimensional organization of hypoglossal motoneurons. **P. S. ULINSKI.** *Loyola Univ., Maywood, IL.*

9:30 **45.5** Organization of synaptic input to defined types of motor *units in cat medial gastrocnemius muscle.* ***R. E. BURKE, W. Z. RYMER*** **J. V. WALSH.** *NIH, Bethesda, MD.*

9:45 **45.6** Comparison of time and spatial averaging of afferent input by motor neurons in decerebrate cats. **D. A. HARRIS.** *Harvard Med. Sch., Boston, MA.*

10:00 **45.7** Influence of intramusclar nerve branching on sensory-motor organization in spinal α-motoneurons. **W. D. LETBETTER** and **S. L. WOLF.** *Emory Univ., Atlanta, GA.*

10:15 **45.8** Three modes of motoneuron repetitive firing and comparisons to firing patterns of epileptic and deafferented CNS neurons. **W. H. CALVIN.** *Univ. of Washington, Seattle, WA.*

10:30 **45.9** Segmental influences of cutaneous afferents on gamma motor neurons. **M. De SANTIS.** *Georgetown Univ., Washington, DC.*

10:45 **45.10** Identification and peripheral regulation of single trigeminal alpha and gamma motoneurones in cat. **L. F. GREENWOOD** and **B. J. SESSLE.** *Univ. of Toronto, Toronto, Canada.*

FRIDAY MORNING

VOLUNTEER PAPERS

46. Limbic System I

8:30 AM—*Senate Room, Town and Country Hotel*

Chairman: **A. SIEGEL**

8:30 **46.1** Hypothalamic modification of drinking response dynamics. **P. VRTUNSKI, T. COMET** and **L. R. WOLIN.** *Cleveland Psychiat. Inst., Cleveland, OH.*

8:45 **46.2** Conditioned aggressive behavior. **O. J. ANDY, L. GIURINTANO** and **J. W. LAING.** *Univ. of Mississippi Med. Ctr., Jackson, MS.*

9:00 **46.3** A search for the brainstem origin of two **hypothalamic**-hippocampal systems mediating hippocampal **theta activity and** desynchronization. **A. W. MACADAR** and **D. B. LINDSLEY.** *UCLA, Los Angeles, CA.*

9:15 **46.4** Brain programed stimulation of the brain. **C. C. TURBES, G. T. SCHNEIDER** and **D. L. JOBE.** *Creighton Univ. Sch. of Med., Omaha, NB.*

9:30 **46.5** Firing of human hippocampal neurons **during memory** testing. **E. HALGREN, T. L. BABB** and **P. H. CRANDALL.** *UCLA, Los Angeles, CA.*

9:45 **46.6** A comparative neuroanatomical analysis **of the differential** projections of the hippocampus to the septum. **A. SIEGEL** and **H. EDINGER.** *New Jersey Med. Sch., Newark, NJ.*

10:00 **46.7** Effects of hippocampal deafferentation and deefferentation on activity, nose poke behavior and operant responding in the rat. **P. W. BOWES** and **R. E. MUSTY.** *Univ. of Vermont, Burlington, VT.*

10:15 **46.8** Are there two ascending activating systems to neocortex and hippocampus with different relations to behavior? **C. H. VANDERWOLF.** *Univ. of Western Ontario, London, Canada.*

10:30 **46.9** Prefrontal and insular projections to the entorhinal area in the monkey. **J. ASTRUC** and **G. R. LEICHNETZ.** *Med. Col. of Virginia, Virginia Commonwealth Univ., Richmond, VA.*

10:45 **46.10** Fiber degeneration following lesions in the medial prefrontal cortex of the squirrel monkey. **G. R. LEICHNETZ** and **J. ASTRUC.** *Med. Col. of Virginia, Virginia Commonwealth Univ., Richmond, VA.*

11:00 **46.11** Operant conditioning of 40 Hz activity in the amygdaloid nuclei of the cat. **T. M. KNAPP** and **J. F. LUBAR.** *Univ. of Houston, Houston, TX, and Univ. of Tennessee, Knoxville, TN.*

VOLUNTEER PAPERS

47. Analysis of Synaptic Transmission

8:30 AM—*Sunset Room, Town and Country Hotel*

Chairman: **M. V. L. BENNETT**

8:30 **47.1** The abdominal ganglion of *Aplysia willcoxi*. **J. E. BLANKENSHIP** and **R. E. COGGESHALL**. *Marine Biomed. Inst. and Univ. of Texas Med. Branch, Galveston, TX.*

8:45 **47.2** Synaptology of an interneuron of the abdominal ganglion of *Aplysia* studied by a new intracellular staining technique. **R. GILLETTE** and **B. POMERANZ**. *Univ. of Toronto, Toronto, Canada.*

9:00 **47.3** Autoradiographic analysis with the light and electron microscope of *Aplysia* identified neurons, their processes, and synapses after intrasomatic injection of ^{3}H-L-fucose. **E. B. THOMPSON, J. H. SCHWARTZ** and **E. R. KANDEL**. *Public Health Res. Inst. and New York Univ. Med. Sch., New York, NY.*

9:15 **47.4** Identified motor neurons controlling the circulation in *Aplysia*: synthesis of transmitters and synaptic pharmacology. **G. LIEBESWAR, J. KOESTER** and **J. E. GOLDMAN**. *Public Health Res. Inst. and New York Univ. Med. Sch., New York, NY.*

9:30 **47.5** Stimulation-induced depletion of synaptic vesicles: reversibility during quiescent recovery. **J. J. PYSH, R. G. WILEY** and **C. W. SPENCER**. *Northwestern Univ. Med. Sch., Chicago, IL.*

9:45 **47.6** Depletion of presynaptic vesicles at a vertebrate central synapse following stimulation. **P. G. MODEL** and **M. V. L. BENNETT**. *Albert Einstein Col. of Med., New York, NY.*

10:00 **47.7** Fatigue of transmission at Mauthner fiber–giant fiber synapses of the hatchet fish. **S. M. HIGHSTEIN** and **M. V. L. BENNETT**. *Albert Einstein Col. of Med., New York, NY.*

10:15 **47.8** Physiological and pharmacological properties of neurons in the subesophageal ganglion of the leech. **A. L. KLEINHAUS** and **J. W. PRICHARD**. *Yale Med. Sch., New Haven, CT.*

10:30 **47.9** Two components of facilitation in motor neurons of *Panulirus interruptus* cardiac ganglion. **W. O. FRIESEN**. *Univ. of California San Diego, La Jolla, CA.*

10:45 **47.10** Function of synaptic modulation of **electrotonic** coupling between neurons. **M. E. SPIRA** and **M. V. L. BENNETT.** *Albert Einstein Col. of Med., New York, NY, and Marine Biol. Lab., Woods Hole, MA.*

11:00 **47.11** Electrotonic decrements within *Aplysia* **neurons. K. GRAUBARD.** *Univ. of Washington, Seattle, WA.*

11:15 **47.12** Equilibrium potential of 5HT action **on neuronal** membrane in mammalian brain. **C. C. HUANG and A. S. MARRAZZI.** *Univ. of Missouri Inst. of Psychiat., St. Louis, MO.*

FRIDAY MORNING

VOLUNTEER PAPERS

48. Neurotransmitters: Amino Acids I

8:30 AM—*Windsor Court Room, Le Baron Hotel*

Chairman: **E. ROBERTS**

8:30 **48.1** Kinetic properties of purified brain L-glutamate decarboxylase. **J-Y. WU** and **E. ROBERTS.** *City of Hope Med. Ctr., Duarte, CA.*

8:45 **48.2** Immunochemical comparison of vertebrate glutamic acid decarboxylase. **K. SAITO, J-Y. WU** and **E. ROBERTS.** *City of Hope Med. Ctr., Duarte, CA.*

9:00 **48.3** Stimulus-coupled secretion of GABA from synaptosomes. **D. A. REDBURN, W. B. LEVY** and **C. W. COTMAN.** *Sch. of Biol. Sci., Univ. of California, Irvine, CA.*

9:15 **48.4** The release of amino acids from sensory and motor roots during stimulation. **D. WEINREICH** and **R. HAMMERSCHLAG.** *City of Hope Med. Ctr., Durante, CA.*

9:30 **48.5** Differences in the binding of GABA and glycine to subcellular particles of rat cerebral cortex and spinal cord. **F. V. DeFEUDIS.** *McGill Univ., Montreal, Canada.*

9:45 **48.6** *N*-Methyl bicuculline and the γ-aminobutyric acid receptor. **E. J. PECK, JR., J. M. SCHAEFFER** and **J. H. CLARK.** *Baylor Col. of Med., Houston, TX, and Purdue Univ., W. Lafayette, IN.*

10:00 **48.7** Amino acid neurotransmitters: cerebrospinal fluid changes in ammonia intoxication. **R. G. DACEY** and **W. J. LOGAN.** *Univ. of Virginia Sch. of Med., Charlottesville, VA.*

10:15 **48.8** Monosodium glutamate—a precursor of acetylcholine synthesis in rat brain in vivo. **S. KUMAR** and **R. GHADIMI.** *Methodist Hosp., Brooklyn, NY.*

10:30 **48.9** Glycine receptor binding in the central nervous system. **A. B. YOUNG** and **S. H. SNYDER.** *Johns Hopkins Sch. of Med., Baltimore, MD.*

10:45 **48.10** Hyperpolarizing and depolarizing receptors to glycine on the frog motoneurons. **A. L. PADJEN, R. A. NICOLL** and **J. L. BARKER.** *NIMH, St. Elizabeths Hosp., Washington, DC.*

VOLUNTEER PAPERS

49. Visual Relay Nuclei

8:30 AM—*Hampton Court Room, Le Baron Hotel*

Chairman: **W. R. ADEY**

8:30 **49.1** Interneurons in monkey lateral geniculate nucleus: participation in "triadic" and "non-triadic" synapses. **P. PASIK, T. PASIK, J. HAMORI** and **J. SZENTAGOTHAI.** *Mt. Sinai Sch. of Med., CUNY, New York, NY, and Semmelweis Univ. Med. Sch., Budapest, Hungary.*

8:45 **49.2** Receptive field properties of lateral geniculate neurons in kittens. **R. L. GLENDENNING** and **T. T. NORTON.** *Duke Univ., Durham, N.C.*

9:00 **49.3** Brightness contrast mechanisms of the primate lateral geniculate. **D. M. SNODDERLY, JR., R. L. DeVALOIS, E. W. YUND** and **N. K. HEPLER.** *Retina Fndn., Boston, MA, Univ. of California, Berkeley, and VA Hosp., Martinez, CA.*

9:15 **49.4** Differential modification of responses of tonic and phasic lateral geniculate units to visual flash stimuli after click-flash pairing. **L. M. CHALUPA, A. W. MACADAR** and **D. B. LINDSLEY.** *Brain Res. Inst., UCLA, Los Angeles, CA.*

9:30 **49.5** Excitability changes of lateral geniculate cells following saccadic eye movements of chronic cats. **H. NODA** and **W. R. ADEY.** *UCLA Sch. of Med., Los Angeles, CA.*

9:45 **49.6** Lateral geniculate postsynaptic responses to light stimuli and their relation to energy summation and visual persistence in human visual psychophysics. **D. N. YOUNG, JR.** and **C. D. HULL.** *UCLA Sch. of Med., Los Angeles, CA.*

10:00 **49.7** An analysis of the connections of the inferior and superior divisions of the pulvinar nucleus of the bushbaby (*Galago senegalensis*). **K. K. GLENDENNING, V. CASAGRANDE, J. A. HALL** and **W. C. HALL.** *Duke Univ., Durham, NC.*

10:15 **49.8** The role of the superior colliculus in relearning following unilateral visual cortical lesions in the cat. **B. S. WOOD.** *Cornell Univ. Med. Col., New York, NY.*

10:30 **49.9** Effects of ablation and cooling of visual cortex on the monkey superior colliculus. **M. P. STRYKER.** *MIT, Cambridge, MA.*

10:45 **49.10** Separation of tectal and thalamic visual functions in the frog. **D. INGLE.** *McLean Hosp., Belmont, MA.*

11:00 **49.11** Ontogenic development of retinotopic organization of the superior colliculus of rabbits. **C. SITTHI-AMORN.** *Univ. of Wisconsin, Madison, WI.*

11:15 **49.12** The mode of innervation of the anterior and posterior pretectal nuclei of the rabbit by axons arising from the visual cortex. **R. A. GIOLLI** and **L. C. TOWNS.** *Univ. of California, Irvine, CA.*

FRIDAY MORNING

VOLUNTEER PAPERS

50. Membrane Biophysics

8:30 AM—*Sheffield Court Room, Le Baron Hotel*

Chairman: **W. J. ADELMAN, JR.**

8:30 **50.1** A model for passive electrochemical dynamics in excitable tissue. **J. FROMKIN.** *USC, Los Angeles, CA.*

8:45 **50.2** Effects of temperature changes on the sodium and potassium conductances of *Myxicola* giant axons. **C. L. SCHAUF.** *Rush Med. Col., Chicago, IL.*

9:00 **50.3** Anatomical basis for apparent paradox concerning conduction velocities of two identified axons in *Aplysia.* **H. M. PINSKER, R. FEINSTEIN** and **R. E. COGGESHALL.** *Marine Biomed. Inst., Univ. of Texas Med. Branch, Galveston, TX.*

9:15 **50.4** Tetanic and post-tetanic changes in membrane potential of single medullated nerve fibers. **G. M. SCHOEPFLE** and **C. R. KATHOLI.** *Univ. of Alabama Med. Ctr., Birmingham, AL.*

9:30 **50.5** Solutions of the Hodgkin-Huxley equations modified for potassium accumulation in periaxonal space. **W. J. ADELMAN, JR.** and **R. FITZHUGH.** *NIH, Bethesda, MD.*

9:45 **50.6** Voltage clamp stability with series resistance compensation. **R. E. TAYLOR** and **F. BEZANILLA.** *NIH, Bethesda, MD, and Univ. of Rochester Med. Sch., Rochester, NY.*

10:00 **50.7** Divalent cation regulation of bursting pacemaker activity in molluscan neurons. **J. L. BARKER** and **H. GAINER.** *NIH, Bethesda, MD.*

10:15 **50.8** Potassium conductance change during normal bursting in the *Aplysia* R15 cell. **D. JUNGE** and **C. L. STEPHENS.** *UCLA Sch. of Dent., Los Angeles, CA.*

10:30 **50.9** Interaction between synaptic events in a dendritic cable. **R. NORMAN.** *Univ. of Connecticut, Storrs, CT.*

10:45 **50.10** Selective permanent blockade of excitatory and inhibitory postsynaptic receptors by *p*-nitrothiophenol and pyridoxal phosphate. **M. SATO** and **J. MARUHASHI.** *Univ. of Oregon Med. Sch., Portland, OR.*

11:00 **50.11** 2,4 Dinitrophenol: effect on membrane permeability of molluscan neurons. **H. LEVITAN** and **J. L. BARKER.** *Univ. of Maryland, College Park, MD, and NIH, Bethesda, MD.*

11:15 **50.12** Diphenylhydantoin and calcium movement. **J. H. PINCUS, S. H. LEE** and **M. HASBANI.** *Yale Univ. Sch. of Med., New Haven, CT.*

STATE OF THE ART PANEL

51. Role of Axoplasmic Transport in Neurotrophism

1:30 PM—*Town and Country Room, Town and Country Hotel*

Chairman: **E. X. ALBUQUERQUE**

Selective blockade of trophic influence on mammalian skeletal muscle. **E. X. ALBUQUERQUE.** *SUNY-Buffalo, Buffalo, NY.*

The control of nerve territory by axoplasmic flow. **J. DIAMOND.** *McMaster University, Hamilton, Ont., Canada.*

Trophic interaction between nerve and muscle. **L. GUTH.** *NIH, Bethesda, MD.*

FEEDBACK COMMENTARY PANEL

Extended discussion of new research lines derived from abstracts presented at this meeting.

52. Are Segmental Reflexes Used to Initiate and Control Movement?

1:30 PM—*San Diego Room, Town and Country Hotel*

Chairman: **E. HENNEMAN**

E. HENNEMAN. *Harvard Med. Sch., Boston, MA.*

H. ASANUMA. *Rockefeller Univ., New York, NY.*

L. M. MENDELL. *Duke Univ. Sch. of Med., Durham, NC.*

VOLUNTEER PAPERS

53. Sympathetic Ganglia

1:30 PM—*Sunrise Room, Town and Country Hotel*

Chairman: **R. LEVI-MONTALCINI**

1:30 **53.1** Histofluorescence study of chromaffin cells in dissociated cell cultures of chick embryo sympathetic ganglia. **D. M. JACOBOWITZ** and **L. A. GREENE.** *NIMH and NIH, Bethesda, MD.*

1:45 **53.2** Fluorescence and electron microscopic studies of developing sympathetic neuroblasts in the fetal rabbit. **V. M. TENNYSON.** *Columbia Univ., Col. of Phys. and Surg., New York, NY.*

2:00 **53.3** Excessive glial cell proliferation in sympathetic rat ganglia by combined nerve growth factor and 6-hydroxydopamine treatment. **R. LEVI-MONTALCINI.** *Lab. Biol. Cell. CNR, Rome, Italy, and Washington Univ., St. Louis, MO.*

2:15 **53.4** Non-neuronal and nerve growth factor influences on mouse ganglionic neurons in dissociated cultures. **S. VARON, P. BURNHAM** and **C. RAIBORN.** *Univ. of California, San Diego Sch. of Med., La Jolla, CA.*

2:30 **53.5** Slow synaptic inhibition and adrenergic antagonism in sympathetic ganglion. **F. F. WEIGHT.** *NIMH, St. Elizabeths Hosp., Washington, DC.*

2:45 **53.6** Blockade by polyvalent cations of transmission through sympathetic ganglia of bullfrogs. **G. P. COOPER, M. HOUSER** and **M. LOWENHAUPT.** *Univ. of Cincinnati Col. of Med., Cincinnati, OH.*

VOLUNTEER PAPERS

54. Somatosensory Mechanisms

1:30 PM—*Council Room, Town and Country Hotel*

Chairman: **W. D. WILLIS, JR.**

1:30 **54.1** Convergence of electroreceptor, common cutaneous and optic input to the tectum and elsewhere in the brain of *Torpedo* and other elasmobranchs. **T. H. BULLOCK, C. J. PLATT, G. CZEH, H. KOVACEVIC, DJ. KONJEVIC** and **M. GOJKOVIC.** *International Brain Res. Lab., Kotor, Yugoslavia.*

1:45 **54.2** Somatosensory afferents to the external nucleus of the inferior colliculus. **D. M. SCHROEDER** and **J. A. JANE.** *Univ. of Virginia Sch. of Med., Charlottesville, VA.*

2:00 **54.3** Splanchnic evoked potentials in the dorsal mesencephalon of the pentobarbital-anesthetized rat. **S. T. HUPRICH** and **J. C. LIEBESKIND.** *UCLA, Los Angeles, CA.*

2:15 **54.4** Control of sensory transmission in spinothalamic tract neurons. **W. D. WILLIS, JR., J. D. COULTER** and **R. A. MAUNZ.** *Marine Biomed. Inst., Univ. of Texas Med. Branch, Galveston, TX.*

2:30 **54.5** Effects of dorsal column stimulation on somatosensory responses of cells in the thalamic posterior group of nuclei. **W. K. DONG** and **I. H. WAGMAN.** *Univ. of California, Davis, CA.*

2:45 **54.6** Blockage of pain responses in thalamic neurons by mechanical stimulation of the vagina in rats. **B. R. KOMISARUK** and **J. WALLMAN.** *Rutgers Univ., Newark, NJ.*

3:00 **54.7** Persistence of pain after spinothalamic tractotomy and its relief by dorsal cord stimulation. **H. I. FIELDS.** *Univ. of California, San Francisco, CA.*

3:15 **54.8** Synaptic organization of spinothalamic projections to the squirrel monkey thalamus. **D. J. FORBES.** *Univ. of Wisconsin Med. Sch., Madison, WI, and Univ. of Minnesota Duluth Med. Sch., Duluth, MN.*

3:30 **54.9** Somatotopic organization and submodality distribution in the ventroposterior nucleus of the thalamus of the macaque. **P. R. LOE, B. L. WHITSEL, D. A. DREYER** and **C. B. METZ.** *Univ. of North Carolina Sch. of Med. and Dental Res. Ctr., Chapel Hill, NC.*

3:45 **54.10** The intrinsic circuitry of the ventrobasal thalamus of the cat. **H. J. RALSTON, III.** *Univ. of California, San Francisco, CA.*

4:00 **54.11** Electroencephalographic correlates of muscle spindle afferents. **M. HOHENBERGER, R. HERMAN** and **M. NEGIN.** *Temple Univ. Health Sci. Ctr., Philadelphia, PA.*

4:15 **54.12** Responses of postcentral cells during active and passive joint movements. **M. SOSO** and **E. E. FETZ.** *Regional Primate Res. Ctr., Univ. of Washington, Seattle, WA.*

4:30 **54.13** Characteristics of the head and face representation in the postcentral gyrus of macaques. **D. A. DREYER, B. L. WHITSEL, P. R. LOE, R. A. ELLIOTT** and **H. H. SMITH.** *Univ. of North Carolina Sch. of Med. and Dental Res. Ctr., Chapel Hill, NC.*

4:45 **54.14** "On" and "off" components in the somatosensory evoked response. **M. FEINSOD, P. BACH-Y-RITA** and **E. SIMOES.** *Smith-Kettlewell Inst. of Visual Sci., San Francisco, CA.*

FRIDAY AFTERNOON

VOLUNTEER PAPERS

55. Human Neuroscience: EEG and Evoked Potentials

1:30 PM—*Chamber Room, Town and Country Hotel*

Chairman: **E. CALLAWAY**

1:30 **55.1** Human somatosensory brain signals: some criteria for clinical use. **H. STOWELL.** *Univ. of Mississippi, Jackson, MS.*

1:45 **55.2** Precision in latency determination of evoked potential. **B. SALTZBERG** and **L. S. LUSTICK.** *Tulane Univ. Sch. of Med., New Orleans, LA.*

2:00 **55.3** Motor and cognitive components of response-related potentials: forcefully dissected. **E. DONCHIN** and **M. KUTAS.** *Univ. of Illinois, Champaign, IL.*

2:15 **55.4** Different spatial distribution of scalp recorded slow potential shifts dependent on differing task demands. **G. R. MARSH, L. POON** and **L. W. THOMPSON.** *Duke Univ. Med. Ctr., Durham, NC.*

2:30 **55.5** Contextual meaning effects on speech evoked potentials. **W. S. BROWN, J. T. MARSH** and **J. C. SMITH.** *UCLA Sch. of Med., Los Angeles, CA.*

2:45 **55.6** Correlation of EEG frequency with temporal resolution in man. **S. COFFIN** and **L. GANZ.** *Stanford Univ., Stanford, CA.*

3:00 **55.7** Average evoked potential/intelligence correlations: long auditory AEP latencies with high IQ. **E. CALLAWAY, H. NAYLOR** and **S. VAN BEENAN.** *Langley Porter Neuropsychiat. Inst., San Francisco, CA.*

3:15 **55.8** Dichotic ear-order effects with nonverbal stimuli. **M. OSCARBERMAN, H. GOODGLASS** and **H. DONNENFELD.** *Aphasia Res. Ctr., Boston VA Hosp. and Boston Univ. Sch. of Med., Boston, MA.*

3:30 **55.9** Normal man and monkey sometimes behave as though "split-brained." **C. R. BUTLER** and **A. C. FRANCIS.** *McMaster Univ., Hamilton, Canada.*

3:45 **55.10** Measurement of the EEG and EKG from novice and experienced sport parachutists during a parachute jump. **J. G. McELLIGOTT.** *Temple Med. Sch., Philadelphia, PA.*

4:00 **55.11** A sleep EEG assessment of the abstinence syndrome following prolonged use of diazepam. **R. P. ALLEN** and **L. COVI.** *Johns Hopkins Univ., Baltimore, MD.*

4:15 **55.12** Stimulus augmenting and reducing in mental disease. **V. MILSTEIN, J. G. SMALL, J. E. MOORE** and **C. CORSARO.** *Larue D. Carter Mem. Hosp. and Indiana Univ. Med. Ctr., Indianapolis, IN.*

4:30 **55.13** The averaged visual evoked potential as a technique for assessing cerebral death. **E. C. BECK, E. M. BEHRENS** and **R. E. DUSTMAN.** *VA Hosp. and Univ. of Utah, Salt Lake City, UT.*

4:45 **55.14** Electroencephalographic correlates of renal disease. **J. R. BOURNE** and **J. W. WARD.** *Vanderbilt Univ., Nashville, TN.*

VOLUNTEER PAPERS

56. Neurotransmitters: Serotonin

1:30 PM—*Cabinet Room, Town and Country Hotel*

Chairman: **M. M. RAPPORT**

1:30 **56.1** Distribution and properties of serotonin-binding protein from rat brain. **H. TAMIR, Y. L. HUANG** and **M. M. RAPPORT.** *New York State Psychiat. Inst. and Columbia Univ. Col. of Phys. and Surg., New York, NY.*

1:45 **56.2** Effect of 5-hydroxytryptamine on cerebral protein synthesis: in vivo mediation and in vitro effects. **W. B. ESSMAN** and **E. HELDMAN.** *Queens Col., CUNY, Flushing, NY.*

2:00 **56.3** Effect of 5,6- and 5,7-dihydroxytryptamine on regional brain chemistry in the rat. **P. J. MORGANE, W. FORBES, W. STERN** and **J. JALOWIEC.** *Worcester Fndn. for Exp. Biol., Shrewsbury, MA.*

2:15 **56.4** The effects of 5,7-dihydroxytryptamine on brain serotonin in the developing rat. **L. D. LYTLE, J. H. JACOBY** and **R. J. WURTMAN.** *MIT, Cambridge, MA.*

2:30 **56.5** Treatment by dimethylsulfoxide of experimental paraplegia subsequent to spinal cord trauma. **J. C. de la TORRE, C. JOHNSON** and **S. MULLAN.** *Univ. of Chicago, Pritzker Sch. of Med., Chicago, IL.*

2:45 **56.6** Platelets as mediators of CNS damage in cold edema. **J. L. COSTA, U. ITO, M. SPATZ** and **I. KLATZO.** *NIH, Bethesda, MD.*

VOLUNTEER PAPERS

57. Cardiovascular Control

1:30 PM—*Forum Room, Town and Country Hotel*

Chairman: **F. R. CALARESU**

1:30 **57.1** Localization of excitatory and inhibitory pathways from medullary nuclei to spinal cardioacceleratory neurons in the cat. **J. L. HENRY** and **F. R. CALARESU.** *Univ. of Western Ontario, London, Canada.*

1:45 **57.2** Dorsomedial hypothalamic interaction with carotid sinus baroreceptor activity. **J. R. ADAIR** and **J. W. MANNING.** *Emory Univ., Atlanta, GA.*

2:00 **57.3** The limbic system as a site of action of antihypertensive drugs. **H. L. GARVEY, B. L. WOODHOUSE** and **N. RAM.** *Howard Univ. Sch. of Med., Washington, DC.*

2:15 **57.4** Decreased norepinephrine turnover in the brain stem of hypertensive rats. **J. de CHAMPLAIN** and **M.-R. VAN AMERINGEN.** *Univ. of Montreal, Montreal, Canada.*

2:30 **57.5** Brain lesions, serum cholesterol levels, and "spontaneous" arteriosclerosis in rabbits. **C. SOMOZA.** *VA Hosp. and Univ. of Cincinnati, Cincinnati, OH.*

2:45 **57.6** Continuous monitoring of internal carotid flow velocity in neurosurgical patients. **C. P. McGRAW** and **K. IWATA.** *Univ. of Texas Med. Branch, Galveston, TX.*

VOLUNTEER PAPERS

58. Brain Stem

1:30 PM—*Senate Room, Town and Country Hotel*

Chairman: **M. GLICKSTEIN**

1:30 **58.1** Dark neurons in the normal and deafferentated lateral vestibular nucleus: experimental effect or artifact? **J. E. JOHNSON, JR.** *Tulane Med. Sch., New Orleans, LA.*

1:45 **58.2** Projections of the primary and secondary auditory fibers in the bullfrog (*Rana catesbeiana*). **P. M. FULLER** and **S. O. E. EBBESSON.** *Univ. of Virginia Sch. of Med., Charlottesville, VA.*

2:00 **58.3** Correlation of periodicities in two preganglionic sympathetic nerves. **P. M. GOOTMAN** and **M. I. COHEN.** *Albert Einstein Col. of Med., New York, NY.*

2:15 **58.4** Synchronized burst activity in the inspiratory network. **M. I. COHEN.** *Albert Einstein Col. of Med., New York, NY.*

2:30 **58.5** Cranial motoneurons: aspects of their motor control. **A. J. MILLER.** *Univ. of Illinois Med. Ctr. Sch. of Med., Chicago, IL.*

2:45 **58.6** Midbrain–facial connections in the opossum, *Didelphis marsupialis virginiana.* **G. F. MARTIN, W. FALLS** and **R. DOM.** *Ohio State Univ. Sch. of Med., Columbus, OH.*

3:00 **58.7** Afferent connections of cells in the superior colliculus of the cat giving rise to the tectospinal tract. **V. C. ABRAHAMS** and **P. K. ROSE.** *Queen's Univ., Kingston, Canada.*

3:15 **58.8** Visual input to pontine nuclei in monkey. **M. GLICKSTEIN, M. HOLLINS** and **E. LaBOSSIERE.** *Brown Univ., Providence, RI.*

3:30 **58.9** Effect of harmaline on inferior olivary neurons. **C. de MONTIGNY** and **Y. LAMARRE.** *Univ. of Montreal, Montreal, Canada.*

3:45 **58.10** Intracellular analysis of the nucleus reticularis tegmenti pontis. **T. KIYOHARA, S. T. KITAI, D. T. KENNEDY** and **J. F. DeFRANCE.** *Wayne State Univ. Sch. of Med., Detroit, MI.*

4:00 **58.11** The differential connectivity of three distinct populations of rubral neurons. **J. S. KING, R. DOM** and **G. F. MARTIN.** *Ohio State Univ. Col. of Med., Columbus, OH.*

4:15 **58.12** Pharmacology of reticular system projecting to the spinal cord in cats. **C. D. BARNES** and **F. P. WHITE.** *Indiana State Univ., Terre Haute, IN.*

4:30 **58.13** Centrally evoked electrodermal responses in the cat: the effects of chlorpromazine and reserpine. **M. A. DAVISON** and **M. C. KOSS.** *Univ. of Oklahoma Health Sci. Ctr., Oklahoma City, OK.*

4:45 **58.14** Nembutal modifies acoustic input in the hypothalamus. **N. DAFNY.** *Univ. of Texas Med. Sch., Houston, TX.*

FRIDAY AFTERNOON

VOLUNTEER PAPERS

59. Amphetamines

1:30 PM—*Sunset Room, Town and Country Hotel*

Chairman: **W. G. CLARK**

1:30 **59.1** Central control of *d*-amphetamine-induced discriminative stimuli. **D. W. RICHARDS III, R. T. HARRIS** and **B. T. HO.** *Texas Res. Inst. of Mental Sci. and Baylor Col. of Med., Houston, TX.*

1:45 **59.2** The role of monoamines in discriminative response control by *d*-amphetamine. **B. T. HO** and **J-T. HUANG.** *Texas Res. Inst. of Mental Sci., Houston, TX.*

2:00 **59.3** Normalizing effects of *d*- and *l*-amphetamine on cerebrovisceral pathology. **E. O'L. CORSON, S. A. CORSON, V. KIRILCUK** and **J. KIRILCUK.** *Ohio State Univ. Col. of Med., Columbus, OH.*

2:15 **59.4** Amphetamine anorexia: interaction with stimulus-bound consummatory behavior. **T. B. WISHART.** *Univ. of Saskatchewan, Saskatoon, Canada.*

2:30 **59.5** Dose-related suppression by amphetamine of spontaneous locomotor shuttling activity in goldfish. **F. PETTY, R. C. BRYANT** and **W. L. BYRNE.** *Brain Res. Inst. and Univ. of Tennessee Med. Units, Memphis, TN.*

2:45 **59.6** Amphetamine induced dyskinesias in cats and monkeys. **A. SUDILOVSKY, E. H. ELLINWOOD** and **L. NELSON.** *Duke Univ. Med. Ctr., Durham, NC.*

3:00 **59.7** Behavior and EEG analysis of chronic amphetamine effect. **E. H. ELLINWOOD, A. SUDILOVSKY** and **L. NELSON.** *Duke Univ. Med. Ctr., Durham, NC.*

3:15 **59.8** The electroencephalographic effects of cocaine and D-amphetamine in the rhesus monkey as described by period analysis. **H. L. ALTSHULER** and **N. R. BURCH.** *Texas Res. Inst. of Mental Sci., Houston, TX.*

3:30 **59.9** *d*-Amphetamine reduces the severity of sound-induced seizures in DBA/2J and C57BL/6J mice. **J. M. GRAHAM, JR., R. A. SCHREIBER** and **J. W. ZEMP.** *Med. Univ. of South Carolina, Charleston, SC.*

3:45 **59.10** Blockade of central effects of amphetamine by other stimulants. **W. G. CLARK** and **L. K. Y. K. YUEN.** *VA Hosp., Sepulveda, and UCLA Sch. of Med., Los Angeles, CA.*

4:00 **59.11** Tissue distribution and excretion of ^{3}H-trifluoperazine in rats. **N. R. WEST** and **W. H. VOGEL.** *Thomas Jefferson Univ., Philadelphia, PA.*

4:15 **59.12** Amphetamine potentiation of psychosocial therapy of violent and hypoinhibitory (hyperkinetic) behavior in dogs. **S. A. CORSON, E. O'L. CORSON, V. KIRILCUK, J. KIRILCUK, L. E. ARNOLD** and **W. KNOPP.** *Ohio State Univ. Col. of Med., Columbus, OH.*

4:30 **59.13** A primate behavioral psychosis, a model for studying neurotransmitters and neuroleptics. **D. L. GARVER, F. SCHLEMMER** and **J. W. MAAS.** *Illinois State Psychiat. Inst., Chicago, IL.*

4:45 **59.14** D or L amphetamine and schizophrenia. **J. M. DAVIS, D. S. JANOWSKY** and **M. K. EL-YOUSEF.** *Illinois State Psychiat. Inst., Univ. of Chicago, Chicago, IL, and Vanderbilt Univ., Nashville, TN.*

FRIDAY AFTERNOON

VOLUNTEER PAPERS

60. Neurotransmitters: Amino Acids II

1:30 PM—*Windsor Court Room, Le Baron Hotel*

Chairman: **M. H. APRISON**

1:30 **60.1** Developmental changes in synaptosomal amino acid transport. **N. A. PETERSON** and **E. RAGHUPATHY.** *Sonoma State Hosp., Eldridge, CA.*

1:45 **60.2** The effect of amino acids and other putative neurotransmitters on the calcium bound to synaptic membranes. **A. T. TAN.** *McGill Univ., Montreal, Canada.*

2:00 **60.3** A unique distribution of aspartate in four giant axons of the central nervous system of the lobster. **M. H. APRISON, A. R. FREEMAN, W. J. McBRIDE** and **L. T. GRAHAM, JR.** *Indiana Univ. Med. Ctr., Indianapolis, IN.*

2:15 **60.4** Changes in amino acid composition of excised toad brain in response to hyperosmotic medium. **J. T. WHITEN** and **C. F. BAXTER.** *VA Hosp., Sepulveda, and UCLA Sch. of Med., Los Angeles, CA.*

2:30 **60.5** Depolarizing action of substance P in in the cuneate nucleus of the cat. **K. KRNJEVIC** and **M. E. MORRIS.** *McGill Univ., Montreal, Canada.*

2:45 **60.6** Variation of endogenous and exogenous piperidine in the brain of active and dormant snails. **H. DOLEZALOVA, M. STEPITA-KLAUCO** and **E. GIACOBINI.** *Univ. of Connecticut, Storrs, CT.*

FRIDAY AFTERNOON

VOLUNTEER PAPERS

61. Morphine and Addiction II

1:30 PM—*Hampton Court Room, Le Baron Hotel*

Chairman: **F. W. KERR**

1:30 **61.1** Characteristics of the binding of ^{3}H-naloxone in the mouse brain. **R. J. HITZEMANN** and **H. H. LOH.** *Langley Porter Neuropsychiat. Inst. and Univ. of California, San Francisco, CA.*

1:45 **61.2** The opiate receptor: influence of enzymes, ions and detergents. **G. W. PASTERNAK** and **S. H. SNYDER.** *Johns Hopkins Sch. of Med., Baltimore, MD.*

2:00 **61.3** Morphine modification of brain amino acid levels. **L. MILLER** and **J. HARRIS.** *Barrow Neurological Inst., Phoenix, and Arizona State Univ., Tempe, AZ.*

2:15 **61.4** Effects of morphine on catecholamine turnover, cyclic 3',5'-AMP concentrations and tyrosine hydroxylase activity in rat tissues. **A. CARENZI, E. COSTA, A. GUIDOTTI** and **A. REVUELTA.** *NIMH, St. Elizabeths Hosp., Washington, DC.*

2:30 **61.5** Effects of morphine administration on the incorporation of uridine-^{3}H into brain nucleotides and ribonucleic acid. **R. A. HARRIS** and **L. S. HARRIS.** *Univ. of North Carolina, Chapel Hill, NC, and Med. Col. of Virginia, Richmond, VA.*

2:45 **61.6** Neurophysiological correlates of heroin addiction in squirrel monkeys. **S. JACOBS, E. T. ANGELAKOS** and **P. LOMAX.** *Univ. of California, Santa Barbara, CA, Hahnemann Med. Col., Philadelphia, PA, and UCLA Sch. of Med., Los Angeles, CA.*

3:00 **61.7** Effects of morphine and antagonists on hypothalamic neurone activity in naive and addicted rats. **J. N. TRIPLETT, G. W. BEELER** and **F. W. L. KERR.** *Mayo Med. Sch., Rochester, MN.*

3:15 **61.8** CNS sites of morphine action: hypo- or hyperalgesia depending on injection site and dose. **Y. F. JACQUET** and **A. LAJTHA.** *New York State Res. Inst. for Neurochem. and Drug Addiction, Ward's Island, NY.*

3:30 **61.9** Localization in the primate brain of the antinociceptive action of morphine. **T. L. YAKSH** and **A. PERT.** *Med. Res. Div., Biomed. Lab., Edgewood Arsenal, MD.*

3:45 **61.10** Effect of cingulate cortex lesions on morphine intake in premedicated and non-premedicated rats. **C. L. TRAFTON** and **M. KAHN.** *Univ. of Arizona, Tucson, AZ.*

4:00 **61.11** Effects of discrete CNS lesions on morphine addiction. **G. LITTLE, K. ROBINSON, PAT D'ENCARNACAO** and **PAUL D'ENCARNACAO.** *Memphis State Univ., Memphis, TN.*

4:15 **61.12** Blockade of drinking of a morphine solution by hypothalamic lesions and 6-hydroxydopamine infusions in rats. **Z. AMIT** and **M. E. CORCORAN.** *Sir George Williams Univ., Montreal, and Univ. of British Columbia, Vancouver, Canada.*

4:30 **61.13** The cholinergic system and nociception in the primate: interactions with morphine. **A. PERT.** *Exp. Med. Branch, Biomed. Lab., Edgewood Arsenal, MD.*

4:45 **61.14** Morphine withdrawal syndrome: similarity to thermoregulatory behavior. **E. WEI, L. F. TSENG, H. H. LOH** and **E. L. WAY.** *Univ. of California Sch. of Public Health, Berkeley, and Univ. of California, San Francisco, CA.*

VOLUNTEER PAPERS

62. Vision: Receptor and Retinal Organization

1:30 PM—*Sheffield Court Room, Le Baron Hotel*

Chairman: **F. RATLIFF**

1:30 **62.1** Electrophysiological measurement of the number of rhodopsin molecules in *Limulus* ventral photoreceptor cells. **J. E. LISMAN** and **H. BERING.** *Harvard Univ., Cambridge, MA.*

1:45 **62.2** Control of membrane permeability in a hyperpolarizing photoreceptor: similar effects of light and metabolic inhibitors. **J. S. McREYNOLDS** and **A. L. F. GORMAN.** *NIH, Bethesda, MD, and Boston Univ., Boston, MA.*

2:00 **62.3** Structural changes associated with illumination in the *Aplysia* giant neuron. **M. HENKART.** *NIH, Bethesda, MD.*

2:15 **62.4** Synaptic organization of the inner plexiform layer in the retina of the larval tiger salamander. **M. T. T. WONG-RILEY.** *NIH, Bethesda, MD.*

2:30 **62.5** Fourier analysis of dynamics of excitation and inhibition in the eye of *Limulus*: amplitude, phase and distance. **F. RATLIFF, B. W. KNIGHT, JR., F. A. DODGE, JR.** and **H. K. HARTLINE.** *Rockefeller Univ., New York, NY.*

2:45 **62.6** Calculating the full space and time dependence of nervous activity in the *Limulus* retinal network. **B. W. KNIGHT.** *Rockefeller Univ., New York, NY.*

3:00 **62.7** Visual acuity of compound eyes. **R. B. PINTER** and **J. PALKA.** *Univ. of Washington, Seattle, WA.*

3:15 **62.8** Intracellular responses from the retina of the cat. **R. NELSON, A. V. LUTZOW** and **P. GOURAS.** *NIH, Bethesda, MD.*

3:30 **62.9** Synapses in the retina of the cat. **E. V. FAMIGLIETTI, JR.** and **H. KOLB.** *NIH, Bethesda, MD.*

3:45 **62.10** Anatomical evidence for two types of receptors in ground squirrel retina. **R. W. WEST.** *Harvard Univ., Cambridge, MA.*

4:00 **62.11** Mechanisms of directional selectivity in retinal ganglion cells of the rabbit. **H. J. WYATT** and **N. W. DAW.** *Washington Univ. Med. Sch., St. Louis, MO.*

4:15 **62.12** Two-flash recovery cycle in relation to the suppression-recovery effect: evoked potential and single unit analysis in the optic tract of the cat. **W. SALINGER** and **C. K. PECK.** *Univ. of North Carolina, Greensboro, NC, and Pomona Col., Claremont, CA.*

4:30 **62.13** Observations on the b-wave of the mammalian electroretinogram in 20 mM potassium. **B. S. WINKLER.** *Oakland Univ., Rochester, MI.*

4:45 **62.14** Effects of hypoxia on retina, optic nerve, and visual cortex of cat. **C. K. ADAMS, J. M. PEREZ** and **W. W. DAWSON.** *Univ. of Florida, Gainesville, FL.*

FEEDBACK COMMENTARY PANEL

Extended discussion of new research lines derived from abstracts presented at this meeting.

63. Functional Significance of Parallel Organization within Major Sensory Pathways

3:30 PM—*Town and Country Room, Town and Country Hotel*

Chairman: **H. L. TEUBER**

H. L. TEUBER. *MIT, Cambridge, MA.*

A. GRAYBIEL. *MIT, Cambridge, MA.*

J. M. SPRAGUE. *Univ. of Pennsylvania Med. Sch., Philadelphia, PA.*

A. L. TOWE. *Univ. of Washington Med. Sch., Seattle, WA.*

F. G. WORDEN. *MIT, Boston, MA.*

FEEDBACK COMMENTARY PANEL

Extended discussion of new research lines derived from abstracts presented at this meeting.

64. Neurophysiological Basis of Habituation and Conditioning

3:30 PM—*San Diego Room, Town and Country Hotel*

Chairman: **R. THOMPSON**

J. OLDS. *California Inst. of Tech., Pasadena, CA.*

C. WOODY. *Univ. of California, Los Angeles, CA.*

D. COHEN. *Univ. of Virginia, Charlottesville, VA.*

J. BUCHWALD. *Univ. of California, Los Angeles, CA.*

VOLUNTEER PAPERS

65. Limbic System II

3:30 PM—*Sunrise Room, Town and Country Hotel*

Chairman: **S. H. SNYDER**

3:30 **65.1** The dose-response relationship between *d* and *l* tranylcypromine and self-stimulation at three loci. **Z. ANNAU, R. HEFFNER** and **S. H. SNYDER.** *Johns Hopkins Univ. Sch. of Hyg. and Publ. Hlth., Baltimore, MD.*

3:45 **65.2** Inhibitory effects of acetylcholine in the lateral septal nucleus of the cat. **J. F. DeFRANCE, S. T. KITAI, R. A. McCREA** and **H. YOSHIHARA.** *Wayne State Univ. Sch. of Med., Detroit, MI.*

4:00 **65.3** Modification of intralimbic evoked potentials by direct application of cholinergic drugs and high frequency stimulation of midbrain central gray substance. **R. G. WILEY** and **C. A. BERRY.** *Northwestern Univ. Med. Sch., Chicago, IL.*

4:15 **65.4** Pineal body and hypothalamic evoked responses following acoustic and amygdala stimulation in freely behaving rats. **R. McCLUNG, N. DAFNY** and **S. J. STRADA.** *Univ. of Texas Grad. Sch. of Biomed. Sci. and Univ. of Texas Med. Sch., Houston, TX.*

4:30 **65.5** A comparison of unilateral and bilateral hippocampal lesions on liver glycogen levels and body weight in the rat. **H. M. MURPHY, C. H. WIDEMAN** and **T. S. BROWN.** *John Carroll Univ., Cleveland, OH, and DePaul Univ., Chicago, IL.*

4:45 **65.6** The effect of time and the light-dark cycle on liver glycogen levels in normal, neocortical lesioned and hippocampal lesioned rats. **C. H. WIDEMAN, H. M. MURPHY** and **T. S. BROWN.** *John Carroll Univ., Cleveland, OH, and DePaul Univ., Chicago, IL.*

VOLUNTEER PAPERS

66. Developmental Neurobiology: Electrophysiology and Reflexes

3:30 PM—*Cabinet Room, Town and Country Hotel*

Chairman: **A. B. SCHIEBEL**

3:30 **66.1** Developmental and regional differences in multiple unit activity of young kitten. **T. L. DAVIES, R. D. LINDSAY, M. E. SCHEIBEL** and **A. B. SCHEIBEL.** *UCLA Sch. of Med., Los Angeles, CA.*

3:45 **66.2** Brain stem influences on evoked thalamic synchronizing activities in kittens. **R. W. HOMAN, R. J. SHOFER** and **D. P. PURPURA.** *Albert Einstein Col. of Med., Bronx, NY.*

4:00 **66.3** Electrophysiology and pharmacology of Purkinje cells in rat cerebellum degranulated by postnatal X-irradiation. **D. J. WOODWARD, J. ALTMAN** and **B. J. HOFFER.** *Univ. of Rochester, Rochester, NY, Purdue Univ., Lafayette, IN, and St. Elizabeths Hosp., NIMH, Washington, DC.*

4:15 **66.4** Development of motor coordination in 17- to 21-day chick embryos. **A. BEKOFF.** *Washington Univ., St. Louis, MO.*

4:30 **66.5** Reflex specificity from supernumerary limbs of *Xenopus laevis.* **L. MENDELL** and **M. HOLLYDAY.** *Duke Med. Ctr., Durham, NC.*

4:45 **66.6** Spontaneous action potentials and the cell cycle in embryonic mouse heart cells. **K. ARMS.** *Cornell Univ., Ithaca, NY.*

VOLUNTEER PAPERS

67. Central Adrenergic Systems

3:30 PM—*Forum Room, Town and Country Hotel*

Chairman: **B. HOFFER**

3:30 **67.1** Morphological organization of monoamine-containing neurons in the turtle brain. **A. PARENT.** *Laval Univ., Quebec, Canada.*

3:45 **67.2** Evolution of a ponto-cerebellar noradrenergic nucleus in the primate. **C. DEMIRJIAN, R. GROSSMAN** and **R. KATZMAN.** *Albert Einstein Col. of Med., New York, NY.*

4:00 **67.3** A projection of the nucleus locus coeruleus to the hippocampus of the rat. **M. SEGAL** and **F. E. BLOOM.** *NIMH, St. Elizabeths Hosp., Washington, DC.*

4:15 **67.4** Responses of cortically modulated rat striatal cells to iontophoretically applied neurotransmitter candidates. **H. J. SPENCER** and **V. HAVLICEK.** *Univ. of Manitoba, Winnipeg, Canada.*

4:30 **67.5** Responses of squirrel monkey auditory cortex neurons to vocalizations: changes produced by microiontophoresis of putative neurotransmitters. **S. L. FOOTE, J. NEWMAN** and **B. J. HOFFER.** *NIMH, St. Elizabeths Hosp., Washington, DC.*

4:45 **67.6** Evidence that 6-hydroxydopamine is a nonspecific neurotoxic agent when administered intracerebrally. **L. L. BUTCHER** and **G. K. HODGE.** *UCLA, Los Angeles, CA.*

5:00 **67.7** Reciprocal firing by two neuronal groups during the sleep cycle. **J. A. HOBSON, R. W. McCARLEY, P. W. WYZINSKI** and **R. T. PIVIK.** *Harvard Med. Sch., Boston, MA.*

VOLUNTEER PAPERS

68. Circulation, CSF and Blood–Brain Barrier

3:30 PM—*Windsor Court Room, Le Baron Hotel*

Chairman: **R. BLEIER**

3:30 **68.1** Effects of hypoxia and hypercapnia on glucose transfer across the blood–brain barrier in rabbits. **F. BERSON, M. SPATZ** and **I. KLATZO.** *NIH, Bethesda, MD.*

3:45 **68.2** Accumulation of a radiolabeled neutral amino acid by canine dura-arachnoid. **L. A. O'TUAMA, M. P. REMLER** and **H. N. NICHOLS.** *Univ. of North Carolina Sch. of Med., Chapel Hill, NC.*

4:00 **68.3** Blood flow and tissue oxygen in experimental paraplegia. **T. B. DUCKER** and **P. L. PEROT, JR.** *Med. Univ. of South Carolina, Charleston, SC.*

4:15 **68.4** The relationship of edema to the development of microvascular obstruction in cerebral ischemia. **G. WISE, M. STEVENS, E. C. SHUTTLEWORTH** and **N. ALLEN.** *Ohio State Univ., Columbus, OH.*

4:30 **68.5** Observation on no-reflow phenomenon in the brain of Mongolian gerbils. **U. ITO, I. KLATZO** and **M. SPATZ.** *NIH, Bethesda, MD.*

4:45 **68.6** Transient global amnesia due to arterial embolism. **E. SHUTTLEWORTH** and **G. WISE.** *Ohio State Univ., Columbus, OH.*

SYMPOSIUM

69. Plasticity in the CNS

8:30 AM—*Town and Country Room, Town and Country Hotel*

Co-Chairmen: **W. M. COWAN**
R. Y. MOORE (Moderator)

Neuronal plasticity in the hippocampal formation. **C. COTMAN** and **G. LYNCH.** *Univ. of California, Irvine, CA.*

The effects of early visual deprivation on synaptic organization in the superior colliculus. **R. LUND.** *Univ. of Washington, Seattle, WA.*

Axonal sprouting in the lateral geniculate nucleus of the kitten. **R. E. KALIL.** *MIT, Cambridge, MA.*

Factors affecting the formation of abnormal retinal projections following early lesions in the superior colliculus. **G. SCHNEIDER.** *MIT, Cambridge, MA.*

Recovery of movement and collateral sprouting in the cat spinal cord. **M. GOLDBERGER.** *Univ. of Chicago, Chicago, IL.*

A critique of axonal sprouting in the spinal nucleus of the trigeminal nerve. **F. W. L. KERR.** *Mayo Clinic, Rochester, MN.*

SYMPOSIUM

70. Underwater Physiology: Changes in Brain Functions at High Pressure

8:30 AM—*San Diego Room, Town and Country Hotel*

Co-Chairmen: **A. J. BACHRACH**
P. B. BENNETT

Neurophysiological problems at high pressure. **A. J. BACHRACH.** *Naval Med. Res. Inst., Bethesda, MD.*

The etiology and prevention of the high pressure nervous syndrome in man during oxygen/helium diving. **P. B. BENNETT.** *Duke Univ. Sch. of Med., Durham, NC.*

Electrophysiological approach to the high pressure nervous syndrome: variations due to the mode of compression. **R. NAQUET** and **J. C. ROSTAIN.** *C.N.R.S., Inst. de Neurophysiologie et de Psychophysiologie, Marseilles, France.*

The critical volume hypothesis and the high pressure nervous syndrome. **K. MILLER.** *Harvard Med. Sch., Boston, MA.*

Genesis of the high pressure neurological syndrome. **R. BRAUER.** *Wrightsville Marine Bio-Medical Lab., Wilmington, NC.*

VOLUNTEER PAPERS

71. Lower Vertebrate and Invertebrate Neuronal Mechanisms

8:30 AM—*Sunrise Room, Town and Country Hotel*

Chairman: **C. C. BELL**

8:30 **71.1** Arousal states and habituation procedure in the mudpuppy, *Necturus maculosus.* **D. A. GOODMAN** and **C. J. SWIGERT.** *Newport Neuroscience Ctr., Culver City, CA.*

8:45 **71.2** A leech with abnormal ganglia containing supernumerary sensory and motor neurons. **D. KUFFLER** and **K. J. MULLER.** *UCLA, Los Angeles, CA, and Harvard Med. Sch., Boston, MA.*

9:00 **71.3** Stimulus specificity of habituation to vibratory stimulus in *Spirostomum.* **W. B. RUCKER** and **J. C. HUBER.** *Mankato State Col., Mankato, MN, and Faribault State Hosp., Faribault, MN.*

9:15 **71.4** Medium receptor mediation of the echo response, an electrical interaction between mormyrid fish. **C. J. RUSSELL** and **C. C. BELL.** *Good Samaritan Hosp. and Med. Ctr., Portland, OR.*

9:30 **71.5** Electrical sensitivity in two sympatric species of gymnotid fish. **E. I. KNUDSEN.** *Univ. of California, San Diego Sch. of Med., La Jolla, CA.*

9:45 **71.6** Connections among leech motor neurons. **C. A. ORT, W. B. KRISTAN** and **G. S. STENT.** *Univ. of California, Berkeley, CA.*

10:00 **71.7** Innervation and reflex activity of the dorsal superficial muscles of the abdomen of the hermit crab, *Pagurus pollicarus.* **W. D. CHAPPLE.** *Univ. of Connecticut, Storrs, CT.*

10:15 **71.8** Anatomy of the hermit crab, *Pagurus pollicarus,* deep abdominal muscle and nervous system. **J. D. MARRELLI.** *Univ. of Connecticut, Storrs, CT.*

VOLUNTEER PAPERS

72. Neurochemistry: Cyclic AMP and Energy Metabolism

8:30 AM—*Council Room, Town and Country Hotel*

Chairman: J. V. PASSONNEAU

8:30 72.1 *Adenosine mediated elevation of cAMP levels in cultured* mouse neuroblastoma cells. **A. J. BLUME, C. DALTON** and **H. SHEPPARD.** *Roche Inst. of Mol. Biol. and Hoffmann-La Roche, Nutley, NJ.*

8:45 72.2 Cyclic AMP and cyclic GMP in normal and degenerative retinae of mice. **D. B. FARBER** and **R. N. LOLLEY.** *VA Hosp., Sepulveda, and UCLA Sch. of Med., Los Angeles, CA.*

9:00 72.3 Regulation of cyclic nucleotides in adrenal medulla of rat: possible involvement of nicotinic receptors. **A. GUIDOTTI, H. GERHARDS, C. MAO** and **E. COSTA.** *NIMH, St. Elizabeths Hosp., Washington, DC.*

9:15 72.4 Adenylate energy levels during brain ischemia and recovery. **C.-L. LIAO** and **F. M. YATSU.** *Univ. of California Sch. of Med., San Francisco, CA.*

9:30 72.5 The potassium dependence of the cytochrome redox potential of brain slices. **R. J. BULL** and **J. T. CUMMINS.** *Environmental Protection Agency, Cincinnati, OH, and VA Hosp., Sepulveda, CA.*

9:45 72.6 Measurement of fast brain responses to K^+ in vitro. **J. T. CUMMINS** and **R. BULL.** *Univ. of California, Irvine, CA, VA Hosp., Sepulveda, CA, and Environmental Protection Agency, Cincinnati, OH.*

10:00 72.7 Measurement of glucose utilization in rat brain in vivo. **R. A. HAWKINS, A. L. MILLER, J. E. CREMER** and **R. L. VEECH.** *NIMH, St. Elizabeths Hosp., Washington, DC.*

10:15 72.8 Oxidation of nicotinamide adenine dinucleotide during intermittent stimulation in dorsal root ganglion neurons. **C. R. RODRIGUEZ-ESTRADA.** *Univ. Central de Venezuela, Caracas, Venezuela.*

10:30 72.9 Regional distribution of pyruvate dehydrogenase in cat brain and its relation to disorders of pyruvate metabolism. **S. F. REYNOLDS, J. P. BLASS** and **R. JOPE.** *UCLA Med. Sch., Los Angeles, CA.*

10:45 **72.10** Changes in energy metabolism in anoxic neonatal rats. **C. L. MOORE** and **J. L. MYERS.** *Univ. of Texas Med. Branch, Galveston, TX.*

11:00 **72.11** The effect of brain injury on cerebral glycogen metabolism and related metabolites and enzymes. **J. V. PASSONNEAU** and **H. WATANABE.** *NIH, Bethesda, MD.*

11:15 **72.12** Effect of ouabain and amobarbital on cortical metabolism associated with evoked potentials and spreading depression in situ. **J. C. LAMANNA, F. F. JOBSIS** and **M. ROSENTHAL.** *Duke Univ., Durham, NC.*

SATURDAY MORNING

VOLUNTEER PAPERS

73. Experimental Morphology

8:30 AM—*Chamber Room, Town and Country Hotel*

Chairman: **E. EIDELBERG**

8:30 **73.1** Unmyelinated fibers in the ventral root. **R. E. COGGESHALL, J. D. COULTER** and **W. D. WILLIS, JR.** *Univ. of Texas Med. Branch, Galveston, TX.*

8:45 **73.2** Projection of supraspinal fibers to the spinal cord of the tegu lizard, *Tupinambis nigropunctatus.* **W. L. R. CRUCE.** *Univ. of Wisconsin, Madison, WI.*

9:00 **73.3** Cat medial superior olivary nucleus: fine structure and dendritic specificity of cochlear nucleus afferents. **B. G. LINDSEY.** *Univ. of Pennsylvania Sch. of Med., Philadelphia, PA.*

9:15 **73.4** Investigations of "nonspecific" thalamic projections to parietal regions of cerebral cortex. **R. T. ROBERTSON.** *Fels Res. Inst., Yellow Springs, OH.*

9:30 **73.5** Central connections of the frog's retina as demonstrated with cobalt impregnation. **K. RUBINSON.** *New York Univ. Sch. of Med. and Public Health Res. Inst., New York, NY.*

9:45 **73.6** Intrinsic connections in the frog optic tectum. **M. C. TRACHTENBERG.** *McLean Hosp., Belmont, MA.*

10:00 **73.7** Axon diameters in the lateral hypothalamus of the rat. **R. H. THALMANN** and **L. A. FORSYTH.** *Baylor Col. of Med., Houston, TX.*

10:15 **73.8** *The fine structure of the thoracic spinal cord following experimental compression.* **C. WAKEFIELD** and **E. EIDELBERG.** *Barrow Neurological Inst. of St. Joseph's Hosp. and Med. Ctr., Phoenix, AZ.*

10:30 **73.9** Evaluation of normothermic spinal cord perfusion after impact injury. **M. S. ALBIN** and **R. J. WHITE.** *Univ. of Pittsburgh Sch. of Med., Pittsburgh, PA, and Case Western Reserve Univ. Sch. of Med., Cleveland, OH.*

10:45 **73.10** Microscopic studies of degeneration in the crayfish brain following antennule removal. **E. A. MAYNARD.** *Univ. of Oregon, Eugene, OR.*

11:00 **73.11** Death of the intrinsic neuron: an electron microscopic study of thalamic retrograde degeneration following cortical ablation. **M. A. MATTHEWS.** *Louisiana State Univ. Med. Ctr., New Orleans, LA.*

11:15 **73.12** Histological patterns of fibrillary neuronal degeneration in Alzheimer's disease and atypical forms of dementia. **L. LISS.** *Ohio State Univ. Col. of Med., Columbus, OH.*

VOLUNTEER PAPERS

74. Central Reflex Analysis

8:30 AM—*Cabinet Room, Town and Country Hotel*

Chairman: **V. B. BROOKS**

8:30 **74.1** Surface electrospinogram recordings in man following synchronous activation of afferent fibers. **A. W. MONSTER.** *Temple Univ. Health Sci. Ctr., Philadelphia, PA.*

8:45 **74.2** Time series analysis of Parkinsonian hand tremors. **R. S. POZOS** and **R. N. STILES.** *Univ. of Tennessee Med. Units, Memphis, TN.*

9:00 **74.3** Patterns of cortical projection to hindlimb motoneurone pools. **F. J. THOMPSON** and **J. J. FERNANDEZ.** *Rockefeller Univ., New York, NY.*

9:15 **74.4** Cortical load compensation during voluntary elbow movements. **B. CONRAD, K. MATSUNAMI, M. WIESENDANGER** and **V. B. BROOKS.** *Univ. of Western Ontario, London, Canada.*

9:30 **74.5** Motor reflexes during operantly conditioned activity (12–14 cps) of the sensorimotor cortex. **M. H. CHASE** and **M. BABB.** *UCLA Sch. of Med., Los Angeles, CA.*

9:45 **74.6** A quantitative description of postural control in the dog during sinusoidal perturbation. **R. E. TALBOTT.** *Univ. of Oregon Sch. of Med., Portland, OR.*

10:00 **74.7** Activity of neurons in the lower precentral cortex of *Macaca mulatta* during jaw movement. **J. P. LUND** and **Y. LAMARRE.** *Univ. of Montreal, Montreal, Canada.*

10:15 **74.8** Synaptic organization and functional identification of inhibitory neurons in the sensorimotor cortex. **L. P. RENAUD** and **J. S. KELLY.** *McGill Univ., Montreal, Canada.*

10:30 **74.9** Initiation of human gait cycle: role of central and peripheral mechanisms. **R. HERMAN, T. COOK** and **B. COZZENS.** *Temple Univ. Health Sci. Ctr., Philadelphia, PA.*

10:45 **74.10** Gating of motor cortex reflexes by prior instruction. **J. TANJI** and **E. V. EVARTS.** *NIMH, Bethesda, MD.*

SATURDAY MORNING

VOLUNTEER PAPERS

75. Tissue Culture

8:30 AM—*Forum Room, Town and Country Hotel*

Chairman: **A. ZALEWSKI**

8:30 **75.1** Biochemical correlates of neuroblastoma differentiation. **V. J. ALOYO, J. B. WITHERINGTON, III, S. V. MOLINARY** and **W. L. BYRNE.** *Univ. of Tennessee Med. Units, Memphis, TN.*

8:45 **75.2** Uptake of ^{3}H-γ-aminobutyric acid by neurons in cultures of dissociated developing rat CNS. **R. S. LASHER.** *Univ. of Colorado Med. Sch., Denver, CO.*

9:00 **75.3** Uptake of choline by clonal lines of astrocytoma and neuroblastoma in culture. **B. HABER, T. COLMORE, K. WERRBACH** and **H. T. HUTCHISON.** *Univ. of Texas Med. Branch, Galveston, TX.*

9:15 **75.4** Quinazoline antifolates as inhibitors of the growth, dihydrofolate reductase and thymidylate synthetase of mouse neuroblastoma cells in culture. **S. C. CARLIN, R. N. ROSENBERG, L. VandeVENTER** and **M. FRIEDKIN.** *Univ. of California San Diego Sch. of Med., La Jolla, CA.*

9:30 **75.5** Protein-induced alteration of cell morphology. **R. LIM** and **K. MITSUNOBU.** *Univ. of Chicago, Chicago, IL.*

9:45 **75.6** Survival and trophic function of homografted neurons by immunosuppression. **A. A. ZALEWSKI** and **W. K. SILVERS.** *NIH, Bethesda, MD, and Univ. of Pennsylvania, Philadelphia, PA.*

10:00 **75.7** The effects of ganglionic non-neuronal cells and nerve growth factor on bioelectric activity in dorsal root ganglion neurons grown in cell cultures. **E. TYSZKA.** *Univ. of California San Diego Sch. of Med., La Jolla, CA.*

10:15 **75.8** Interaction between the nerve fiber and the glial cell during growth in cultures of the central nervous tissue. **H. M. SOBKOWICZ, D. GOLUEKE** and **B. L. LOWRY.** *Univ. of Wisconsin Sch. of Med., Madison, WI.*

10:30 **75.9** Effects of gold thioglucose on the mouse ventromedial hypothalamus in vitro. **M. M. HERMAN** and **M. B. BORNSTEIN.** *Stanford Univ. Sch. of Med., Stanford, CA, and Albert Einstein Col. of Med., Bronx, NY.*

10:45 **75.10** A tissue culture model for studies of regeneration and formation of new functional connections in adult CNS. **S. M. CRAIN** and **E. R. PETERSON.** *Albert Einstein Col. of Med. and Rose F. Kennedy Ctr., Bronx, NY.*

11:00 **75.11** Rhythmic neural activity in tissue culture. **F. D. WALKER.** *Indiana Univ. Med. Ctr., Indianapolis, IN.*

11:15 **75.12** Electrophysiological studies on superior cervical ganglion neurons in tissue culture. **H. BURTON, C-P. KO, R. BUNGE** and **R. REES.** *Washington Univ. Sch. of Med., St. Louis, MO.*

VOLUNTEER PAPERS

76. Neurohormones II

8:30 AM—*Senate Room, Town and Country Hotel*

Chairman: **J. N. HAYWARD**

8:30 **76.1** Control of synthesis and release of thyrotropin releasing factor by hypothalamic fragments from newts (*Triturus viridenses*) incubated in vitro. **Y. GRIMM-JORGENSEN** and **J. F. McKELVY.** *Univ. of Connecticut Health Ctr., Farmington, CT.*

8:45 **76.2** Neurotransmitter regulation of growth hormone release. **G. M. BROWN, J. W. CHAMBERS** and **J. FELDMANN.** *Clarke Inst. of Psychiat. and Univ. of Toronto, Toronto, Canada.*

9:00 **76.3** Cyclic nucleotide stimulated protein kinase activity in the hypothalamic median eminence. **E. MARTIN** and **J. F. McKELVY.** *Univ. of Connecticut Health Ctr., Farmington, CT.*

9:15 **76.4** Cyclic AMP involvement in luteinizing hormone releasing hormone induced luteinizing hormone release? **A. RATNER, M. C. WILSON** and **G. T. PEAKE.** *Univ. of New Mexico Sch. of Med., Albuquerque, NM.*

9:30 **76.5** Effect of septal lesions on plasma levels of corticosterone, growth hormone, prolactin and melanocyte stimulating hormone before and after stimulation. **J. A. SEGGIE, G. M. BROWN, I. V. UHLIR, A. SCHALLY** and **A. J. KASTIN.** *Clarke Inst. of Psychiat., Toronto, Canada, and VA Hosp. and Tulane Univ., New Orleans, LA.*

9:45 **76.6** Immunohistological localization of melatonin in the pineal gland and the cerebellum. **G. A. BUBENIK, G. M. BROWN** and **L. J. GROTA.** *Clarke Inst. of Psychiat., Toronto, Canada, and Univ. of Rochester, Rochester, NY.*

10:00 **76.7** Location of action of centrally acting drugs on inhibition of LH release in rats. **C. A. BLAKE.** *Duke Univ. Sch. of Med., Durham, NC.*

10:15 **76.8** Blockade of cortical spreading depression's effects on prolactin levels in female rats by surgical isolation of the amygdala. **J. A. COLOMBO, R. J. KRIEG** and **C. H. SAWYER.** *UCLA, Los Angeles, CA.*

10:30 **76.9** Effect of sex on the neuroendocrine response to psychoactive agents. **J. A. CLEMENS, E. B. SMALSTIG** and **B. D. SAWYER.** *Eli Lilly Res. Labs., Indianapolis, IN.*

10:45 **76.10** Stimulation of vasopressin biosynthesis in organ cultures of the hypothalamo-neurohypophysial complex by fetal hypothalamic factor (s). **D. B. PEARSON** and **H. SACHS.** *Roche Inst. of Mol. Biol., Nutley, NJ.*

11:00 **76.11** Binding of dexamethasone by rat brain cytosols. **W. STEVENS, D. J. REED** and **B. I. GROSSER.** *Univ. of Utah Col. of Med., Salt Lake City, UT.*

VOLUNTEER PAPERS

77. Brain Lesions and Behavior

8:30 AM—*Sunset Room, Town and Country Hotel*

Chairman: **S. P. GROSSMAN**

8:30 **77.1** Trigeminal structures and feeding behavior in rat and pigeon. **H. P. ZEIGLER** and **H. J. KARTEN.** *Hunter Col., CUNY, New York, NY, and MIT, Cambridge, MA.*

8:45 **77.2** An anatomical connection between the anterior thalamus and the telencephalon in the frog. **E. KICLITER.** *Upstate Med. Ctr., Syracuse, NY, and Univ. of Virginia Sch. Med., Charlottesville, VA.*

9:00 **77.3** Transection and chemical lesion of nigro-striatal pathways: comparison of effects on learned behavior. **E. W. KENT, M. REZAK** and **S. P. GROSSMAN.** *Univ. of Illinois at Chicago Circle and Univ. of Chicago, Chicago, IL.*

9:15 **77.4** Effect of septal lesions on female sexual behavior in the rat. **D. M. NANCE, J. SHRYNE** and **R. A. GORSKI.** *UCLA Sch. of Med., Los Angeles, CA.*

9:30 **77.5** Septum and hippocampus: further evidence for functional communality. **J. D. MASER, F. T. DIENST** and **E. O'NEAL.** *Tulane Univ., New Orleans, LA.*

9:45 **77.6** Effects of limbic system lesions during late gestation on maternal behavior in primiparous rats. **L. R. HERRENKOHL.** *Temple Univ., Philadelphia, PA.*

10:00 **77.7** Brain lesion effects on conditioned vocalization in rhesus monkeys. **D. SUTTON, C. R. LARSON** and **R. C. LINDEMAN.** *Virginia Mason Res. Ctr., Seattle, WA.*

10:15 **77.8** Monocular visual processing capacity loss in the split-brain cat: sensory or central? **J. S. ROBINSON.** *Brain-Behavior Res. Ctr., Sonoma State Hosp., Eldridge, CA.*

10:30 **77.9** Hemispheric specificity, complementarity, and self-referential mappings. **J. E. BOGEN.** *Ross-Loos Med. Group, Los Angeles, CA.*

10:45 **77.10** A nonverbal form of the street silhouette completion test. **S. KUMAR, M. BINDER** and **J. E. BOGEN.** *Ross-Loos Med. Group, Los Angeles, CA.*

SATURDAY MORNING

VOLUNTEER PAPERS

78. Human Neuroscience

8:30 AM—*Windsor Court Room, Le Baron Hotel*

Chairman: **J. W. CRAYTON**

8:30 **78.1** Neuromuscular pathology in psychotic patients. **J. W. CRAYTON** and **H. Y. MELTZER.** *Pritzker Sch. of Med., Univ. of Chicago, Chicago, IL.*

8:45 **78.2** Effect of dantrolene sodium on human skeletal muscle. **N. H. MAYER** and **R. HERMAN.** *Temple Univ. Health Sci. Ctr., Philadelphia, PA.*

9:00 **78.3** Muscle pain and posture or why Moses needed help. **P. A. McGRATH** and **R. M. STEINMAN.** *Univ. of Maryland, College Park, MD.*

9:15 **78.4** Prosthetic arm control by pattern recognition. **F. R. FINLEY, R. W. WIRTA** and **D. TAYLOR.** *Temple Univ. Health Sci. Ctr., Philadelphia, PA.*

9:30 **78.5** The effects of 50 ft/min and 100 ft/min compression rates in excursions from 870 ft to 1000 ft on force microtremor and tremor "signatures." **A. E. FINDLING, A. J. BACHRACH** and **P. B. BENNETT.** *US Naval Med. Res. Inst., Bethesda, MD, and Duke Univ. Med. Ctr., Durham, NC.*

9:45 **78.6** Temporal summation at the absolute threshold for warmth. **J. C. STEVENS.** *J. B. Pierce Fndn. Lab. and Yale Univ., New Haven, CT.*

10:00 **78.7** Computer analysis of serial EEGs from stroke patients. **B. A. COHEN, E. J. BRAVO-FERNANDEZ** and **R. S. HOSEK.** *Marquette Univ. and VA Ctr., Wood, WI.*

VOLUNTEER PAPERS

79. Visual Mechanisms

8:30 AM—*Hampton Court Room, Le Baron Hotel*

Chairman: **D. B. LINDSLEY**

8:30 **79.1** Photoreceptor responses and central conduction in the eye of a nudibranch mollusc. **R. CHASE.** *McGill Univ., Montreal, Canada.*

8:45 **79.2** Information coding in the crayfish optic nerve: motion detector activity predicts the occurrence of visually guided behavior. **R. M. GLANTZ.** *Rice Univ., Houston, TX.*

9:00 **79.3** Retinal projections in the lizard *Gekko gecko.* **A. B. BUTLER** and **R. G. NORTHCUTT.** *Univ. of Virginia Sch. of Med., Charlottesville, VA, and Univ. of Michigan, Ann Arbor, MI.*

9:15 **79.4** Retinal projections in a teleost (*Malapterurus electricus*). **D. E. O'DONNELL** and **S. O. E. EBBESSON.** *Univ. of Virginia Sch. of Med., Charlottesville, VA.*

9:30 **79.5** Retinogeniculate projections of C57BL/6J mice. **I. S. WESTENBERG** and **R. A. GIOLLI.** *Univ. of California, Irvine Sch. of Biol. Sci., Irvine, CA.*

9:45 **79.6** Depth discrimination in the cat contingent upon positive reward. **M. GOLLENDER** and **C. B. PITBLADO.** *Pacific Univ. Col. of Optometry, Forest Grove, OR.*

10:00 **79.7** Thalamic electroencephalographic correlates of discriminative performance in the monkey. **A. COSTIN** and **S. L. MOISE, JR.** *UCLA Sch. of Med., Los Angeles, CA.*

10:15 **79.8** Visual evoked responses and selective masking with pattern flashes of different spatial frequencies. **M. MUSSO** and **M. R. HARTER.** *Univ. of North Carolina, Greensboro, NC.*

10:30 **79.9** Topography of late visual evoked responses in man. **M. W. DONALD.** *Queen's Univ., Kingston, Canada.*

10:45 **79.10** Changes in the late components of visual evoked potentials with visual information processing. **D. B. LINDSLEY, D. M. SEALES** and **G. F. WILSON.** *Brain Res. Inst., UCLA, Los Angeles, CA.*

11:00 **79.11** Concurrent behavioral and lateral geniculate spectral response for rhesus monkey. **M. L. J. CRAWFORD** and **H. G. SPERLING.** *Univ. of Texas, Graduate Sch. of Biomed. Sci., Houston, TX.*

11:15 **79.12** Interocular transfer of McCollough effect. **H. H. MIKAELIAN.** *Univ. of Georgia, Athens, GA.*

VOLUNTEER PAPERS

80. Developmental Neurobiology: Neurochemistry

8:30 AM—*Sheffield Court Room, Le Baron Hotel*

Chairman: **P. J. MORGANE**

8:30 **80.1** Effect of pyrithiamine induced thiamine deficiency on rat myelination. **D. McCANDLESS** and **M. J. MALONE.** *George Washington Univ. Med. Sch., Washington, DC.*

8:45 **80.2** The neurochemistry of prenatal malnutrition in rhesus monkey. **J. M. DAVIS** and **W. A. HIMWICH.** *Galesburg State Res. Hosp., Galesburg, IL, and Nebraska Psychiat. Inst., Omaha, NB.*

9:00 **80.3** Chronic protein malnourishment and the development of brain functioning in rats. **W. B. FORBES, W. C. STERN, J. D. BRONZINO** and **P. J. MORGANE.** *Worcester Fndn. for Exp. Biol., Shrewsbury, MA.*

9:15 **80.4** Essential amino acids and prenatal brain development. **S. M. HALL, L. GRAUEL, E. VAN MARTHENS** and **S. ZAMENHOF.** *Brain Res. Inst. and Mental Retardation Ctr., UCLA, Los Angeles, CA.*

9:30 **80.5** Effect of fat-free diet on the developing infant brain. **H. B. WHITE, JR., M. D. TURNER** and **R. C. MILLER.** *Univ. of Mississippi Sch. of Med., Jackson, MS.*

9:45 **80.6** Developmental aspects of acetylcholinesterase. **A. D. VANKER** and **H. MIZUKAMI.** *Wayne State Univ., Detroit, MI.*

10:00 **80.7** Induction of glycerolphosphate dehydrogenase by hydrocortisone in primary rat brain cultures. **G. A. M. BREEN, J. de VELLIS** and **R. COLE.** *Mental Retardation Res. Ctr., UCLA, Los Angeles, CA.*

10:15 **80.8** The blocking effects of cycloheximide on the sensory induction of susceptibility to audiogenic seizures. **S. C. MAXSON** and **P. Y. SZE.** *Univ. of Connecticut, Storrs, CT.*

10:30 **80.9** The effect of early input of ethanol on mice on their susceptibility to audiogenic seizures. **J. YANAI** and **B. E. GINSBURG.** *Univ. of Connecticut, Storrs, CT.*

ABSTRACTS

1.1 POST-CONTRACTILE CHANGES IN STATIC DISCHARGE OF MUSCLE SPINDLES. R. S. Hutton , E. Eldred , and J. L. Smith. School of Physical and Health Education, Univ. Washington, Seattle, WA 98195, and Depts. of Anatomy and Kinesiology, Univ. California, Los Angeles, CA 90024

Isometric contraction induced by electrically stimulating the medial gastrocnemius (MG) via appropriate ventral roots or the muscle nerve produced a persistent post-tetanic sensory discharge (PTSD) in dorsal roots L_7, S_1 of cats. PTSD, typically characterized by an early, maximal, and late phase, was abolished by subsequent stretch of the MG tendon but was uninfluenced by muscle twitches or temporary release of muscle tension. Samples of muscle spindle units showed that Ia afferents contribute significantly to PTSD, Group II units exhibited a lesser tendency to discharge, while no Ib fibers sampled showed PTSD. Sensory discharge to vibratory stimuli as seen in spindle units or DR activity was markedly potentiated by vibratory stimuli during the PTSD period as compared to pre-contractile levels. Results obtained with gradation in strength of stimulation, progressive neuromuscular block with gallamine, and increase in frequency of stimulation beyond that necessary for tetanic fusion suggested that alteration in contractile status of both the intra- and extrafusal fibers contribute to the effect. No indication was seen that the response was an aftermath of ionic or metabolic change in the contracting muscle. Spindle afferent discharge appears to contribute to a significant portion, if not all, of PTSD. The possibility that PTSD influences subsequent motor behavior might be considered.

This work has been supported by USPHS Grants NS 01143, MH 5 TI 6415-13 and NIH RR-07096.

1.2 FUSIMOTOR INNERVATION AND RESPONSE CHARACTERISTICS OF THE PRIMATE MUSCLE SPINDLE. P. D. Cheney* and J. B. Preston. Dept. Physiol., SUNY Upstate Med. Ctr., Syracuse, N.Y.

The baboon's soleus muscle has been used to study the innervation and response characteristics of the primate muscle spindle. Spindle afferents can be separated into two distinct populations on the basis of conduction velocity and response to stretch. The population of rapidly conducting afferents has a mean conduction velocity of 81 M/sec (58 units) while the slower conducting population has a mean of 41 M/sec (23 units). The effects of stimulating isolated fusimotor fibers on the response of primary and secondary endings to ramp stretch and release at different rates has been studied. As in the cat, baboon fusimotor fibers can be divided into static and dynamic types on the basis of their effect on the dynamic index of the Ia afferent response to stretch. The dynamic index of both group Ia and group II fibers increases with the rate of stretch; however, the dynamic index of the group Ia fibers is generally much larger than that of the group II fibers and the dynamic sensitivity is slightly greater for group Ia fibers. Stimulating dynamic fusimotor fibers increases the dynamic sensitivity while stimulating static fusimotor fibers decreases it. The effect of fusimotor stimulation on steady state discharge for different amplitudes of stretch has also been studied. Preliminary results indicate that the mean position sensitivity of group Ia units is less than the mean of group II units. Static fusimotor stimulation slightly increases the mean position sensitivity of Ia fibers while dramatically increasing that of group II fibers. The increase for group II fibers is related to the frequency of fusimotor stimulation. On the other hand, the mean position sensitivity for group Ia fibers activated by dynamic fusimotor stimulation is either unchanged or decreased for most frequencies of fusimotor drive.

1.3 ON THE ORIGIN OF PRIMARY AFFERENT DEPOLARIZATION (PAD) IN THE FROG CORD. S.Glusman*, E.Rivaud* & P.Rudomín. Centr. Invest. IPN México 14, DF. (Partly supported by NIH grant NS 09196).

Implicit in the hypothesis that PAD results from current flows generated by interneurons (Lloyd & McIntyre, J. Gen. Physiol. 32, 409,1949), is the idea that adequate activation of these interneurons generates the potential field leading to PAD independently of whether or not afferent fibers are present in the region. In the frog cord, in addition to the PAD produced by afferent fibers, antidromic stimulation of motor nerves (MN) also produces PAD. We studied the distribution of the potential fields generated by antidromic stimulation of hindlimb MN in normal cords and in cords with chronic section (6-8 days) of the left dorsal root (L9-L10). In the normal cord, or in the intact side of the operated cord, MN stimulation produced a potential field with an initial component due to antidromic activation of motoneurons and a delayed slow potential (MN-SP) corresponding to the PAD recorded from the dorsal roots. The negative MN-SP was largest 500-700μ from the dorsal surface, where most afferent fibers terminate. We have not recorded MN-SPs in the deafferented side by stimulation of the ipsilateral MN although there were clear signs of antidromic invasion of motoneurons, which also generated monosynatic responses by stimulation of the ipsilateral ventrolateral tract. This suggests that PAD in the frog cord is not due to current flows generated by interneurons imposed onto afferent fibers. Rather, the potential fields associated with PAD seem to be due to current flows initiated by changes occurring in the afferent fibers themselves.

1.4 PRIMARY AFFERENT HYPERPOLARIZATION AND PRESYNAPTIC DIS-INHIBITION OF Ia FIBER TERMINALS PRODUCED BY LARGE CUTANEOUS FIBERS IN THE CAT CORD. P.Rudomín*, R.Núñez*, J.Madrid* & R.E. Burke Centr. Invest. del IPN México 14, DF. & Lab. of Neural Control NINDS, Bethesda, Md.(Partly supported by NIH Grant NS 09196).

In the unanesthetized cord deprived of supraspinal control, stimulation of the lowest threshold fibers in the sural (SU) nerve produced a small, but consistent (7-10%) excitability reduction of flexor and extensor Ia terminals in the motor nucleus. Hypoexcitability started 15-20ms after SU conditioning and reached a maximum between 40-60ms. This effect was often associated with increased Ia monosynaptic EPSPs without noticeable changes in their falling phase. SU conditioning could also reduce the excitability fluctuations of the Ia terminals, the coefficient of correlation between the antidromic responses of Ia fibers recorded from synergistic or from antagonistic nerves (which ranged from 0.3 to 0.7) and the fluctuations of Ia monosynaptic EPSPs. The effects of SU conditioning on the excitability (mean & variance) of Ia terminals could be fully reproduced by injection of nembutal (10-15 mg/kg). These results suggest that the same set of interneurons is responsable for the correlated membrane potential fluctuations of Ia fiber terminals and for their maintained depolarization. The former introduces variability of Ia monosynaptic EPSPs and the latter reduces synaptic effectiveness. Inhibition of interneurons by stimulation of large cutaneous fibers leads to presynaptic dis-inhibition and reduces the Ia EPSP fluctuations. The effects on cell firing will largely depend on the interplay between these two factors.

1.5 ANALYSIS OF SPIKE ACTIVITY OF THE DORSAL ROOT REFLEX. G.K. Matheson and R.D. Wurster. Depts. Anat. and Physiol., Stritch Sch. Med., Loyola Univ., Maywood, Ill. 60153

Interest in the dorsal root reflex has generally centered on long duration, slow wave velocity, while spike activity has not received much attention. Lumbosacral laminectomies were performed on pentobarbital anesthetized, artificially ventilated cats, immobilized with gallamine. Lumbosacral ventral roots were cut, and the cord was maintained between 36-38 C by means of a heated oil bath. Lumbar dorsal root and/or cutaneous and muscle nerve activity was recorded by means of an AC-coupled amplifier and computer analyzed. Spontaneous dorsal root activity was recorded from the central end of cut dorsal roots. In some single fiber preparations this spontaneous activity correlated with respiration; other fibers could not be correlated with either respiratory or cardiovascular responses. Stimulation of another dorsal root could evoke expected dorsal root or peripheral nerve responses which appear as single or multiple burst activity. Stimulation of lumbar ventral roots was also capable of generating evoked dorsal root potentials.

The effect of paired dorsal root stimulations on the dorsal root reflex of a third dorsal rootlet was studied with the condition-test technique. A condition-test interval between 2-500 msec had an inhibitory effect on the dorsal which is similar in pattern and time course to that characteristically seen in presynaptic inhibition. Similar effects on the dorsal root reflex were observed with condition-test stimulation of either a ventral root-dorsal root pair, or when both stimuli were applied to a single dorsal or ventral root. (Supported by GRSG SOl RR05368 and HE 08682.)

1.6 EFFECTS OF SECONDARY MUSCLE SPINDLE AFFERENT DISCHARGE ON EXTENSOR MOTONEURONES IN THE DECEREBRATE CAT. William Z. Rymer* and John V. Walsh, Laboratory of Neural Control, NIH, NINDS, Bethesda, Md. 20014

Recordings from dissected ventral root fibers, selective electromyography with fine tungsten microelectrodes and standard intracellular recording techniques were used to investigate the response of gastrocnemius and soleus motoneurones to secondary afferent input from the homonymous muscle. Identifiable effects of secondary afferents were produced by combining vibration and slow stretch of the muscle tendon. High frequency (150-200 Hz) small amplitude (100-120 μ)longitudinal vibration is known to produce phase locked discharge of all primary endings in the muscle, giving a fixed firing frequency. Slow sinusoidal stretch was superimposed in order to excite secondary endings, and correlated effects were observed on motoneuronal discharge frequency and membrane potential. Motoneurones showing maintained spike discharge in response to vibration alone also demonstrated increased discharge frequency during added muscle stretch. Motoneurones not responding with spikes consistently demonstrated sinusoidal variations of membrane potential, in which maximal depolarization occurred during muscle lengthening. Electromyographic data provided evidence that additional motor units were recruited during combined slow muscle stretch and vibration. These data support P.B.C. Matthews' hypothesis (J. Physiol. 1969, 204:365-393) suggesting an excitatory effect of secondary spindle afferents on extensor motoneurones in the decerebrate cat.

1.7 THE IDENTIFICATION OF GROUP Ib INTERNEURONS. Mary E. Lucas*, Wm.D.Willis, Jr. Dept. of U.S. Army, Office of Surgeon General and Marine Biomedical Institute, University of Texas Medical Branch, Galveston, Texas 77550.

Interneurons in the intermediate nucleus of the spinal cord were considered to mediate reciprocal inhibition in the stretch reflex until recent evidence showed that ventral horn interneurons are responsible. The afferent input to the interneurons of the intermediate nucleus was re-examined using a combination of brief stretches of muscle and electrical stimulation of muscle nerves to identify the muscle receptors involved. 38 spinal cats anesthetized with α-chloralose were used. The hindlimb was denervated, except for the triceps surae nerves. Group Ia, Ib and II afferents from primary endings of muscle spindles, Golgi tendon organs and secondary endings of muscle spindles, respectively, were excited by electrical stimulation of the nerves and by quick stretches of the muscles. Recordings from 128 Ia, 117 Ib and 106 group II afferents in dorsal root filaments showed that quick stretches of less than 100μ (muscle tension 100g) activate almost exclusively Ia fibers.

Microelectrodes placed in the intermediate nucleus recorded the activity of 50 interneurons extracellularly and 4 intracellularly. The interneurons were selected by monosynaptic responses to group I volleys evoked by electrical stimulation. Only 3 of the cells studied by extracellular recording and 2 of the interneurons examined by intracellular recording were excited by brief stretches of 100μ or less. The vast majority of the interneurons could be fired only by large amplitude quick stretches, if at all.

These findings suggest that the group I activated interneurons in the intermediate nucleus belong to a pathway from Golgi tendon organs.

(Supported by NIH Grant NS 09743, a grant from the Moody Foundation, and the Dept. of U.S. Army, Office of Surgeon General.)

1.8 Segmental Reflexes Mediated by Joint Afferent Neurons
Peter Grigg Department of Physiology University of Massachusetts Medical School, Worcester, Mass. 01604.

Joint afferent neurons innervating the knee joint of the cat were activated by rotating the joint with a stepping motor. Cats were decerebrate and spinal. Reflex effects were observed by monosynaptic reflex testing in knee flexors. The nerve to PB-ST was cut and electrically stimulated. Reflex discharge was recorded in cut ventral roots. The limb studied was completely denervated except for the medial articular nerve (MAN). Control measurements were obtained by repeating observations after section of the MAN.

Reflex effects were in general observed only at positions of extreme flexion or extension. When the knee was moved into extension, the PB-ST monosynaptic reflex discharge was increased, and when the knee was moved into full flexion it was reduced. The magnitude of these effects was related to the degree of flexion or extension.

Since PB-ST are flexors of the knee these effects constitute negative feedback onto flexor motoneurons. This reflex tends to oppose movements of the joint, and since effects were observed primarily at extreme angular positions it is suggested that this reflex may serve to limit the angular range of active movements of the joint.

Supported by NIH grant NS-10783-01.

1.9 THE INVOLVEMENT OF GAMMA MOTONEURONS IN THE AUDIOSPINAL REFLEX. G-M. Moolenaar and C.D. Barnes. Howard Univ. Med. Sch., Wash., D.C. and Indiana State Univ., Terra Haute, Ind.

The participation of gamma motoneurons in the acoustically evoked startle reflex was investigated in adult cats anesthesized with chloralose (50 mg/kg). Computer analysis of conduction velocities in ventral roots as well as the observed latency difference between the click-evoked responses of dorsal root filaments and the ventral root of the same segment indicated that the gammas were activated in advance of the alpha motoneurons. While both static and dynamic gammas were influenced by the click, results showed that gamma activity is not necessary for the mediation of the audiospinal reflex but is additive to the direct, descending supraspinal influences impinging on the alpha motoneurons. It is suggested that gamma activation as a result of sudden, intense sensory stimulation may serve to increase the static and dynamic sensitivity of muscle spindle afferents in anticipation of subsequent movements in response to that stimulus.

1.10 AN ELECTROPHYSIOLOGICAL STUDY OF THE SPINAL CORDS OF DEAFFERENTED MONKEYS. R.M. Wylie, G. Barro*, P.N. Perrella*, S.G. Weinberg* and E. Taub. Dept. Neurophysiol. Walter Reed Army Medical Center, Washington, DC 20012 and Institute for Behavioral Research, Silver Spring, MD 20910.

In anaesthetized, chronically deafferented monkeys*, we have electrically stimulated forelimb nerves while recording from different depths in the spinal cord to determine whether there is any afferent input at the segmental level which might underlie the recovery of function observed in these animals. Unlike the response to peripheral stimulation observed in normal monkeys, in the deafferented monkeys, the responses at the cord surface were small and of short duration. The potentials reached maximum amplitude only when the electrode was in the ventral horn. Small late waves were observed in some preparations, often with spikes resembling Renshaw cell discharges riding on them. All of the potentials we have recorded in the spinal cords of chronically deafferented monkeys can be attributed to the antidromic invasion of motoneurons. Although we cannot exclude the possibility that some afferent activity may be carried in intact rootlets missed in our explorations or in small diameter fibers, segmental afferent input as observed in normal monkeys is clearly absent from chronically deafferented monkeys.

*In conducting this research, the investigators adhered to the "Guide for Laboratory Animal Facilities and Care," of the Institute of Laboratory Animal Resources, National Academy of Sciences - National Research Council. (Supported in part by PHS Grant No. MH 16954.)

2.1 FREEZE-FRACTURE STUDY OF EXCITATORY AND INHIBITORY SYNAPSES. Dennis M. D. Landis* and T. S. Reese. Lab. Neuropath. Neuroanat. Sci., NINDS, NIH, Bethesda, Md. 20014

Synapses in cerebellar cortex and olfactory bulb from morphine-treated mice and rabbits were examined in replicas of freeze-fractured tissue fixed in aldehydes and glycerinated prior to freezing. Fractures presumably split membranes, revealing the inner surface of outer leaflets or the outer surface of inner leaflets. The inner and outer leaflets of both the pre- and postsynaptic membrane were studied in each of six types of synapse. At synapses reported to be excitatory (mitral dendrites to gemmules in the olfactory bulb and, in the cerebellum, parallel fibers to Purkinje spines and mossy or climbing fibers to granule dendrites) an array of particles was found on the outer leaflet of the postsynaptic membrane coextensive with the widened portion of the synaptic cleft. A corresponding array of pits was found on the inner leaflet. Similar arrays of outer leaflet particles were coextensive with the widened intercellular cleft at desmosomes between cerebellar granule cell dendrites. At synapses reported to be inhibitory (granule cell gemmules to mitral dendrites in the olfactory bulb and, in the cerebellum, basket cell axons to Purkinje somata and stellate cell axons to Purkinje dendrites) there were no particles specifically associated with either leaflet of the postsynaptic membrane at the synaptic junction. "Presynaptic membrane modulations" (Streit, et al., Brain Res., 1972) were adjacent to rather than coextensive with the synaptic junctions at some of the excitatory and inhibitory synapses. No other specializations were consistantly found on presynaptic membranes. Inner leaflets around Purkinje, stellate, and basket cell somata had large arrays of particles which typically lay opposite flattened glial processes. No structure of corresponding size and distribution has been identified yet in thin sections.

2.2 EFFECTS OF OSMOLARITY OF FIXATIVES ON FINE STRUCTURE OF SYNAPTIC VESICLES OF NERVE TERMINALS IN THE CRAYFISH STRETCH RECEPTOR. A. D. Tisdale* and Y. Nakajima. Dept. of Bio. Sci., Purdue Univ., W. Lafayette, Ind. 47907

A variety of fixation procedures with varying osmolarities were used for EM preparations of crayfish stretch receptor organs after dissection in physiological solution (440 mOsm). The control procedure was primary fixation with phosphate buffered 1.6% glutaraldehyde, wash with phosphate buffer, and postfixation with phosphate buffered 1% OsO_4, all isosmotic with the physiological solution. Under these conditions, we encountered two types of nerve terminals; small-vesicle terminals (SVT) containing small elongate vesicles of about 330 Å and large-vesicle terminals (LVT) containing larger round vesicles about 440 Å. Their location and physiological evidence suggest that SVT and LVT are inhibitory and excitatory, respectively (Uchizono, 1967; Atwood and Morin, 1970; Nakajima and Tisdale, 1973). Primary fixatives, made hypertonic (880 or 1320 mOsm) by increasing glutaraldehyde concentration gave results similar to the control, while primary fixatives made hypertonic by increasing the buffer concentration distorted the entire specimen. Preparations washed with hypertonic buffer (880 or 1320 mOsm) showed elongation of vesicles in SVT and LVT, while washing with hypotonic buffer (145 mOsm) rendered vesicles in both types round. However, vesicles in SVT were always smaller than those in LVT. Skipping the washing procedure of the control had little effect on the morphology of vesicles. Direct fixation with isosmotic OsO_4 resulted in irregularly elongated vesicles in SVT and irregularly round vesicles in LVT. The results suggest that the basic morphological difference in vesicles between SVT and LVT is size rather than shape, and that shapes of synaptic vesicles are altered by concentration of buffer rather than that of glutaraldehyde. (Supported by PHS grants NS-10457 and NS-08601).

2.3 EFFECTS OF OSMOLARITY OF FIXATIVES ON THE FINE STRUCTURE OF SYANPTIC VESICLES IN THE NEUROMUSCULAR JUNCTIONS OF THE FROG. Y. Nakajima and T. Naab*. Dept. of Bio. Sci., Purdue Univ., W. Lafayette, Ind. 47907.

A variety of fixation procedures with varying osmolarities were used for EM preparations of the cutaneous pectoris muscle of the frog after dissection in Ringer's solution (226 mOsm), and a quantitative investigation of the size and shape of synaptic vesicles in the neuromuscular junctions was conducted. In the control procedure (primary fixation with phosphate buffered 0.85% glutaraldehyde, wash with phosphate buffer, and postfixation with phosphate buffered 1% OsO_4 - all solutions isosmotic with Ringer solution), the synaptic vesicles appeared uniformly round, about 530 Å in diameter. Skipping of wash from the control procedure gave similar results. On the other hand, direct fixation with the isosmotic phosphate buffered OsO_4 resulted in irregularly shaped and moderately elongated vesicles. Primary fixative made hypertonic (678 mOsm) by increase in glutaraldehyde concentration gave similar results to the control, while fixatives made hypertonic by an increase in buffer concentration caused severe shrinkage of the nerve terminal due to the decrease of the intracellular space, but had only a little effect on the shape of vesicles. Preparations washed with hypertonic buffer (678 mOsm) (primary and post-fixatives were isosmotic) showed severe elongation and distortion of synaptic vesicle shape. Treatment with either hypotonic primary fixative or hypotonic wash had little effect on synaptic vesicle shape. These results suggest that the shapes of the synaptic vesicles are altered by the concentration of buffer rather than by that of glutaraldehyde. (Supported by PHS grant NS-10457).

2.4 CYTOCHEMICAL STUDIES OF SYNAPTIC VESICLES AND RELATED STRUCTURES IN FROG RETINAL PHOTORECEPTOR CELLS. Samuel Schacher* and Eric Holtzman. Dept. Biol., Columbia Univ., N.Y. 10027

Photoreceptor cells in isolated frog retina preparations show considerable uptake of horseradish peroxidase into small vesicles in synaptic regions and into multivesicular bodies and other lysosome-related structures in synaptic regions and in the vicinity of the Golgi apparatus. Since such uptake is substantial in retinas maintained in the dark throughout the experiment, it appears quite probable that the receptor cell synapses are active in the dark, at least in the presence of peroxidase. Initial experiments utilizing varying conditions of illumination or alterations in the ionic composition of the bathing medium suggest that the extent of peroxidase uptake changes with varying states of the cells. Thus, such uptake may be useful in evaluating or mapping synaptic activity of rods and cones (and other retinal cells) under different physiological conditions.

Most synaptic vesicles in the photoreceptors show electron dense deposits in preparations incubated in a medium intended for demonstration of glucose-6-phosphatase activity. Since such deposits are seen whether or not substrate (glucose-6-P) is included in the medium, they probably reflect the capacity of vesicle membranes to bind lead. This is of interest in light of the supposed metal (e.g. Zn) or ion binding capacities of some other types of synapses. In addition, since rough and smooth endoplasmic reticulum and some Golgi-associated membranes of the receptor cells also can bind lead, the observations may provide clues to the origins of the synaptic vesicles.

2.5 AN ELECTRON MICROSCOPIC STUDY OF ALTERATIONS IN HIPPOCAMPAL DENTATE GYRUS SYNAPTIC MORPHOLOGY AND ASSOCIATED ELECTRON DENSITIES: IMMEDIATE POST-MORTEM EFFECTS. Aryeh Routtenberg and Sally Tarrant*. Dept. Psychol., Cresap Lab. Neurosci. Behav., Northwestern Univ., Evanston, Ill. 60201

In order to understand the functions of the synapse, it is necessary to evaluate the methods by which this structure is known. One salient feature of all methods used to date is the obligatory transition of the synapse from the awake animal to a test tube or plastic-epoxy embedment. Using both immersion and perfusion fixation, young and adult albino rat brain tissue was fixed in a glutaraldehyde-formaldehyde mixture while anesthetized ("alive condition"), when breathing stopped, but heart was still beating (0 min condition), breathing and heart stopped (1 min), and 5 min and 10 min after breathing stopped. The present findings using a quantitative and statistical approach indicated that, as a function of post-mortem time, there was rapid increase in spherical densities 1000 Å in diameter in the cell body, dendrites and adjacent to the post synaptic membrane thickening. These densities were seen only rarely in "alive" tissue, but were obvious in the 0 min condition. Synaptic curvature was also found to be altered following post-mortem treatment. In the "alive" condition the synaptic cleft was concave while in the post-mortem material the mean cleft curvature became increasingly convex. Even in the 0 min condition such alterations occurred in cleft curvature, although they were greater at later post-mortem times (e.g., 10 min). These results bear on the issue of the in vivo morphology of the synapse, and point to, during the transition from life to death, rapid alterations in synaptic morphology, as well as suggesting possible alterations in synaptic chemistry.

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2.6 SYNAPTIC PROFILES ON SOMATA AND DENDRITES OF THE TUBEROINFUNDIBULAR NUCLEUS OF THE MOUSE. N. Lemkey-Johnston and V. Butler*. Illinois State Pediatric Institute and Dept. Anat., Univ. of Ill. at the Medical Center, Chicago, Il. 60608.

Sampling of somatic and dendritic profiles from tuberoinfundibular nuclear cells immediately above the median eminence has revealed that synaptic profiles can be divided into at least 7 morphological classes. The two most abundant types of profiles present are "systems" of unmyelinated axons which expand into multiple, large, irregular varicosities containing abundant clear agranular vesicles as well as dense core vesicles. The "systems" differ in that one contains light axoplasm and forms asymmetrical adhesions while the second has dark axoplasm and forms symmetrical adhesions. The next largest class consists of small to medium-sized boutons in which clear round synaptic vesicles are randomly distributed, few dense core vesicles occur and the adhesions are asymmetrical. In smaller numbers are found medium-size boutons forming multiple symmetrical adhesions, and small boutons filled with round clear vesicles clustered around an asymmetrical adhesion. Few boutons with abundant ellipsoid or "flattened" vesicles were found in our sample. These results represent preliminary observations in a systematic study of the synaptic organization of the tuberoinfundibular nucleus, with its ultimate goal to determine possible cellular heterogeneity on the basis of synaptic patterns.

2.7 THE DEVELOPMENT OF SYNAPSES IN THE CEREBELLUM OF THE CHICK EMBRYO. Rainer F. Foelix* and Ronald W. Oppenheim. N. C. Dept. Mental Health, Research Div., Neuroembryology Lab., Raleigh, N. C. 27611

Cerebelli of chicken embryos were studied electron microscopically at 8,9,10,12,14 and 18 days of incubation. At day 8 very few immature axo-dendritic synapses are detected in the future molecular layer; very few synaptic vesicles (2-3) and a slight membrane thickening is typical. By day 9 the number of synapses has increased, there are more synaptic vesicles per terminal (~10) and the membrane thickenings are slightly asymmetrical. Synapses are axo-dendritic and axo-somatic (on soma of Purkinje cells). At day 10 fairly mature synapses appear, e.g. more synaptic vesicles and further membrane differentiation is observed. Synapses at 12, 14 and 18 days differ structurally very little from a 10-day synapse. All synaptic vesicles are spherical (S-type); dense-core vesicles are abundant in early stages but decrease after day 10. Most synapses are on Purkinje cell dendrites. EPTA- staining of synapses was successful on day 10 and later but failed in earlier stages. Morphologically mature synapses appear in the cerebellum within 3 days after onset of synaptogenesis whereas the synaptogenic period is about 10 days in the spinal cord of the chick.

2.8 THE ANTEROVENTRAL NUCLEUS OF THE THALAMUS: SYNAPTIC ORGANIZATION IN THE ALBINO RAT. Nicholas J. Lenn. Dept. Pediat., Univ. Chgo., Chicago, 60637

The anteroventral nucleus contains a single neuronal population with 12-14 by 16-18 micron diameter perikarya in Nissl stain, and spherically radiate dendritic trees as seen in three planes with Golgi impregnation. By routine electron microscopy the neuronal perikarya are unremarkable except for the virtual absence of axosomatic synaptic contacts. The neuropil contains dendrites of various sizes with occasional spines, and two types of nerve endings. Type I endings are the large majority, are 0.5 to 1.0 micron in diameter, contain spherical synaptic vesicles, and form asymmetrical contacts with the shafts of distal dendrites. Endings of type Ia and Ib underwent dense degeneration after lesions of hippocampus and mammillary body, respectively. Type Ia and Ib could not be distinguished from each other in the normal material. Type II endings are few in number, are 2 to 4 microns in diameter, also contain spherical synaptic vesicles regardless of tonicity of fixative or post-fixation buffer wash, and form symmetrical contacts with proximal dendrites. They did not degenerate after hippocampal and mammillary body lesions. The anteroventral nucleus is thus simpler than other thalamic nuclei in not containing Golgi type II neurons, not exhibiting diversity of synaptic vesicle morphology, and not containing serial synapses or glomeruli. The significance of the convergence of hippocampal and mammillary body afferents, and the origin of the type II endings remain to be clarified.

2.9 A QUANTITATIVE ULTRASTRUCTURAL ANALYSIS OF THE SACRAL PARASYMPATHETIC NUCLEUS OF THE RABBIT. R. William Soller* and Leonard L. Ross. Dept. Anat., Cornell University Medical College, New York, N. Y. 10021

Seven inputs have been proposed to the sacral parasympathetic nucleus (SPN) of the rabbit. Quantitative electron microscopy has been used to characterize these inputs morphologically. Within the ventral subgroup of the SPN two different neurons can be distinguished on the basis of size, shape, and synaptic input. One is medium-sized (20-25u) and multipolar; the other is small (10-15u) and spindle shaped.

At the ultrastructural level the synaptic input to the SPN has been identified by degeneration after dorsal rhizotomy and T10 transection. The primary afferent input is bilateral to both neurons. It is represented by an F (flattened vesicle) type bouton. These F boutons are found in higher numbers and with an even distribution over spindle cells, while on multipolar cells they are confined to the soma and proximal dendrite. Two suprasegmental S (spherical vesicle) type boutons contact both neurons. One is large and is found mainly on primary and secondary dendrites; the other is smaller, contains large dense core vesicles, and occurs mainly on the dendritic trunks of both cells. In addition, a descending F bouton is rather evenly distributed over both neurons. The interneuronal S bouton typically exhibits bodies of Taxi. While it is evenly distributed over both cells, it occurs in greater number on spindle neurons. No certain identification of an interneuronal F bouton could be made.

Thus, of the seven proposed inputs to the SPN the terminations of five have been demonstrated morphologically. These synapses correspond to primary afferent, suprasegmental, and interneuronal inputs.

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2.10 ULTRASTRUCTURE OF EPENDYMAL CELLS AND TANYCYTES OF THE HYPOTHALAMIC THIRD VENTRICLE. Ruth Bleier and Grayson Scott* Depts. Neurophysiol. and Anat. Univ. of Wis. Med. School, Madison, Wis. 53706

A previous study has demonstrated with the Golgi-Cox technique that ependymal cells throughout the hypothalamus send basal processes into every hypothalamic cell group and area. The branches of such ependymal cells (tanycytes) were seen to form intricate morphological relationships-loops, calyces, claws - with neurons and capillaries. The present study examines the ultrastructure of hypothalamic ependymal cells and of interependymal cell, tanycyte-neuronal and tanycyte-capillary relationships. Hypothalamic blocks are fixed in glutaraldehyde-paraformaldahyde/sucrose-sodium phosphate buffer, post-fixed in osmic acid-buffer, and stained with uranyl and lead acetate. A great variety of ependymal forms is seen. The ependyma appears to constitute a mosaic with adjacent cells or groups of cells showing variations in morphological features: ventricular surface characteristics (presence or absence of cilia and microvilli); cell body and nuclear shape and size; electron density of the cytoplasm; types and numbers of organelles, dense bodies, vacuoles and vesicles; basal features (presence or absence of processes); intricate desmosomal and interdigitating cytoplasmic intercellular relationships. The variety of morphological types suggests a variety of functions which may include secretory and transport mechanisms in hypothalamic regulation of the adenohypophysis.
(Work supported by NSF grant GB-17835 and NIH grant 5-P01-NS-06225.

3.1 HEMISPHERECTOMY AND FUNCTIONAL PLASTICITY OF THE HUMAN BRAIN. AARON SMITH Univ. Mich. Med. Sch., Ann Arbor, Mich. 48104. Standardized neuropsychologic tests of 41 patients with hemispherectomy for infantile hemiplegia, glioma or shrapnel wounds showed marked differences in effects of hemispheric removals as a function of the age at which brain insults occurred. Language and mental functions generally improved, with no differences between left or right hemispherectomy for early brain insults. After left hemispherectomy at age 6, a 23 yr. old boy had completed 3 years of college. In 6 adults (5 with glioma, 1 shrapnel wound), effects of hemispherectomy differed drastically. Left dominant hemispherectomy resulted in severe speech, reading and writing defects. However, speech comprehension was relatively spared, and nonverbal intellectual capacities remained intact. Right hemispherectomy resulted in severe nonverbal intellectual defects but language and verbal intelligence were intact. Despite the severity of selective verbal or nonverbal defects, no patients had prosopagnosia; anosognosia; color agnosia; word deafness, blindness or mutism; amusia; complete constructional apraxia or other total defects variously described in adults with focal lesions in either hemisphere. The results indicate (1) a single intact infant hemisphere alone - either the left or right - will suffice for the development of normal adult language and intelligence (2) normal adult hemispheric functions differ quantitatively rather than qualitatively. Although the plasticity of the developing infant brain diminishes with increasing specialization of each hemisphere in language or visual indeational functions, recovery or improvement of impaired functions after hemispherectomy in adults as well as children reflects the removal of inhibitory influences radiated from the diseased to the intact hemisphere; and the capacities of the remaining hemisphere to compensate in varying degrees for functional losses resulting from removal of a diseased hemisphere.

3.2 RECOVERY OF STRUCTURE IN INJURED MAMMALIAN BRAIN. Anne F. Marks. Dept. of Biophysics, Johns Hopkins Univ., Baltimore, Md. 21218.

Cuts through living brain are made with the dorsoventral motion of 0.9-5.0 mm crossbars of 89μm wire loops which remain in situ until after fixation. Pairs of dorsoventral holes, remaining after ventral removal of the wire arms, mark the incision. Sections of pyridine silver impregnated brain are counterstained with Luxol Fast Blue and Nuclear Fast Red. Brains are fixed shortly after incision (19 rats, 45 cuts) or after survival of 30 minutes to 231 days (48 rats, 62 cuts). Two Rhesus monkeys had cuts for zero (3), two (5) and sixty (10) days. Such cuts are sometimes: reoccupied by brain tissue of normal appearance; crossed by axons of normal orientation; without interruption detectable with the light microscope. Such restoration can occur by two hours (cortex, corpus callosum, fimbria) and be evident after 206 days (internal capsule, corpus callosum, septum). The more common recovery of structure is a gradual relocalization of an intercepted tract so that its orderly, myelinated axons massively bypass one or both ends of an incision. This phenomenon is first shown by fibers at the end of the cut and later by those at its center. It does not occur when the cut is much larger than the tract. These two types of repair are associated with axon terminal formations detectable only near the cut, at early times, and with little to no axon and myelin degeneration distal to the cut at later times. The speed of repair and absence of degeneration indicate reconnection of perikaryon-free axons with those from a trophic center, after elongation [Marks, Anat. Rec. 175:383 (1973)] across or around an incision, in normal adult rats and monkeys. [Supported by grant NIH 5-RO1-NM08385-3 and the Department of Biophysics].

3.3 AXON SPROUTING IN THE HIPPOCAMPAL FORMATION AND BEHAVIORAL RECOVERY FOLLOWING UNILATERAL ENTORHINAL CORTEX LESIONS. R.L. Smith, O. Steward, C. Cotman and G. Lynch (SPON: R.F. Thompson) Dept. Psychobiology, University of California, Irvine 92664

Following unilateral ablation of the entorhinal cortex (EC) in rats, we have examined (1) the redistribution of the efferent projections of the remaining, contralateral EC; (2) the electrophysiological capacity of the redistributed terminal projection; and (3) the behavioral consequence of lesion and subsequent fiber redistribution. In normal rats, the EC sends a massive projection to the ipsilateral dentate gyrus (DG), but sends no projection to the contralateral DG; whereas, following unilateral EC lesions, we demonstrate autoradiographically the presence of a new terminal projection which occupies the synaptic territory vacated by the ipsilateral EC afferents. Furthermore, this new projection is electrophysiologically functional. In normal animals, unilateral stimulation of the EC never results in short latency activation of the contralateral DG, though in the operated animals, a short latency response to contralateral EC stimulation becomes apparent by 9 days post-lesion. Behaviorally, animals with unilateral or bilateral EC lesions show a deficit in spontaneous alternation (SA) immediately post-lesion. While animals with bilateral lesions alternate at chance rates throughout testing, the rats with unilateral lesions recover normal SA levels by 10 days post-lesion. To show that the behavioral recovery is correlated with fiber redistribution, we lesioned the dorsal psalterium (the fiber tract through which CEC projects) in recovered animals. This lesion resulted in an immediate and apparently permanent return to chance levels of alternation, characteristic of the immediate post-EC lesion state. In addition, when the dorsal psalterium was destroyed prior to the unilateral EC ablation, the animals never recovered a control rate of SA. This implies that, in this instance, behavioral recovery depends on sprouting of CEC fibers into the deafferented DG.

3.4 SPROUTING OF NORADRENERGIC NERVE TERMINALS SUBSEQUENT TO FREEZE LESIONS OF RABBIT CEREBRAL CORTEX. Florry P. Bowen, Charles Demirjian*, Stephen E. Karpiak* and Robert Katzman, Dept. Neurol., Columbia Univ., Coll. Phys. & Surgeons, New York 10032 & Dept. Neurol., Albert Einstein Medical Ctr. New York, 10461.

Previous studies have reported sprouting and growth of catecholamine-containing nerve fibers after interruption of pathways in the spinal cord and mesencephalon. The present study examined the histological changes in situ associated with freeze lesions of the rabbit motor cortex using the histofluorescent technique of Falck (1962). Within three hours after cryosurgery noradrenaline accummulated in the nerve terminal varicosities and further increased after 24 hours which resulted in swollen and distorted terminals. After one week, the area of the lesion was infiltrated with autofluorescent macrophages and autofluorescent pyknotic motor cortex cells were visible. Bordering the damaged region were many abnormal noradrenergic nerve terminals as well as terminals that sprouted fibers growing into the necrotic tissue. 12 and 16 weeks post-surgery, many more nerve terminals were visible in the lesion area than in similar sections taken from a sham operated control or sections posterior to the lesion. Fluorescence of noradrenergic innervation of pial and intracortical vessels also increased in the damaged area. Microspectrofluoremetric examination of the tissue according to Björklund (1968) confirmed that the emission and excitation spectra of the terminals surrounding the lesion were noradrenergic. Pretreatment of animals with reserpine abolished all catecholamine fluorescence. It is suggested that reorganization of noradrenergic innervation reflects a more general process that contributes to the development of epileptogenic foci subsequent to freezing.

This work supported by NS-05184 and NS-09649.

3.5 A REVERSIBLE REDUCTION IN ACCUMULATION OF TYROSINE HYDROXYLASE ENZYME PROTEIN IN LOCUS COERULEUS AFTER HYPOTHALAMIC LESIONS. Robert A. Ross, Tong H. Joh* and Donald J. Reis. Dept. Neurol., Lab. Neurobiol., Cornell University Medical College, New York, 10021.

Transection of axons of noradrenergic neurons of n. locus coeruleus (LC) by electrolytic lesions of lateral hypothalamus results in a reversible reduction of activity of the enzyme dopamine-β-hydroxylase (DBH) in the LC (Reis & Ross. Brain Res. 1973 in press). Enzyme activity falls to 50% by day 14 returning to control levels by day 28. This change has been viewed as a concomitant of the retrograde reaction of central noradrenergic neurons. To determine if such lesions evoke a parallel reduction in the activities of other enzymes involved in catecholamine metabolism we assayed the activities of tyrosine hydroxylase (TH), dopa decarboxylase (DDC) and monoamine oxidase (MAO) at 14 and 28 days after a lesion. Unilateral lesions of posterolateral hypothalamus transecting noradrenergic axons resulted in reversible changes in TH and DBH activities in LC. Enzyme activities fell to 50-60% of control by day 14 returning to normal by day 28. DDC and MAO activities were unchanged. Immunochemical titration with a specific antibody to TH demonstrated that the reduction in TH activity was entirely attributable to reduction in the amount of specific TH enzyme protein and not to inhibition of enzyme activity. We conclude that during the retrograde reaction of central noradrenergic neurons there is a reversible accumulation of enzymes subserving synthesis of the neurotransmitter. Such changes may reflect reordering of protein biosynthetic pathways. (Supported by NIH grant NS 06911 and Harris Foundation.)

3.6 ENZYMATIC DEVELOPMENT AND BIOCHEMICAL PLASTICITY WITHIN A DEVELOPING CHOLINERGIC PROJECTION IN THE CNS. J. Victor Nadler, Dee Ann Matthews*, Carl W. Cotman, and Gary S. Lynch. Dept. Psychobiol., Sch. Biol. Sci., UCI, Irvine, Cal. 92664

The cholinergic innervation of the rat hippocampal formation is derived predominantly from septal afferent input, and thus changes in biochemical parameters of cholinergic transmission can be related to development within a single morphological entity. The postnatal development of choline acetyltransferase (ChAc) and acetylcholinesterase (AChE) activities has been studied within discrete layers of the dentate gyrus by quantitative histochemical analysis. The specific activity of ChAc increases several-fold to adult values within a brief period around 16-17 days after birth. We interpret this abrupt change as a correlate of cholinergic synaptogenesis. It is not accompanied by an increase of similar magnitude in AChE activity, which attains mature values later and at a more gradual rate. Removal of the entorhinal cortex at 11 days of age strikingly alters the discrete laminar distribution of these enzyme activities. The outer part of the molecular layer on the operated side becomes enriched in both ChAc and AChE activities relative to the control side. However, the differences between the two sides disappear before maturity. A slowly-developing, permanent bilateral depletion of AChE activity was also observed in all layers of the dentate gyrus, but specific activities of ChAc in adult animals were normal. These changes were localized to septo-hippocampal elements. They demonstrate a remarkable degree of biochemical plasticity within a developing CNS projection. These data are consistent with histochemical evidence which suggests a relocation of septo-hippocampal synaptic terminals and neuropil in response to entorhinal lesion. (Supported by NIMH Grant MH 19691 amd NSF Grant GB 35315X.)

3.7 SITE SPECIFIC REGENERATION OF TYPE I CUTANEOUS RECEPTORS IN THE CAT. K. W. Horch, K. B. English*, L. J. Stensaas and P. R. Burgess. Dept. Physiol., Coll. Med., Univ. Utah, Salt Lake City, 84112.

Earlier work by Burgess and Horch (J. Neurophysiol. 36:101-114, 1973) showed that regenerating cutaneous sensory fibers in adult cats re-establish receptor properties similar to those they had before nerve transection. For instance, Type I fibers, which normally innervate small dome-like elevations (Haarscheiben) on the cat's skin, are uniquely associated with these domes after regeneration, and have response patterns indistinguishable from those seen before transection. In the present study, the distribution of domes innervated by the femoral cutaneous nerve was mapped and the nerve was cut. The denervated domes atrophied and the specialized epithelial Merkel cells normally found within these domes disappeared. Return of the nerve caused the reappearance of normal domes. Although some of these structures were found at new sites, there was a significant tendency for regenerated domes to appear at old dome loci. This indicates that some agent acted to direct returning Type I fibers to form terminals at the old sites.

3.8 PRECISION AND PLASTICITY IN A REGENERATING SENSORY SYSTEM. John Palka and John S. Edwards*, Dept. Zool., Univ. Washington, Seattle 98195.

The cerci of orthopteroid insects, abdominal appendages covered with a variety of sensilla, regenerate readily if removed in any of the immature instars. In house crickets (Acheta domesticus) axons from long, socketed cercal hairs synapse in the terminal abdominal ganglion with a few giant interneurons, in particular with the two largest ones on the ipsilateral side, the lateral and medial giant interneurons (LGI and MGI). Evidence for the pattern of synaptic connections comes from staining of terminals of sensory axons following short-term degeneration, from analysis of response characteristics of the LGI and MGI to acoustic and other sensory stimulation of the cerci and of non-cercal receptors, and from intracellular recording and dye injection of the interneurons (with R.K. Murphey).

Appropriate connections from the filiform hairs to the MGI and LGI, preserving even such details as the shape of the directional sensitivity curve, are restored if the cerci regenerate symmetrically, even if they were removed at hatching and all primordia were removed until the 7th of the 9 larval instars. But marked synaptic rearrangements occur if: (a) only one cercus is removed and the other allowed to grow normally throughout postembryonic development; (b) both cerci are removed for 6 instars and then only one is allowed to regenerate; (c) only one of the cerci is removed for 6 instars and is then allowed to grow for the first time while the first cercus is removed; (d) one of the connectives anterior to the terminal ganglion is crushed or cut in the 7th instar, regardless of whether the cerci are forced to regenerate or are left intact. Possible anatomical substrates for functionally recognized rearrangements include both mislocation of primary sensory axonal terminals and changes in the dendritic morphology of the MGI and LGI.

4.1 CONDITIONED RESPONSES IN THE RETICULAR FORMATION. Jacques Montplaisir* and James Olds. Division of Biology, California Institute of Technology, Pasadena, 91109.

Olds et al. (J. Neurophysiol. 35: 202, 1972) reported primary changes of reticular units in the midbrain and the pons as a consequence of learning. The present experiment is an extension of this original study using a larger number of units and a finer grain of temporal analysis. The response of 225 units were recorded from 49 freely moving rats during an appetitive classical conditioning situation. Seventy per cent of these neurons showed a sensory response to the conditioned stimulus (a tone of 1,000 Hz frequency and 300 msec duration) prior to conditioning. More than 75% of all units showed a learned excitatory response (i.e., a response which arose de novo or increased greatly during conditioning). Forty percent of these responses had a latency less than 30 msec, shorter than any detectable behavioral conditioned response. Learned unit responses were observed in all areas of the reticular formation (RF). But, the shortest latency changes (4.5 to 12 msec.) occurred preferentially in the ventral part of the caudal midbrain and the pontine RF. Further, they were more numerous in the midlateral subdivision of this region. Marked inhibitory learned responses were recorded from 5% of the neurons, and these cells were located mainly in the area surrounding the red nucleus (perirubral area). More than 100 of the 225 units were also monitored during several episodes of sleep and wakefulness. Results will be discussed in relation to the spatio-temporal distribution of learned responses in the RF and the possible correlation of these changes with general or selective arousal mechanisms.

4.2 HABITUATION AND MODIFICATION OF RETICULAR FORMATION NEURON RESPONSES IN CATS. David F. Lindsley, Susan K. Ranf*, Marjorie J. Sherwood* and William G. Preston*. Dept. Physiol., Sch. Med., Univ. Southern Calif., Los Angeles, Calif. 90033.

In order to study the response plasticity of reticular formation (RF) neurons a stimulus paradigm was used that has been worked out by Chow et al. (J. Neurophysiol. 31: 729, 1968). Extracellular microelectrode experiments were performed on 22 acute, paralyzed cats. Twenty-one of 36 medullary and midbrain RF cells showed response habituation after 5-15 min of repetitive sciatic stimulation at one/3 sec. Two types of changes appeared in the poststimulus time histogram or dot displays: either response decrements or latency alterations. Recovery of the prehabituated responses occurred within 10-30 min. Comparison of responses to pre- and post-habituation control stimulation of either the other sciatic nerve or forepaw indicated that habituation was not due to some nonspecific process but resulted from repetition of the stimulus. Ten of 18 neurons, tested completely, showed response modification to stimulation of one sciatic nerve after pairing for 10-15 min with a stimulus to the other sciatic or forepaw. Extinction of the modified response and comparison of pre- and post-pairing control responses support the conclusion that the response modification is specifically related to the pairing experience. Stimulus pairing also led to sensory interaction, i.e. the neurons responded in a different way to pairing of the stimuli than to either stimulus alone. Of 12 cells showing sensory interaction, 9 subsequently demonstrated response modification after pairing. Also 6 of 10 modifiable units had previously shown habituation. Thus response modification appears to be characteristic of many RF cells which also show other dynamic properties such as habituation and sensory interaction. (Supported by NSF grant GB 31540 and NIH grant NS 07865).

4.3 EFFECTS OF REPEATED PRESENTATION OF ACOUSTIC STIMULATION UPON EVOKED POTENTIALS IN THE AUDITORY CORTEX OF THE CAT. Norman M. Weinberger, Irwin S. Westenberg*, Gary Paige*, Barry Golub* and Michael Esposito*
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Decrements in the amplitude of evoked potentials (EP) at the auditory cortex (ACx) during repeated acoustic stimulation have been interpreted as habituatory. Demonstrations of dishabituation and accelerated decrement during a second run following spontaneous recovery (savings) would support this interpretation, particularly if obtained during ensured stimulus constancy at the receptor. Cats bearing chronically implanted electrodes over four loci of ACx field AI were tested while paralyzed (gallamine) with clicks presented binaurally via earphones. Average EP (32 clicks) were analyzed by computer and evaluated statistically. In the first experiments (N=5) 1/sec stimulation for 30' yielded amplitude decrements. Pawshock failed to produce dishabituation although it was behaviorally effective (pupillary dilation); following a break of 15', there was spontaneous recovery and replication of decrements obtained in the first run, but not savings. In a second experiment (N=5), clicks were presented at 5/sec in trains of 6.4 sec at approximately 1 min intertrial intervals for 40'. Amplitude decrements were found but there was no dishabituation or savings. In both studies, EP decrements did not occur at all AI loci within each subject. Therefore, the decrements cannot be attributed to a general change in the animals' state. The decrements in Exp. 1 might be attributed to neural refractoriness, but this explanation is precluded for Exp. 2 because of the long intertrial interval. These findings suggest EP decrements at AI are not habituatory, and demonstrate differential effects of repeated stimulation within subfields of the primary auditory cortex.

4.4 SLOW POSITIVE POTENTIALS IN NUCLEUS RETICULARIS THALAMI DURING CONDITIONED EXPECTANCY IN CHRONIC CATS. J. E. Skinner and C. D. Yingling*. Neurophysiol. Dept., The Methodist Hosp., Baylor Coll. Med., and Rice Univ., Houston, 77025

Cats were implanted with platinum-black electrodes in frontal cortex and rostral thalamus and bilateral cryoprobes in the vicinity of the inferior thalamic peduncle (ITP). DC-coupled recordings were made from the thalamus referenced to frontal sinus bone and from the cortical surface referenced to the underlying white matter. Each conditioning trial consisted of a half-sec tone followed 4 sec later by a brief 60 V shock. After acquisition of conditioning, the tone elicited a slow positive response of 2000 μV from nucleus reticularis thalami (R) concomitantly with a surface-negative, depth-positive response from the anterior sigmoid cortex (AS). Conditioned responses (CRs) were not recorded from control structures in the cortex and thalamus. The CRs habituated after repeated trials at 15 to 45 sec intervals. Lengthening the interval to 2 to 4 min resulted in restoration of the CRs. When the interstimulus interval was changed abruptly from 4 to 6 sec, the CRs continued to peak at 4 sec. Orientation to novel stimuli and investigation of familiar objects were also accompanied by slow-potential shifts similar to the CRs. Temporary cryogenic blockade in ITP abolished the thalamic and cortical slow potentials. It is interpreted that 1) the state of expectancy and attention results in the CRs, and 2) the CR in either R or AS can be manifested only if the interconnections between these structures remain intact.

4.5 CORTICAL STEADY POTENTIAL SHIFT AND INTEGRATED MASS UNIT ACTIVITY IN FORMS OF TEMPORAL CONDITIONING. Patrick Sheafor,* and Vernon Rowland. Dept. of Psychiatry, Case Western Reserve School of Medicine, Cleveland, Ohio 44106. Graded cortical steady potential shifts (SPS) of more than one minute duration are acquired and observed following and preceding food reinforcements automatically offered at a fixed interval (temporal conditioning). The relation of such shifts to an integration of mass unit (action potential) activity (IMU), the oscillatory electrocorticogram (ECoG), and peripheral behavioral measures (lickometer and electro-oculogram, EOG) is sought in implanted, restrained cats. Homogenized milk-fishmeal is delivered either to a small cup fixed one inch from the cat's nose or directly by implanted cannula into the mouth. Two basic types of schedules are used: uncued reinforcements at fixed intervals or CS (tone) paired with US (food) trials alternating at fixed intervals with CS alone ("single alternation"). Interval SPS were acquired in visual and auditory cortex, having a positive polarity during a recovery phase (from shift during reinforcement) followed at mid-interval by a negative "expectancy phase" preceding the next reinforcement. ECoG synchrony, and EOG and lickometer quiescence were observed, lasting well into the negative expectancy phase SPS in some subjects. IMU in this relation was usually holding at low levels, suggesting independence of the expectancy SPS from direct relation to action potentials. This overall pattern is named "quiet expectancy." Late in the expectancy phase, ECoG desynchronization, EOG activity, and IMU activation occurred together replacing the quiet expectancy with an active expectancy pattern. The effect of an interpolated CS in single alternation is under evaluation. From these findings a division of cortical SPS into two basic types is proposed, SPS-1 which is stimulus-bound and correlates highly with ECoG and IMU, and SPS-2 which under special circumstances ("quiet expectancy" in temporal conditioning) appears to be relatively independent of external cues and action potential activity.

4.6 DIFFERENTIAL CONDITIONING OF EYE BLINK IN CATS FOLLOWING BILATERAL DECORTICATION OR REMOVAL OF CAUDATE NUCLEUS. R.J. Norman*, J.A. Schwafel*, K.A. Brown*, J.R. Villablanca, and J.S. Buchwald. Depts. Psychiat. & Physiol., Mental Retardation Ctr., UCLA, Los Angeles, CA 90024

The purpose of this experimental series is to determine the minimal brain circuitry which is necessary for the acquisition and maintenance of a differential, classically conditioned motor response. The eye blink reflex was conditioned in cats using a 400 msec white noise as the conditioned stimulus (CS) reinforced by a 70 msec shock train to the posterior margin of the eye (US) which terminated with the CS. An unreinforced 1 kHz tone was randomly presented as the discriminative stimulus (DS) in a differential conditioning paradigm. EMG activity was recorded bipolarly from the orbicularis oculi muscles of both eyes. No EMG reflex activity was induced by the auditory CS during initial conditioning trials, but conditioned EMG responses began to appear within the first 50-100 pairings These responses were initially bilateral, but became unilateral with extended training. The conditioned EMG response latency was closely related to the CS-US interval, i.e., if the interval was increased, the CR latency increased. Response discrimination between the white noise CS and nonreinforced tone DS was acquired by all subjects. Bilateral decortication or bilateral removal of the caudate nucleus in naive cats had little effect on the animals' subsequent ability to acquire the conditioned response or to withhold responses to the discriminative stimulus. Further, retention over successive days was observed. By a number of criteria, the observed responses are believed to represent true conditioning and not sensitization or pseudo-conditioning. These results combined with other published reports suggest that telencephalic structures are not essential for differential conditioning. Continuing work in this laboratory will examine the role of thalamic and midbrain mechanisms in conditioning. (Supported by USPHS HD-04612, MH-05437, and HD-00345.)

4.7 ACQUISITION OF A CLASSICALLY CONDITIONED EYEBLINK BY PAIRING CLICK-CS WITH ELECTRICAL STIMULATION OF FACIAL NERVE. P. Black-Cleworth*, C.D. Woody and J. Niemann*. Laboratory of Neurophysiology, Mental Retardation Center, UCLA, Los Angeles, Ca. 90024

In the usual classical conditioning paradigm, the unconditioned stimulus (US) initiates production of the unconditioned response (UR) and also provides considerable sensory stimulation. It is known that function of peripheral effectors, e.g., muscles, and sensory feedback from them, is unnecessary for successful conditioning. Our experiments tested the hypothesis that electrical stimulation of the efferent neuronal pathway involved in production of a UR is an adequate replacement for the usual sensory US. Cats were trained to blink to a click conditioned stimulus (CS) by repeatedly pairing the click with unilateral bipolar shock (300μa-2ma; 100 msec train of 1 msec pulses) to the temporal zygomatic branch of the facial nerve (400 msec interval between CS and nerve stimulation). Both intact (N=3) and trigeminal rhizotomized cats (Vth nerve cut next to brain stem on side of stimulation) (N=3) learned a bilateral conditioned response (CR) with this paradigm. The mean number of training sessions to reach 50% CR performance levels (stimulated side) was 11 for the intact and 18 for the trigeminal rhizotomized cats, compared to 8 sessions for 9 cats trained with a sensory US (glabella tap). The mean latency of the CR was 18 msec on the stimulated side and 20 on the unstimulated, as measured from EMG responses. The CR could be extinguished by reversing the pairing order of CS and nerve stimulation and could be readily relearned. Further control experiments indicated that facial nerve afferents were probably not significantly involved in development of the CR. The results suggest that click paired with antidromic activation of facial motoneurons projecting to orbicularis oculis is a sufficient condition to produce a blink CR and that trigeminal sensory activation is unnecessary in this case. (Supported by USPHS HD-05958, HD-04612 and California D.M.H.)

4.8 HYPERTHERMIA AND OPERANT RESPONDING FOR HEAT EVOKED IN THE MONKEY BY INTRAHYPOTHALAMIC PROSTAGLANDIN. M. B. Waller* and R. D. Myers. Laboratory of Neuropsychology, Purdue University, Lafayette, Indiana, 47907.

In a previous study by Milton and Wendlandt (J. Physiol., 218, 325, 1971) a minute amount of a prostaglandin (PGE_1) injected into the cerebral ventricles of the cat or rabbit was found to produce an intense hyperthermia. When PGE_1 is micro-injected into the anterior hypothalamus of the cat, a similar pyrexic response is evoked (Feldberg and Saxena, J. Physiol., 219, 739, 1971). In view of these results, the present study was designed to examine the action on body temperature of PGE_1 in the hypothalamus of the primate. An array of stainless-steel guide cannulae was implanted stereotaxically above the hypothalamus in male monkeys (Macaca nemistrina) previously trained to lever-press for heat. An injection cannula was lowered through the guide so that PGE_1, in 1-50 nanogram amounts, could be injected into the rostral hypothalamus. At certain sites, PGE_1 evoked a transient increase in body temperature of 1.0 - 1.7°C. Although vasoconstriction was pronounced, there was no evidence of shivering. However, the rate of lever pressing for a 4 sec. period of warmth from an infrared heat lamp increased sharply along with the rise in body temperature. Thus, the behavioral response to obtain heat paralleled the physiological response to intrahypothalamic prostaglandin. These results strengthen the hypothesis that PGE_1 may be a general mediator within the cells of the diencephalon for raising body temperature in the pathological condition attendent to fever. This mediation is apparently consistent across all species examined thus far. In addition, the probable site of action is the anterior hypothalamus.

4.9 OPERANT CONDITIONING OF CORTICAL STEADY POTENTIAL SHIFTS IN MONKEYS. Steven C. Rosen, David L. Loiselle*, and John S. Stamm. SUNY at Stony Brook, N.Y. 11790

Nonpolarizable electrodes were chronically implanted in monkeys' prefrontal, precentral, and occipital cortex, and subcutaneously across the monkeys' eyes. Steady potential (SP) shifts were recorded with DC amplifiers while the animals were restrained in a chair in a dimly illuminated, soundproof chamber. The electrocorticographic data were led on-line to a PDP-12A computer which was programmed to detect the occurrence of either surface negative or positive SP shifts at the rate of 15-25 μV/sec for periods of 3 sec. The rate of occurrence of criterion shifts was determined for: (a) baseline recording sessions in which the monkeys received no rewards, (b) conditioning sessions in which sugar pellet rewards were delivered to the mouth, via a metal tube, within 200-300 msec of the occurrence of a criterion SP shift, and (c) extinction sessions when rewards were delivered randomly. Conditioning for either prefrontal or occipital shifts resulted in increased rates of criterion shifts to 40% above the baseline or extinction levels. Off-line data analyses indicated that conditioned prefrontal shifts were associated with similar shifts in other cortical areas, whereas the conditioned occipital shifts were specific to the recorded site. Simultaneous videotaping of polygraph recordings and the monkeys' behavior indicated that conditioned SP shifts were not the direct result of gross body movements or eye movements, although complex patterns of eye movements were occasionally observed in relation to the source of illumination. The data suggest that monkeys can control cortical SP shifts by means of central processes affecting cortical excitability. (Supported by NSF Grant 31-741A.)

5.1 SOME ELECTRICAL AND CHEMICAL PROPERTIES OF ARCUATE NEURONS ANTIDROMICALLY IDENTIFIED BY STIMULATION OF THE MEDIAN EMINENCE. Robert L. Moss and Peter Riskind*. Dept. of Physiology, Univ. of Texas Southwestern Medical School, Dallas, Texas 75235.

Forty-five extracellular action potentials were recorded from the arcuate nucleus in intact normal cyclic female rats anesthetized with urethane. Thirty-six of these potentials were found to be antidromically identified in response to electrical stimulation of the median eminence and were recorded at a mean latency of 10 msec; the upper limit of conduction velocity was estimated to be 0.05 m/sec. Seventeen out of 36 were not discharging spontaneously and would have been undetected in the absence of antidromic stimulation. Only about one-fifth of all the neurons recorded (N=9) could not be driven antidromically. The spontaneous firing rate of antidromically identified arcuate neurons varied from less than 1/sec to 5/sec while unidentified cells discharged at rates from less than 4/sec to 8/sec. It is concluded that eighty percent of the neurons of the arcuate project to the median eminence and that these are capable of generating action potentials and conducting impulses. In subsequent studies, norepinephrine, dopamine and glutamate were applied microelectrophoretically to cells in the arcuate nucleus of the rat hypothalamus. Successful drug applications and extracellular recordings were made on 20 cells of which 11 were identified by antidromic stimulation of the median eminence. The remaining 9 cells, though located in the arcuate nucleus, were not antidromically invaded. Norepinephrine and glutamate excited all the identified arcuate cells while dopamine excited 6 and inhibited 5 cells. Glutamate was shown to excite all the uninvaded cells but norepinephrine and dopamine was demonstrated to have no effect on them. These are preliminary findings and therefore no conclusions have been formulated at the time of this writing.

5.2 SENSORY INPUT AND FIRING PATTERNS OF ANTIDROMICALLY IDENTIFIED SUPRAOPTIC NEURONS IN UNANESTHETIZED MONKEY. James N. Hayward and Karol Murgas*. Depts. Neurology & Anat., Reed Neurol. Res. Ctr., Sch. Med., UCLA, Los Angeles, Calif. 90024

We find that the response characteristics of single supraoptic neurons to afferent input depends upon the nature of the stimulus, the level of activity of the cell and the 'significance' of the stimulus to the animal. We recorded spontaneous and evoked activity of single cells in the hypothalamus of trained, unanesthetized monkeys with tungsten recording microelectrodes and pituitary stimulating electrodes. Spontaneous arousal from slow sleep usually had no associated change in supraoptic discharge. An auditory stimulus without arousal caused no alteration in firing patterns. A particular high frequency auditory signal caused both arousal and accelerated discharge. Noxious 'hard touch' on the side of the face with an air jet produced an accelerated discharge at the first trial but with sequential trials the unit response decreased in magnitude ie. habituation. A similar habituation occurred with repetitive noxious cutaneous electrical stimuli and repetitive noxious sound stimuli. Supraoptic neurons firing at high discharge frequencies responded to cutaneous electrical, 'hard touch' and noxious auditory stimuli. Cells firing at an intermediate level could be accelerated only by cutaneous electrical and 'hard touch' stimuli. Very slowly firing supraoptic neurons could not be driven by any of these sensory stimuli. We conclude that our three functional cell types, 'silent' 'burster' and 'continuously active' in the supraoptic nucleus can be driven by sensory input depending upon the nature of the stimulus, the 'meaning' of the stimulus to the animal and the firing level of the cell under study.

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5.3 STUDY OF NEUROSECRETORY CELLS IN VITRO: THEIR FACILITATION AND INHIBITION THROUGH AXON COLLATERALS. K. Koizumi and T. Ishikawa*. Dept. of Physiol., State Univ. of N. Y., Downstate Medical Center, Brooklyn, N. Y., 11203.

Recent studies have suggested operation of an inhibitory recurrent collateral system in neurosecretory cells of goldfish and mammalian hypothalamus. Our study indicates that not only inhibition but also facilitation can be produced by these collateral systems. Bullfrogs were pithed; the hypothalamus was isolated with pituitary gland attached and perfused by circulating frog Ringer's solution saturated with 95% O_2-5% CO_2 mixture at 17-18° C. 3MKCl glass capillary electrodes were used for recording. The neural lobe was stimulated by inserting a fine bipolar silver electrode. When two successive stimuli, subthreshold for antidromic excitation, were separated by 5 to approximately 70 msec. the conditioning stimulus facilitated the test response so that an action potential was evoked. In some neurons the facilitatory effect lasted as long as 200 msec. Facilitated responses had longer latencies than threshold responses, particularly when two stimuli were separated by long intervals. When conditioning and testing stimuli were both suprathreshold and separated by 20-50 msec. antidromic response from testing stimuli showed only an A spike; the B spike was blocked. Recovery of B spike required 300 to 500 msec. The facilitatory action of neurosecretory cells by antidromic stimulation may be explained by axon collaterals which have a lower threshold than do inhibitory ones. This also explains the findings that an antidromic stimulus occasionally produced two action potentials with a 20 msec. interspike interval and that a slight increase in neural lobe stimulus intensity shortens latency of an action potential of the same neuron by 20-25 msec. (Supported by Grant #NS-06537).

5.4 BLOCKADE OF ANGIOTENSIN-INDUCED THIRST BY 1-SAR-8-ALA ANGIOTENSIN II ANALOG. A. N. Epstein, S. Hsiao* and A. K. Johnson*. Inst. of Neurological Sciences, Univ. of Penna., Philadelphia, Pa. 19174.

The dipsogenic dose of peripheral angiotensin II (A II) is now at physiological levels (Hsiao & Epstein, Fed. Proc., 1973, 32). Rats infused i.v. with 16-32ng/min of 5-Ile-A II drink after cumulative doses of 70-190ng/rat. Sensitivity is doubled by nephrectomy. These low doses make experiments with competitive inhibitory analogs feasible. The 1-Sar-8-Ala-A II analog (P-113, Norwich Pharmacal) specifically antagonizes the pressor effect of A II (Pals et al, Circ.Res., 1971, 29). We report here that P-113 blocks the dipsogenic effect of the hormone when infused with it both i.v. and intracranially. In intravenous studies rats (400g♂) were infused for 17.5 min. through chronic precaval catheters at 0.01ml/min while in their home cages with water and pellets available. Ten rats, all responding on the previous day to 32ng/min of 5-Ile-A II (mean latency:6'31", mean intake:3.22ml), were preinfused for 20min. with 285ng/min P-113 (10X the molal dose of A II) followed immediately by 32ng/min A II plus 285ng/min P-113. Only two drank (latencies:9'2" & 7'15", intakes:3.0 & 0.8ml). Intravenous 5-Ile-A I was also blocked by 10:1 P-113. The blockade was equally effective for intracranial A II. Five of eight rats that drank rapidly (mean latency: 61.6") and copiously (mean intake:6.5ml) to 10ng of A II (Hypertensin) injected into the anterior forebrain did not drink when the hormone was accompanied by 100ng of P-113 analog. Drinking in the other three was delayed and reduced in volume. Drinking to intracranial A I was not attenuated by P-113 until 100:1 ratio of blocker to decapeptide was used. This work shows that the 1-Sar-8-Ala-angiotensin II analog antagonizes the dipsogenic effect of angiotensin both intravenously and in the brain, and it suggests that the hormone's receptor system in the brain for thirst is similar to that for the pressor effect in the periphery but may include receptors for the unconverted decapeptide. Supported by NDS 03469.

5.5 HORMONAL MODULATION OF AGGRESSIVE BEHAVIOR IN FEMALE HAMSTERS. Owen R. Floody* and Donald W. Pfaff. Rockefeller Univ., New York, N. Y. 10021

The progress of fights between nonestrous female hamsters is stereotyped and may be summarized by a flowchart of specific behavioral components. Detailed knowledge of the response sequences involved in fighting facilitates the selection of sensitive indices of aggression and the interpretation of hormonal effects on aggression. On nonestrous days of the estrous cycle, female hamsters exhibit intense aggression toward conspecifics of either sex. In dramatic contrast, the estrous female hamster is not aggressive and spends a large proportion of time in lordosis, indicative of sexual receptivity. The inhibition of fighting on estrous day depends upon estrogen and progesterone. Adrenalectomized-ovariectomized female hamsters receiving only control oil injections fight at levels comparable to those shown by intact nonestrous females, and considerably above levels characteristic of intact estrous females. The combination of 17β-estradiol benzoate (EB) and progesterone (P) suppressed fighting completely, creating a situation identical to that typical of estrous day. On the other hand, replacement therapy with testosterone propionate, P or EB individually did not exert consistent significant effects upon the aggressiveness of adrex-ovariex females. Furthermore, hypophysectomized female hamsters also fight at levels comparable to those characteristic of intact nonestrous females, indicating that high levels of pituitary protein hormones are not obligatory for the appearance of vigorous aggressive behavior. These results emphasize the roles of estrogen and progesterone in synchronizing important social responses, e.g., aggression, with the female hamster's current reproductive status.

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5.6 SUPPRESSION OF SEXUAL RECEPTIVITY IN THE HORMONE-PRIMED FEMALE HAMSTER BY ELECTRICAL STIMULATION OF THE MEDIAL PREOPTIC AREA. Charles W. Malsbury and Donald W. Pfaff. Rockefeller University, New York, New York 10021.

The behavior of the female hamster toward the male is altered radically by estrogen and progesterone. Her aggression gives way to sexual receptivity, and the lordosis posture will commonly be maintained in the presence of a sexually active male for greater than 10 min. at a time. With autoradiography it has been demonstrated that neurons of the medial preoptic area (MPO), as well as other hypothalamic and limbic areas, preferentially accumulate radioactive estradiol in the female hamster (Floody & Pfaff, 1973). For this reason we explored the effects of electrical stimulation (ES) of the MPO in unanesthetized, freely-moving females in the presence of sexually active males. Each adult female was ovariectomized and stainless steel monopolar electrodes were implanted in the MPO. ES consisted of 60 sec trains of 100 HZ, 0.2 msec, biphasic, square-wave pulses. It was found that in females made sexually receptive by injections (subcutaneous in sesame oil vehicle) of 10 μg estradiol benzoate followed 41-43 hrs later by 200 μg progesterone, and then tested 4-8 hours later, the lordosis response to male contact was prevented from occurring during ES at certain MPO sites. ES would also terminate the posture if it was being maintained at the time of ES onset. Similar results have been found with female rats (R. Moss, personal communication). It appears that some neurons in MPO may act to suppress sexual receptivity and that one of the ways by which ovarian hormones could facilitate lordosis is through reduction of the suppressive activity of these neurons.

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5.7 STRAIN DIFFERENCES IN BEHAVIORAL SENSITIVITY TO TESTOSTERONE AND ITS NEURAL METABOLITES IN MICE. W.G. Luttge and N.R. Hall*. Dept. of Neuroscience, Univ. of Florida Coll. of Med., Gainesville, Florida 32601

In three separate studies we examined the relative effectiveness of androgens naturally occurring in the brain to induce either sexual or agonistic behavior in two strains of outbred albino mice. In the first study using CD-1 mice (Horm. Behav. 3: 71, 1972) testosterone (T), but not dihydrotestosterone (DHT) or androstenedione (AE) was found to induce fighting behavior. All three androgens maintained the seminal vesicles at levels equal to, or greater than those found in non-castrates. In the second study using Swiss-Webster mice (SW) we again found that T readily induced fighting; however, relative to T DHT induced fighting in more SW mice than it did in CD-1 mice. There were no obvious strain differences in the seminal vesicle response to these androgens. In the third study we directly compared the abilities of T, DHT, AE and androstanedione (AA) to induce copulation in both CD-1 and SW male mice. In CD-1 males T was the only androgen with significant behavioral activity, while in SW males DHT was nearly as effective as T in inducing mounts with intromissions. AE and AA were both relatively ineffective in stimulating sexual behavior.

In an initial attempt to uncover possible mechanisms for these strain differences we are currently comparing the uptake and metabolism of ^{3}H-T and ^{3}H-DHT in limbic, diencephalic and mesencephalic brain regions of CD-1 and SW male mice. We are also examining other possible strain differences in brain sensitivity to DHT such as negative feedback suppression of LH secretion. Our present behavioral findings are especially interesting in light of Phoenix's report (Primate News 10: 12, 1972) that both T and DHT can restore copulation in castrate male rhesus monkeys. Thus, in at least two species DHT has been shown to be effective in stimulating androgen induced behaviors, while in the rat (Horm. Behav. 2: 117, 1971) and CD-1 mouse it lacks these effects.

5.8 SEX DIFFERENCES IN THE EFFECTS OF DEXAMETHASONE PHOSPHATE ON BEHAVIOR IN RATS. James A. Mulick, J. M. Joffe, John M. Peterson*. Dept. of Psychology, University of Vermont, Burlington, Vermont, 05401

Previous work has established a relationship between adrenalectomy and open-field behavior (Joffe et al., Horm. and Behav. 3:87, 1972), but the question of the relative contribution of adrenal steroids and ACTH changes awaits further investigation. The present experiments assessed the effect of dexamethasone phosphate (DEX), a powerful ACTH suppressor, administered in rats' drinking water (approx. dosage: 50 µg/rat/day) with respect to running activity and open-field behavior. In Experiment I males were given DEX continuously from either five days or one day prior to and throughout testing. Only 5-day treatment significantly increased running-wheel activity (four daily 30 min sessions) over controls. DEX had no significant effect on males' four-day open-field activity, but significantly reduced open-field and home-cage defecation. In Experiment 2 females given DEX defecated significantly more in the open-field than controls. This effect on females does not appear to be due to a general metabolic change, since DEX females, like males, defecated significantly less than controls in the home-cage. Females' open-field activity was not significantly affected. Weight loss and plasma corticosterone analysis confirmed the effectiveness of the dosage used. Results suggest that weight loss correlated effects of DEX (Beatty et al., Physiol. and Behav. 7:869, 1971) on activity do not show up in open-field situations. There appears to be a sex difference in the effects of DEX on open-field defecation, possibly due to the interaction with gonadal hormones. Experiments are now in progress to investigate this possibility. (Supported by NICHD Grant No. R01 HD-05571).

5.9 WEANLING RAT VENTROMEDIAL VERSUS DORSOMEDIAL HYPOTHALAMIC SYNDROME. L.L. Bernardis, J.K. Goldman*, L.A. Frohman* and J.D. Schnatz*, Depts. of Surgery, Pathology, and Medicine, SUNY at Buffalo, and VA Hospital, Buffalo, New York, 14215.

Electrolytic lesions (L) in the ventromedial hypothalamic nuclei (VMN) of the weanling rat cause increased carcass fat, normal body weight, hyperinsulinemia, hypertriglyceridemia and hypercholesterolemia, normophagia and normoglycemia. Glucose-U-C 14 oxidation (GLUCOX) and incorporation (GLUCINC) into adipose tissue are increased but palmitate-1-C 14 oxidation (PALMOX) is decreased and incorporation (PALMINC) enchanced. This set of changes has been termed "Weanling Rat Ventromedial Syndrome". It is also characterized by reduced linear growth and decreased pituitary and plasma growth hormone (GH) levels. The consequences of L in the dorsomedial hypothalamic nuclei (DMN) on the above parameters were investigated and show that carcass fat and protein are normal or slightly elevated, body weight is decreased and plasma insulin, triglyceride, cholesterol and glucose levels are normal while food intake is decreased. GLUCOX and GLUCINIC into adipose tissue are normal but PALMINC is enhanced. While linear growth is greatly retarded plasma GH levels are normal or slightly increased. The following changes were also observed: both VMNL and DMNL cause reduced spontaneous (running wheel) activity and adrenal weights. Thyroid and testes weights were reduced by VMNL only. The data indicate the existence in the medial hypothalamus of two neuronal assemblies, separated by a narrow, cell-free zone, that exert opposite effects on many neuroendocrine and extrapituitary homeostatic mechanisms.

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6.1 MONKEY SUPERIOR COLLICULUS AND EYE-HEAD MOVEMENTS. David Lee Robinson and Charlene D. Jarvis. Lab. of Neurobiology, NIMH, Bethesda, Md. 20014

Recent studies have implicated the superior colliculus in either visual guidance of eye movements and/or a shift of attention and facilitation of eye movements. These studies, using monkeys with their heads restrained, showed that collicular cells in the intermediate layers discharge before saccadic eye movements to the contralateral field. To study these cells during both head and eye movements, we fitted monkeys with a light-weight head holder permitting either head restraint or horizontal head movements. We trained two animals to fixate a small spot of light and shift their gaze to another light when it appeared at a new position in the visual field. We then recorded intermediate layer cells and identified those related to eye movements in the light and dark with the head restrained. Next, the animal's head was released to determine the relationship of these same cells to head movements. Target acquisition was then accomplished by head and eye movements of varying coordination. All 73 intermediate layer cells discharged before and in close synchrony with saccadic eye movements whether or not the head moved. The discharges of collicular neurons often varied when the monkey repeated the same eye movement with his head restrained, but this variability persisted even when he was free to make head movements but did not. The amplitude of eye movements coupled with head turning was shortened by peripheral feedback from the head movement; discharges of collicular neurons were the same as if the full eye movement had been made. Twenty-three other intermediate and deep layer cells which showed no relationship to eye movements were studied; none discharged in relation to head movement or head position. These data suggest that the monkey superior colliculus is involved in the control of eye movements and not head movements; eye-head integration must occur at other neural levels.

6.2 PROGRAMMING OF SACCADIC EYE MOVEMENTS AS FUNCTION OF STIMULUS ECCENTRICITY. D. O. Frost* and E. O. E. Poeppel. Dept. Psychol., M. I. T., Cambridge, Mass. 02139

These studies were undertaken to determine how human saccadic eye movements are programmed. Starting with the eyes in either primary position or eccentrically deviated, subjects made saccades to a random sequence of spots presented at one of 8 positions placed 5° apart on the horizontal meridian. Targets were viewed monocularly in a HARMS perimeter and flashed for 100 msec. or 3 sec. against a homogeneous photopic background. Eye movements were recorded using d.c. electrooculography. The saccade magnitude, latency, velocity, and intersaccadic interval were recorded. The functional dependence of these parameters upon the retinal eccentricity of the target was derived. Correlations between various parameters were obtained. We found 1) that the amplitude and velocity of the first saccade to a suddenly presented visual target are independent of target duration and depend upon the retinal eccentricity of the target, 2) that the occurrence of corrective saccades depends upon both the retinal eccentricity of the target and the presence of visual error information during a critical interval after the completion of the first saccade, 3) that the duration of the intersaccadic interval is much less variable than that of latency and is negatively correlated with the size of the initial undershoot (which suggests the release of a central motor program by a visual error signal), 4) that eccentricity dependent changes of saccadic eye movement parameters may be correlated with the distribution of contrast sensitivity throughout the visual field. This later observation suggests that there is a limited range of positions over which visual input is adequate for the central motor program to accurately control saccadic eye movements.

6.3 THALAMIC INVOLVEMENT IN INITIATION OF EYE MOVEMENTS. John Schlag, Ilkka Lehtinen* and Madeleine Schlag-Rey*. Dept. Anat., Sch. Med., UCLA, Los Angeles, 90024.

Microelectrode recordings were made in the thalamic internal medullary lamina of alert cats. Changes of firing were observed in 49 neurons in relation with saccadic eye movements. These movements were neither triggered nor paced by external stimuli and their spontaneous occurrence was rewarded by milk. In many cases, the changes of activity started 50 to 150 msec prior to the movements both in light and in complete darkness. It is concluded that neurons of that thalamic area are involved in initiation of eye movements. This is consistent with previous findings of stimulation and lesion experiments, namely that: (1) threshold stimulations of the lamina elicit a contraversive rotation of the head with a saccadic contraversive deviation of the eyes, (2) lesions selectively destroying most of the lamina produce a syndrome of contralateral visual neglect.

(Supported by a Bob Hope Fight for Sight Postdoctoral Research Fellowship, and USPHS Grants NB-04955 and NB-21633).

6.4 DIFFERENTIATION OF DORSAL AND VENTRAL ABDUCENS NEURONS BY MEANS OF MOTOR UNIT RESPONSES. S. J. Goldberg*, G. Lennerstrand* and C. D. Hull. (SPON: G. M. Ling) Depts. Anat. & Psychiatr., Mental Retardation Res. Ctr., NPI, University of California, Los Angeles 90024.

Intracellular records were made from two populations of neurons in cat abducens nucleus in response to ipsilateral 6th nerve stimulation. Cells in the dorsal aspect of the abducens nucleus (0.5 to 0.9 millimeters beneath the floor of the 4th ventricle) responded orthodromically with latencies of 1.5 to 10 milliseconds to 6th nerve stimulation. EPSPs, variable latencies and lack of high-frequency following characterized these responses. Ventrally in the nucleus (0.9 to 2.5 millimeters deep) antidromic responses were recorded. These lacked EPSPs, had latencies of less than 1 millisecond and followed stimuli of 300 to 600 Hz. Both types of cells were seen with either Nembutal or alpha-chloralose anesthesia. In preliminary experiments, short depolarizing current pulses were delivered through the intracellular pipette to cells penetrated in the abducens nucleus. Mechanical responses of single motor units to this intracellular stimulation were recorded with the lateral rectus muscle tendon connected to a strain gauge force transducer. Activation of the ventral motor neurons elicited characteristic twitch and tetanic responses. Motor unit contraction was not observed when the dorsal cells were stimulated. These results suggest that the dorsal cells from which these orthodromic responses were recorded are not motor neurons, but represent a separate cell population of different function in the abducens nucleus.

Supported by USPHS MH-07097, HD-05958 and HD-04612.

6.5 BRAINSTEM NEURONS ASSOCIATED WITH VERTICAL EYE MOVEMENTS. W. Michael Davis-King* and Albert F. Fuchs, Dept. Physiology & Biophysics and Primate Center, University of Washington, Seattle, Washington 98195.

It has been suggested that neurons in the pontine reticular formation play a role in generating the horizontal component of eye movement. Our study suggests that certain mesencephalic nuclei may play an analogous role in the generation of the vertical component.

Eye movements and extracellular unit responses were recorded from alert monkeys trained to perform a visual tracking task. Based on anatomical location and discharge pattern, two populations of units were distinguished.

Units in the mesencephalic reticular formation responded with a high frequency burst of spikes prior to saccades (rapid eye movements) in a preferred vertical direction while responding with fewer spikes during saccades in the opposite direction. The duration of the burst was correlated with saccade duration. These units responded later in time and with lower average burst frequencies during horizontal saccades. Except for their vertical preference, these units behave similarly to the pontine reticular formation neurons implicated in the generation of horizontal eye movements.

Units in the periaqueductal gray, rostral to the oculomotor complex, exhibited burst-tonic responses to vertical eye movements, qualitatively like those previously described for oculomotor neurons. A high frequency burst preceded saccades in a preferred vertical direction while a pause accompanied saccades in the opposite direction. During fixation the units discharged with regular firing rates linearly related to eye position above a threshold value. Average steady firing rates during fixation were less than those typically described for extraocular motor neurons.

6.6 THE RESPONSE OF FRONTAL EYE FIELD NEURONS TO VISUAL STIMULI AND SACCADIC EYE MOVEMENTS IN MONKEY. Charles W. Mohler, Michael E. Goldberg and Robert H. Wurtz. Lab of Neurobiology, NIMH, Bethesda, Md. 20014

The widely held belief that the frontal eye fields (FEF) initiate saccadic eye movements is based on the finding that electrical stimulation of this area produces eye movements, but FEF neurons discharge after the onset of saccades. Because of this inconsistency and because most saccadic eye movements of awake animals are triggered by visual stimuli, we studied the relation of 137 FEF neurons to visual stimuli and visually initiated saccades in two awake rhesus monkeys. The monkeys fixed their eyes on a stationary spot of light to allow mapping of visual receptive fields and saccaded between two spots of light to permit study of eye movements. Nearly 50% of FEF neurons responded to stationary 1°x1° spots of light. Visual receptive fields were large, varying from 20° of arc in diameter up to fields which covered an entire hemifield. Receptive fields were always contralateral with some fields also crossing midline by 10° to 20°. Spots larger than 1° were not more effective in driving these cells nor were moving stimuli any better than stationary. In nearly half of these visually related cells in FEF, the on-response to a 1° spot was enhanced if the spot was the target of a visually guided saccade. These neurons are therefore similar to those with visual receptive fields in the superficial layers of the monkey superior colliculus and very unlike those in striate cortex. An additional 23% of FEF neurons discharged within 30 msec after onset of saccadic eye movements. One portion of these saccade related units did not discharge after saccades in darkness but appeared to discharge only after visually guided saccades. We conclude that 1) the FEF is not a motor area for eye movement, 2) the area has some visual function. Electrical stimulation of FEF could produce eye movements because it presents visual information to brainstem areas, not because it presents a motor program.

6.7 VISUAL INHIBITION OF NYSTAGMUS BY THE FLOCCULUS. Bernard Cohen and Setsuko Takemori*. Department of Neurology, Mount Sinai School of Medicine, New York, N.Y. 10029.

In normal monkeys the presence of vision causes a decrease of about 50% in the velocity of slow phases of caloric nystagmus or in the total deviation of the eyes during spontaneous nystagmus. Positional alcohol nystagmus (PAN) and optokinetic after-nystagmus (OKAN) are also suppressed by vision. Floccular Purkinje cells are strongly activated by the visual system (Maekawa & Simpson, Brain Res. 1972) and project inhibition to cells in the vestibular nuclei. Therefore, the flocculus could mediate at least part of the visual effects on vestibular nystagmus. Visual suppression was studied in rhesus monkeys before and after floccular lesions. Visual suppression was defined as the percent reduction in velocity of slow phases of nystagmus in light over that in darkness. Partial floccular lesions caused positional nystagmus and almost normal visual suppression. Total unilateral flocculus destruction caused a loss of visual suppression of caloric nystagmus to the ipsilateral side. After bilateral flocculus lesions visual suppression of caloric nystagmus in either direction was strongly diminished or lost. Visual suppression of PAN and spontaneous nystagmus was also reduced or abolished in these animals. The data support the hypothesis that the flocculus plays an important role in suppressing nystagmus and possibly vertigo of vestibular origin.

Supported by USPHS Grants NS-00294 and 1K3-34,987.

6.8 REGULATION OF EXTRAOCULAR MOTONEURON DISCHARGE AT LOW FREQUENCIES. N. H. Barmack and M. L. Daley*, Laboratory of Neurophysiology, Good Samaritan Hospital & Medical Center, Portland, Oregon 97210

In the alert monkey extraocular motoneuron discharge rate is related linearly to maintained eye position, with coefficients of variation less than 10% over a frequency range of 20-300 spikes/sec. During a saccade motoneurons which innervate the agonist muscle transiently discharge at 200-800 spikes/sec. By intracellular stimulation of antidromically identified extraocular motoneurons we have demonstrated that an adaptive process at the level of the extraocular motoneuron membrane may account for the short duration high frequency bursts (saccadic discharges) evoked by steps of intracellular current. In addition we have sought evidence which could account for the high correlation between the steady state discharge and eye position. By stimulating abducens and trochlear motoneurons with current steps of varying amplitude we have obtained mean steady state frequency-vs-current curves. Maintained repetitive discharge of low variability can be evoked in these motoneurons only in the range of 250-350 spikes/sec. This limited higher range of steady state repetitive firing can be attributed to the relatively brief after-hyperpolarization, AHP, (2-3 msec) following each spike. However, this short AHP cannot regulate frequencies at which the interspike intervals exceed the combined duration of the spike and the AHP. Therefore, we infer that the lower range of discharge rates (20-300 spikes/sec) recorded from chronic animals, is caused by a cyclic variation in synaptic current. Hence the large frequency bandwidth of extraocular motoneurons would be the dual consequence of: 1) Cyclic synaptic currents which regulate discharge at lower frequencies, and 2) The summated direct current effect of these cyclic inputs causing characteristics of the motoneuron membrane to regulate discharge at higher frequencies. (Supported by NIH Grant EY00848)

6.9 EYE MOVEMENT POTENTIALS FOLLOWING VISUAL DEAFFERENTATION IN CATS.

John B. Munson. Department of Neuroscience, College of Medicine, University of Florida, Gainesville, Florida 32610.

Eye movements of alert and sleeping cats are accompanied by grossly recorded electrical spikes in lateral geniculate nuclei (LGN) and visual cortex (VC). Similar spikes are seen in late slow-wave sleep and following reserpine administration. Previous reports are inconsistent concerning the effects of optic nerve (ON) section on these LGN and VC spikes; thus we have reinvestigated this problem in five chronically implanted cats. Intraorbital section of one ON reduces the amplitude of all LGN spikes bilaterally by about 25%, commencing about the 4th day. Subsequent section of the 2nd ON is followed in about 4 days by further reduction of all LGN spike amplitudes to about 50% of control values, except for the LGN spikes accompanying caloric nystagmus in the alert cat, which disappear. One-stage bilateral ON section also produces all of these latter effects on about the 4th day. Bilateral more than unilateral ON section intensifies VC spiking during fast-wave sleep (FWS). The rhythmic 3-5 Hz LGN activity also seen during FWS is unaffected by ON section. Integrated multiple unit activity from LGN accompanying FWS rapid eye movement shows little or no change following ON section. Therefore: 1) depolarization of ON terminals in part generates LGN spikes; 2) FWS LGN spikes and the correlated peaks of integrated multiple unit activity are dissociable phenomena; 3) mechanisms generating LGN spikes in alert cats differ in part from those active in sleeping and reserpine-treated cats; 4) the 3-5 Hz LGN activity does not depend upon retinal input. (Supported by NSF Grant GB-7622)

6.10 NEURONAL CONTROL OF EYE MOVEMENTS.

A. Terry Bahill* and Lawrence Stark. Dept. EECS, Univ. Calif., Berkeley

Simulation of an expanded quasi-analog McCullough-Pitts neuronal model, employing reciprocal inhibition, is used to explore apparent complexity of recent neurophysiological data[1] on oculomotor neurons. A single reciprocal innervation 'effectiveness' parameter controls the slope and the intercept of the function relating output frequency of the oculomotor neuron and eye position, and, as well, completeness of inhibition of the antagonist neuron, the latter being crucial in effecting the fast time-optimal saccadic trajectory.

It has been clear, since the sampled-data model for the discrete saccadic system was first proposed, that neither the sensory system, nor the mechanical output plant is responsible for the intermittency, or 200 ms. refractory period. The present model demonstrates that the oculomotor neurons cannot be the locus of the sampling: the input region cannot be the locus, because both agonist and antagonist neurons are effected, and the antagonist has not been subjected to a high frequency burst; reciprocal innervation cannot help, because vergence and smooth pursuit occur during the interval following a saccade. Recent data[2] have shown intermittent output from continuous stimulation of the superior colliculus. Although the locus of the sampled-data operator is not yet known, it appears to lie in some brain stem structure which functionally follows the superior colliculus and preceeds the oculomotor neurons.

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1. P. Bach-y-Rita; N. Barmack; E. Bizzi; B. Cohen & V. Henn; A. Fuchs & E. Luschei; E. Keller; D. Robinson; R. Wurtz & M. Goldberg.

2. P. Schiller & M. Stryker.

9 SYMPOSIUM

BRAIN MECHANISMS OF SOCIAL BEHAVIOR

Chairman: Paul D. MacLean, M.D.

Role of striatal complex in species typical behavior of the squirrel monkey (Saimiri sciureus).

P.D. MacLean, Laboratory of Brain Evolution and Behavior, NIMH, Bethesda, MD

Changes in social behavior evoked by hypothalamic stimulation in rhesus monkeys.

A.A. Perachio, Yerkes Regional Primate Research Center, Atlanta, GA

Limbic lesions and the agonistic and gamopractic behavior of the golden hamster.

B.N. Bunnell, Dept.of Psychol., Univ.of Georgia, Athens, GA

Amygdalectomy, testosterone, and social behavior in the macaque.

A. Kling, Dept. of Psychiatry, Rutgers Medical School, Piscataway, NJ

As yet, little is known about neural mechanisms of genetically constituted, species-typical patterns of behavior that provide the basis for a wide range of animal activities. High in importance are socially oriented behaviors such as the establishment and defense of territory; mating and breeding; formation and perpetuation of social groups; foraging and hunting; homing and migration. Variously involved are neural substrates for ritualistic, deceptive, or imitative expression. The present symposium examines neural and endocrine mechanisms underlying certain forms of species-typical, social behavior.

10.1 SYNTHETIC SCOTOPHOBIN: ANALYSIS OF EFFECTS ON MICE. David H. Malin and Glen J. Radcliffe, Jr. Mental Health Res. Inst., U. Michigan, Ann Arbor, Michigan 48104; and Baylor Coll. Med., Houston, Texas 77025.

Scotophobin is a polypeptide, previously identified by Ungar as the active factor in brain extract of rats trained in passive dark avoidance, which appears to induce avoidance of the dark chamber when injected into mice. Ungar and colleagues have analyzed and synthesized this molecule and provided samples of synthetic scotophobin for testing at U. of Mich. Experiments confirmed the induction of dark chamber avoidance by injection of synthetic scotophobin. When precautions were taken against chemical degradation, the dose-response relationship resembled that found by Ungar for natural scotophobin from the brains of rats trained to avoid the dark box. Content analysis of all mouse behavior in the black/white choice apparatus revealed a more detailed scotophobin behavior pattern (approaching and turning away from the dark box entrance, prolonged hesitation in the entrance, sitting and grooming in the corners farthest away from the dark box). Recipients showed maximum avoidance of the dark box as presented in the original donor training; changes involving wall color, illumination or the grid floor lessened the effect. Scotophobin recipients showed more emotionality than controls (as measured by defecation rate) when locked inside the black box and less than controls when locked inside the white chamber. The groups were not significantly different when tested in a neutral (transparent) environment. Scotophobin did not affect the activity level (inter-box crossings) of mice in three connected light boxes. Scotophobin did not reduce visual sensitivity at low illumination, measured by the efficiency of visually guided escape behavior as a function of varying degrees of dim illumination. (Supported by HEW grant no. OEG-0-72-0699).

10.2 DARK-AVOIDANCE FACTOR FROM TRAINED FISH BRAIN. Judith L. Warren,* Rodney C. Bryant, Frederick Petty, and William L. Byrne. Brain Research Institute and Department of Biochemistry, University of Tennessee Medical Units, Memphis, Tennessee, 38103.

It has been previously reported that synthetic rat scotophobin is active in goldfish (Bryant, R. C., Society for Neuroscience, First Annual Meeting, 1971; Bryant, R. C., et al., Science, 177:635-636, 1972; Guttman, H. M., et al., Nature New Biology, 235:26, 1972). A behavioral bioassay has been developed for fish scotophobin (dark-avoidance fish factor or factors [DFF]). The DFF and synthetic rat scotophobin (SP) are effective under specific conditions which produce little change in general shuttling activity. Differences are found in response of fish to DFF depending on the number of days dark-avoidance training of donors in a shuttlebox. Partial pretraining of recipients is used in the routine bioassay for DFF, and the DFF enhancement of unreinforced dark-avoidance responding is superimposed on the extinction of dark-avoidance observed in animals injected with extract prepared from untrained (naive) donors.

10.3 ISOLATION FROM GOLDFISH BRAIN OF TWO PEPTIDES CODING FOR COLOR DISCRIMINATION-BASED AVOIDANCE BEHAVIOR. L. Galvan and G. Ungar. Baylor Coll. Med., Houston, Texas 77025.

Two groups of goldfish (Carassius auratus) were trained in a divided tank to avoid either the compartment lighted with blue (BA) or the compartment lighted with green (GA). At the completion of training, the brains were removed and the substances corresponding to the two avoidance behaviors were isolated. The purification procedures were guided by bioassay: at each step, the fractions were tested for their behavioral activity (avoidance of the same color as the corresponding donors) after intracranial injection into naive fish (Ungar et al., Experientia, 28:1026, 1972). After dialysis of crude RNA preparations at pH 3.7, the active materials were found in the dialyzate. On gel filtration (Sephadex G-25), both substances were found in the same eluate fraction. Further purification was done by thin-layer chromatography in three solvent systems: 1) n-butanol-acetic acid-water (4:1:1), 2) n-amyl alcohol-pyridine-water (35:35:30), 3) n-propanol-ammonia (67:33). In solvent system (1) BA-inducing material had Rf 0.13, GA-inducing substance 0.58. In system (2) the respective values were 0.24 and 0.20 and in system (3) 0.30 and 0.34. The spots were detected by fluorescamine. The BA material is inactivated by trypsin and the GA substance by chymotrypsin. Both substances are peptides having 10 to 15 amino acid residues. At the present stage, 7000 brains have been extracted for each of the substances but only their partial purification has been achieved, as judged by the two-dimensional TLC of their dansyl derivatives. When identified, the two peptides may provide some insight into a possible molecular coding of behavior. (Supported by HEW grant no. OEG-0-72-0699)

10.4 PURIFICATION FROM GOLDFISH BRAIN OF A PEPTIDE FACILITATING A LEARNED MOTOR ADAPTATION. J. A. Heltzel and G. Ungar. Baylor College of Medicine, Houston, Texas 77025.

Goldfish (Carassius auratus) were trained to adapt their swimming behavior to the buoyancy created by a polystyrene foam float attached to their ventral surface (Shashoua, Nature, 217:238, 1968). Although most of the fish learn to adapt within three to four hours, the best yield of active material was obtained when the float was kept on for four days. At the end of this period, the brains were removed, extracted and purified by the following procedures: preparation of a crude RNA extract, dialysis at pH 3.7, concentration of the dialyzate, gel filtration on Sephadex G-25 (fine). Further purification was done by thin layer chromatography with two solvent systems: n-butanol, ethanol, acetic acid, water (8:2:1:3) and ethanol, ammonia, water (7:1:2). At each step of purification the active fraction was determined by bioassay. The material was injected intracranially to goldfish whose adaptation to the float was tested and compared with the performance of appropriate controls (Soc. Neurosci. Houston meeting, p. 75, 1972). - After thin-layer chromatography and a second passage through Sephadex G-25 (superfine), a peptide was obtained consisting of 20 to 25 amino acid residues and which was inactivated by incubation with trypsin. Purity of the material is indicated by a) a single fluorescamine-positive spot on TLC, b) a single dansyl derivative obtained in three different two-dimensional solvent systems and c) a single N-terminal amino acid obtained by dansylation followed by acid hydrolysis. The yield of this substance is about 200 ng/g of brain. Further material is being accumulated for amino acid analysis and sequence determination. (Supported by HEW grant no. OEG-0-72-0699).

10.5 COMPARISON OF DIRECT VS. INDIRECT ASSESSMENTS OF BIOCHEMICALLY TRANSFERRED CLASSICAL CONDITIONING EFFECTS IN GOLDFISH. William G. Braud and Porter V. Laird. Dept. Psychol., Univ. of Houston, Houston, Texas 77004

Three experiments are reported in which different methods of assessing the activity of brain extracts from classically conditioned donors were compared. Exp. 1 involved a "direct" assessment in which recipients were tested under nonreinforced conditions for the presence of a response identical to that conditioned in the donors. Diminution of respiratory activity (mouth movements) was classically conditioned to a color stimulus paired with shock (CS^+); another color was presented equally often but was never paired with shock (CS^-). Although donor fish showed very good classical conditioning, nonreinforced presentations of the color stimuli to injected recipients yielded no evidence for biochemical transfer. Exp. 2 involved a "nonreinforced-indirect" assessment procedure in which naive recipients were tested for a generalized preference or aversion for stimuli which had been associated or not associated with shock for their appropriate donors. Here, moderate but significant evidence for transfer was obtained: recipients of trained extract spent less time than comparable controls in the presence of the light color which their donors had associated with shock. Exp. 3 involved a "reinforced-indirect" assessment in which naive recipients learned to avoid either the stimulus associated with shock or the stimulus associated with nonshock (for their appropriate donors). Here, very dramatic and significant evidence for transfer of classical conditioning was obtained: recipients of trained extract learned to avoid what had been CS^+ for their donors much faster than they learned to avoid what had been CS^-. Recipients of control extract learned to avoid CS^+ and CS^- equally well. The differential sensitivity of different recipient testing procedures will be discussed with emphasis upon the role of reinforcement, arousal, instrumental activity, and restraint in recipient assessment paradigms.

10.6 BIOCHEMICAL TRANSFER OF A CLASSICAL CONDITIONING EFFECT IN GOLDFISH WITH NONREINFORCED PREFERENCE TESTING OF RECIPIENTS. Porter V. Laird and William G. Braud. Dept. Psychol., Univ. of Houston, Houston, Texas 77004

In successful "behavioral bioassay" or "memory transfer" experiments using vertebrate subjects, donor training has invariably involved instrumental conditioning. Successful attempts to transfer a classical conditioning effect have not yet been reported. In the six experiments reported here, donor goldfish were trained using a classical defense conditioning procedure, extracts of their brains were prepared, and the activity of the extracts was tested (in naive recipients) using a nonreinforced preference testing procedure. In the first three experiments, the normal preference of our goldfish donors for green illumination was reversed by a classical conditioning paradigm in which a green light (CS^+) was paired with pulsating electric shock (US); a red light (CS^-) was presented equally often, but was never paired with shock. Twenty such differential conditioning trials were given on each of six training days. Donors were killed 16-20 hr. after training and an "RNA-protein" brain extract was prepared (cold phenol method). Naive donors provided an untrained control extract. Naive recipients were tested 48 and 72 hr. after an intracranial injection of 1.5 brain equivalents of either trained or control extract. Amount of time spent in the red and the green illuminated ends of a tank provided the preference measure. In the next three experiments, blue light served as the CS^+) and green light as CS^-. Donor training was extended to 9 days, a dosage of 2.0 brain equivalents was used, and recipients were tested at 72 hr. only. In all six experiments, recipients of trained extract spent less time than did comparable control recipients in the presence of the light color which their donors had associated with shock. The "transfer" effect was greatest at 72 hr. It appears that a nonreinforced preference test (which includes an instrumental swimming component) may detect chemically transferred classical conditioning.

10.7 ENHANCED ACQUISITION AND THE EFFECTS OF UCB 6215 ON THE ERG AND EP. Otto L. Wolthuis and Henk de Vroome*. Medical Biological Laboratory TNO, Rijswijk Z.H., The Netherlands

Light flashes were administered to the right eye of the curarised, artificially ventilated rat. The electroretinogram (ERG), as well as the evoked potential (EP) in area 18a of the contralateral cortex was recorded. In this cortical area a new type of long latency all or none EP was found. At low light intensities there existed no one to one relationship between flash and EP. With increasing light intensity the probability for an EP to occur increased. The EP amplitude appeared to be independent of the light intensity. The latency between flash and EP decreased with growing light intensity even beyond the point where 100% EP's occur.

UCB 6215 (2-pyrrolidone acetamide), previously shown to enhance acquisition in rats, caused an increase in the number of EP's in area 18a without affecting the duration of the latency periods and the shape of the EP's. Injections during 4 days were more effective than a single dose. Since the ERG is not influenced by UCB 6215 and the EP proved to be cortical in nature, it is suggested that this compound enhances learning by its effect on central information processing, i.e. by increasing the efficiency whereby information is relayed to secondary sensory areas.

10.8 **EFFECTS OF MOTIVATIONAL CHANGES ON MULTIPLE UNIT CORRELATES OF DISCRIMINATION TRAINING.** Stephen I. Sideroff* and Dalbir Bindra*. (SPON: R. Malmo) Dept. Psychology, McGill University, Montreal 101, Canada

Multiple unit (MU) activity was examined in the motor cortex, hippocampus, and hypothalamus of water deprived rats while they learned and performed a conditioned discrimination task. Each conditioning trial started with the presentation of a ready signal (a house light) lasting 1.6 sec., which was followed by a positive (CS+) or negative (CS-) conditioned stimulus (a tone of 1-kHz or 9-kHz) lasting 1.6 sec., and a drop of water in the case of a CS+ trial. After stable discriminative performance had been established, the level of motivation was varied by injecting insulin or changing the level of deprivation. The conditioning procedure produced an increase in MU activity during the light period above the level obtained during pseudo-conditioning trials. Discriminative responding to the tones was accompanied by a further increase in MU activity during the CS+ and an initial increase followed by a decrease (not falling below baseline) during the CS-. The increase in MU activity was more marked in the hippocampus and the hypothalamus than in the motor cortex. When satiated, the neural responses to both light and the tones were greatly attenuated in the cortex and hypothalamus, but were minimally affected in the hippocampus. The higher deprivation level employed had no observable effect. Finally injection of insulin produced an increase in only the hypothalamic neural responses with respect to the baseline. These results indicate that different brain regions or systems may serve different functions in the learning processes.

10.9 DISCRETE LESIONS IN THE AREA DENTATA OF THE MOUSE HIPPOCAMPUS: MEMORY DEFICITS FOR AN INHIBITORY AVOIDANCE RESPONSE. Carl A. Boast* and Steven F. Zornetzer. Dept. Neurosci., Col. Med., Univ. of Fla., Gainesville, Florida 32610.

Recently we reported (Zornetzer et al., Behav.Biol., 1973, 8:507) that bilateral electrical stimulation of the dentate region of the hippocampus of chronically implanted mice resulted in retrograde amnesia for inhibitory avoidance of the step-through response. These data suggested further, that the amnesic effect depended upon the bilaterally symmetrical location of both stimulating electrodes in the area dentata. The present study explored further the role of specific hippocampal subfields, and in particular the area dentata, in the development of this memory deficit. Mice were chronically implanted bilaterally in different regions of the hippocampus with bipolar electrodes (total diam. approx 0.35 mm). Mice were assigned to one of the following groups: Bilateral electrical stimulation (0.1 sec @ 100 Hz, 1.0 ms pulses biphasic); unilateral stimulation only; unilateral stimulation + contralateral small lesion; unilateral lesion only; bilateral implanted controls. All lesions were made electrolytically via the indwelling electrodes at least one week prior to training. Electrical stimulation was delivered within 20 sec of training on the single-trial step-through apparatus. Mice were tested for retention 24 hrs. later.

Regardless of group designation, mice having electrode tips located in the area dentata appeared amnesic. Electrode placements located symmetrically in other hippocampal subfields or in dorsolateral thalamus were ineffective in producing amnesia regardless of the group designation. Supported by NIMH Grant No. 1 RO 3 MH 23899 MSM.

10.10 DEFICIT OF DELAYED COLOR MATCHING BY LOCALIZED CORTICAL COOLING. Richard H. Bauer* and Joaquin M. Fuster. Department of Psychiatry and Brain Research Institute, School of Medicine, University of California, Los Angeles, Calif. 90024.

Two rhesus monkeys were trained to perform a delayed matching-to-sample (DMS) task. A trial consisted essentially of the following sequence: 1), presentation of a sample color (red or green) in a centrally located translucid button; 2), termination of the sample by the monkey's pressing of the button; 3), a delay of variable duration (0, 1, 4, 16 or 32 sec.); and 4), illumination of two lower buttons, one red and the other green. Pressing the button with the same color as the sample was followed by fruit-juice reward. The colors on all three buttons were quasi-randomly changed from trial to trial. After training, cryogenic probes were implanted bilaterally on the surface of the dura overlaying prefrontal and parietal cortex. Bead thermistors were implanted subdurally for temperature control. Bilateral prefrontal cooling to 20°C induced a marked and fully reversible deficit of DMS performance: frequency of matching errors increased, especially after delays of longer duration. No impairment was observed at zero delay or on simultaneous matching-to-sample. Unilateral cooling resulted in a DMS defect of lesser magnitude than that induced by bilateral cooling. No defect resulted from cooling parietal cortex to the same temperature (20°C). Inasmuch as correct DMS performance is contingent on mnemonic retention of a hue and not a particular spatial configuration, the results are interpreted as evidence for a functional involvement of the prefrontal cortex in nonspatial short-term memory.

10.11 DETAILED ANALYSIS OF THE DEVELOPMENT AND DECLINE OF HUMAN MEMORY AND LEARNING BY SELECTIVE REMINDING. Herman Buschke. The Saul R. Korey Dept. Neurology, Albert Einstein College of Medicine, Bronx, N.Y. 10461.

Selectively reminding a learner of only those items which were not recalled on the immediately preceding trial, while the learner attempts to recall all of the items in the list, provides a powerful but simple new paradigm for the study of learning. Selective reminding both maximizes the opportunity to learn, by selective presentation of just those items which were not recalled on the preceding trial, and provides the earliest opportunity to show that an item has been learned, by permitting recall without further presentation. Selective reminding provides a precise, detailed analysis of what happens during learning, because recall without further presentation demonstrates retrieval from long-term storage (LTS), so that total recall is separated into retrieval from LTS (LTR) and recall from short-term storage (STR). The number of items learned (LTS) is given by the total number of items retrieved from LTS at least once, under the defensible assumption that items are not lost from LTS (so that failure to recall an item previously retrieved from LTS represents retrieval failure). Since total LTR can be separated into CONSISTENT LTR of items retrieved reliably on all subsequent trials and RANDOM LTR, the proportion of LTS retrieved by random and by organized search can be evaluated. Because CONSISTENT LTR also provides a measure of the degree to which items have been learned as part of a list, item learning and list learning can be compared. This measure of CONSISTENT LTR or LIST LEARNING is very useful, not only because it provides an indisputable, direct measure of retrieval, but also because it accounts for much of the major differences in learning by younger children, older children, young adults, older adults, and patients with impaired memory and learning due to neurological disease which are reported here.

10.12 A THIRTY-YEAR RETROGRADE AMNESIA FOLLOWING ELECTROCONVULSIVE THERAPY IN DEPRESSED PATIENTS. Larry R. Squire. Dept. of Psychiatry, Sch. Med., Univ. California, San Diego, La Jolla, California, 92037

Depressed patients receiving a series of electroconvulsive therapy treatment (E.C.T.) were given a remote memory test dealing with public events occurring between the years 1940-1972. Patients took one of three equivalent forms of the test on each of three occasions: before the first treatment, 40 minutes after the second treatment, and 40 minutes after the fifth treatment. In addition, all patients were given the verbal subtest of the Wechsler Adult Intelligence Test before the first treatment and 40 minutes after the sixth treatment. No change in verbal I.Q. score was evident as a result of six treatments. Patients scored slightly above the normal mean for the population on each occasion that they were tested. On the remote memory test, patients performed the same after the second treatment as before the first. After the fifth E.C.T., however, patients were impaired in their performance on the remote memory test. This deficit extended across thirty years and was greatest for events occurring in the most recent decade. The results of further tests indicated that this deficit was still apparent 24 hours after the fifth treatment.

11.1 THE UPTAKE AND INCORPORATION OF AMINO ACIDS INTO SUBCELLULAR BRAIN PROTEINS OF TRAINED MICE. Moshe Hershkowitz* (SPON: J. E. Wilson). Dept. Biochem., Sch. Med., UNC, Chapel Hill, N.C. 27514

C57BL/6J mice were trained for 20 min to drink milk from a dipper. The animals were then injected subcutaneously with ^{3}H-L-Lysine, ^{35}S-L-Methionine or ^{3}H-L-Leucine, and returned to the training box for 20 min. A control group was injected in the same manner and returned to the home cages. The animals were then decapitated and their brains were subcellularly fractionated (Whittaker et al. Biochem. J. 90, 293, 1964). The nuclei were purified further. When lysine was used as a precursor a significant increase in incorporation was found in nuclear proteins of the brains of trained mice, and a decrease was found in incorporation into cytoplasmic soluble proteins. No changes were observed in the free amino acid pool. When methionine was used as precursor an enhancement occurred in the uptake of the labeled methionine into the free amino acid pools of trained animals' brains. An increase in specific radioactivity was found in nuclear proteins, but when corrected for the change in the amino acid pool no difference was found between experimental and control groups. Trained animals injected with leucine showed a significant increase in the tritium in the water of the brain, but no change in the free amino acid pool or in incorporation into proteins of any of the subcellular fractions. These experiments suggest that a behavioral treatment has a selective influence on the uptake and intermediary metabolism of amino acids.

11.2 THE CONTRIBUTION OF PLASMA GLUCOSE CARBON TO PROTEINS AND LIPIDS OF BRAIN IN FED AND FASTED RATS. Amiram Barkai, Sahebarao Mahadik* and Maurice M. Rapport. New York State Psychiatric Inst. and Columbia Univ., College of Physicians and Surgeons, New York, N. Y. 10032.

The quantitative relationship between plasma glucose precursor and both protein and lipid end-products in brain, in vivo, was studied by measuring the flow of glucose carbon into these brain constituents. Adult male Wistar rats were deprived of food for various periods (up to 72 hrs.), anesthetized (Pentobarbital, 35 mg/kg i.p.) and injected with tracer amount of [U-^{14}C]-D-glucose (50 μC) into the circulation. The specific activity vs. time curve for plasma glucose was established for each animal over 180 minutes. Specific activity values of brain proteins (both soluble and structural) and of several brain lipids, were obtained at 180 minutes. Rates of glucose carbon flow (R) into these end-products were measured by a semicompartmental approach based on steady state kinetics (Baker and Huebotter, J. Lipid Res., 1972). The following ranges were obtained for R values (ng C per min. per mg end-product) in non-fasted rats: soluble protein 7-9; structural protein 11-14; cholesterol 3-6; phospholipids 3-6; cerebrosides 2-5; gangliosides 7-10. Starvation (72 hrs.) caused a 30% reduction in R values for soluble brain protein but did not affect R values for either structural protein or lipids in brain, in spite of a considerable decrease in the rate of irreversible disposal of glucose carbon in the whole body. Thus brain mechanisms for conversion of glucose into lipids and structural proteins appear to be less susceptible to the effects of starvation than mechanisms involved in the biosynthesis of soluble proteins.

11.3 BINDING OF VINBLASTINE AND COLCHICINE TO MACROMOLECULAR COMPONENTS IN A SOLUBLE FRACTION FROM IMMATURE RAT BRAIN. S. L. Twomey, S. Raeburn* and C. F. Baxter. Neurochem. Labs, V.A. Hospital, Sepulveda 91343; City of Hope National Med. Ctr., Duarte 91010; Dept. Physiol., UCLA Sch. Med., Los Angeles, Calif. 90024.

Inhibition of intraneuronal transport and exocytotic release processes by vinblastine (VLB) and colchicine (CLC) is most often interpreted to be the result of the non-competitive binding of these alkaloids to microtubular protein (tubulin). We have examined the post-microsomal supernatant fraction (PMS) from rat brain for components that bind tightly both VLB and CLC. By the criterion of isoelectric focusing, the PMS contained a single [^{3}H]CLC-binding macromolecule with a pI of 4.7 to 5.1 and three macromolecular species which bound [^{3}H]VLB having pI's of 3.2, 4.6 and 7.5, respectively. PMS incubated with [^{3}H]VLB and [^{14}C]CLC revealed upon DEAE cellulose chromatography several components that bound VLB, but only one that bound CLC. The latter did not coincide with any VLB-binding material. When the [^{3}H]VLB and [^{14}C]CLC-labeled PMS was subjected to gel filtration on Sephadex G-200, three components were observed that bound VLB and one component of 120,000 mol wt that bound CLC. The major VLB-binding component was excluded from the gel. The CLC-labeled protein peak bound, on a molar basis, ten times more CLC than it did VLB. These results demonstrate that the bulk of the protein in rat brain PMS which bound VLB differed from that which bound CLC. (Supported in part by NIH Grant NS 03743.)

11.4 THE CIRCADIAN RHYTHM OF PROTEIN SYNTHESIS IN A MOLLUSCAN NEURON R15 OF APLYSIA. Y. Peng Loh* and R. Price Peterson. Depts. Mol. Biol. and Anat., Sch. Med., Univ. of Pennsylvania, Philadelphia, Pa. 19174

R15, is an endogenously bursting (Alving, 1968), neurosecretory neuron in the abdominal ganglion of Aplysia (Frazier et al. 1967). This neuron has been shown to have a light cued circadian rhythm of firing which increases around dawn. (Strumwasser, 1965; Lickey, 1967; Jacklet, personal communication). We have investigated the possibility of a circadian rhythm of protein synthesis in this neuron, which might be correlated with the electrophysiology. Aplysias were entrained to at least seven dark/light cycles, 12hours/12hours. One animal was dissected every two hours over 24 hours and the ganglion removed and pulse labeled in 13uM ^{3}H leucine, for one hour @18°C. The soma of neuron R15 was then dissected from the ganglion and frozen. Protein was extracted and analysed electrophoretically on 15% SDS acrylamide gels. Only proteins in the 12,000 and above 90,000 molecular weight regions showed marked variation in the rate of ^{3}H leucine incorporation as a function of time of the day, others such as tubulin remained constant. Incorporation into the 12K protein which is probably neurosecretory, was significantly enhanced at dawn. The above 90K protein also showed a marked increase in incorporation once/24hours. The former is likely a result of increase in firing at dawn, the latter possibly causal.

11.5 SYNAPTIC REGULATION OF SPECIFIC PROTEIN SYNTHESIS IN AN IDENTIFIED NEURON. Harold Gainer and Jeffery L. Barker. Behav. Biol. Branch, NICHD, NIH, Bethesda, Md. 20014

The bursting pacemaker neuron, R_{15}, in the abdominal ganglion of Aplysia californica exhibits a specific pattern of protein synthesis when incubated in ^{3}H-Leucine. SDS-polyacrylamide gel electrophoresis shows that 20-25% of the de novo synthesized proteins of the cell is accounted for by a single molecular weight class (around 12,000 daltons). Stimulation of the branchial nerve for 5 hours at a rate of 5/sec, hyperpolarized the cell and blocked all spontaneous spike activity. Comparisons of the protein synthesis patterns of synaptically inhibited neurons and spontaneously active control neurons showed that synaptic inhibition produced a selective 30% decrease in the synthesis of the 12,000 dalton peak. The putative inhibitory transmitter, dopamine, produced the same selective inhibition when added to the bathing medium. Depolarization of the cell by increasing the potassium ion concentration of the medium, selectively stimulated the synthesis of the 12,000 dalton protein by 50-70%. Thus, the rate of synthesis of the 12,000 dalton protein in R_{15} may be regulated by the membrane potential of the cell, which in turn is under control of a dopaminergic inhibitory synapse.

11.6 ELECTROPHORESIS OF HUMAN GLIA-SPECIFIC PROTEINS. Eric G. Brunngraber, Jean P. Susz*, and Krystyna Warecka*. Ill. State Psychiatric Instit., Chicago, Ill., 60612 and Neurochem. Labor der Psychiat.-Neurol. Klinik, Lübeck, Germany.

A human glia-specific glycoprotein has been isolated by means of Sepharose immunoadsorbents (WARECKA, et al., J. Neurochem. 19, 719,1972). In the final step of this procedure, extracts from human white matter were applied to a sepharose column coupled with brain-specific antibodies. The brain-specific proteins, which bind to the column, were eluted with 0.15 M glycine, pH 1.8. The eluted proteins were studied by electrophoresis in both continuous and discontinuous (multilayered) polyacrylamide gel systems in the presence of sodium dodecyl sulfate. The gels were stained with periodic acid-Schiff reagent (for glycoproteins) and with Buffalo Black NBR (for proteins). One strong periodic-acid-Schiff positive band, corresponding to the glia-specific glycoprotein was noted. This glycoprotein migrated with an apparent molecular weight of approximately 50,000. In addition to the glycoprotein, four strong protein bands of more rapid electrophoretic mobilities, were also found. These proteins possessed molecular weights ranging from about 12,000 to 40,000. Supported in part by NATO Research Grant No. 584.

11.7 IMMUNOFLUORESCENT LOCALIZATION OF BRAIN-SPECIFIC PROTEINS S-100 & 14-3-2. K.L. Sims and B.W. Moore*, Laboratory of Neuropharmacology, NIMH, Wash., D.C., 20032, and Washington Univ. School of Medicine, St. Louis,63110.

The function of S-100 and 14-3-2, two acidic proteins unique to nervous tissue, has not been defined. The relative distribution of these proteins within the various cell populations of nervous tissue and within classes of cellular organelles may provide some insight into their role in brain metabolic (or regulatory) processes. Using specific rabbit antisera (both antigens purified from beef brain), indirect immunofluorescent techniques were used to characterize their distribution in tissue sections. The effect of the following variables on the initial antigen-antibody reaction between the brain protein and its specific antisera was assessed: antisera concentration; pretreatment of antisera with the corresponding purified antisera prior to use of the antisera on sections; length and temperature of antisera incubation with tissue; prior tissue fixation with glutaraldehyde, formaldehyde, or carbodiimide fixatives; addition of divalent cations or their removal via added EDTA; and preincubation of sections in 10mM 2-Mercaptoethanol. In addition to standard controls, reaction of the specific antisera for S-100 and 14-3-2 with liver and kidney tissue was examined, and antisera to other proteins (albumin and IgG) were used on seriatim sections to determine non-specific fluorescence. S-100 was visualized only within glial cellular elements and prominent staining of their processes was particularly evident; glial nuclei were unstained as were neuronal nuclei, perikarya, and processes. On adjacent sections, fluorescence secondary to the 14-3-2 reaction was observed in neuronal cell populations with neuronal perikarya exhibiting intense fluorescence. Neuronal nuclei with striking exception of the nucleolus portion were unstained, and staining of neuronal processes following the 14-3-2 reaction was not as prominent as the analogous fluorescence of glial processes observed after the S-100 procedure.

11.8 GENETIC TRANSCRIPTION IN THE CEREBRUM AND CEREBELLUM OF THE PRIMATE BRAIN. William E. Hahn. Dept. of Anat., Univ. of Colo. Sch. Med., Denver, CO 80220

Non-repeated sequence H^3 -DNA prepared from cultured Green Monkey cells, Cercopithecus aethiops, was hybridized to nuclear RNA from the cerebrum and cerebellum of the Green Monkey according to methods previously described (Hahn and Laird, 1971, Science 173 158). RNA prepared from nuclei from the cerebrum excluding the occipital lobe, hybridized with 14.1% of the H^3 -DNA. Nuclear RNA from the occipital lobe and the cerebellum hybridized with 13.2 and 13% of the H^3 -DNA respectively. Mixtures of frontal-temporal lobe RNA + cerebellar RNA and frontal-temporal lobe RNA + occipital lobe RNA hybridized with 13 - 14% of the H^3 -DNA. These results indicate that approximately 400,000 genes of an average sequence length of 1000 nucleotides are transcribed in both the cerebellum and cerebrum of the primate brain. The results of the mixture experiments of cerebellar and cerebral RNA indicate that most of the sequences in DNA "titrated" by RNA/DNA hybridization are commonly expressed in these two major regions of the brain. This result does not imply that RNA species unique to a given specific region of the brain do not exist because these RNA species may be in far too low a concentration to "saturate" complementary sequences in H^3 -DNA. Preparations of nuclei contained about 7 times more glial than neuronal nuclei. Hence much of the RNA used in these experiments is glial RNA. This suggests a high level of transcriptional diversity occurs in glial cells.

11.9 PROTEIN COMPOSITION OF BOVINE MYELIN-FREE AXONS. G. H. De Vries*, M. G. Hadfield, L. F. Eng and B. H. Liwnicz*. Health Sciences Div., Va. Comm. Univ., Richmond, Va. 23298; Veterans Adm. Hosp., Palo Alto, Calif. 94304 and Albert Einstein Coll. Med., Bronx, N. Y. 10461.

Axons derived from myelinated axons and isolated as myelin-free entities were isolated from corpus callosum of bovine brain by our procedure (Science 175:1370, 1972). The preparation consisted of axonal fragments with typical neurofilaments and mitochondria but lacking an axolemma as well as fibers containing only tightly packed filaments. Neurotubules (NT) were not evident morphologically although colchicine-binding activity indicated the presence of NT protein. Polyacrylamide electrophoresis in sodium dodecyl sulfate (SDS) containing gels showed proteins which range in molecular weight from approximately 150,000 to 20,000. The majority of the proteins have a MW greater than 40,000 and there is a major protein band at the 50,000 MW region. Immunodiffusion of a pH 8.8 extract showed the presence of glial fibrillary acidic protein (GFAP) as well as protein which interacted with myelin basic protein to give a precipitin line. The presence of GFAP was also confirmed by a specific radioimmunoassay. The filament protein, GFAP and NT protein have been identified in the SDS polyacrylamide gels of the axonal proteins. (Supported by NIH grant NS 10821-01 and an A. D. Williams Fund grant; MN 06418 and ID 4625).

11.10 THE EFFECTS OF WALLERIAN DEGENERATION ON THE PROTEINS AND LIPIDS OF RAT SCIATIC NERVE. J. G. Wood and R. M. C. Dawson*. Inst. of Animal Physiol. Babraham, Cambridge, England.

There is preliminary evidence to suggest that protein breakdown may precede lipid breakdown in demyelination (1). Polyacrylamide electrophoresis and thin layer chromatography (TLC) were used in this study to determine the early effects of Wallerian degeneration on the proteins and lipids of sciatic nerve. At 1, 3, 4, 5, 6, 8, 10 and 14 days after nerve section, degenerating nerves and nerves from the non-operated side were crushed in chloroform-methanol (2:1) and extracted overnight. The chloroform-methanol extract was analysed for lipids. The extracted nerves were washed with acetone and solubilized in 1% sodium dodecyl sulphate (SDS) before used for polyacrylamide electrophoresis of the proteins. Beginning three days after nerve section, a major protein of myelin, which we have recently shown to be a glycoprotein (J. Neurochem., in press), began to break down. A breakdown product appeared which could not be distinguished by electrophoresis from the basic protein of myelin. We have shown that the amino acid analyses of the glycoprotein and myelin basic protein are very similar and suggest that the protein moiety of the glycoprotein may be the myelin basic protein. No changes in the phospholipids could be detected at this stage. Cholesterol esters, however, previously thought to be formed from the 8th day of degeneration, were shown to accumulate from the 3rd day. Thus, protein breakdown involving a myelin glycoprotein is a very early event in Wallerian degeneration, but it is accompanied by at least one change in the lipids as well.

1. Adams et al. (1972) J. Neurochem. 19, 2043.

11.11 ALTERATION OF BRAIN PROTEINASE ACTIVITIES WITH HYPERCAPNIC HYPOXIA, ACUTE ASPHYXIA, ANESTHESIA, AND CONFINEMENT ACCORDING TO TIME OF DAY. George F. Buletza, Jr.* and W. B. Quay. Dept. Zoology, University of California at Berkeley, Ca. 94720

Microfluorometry of calcium-inhibited neutral proteinase activity (PA) using as substrate Nα-carbobenzoxydiglycyl-L-arginine-2-naphthylamide (GGANA)[Enzyme 12:311, 1971] was applied in the comparison of effects of hypercapnic hypoxia, acute hypercapnic asphyxia, ether, Nembutal, and confinement without hypoxia or anesthesia at two times (3 & 8 hr after onset light; = AM versus PM) during the day under a fixed photoperiod (LD 14:10) and using sibling male rats of the S_1 strain. PA was studied in six brain regions, after three recovery periods and in six replications. Ether anesthesia for 30 min resulted in ↑PA in AM and ↓PA when administered in PM. Changes were also dependent on brain region and length of recovery period. Greatest changes following ether occurred in the head of the caudate, with a 27% ↑PA ($P<0.002$) in AM with 90 min recovery, and with a 16% ↓PA ($P<0.01$) in PM. Nembutal (50 mg/kg) in AM gave initial values comparable to those after ether, while asphyxia caused an initial 15% ↓PA. Hypercapnic hypoxia for 30 min resulted in ↓PA, ↓calcium-enhanced neutral proteinase, and ↓cathepsin B in AM and PM. Within each brain region the three proteolytic enzymes exhibited similar patterns of change during hypoxia and recovery, but lower in amplitude and less variable than for asphyxia. Best recovery rates occurred in cerebellum in AM. Metabolic and functional meanings of brain proteinases need further study, but the marked effects and circadian dependencies of hypoxia and anesthesia on brain PA indicate the probable importance of investigation on this subject.
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12.1 INTRACELLULAR RECORDINGS FROM APLYSIA STATOCYST RECEPTOR CELLS.
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The Aplysia statocyst is a spherical organ, approximately 200 um in diameter, filled with fluid and small (6-20 um), dense statoconia. The wall of the statocyst consists mainly of 13 large receptor cells, each bearing multiple cilia which project into the cyst lumen. As the animal rolls or pitches, the statoconia fall to deflect cilia on different cells, leading to depolarization of the receptor cells and initiation of impulses in their axons. The fine structure of the cilia and their associated basal bodies appears similar to those of vertebrate hair cells, suggesting that similar transduction mechanisms may be operative. The statocyst receptor cells have been penetrated with micropipette electrodes of 25 to 60 megOhm resistance. Resting membrane potentials from -40 to -65 mV have been observed. At rest there are ongoing fluctuations in membrane potential ranging from 2 to 15 mV peak-to-peak amplitude. Current-voltage relations have been measured using a bridge amplifier. The receptor-cell membrane has a time constant varying from 20 to 60 msec. Thus it is relatively easy to separate the time constants of cell and recording system, allowing accurate bridge balance to be obtained. Receptor-cell input resistances have varied from 20 to 70 megOhms. Current-voltage relationships are nearly linear from -25 to +5 mV relative to the resting membrane potential. Movements of the preparation can elicit a depolarizing receptor potential as great as 25 mV. No directional sensitivity or hyperpolarizing receptor potentials have been observed.

12.2 THE FUNCTIONAL ALLOMETRY OF THE SEMICIRCULAR CANALS OF FISHES.
Howard C. Howland. Section of Neurobiology & Behavior, Cornell University, Ithaca, N.Y. 14850, and MPIV 8131, Seewiesen, Germany

The parameters describing the working frequency range of vertebrate semicircular canals are functions of several variables including the tube radii and radii of curvature of the canals. The allometries of these two radii were determined for an ontogenetic series of sunfish (n=86) and a phylogenetic series of small fishes. (n=33). The allometries found were:

Ontogenetic (2-20g) (Lepomis gibbosus)	Phylogenetic (.4-400g) (33 species, 19 families)
$\bar{R} = .694\ M^{.266 \pm .002}$	$R = .671\ M^{.264 \pm .038}$
$\bar{r}_o^2 = .019\ M^{.297 \pm .004}$	$\bar{r}_o^2 = .011\ M^{.348 \pm .077}$

where $\bar{R}$ is the average radius of curvature of the semicircular canal and $\bar{r}_o$ is the outer tube radius of the canal.

These allometries imply that the sensitivities of the semicircular canals increase with increasing body mass while their working frequency range, in all probability, decreases.

Significant differences in the growth constants of radii of curvature of anterior and posterior vertical semicircular canals were found in both series. In addition, the tube radii of the horizontal semicircular canals were found to be uniformly smaller than those of the vertical canals. These differences are discussed in terms of the tuning of the semicircular canals to the spectra of angular frequencies about their axes and the breadth of frequencies that the canals must detect.

12.3 SCANNING ELECTRON MICROSCOPY OF THE NEUROMORPHOLOGY OF THE PERIPHERAL VESTIBULAR SYSTEM IN THE PIGEON AND ITS FUNCTIONAL IMPLICATIONS. M.J. Correia, E. R. Young*, and J.P. Landolt*. Dept. Otolaryng., UTMB, Galveston, Texas, and DCIEM, Downsview (Toronto), Canada.

The major neural elements of the peripheral vestibular apparatus include the crista ampullaris, its sensory hair cells, and the primary nerve fibers which originate from the bipolar cells of Scarpa's ganglion.

One of the fundamental differences in the gross morphology of the cristae ampullares of the vertical and lateral membranous ampullae is the saddle-shape of the former and the ✓-shape of the latter. This complex geometry causes the hair cells which emanate from the crista ampullaris to have a wide variety of planes of projection. The planes of projection and the positions of the hair cells on the crista surface have a potential functional significance in determining the threshold and recruitment characteristics of these neural units to cupula deflection.

In addition to illustrating the complex geometry of the cristae, scanning electron microscope (SEM) photomicrographs show the nerve fiber myelin sheaths and their axis cylinder components. The inherent depth-of-field of the SEM is used advantageously to outline the varied geometry of the bipolar ganglion cells and permits calculation of their sizes. These cells range in size from (6.2μm times 16.0μm) to (17.1μm times 32.0 μm)(transverse diameter times longitudinal dimension).

12.4 DYNAMIC RESPONSE CHARACTERISTICS OF PIGEON PRIMARY VESTIBULAR NEURONS. J.P. Landolt* and M.J. Correia.(SPON: R. Feinstein) DCIEM, Downsview (Toronto), Canada, and Dept. of Otolaryng. UTMB, Galveston, Texas.

A frequency analysis was performed on the integrated neural responses from primary afferent single units in the vestibular ganglion of the pigeon. A wide variety of rotary stimuli were used. Frequency of oscillation (f) was varied from f= 0.01 Hz to f=10.0 Hz. Peak angular acceleration (α) and peak angular velocity (ω) at each f was varied from $\alpha=2^{o}/sec.^{2}$ to $\alpha=20^{o}/sec.^{2}$ (Peak angular velocities range from $\omega=191^{o}$/sec. at f=0.01 Hz. to $\omega=0.03^{o}$/sec. at f=10.0 Hz).

Various types of non-linearities were found between the 1st harmonic neural responses and the peak angular accelerations over the frequency range from 0.01 Hz to 10.0 Hz. These types include (a) higher-order harmonic distortion of the integrated neural response, (b) neural response rectification, (c)non-linearities of neural response transfer characteristic curves (1st harmonic neural response as a function of angular acceleration with frequency as a parameter). However, for data from the linear range of the stimulus-response relationship, transfer functions were approximated which relate 1st harmonic neural output to the peak angular acceleration. These transfer functions deviate from the classical torsion pendulum model and therefore must incorporate physiologically meaningful terms (e.g.adaptation) to describe the dynamics of the vestibular end organ.

12.5 BRANCHING OF VESTIBULOSPINAL AXONS. B.W. Peterson, C. Abzug, M. Maeda* and V.J. Wilson. The Rockefeller Univ., New York City 10021.

An important factor in understanding the function of a pathway is knowledge of the divergence of projections of individual neurons that comprise that pathway. Using microstimulation techniques we have found that individual Deiters' neurons that project in the lateral vestibulospinal tract (LVST) of the cat may give off branches at several levels of the spinal cord. Activity of Deiters' neurons was recorded extracellularly in anesthetized cerebellectomized cats while the ipsilateral spinal cord was stimulated locally with fine lacquer or glass insulated electrodes (20-100μ uninsulated tips). Antidromic responses were identified by their fixed latencies, ability to follow 250/sec. stimulation and by the characteristics of collision block. When a neuron was activated antidromically from two different spinal levels the critical intershock interval for collision block was approximately equal to the difference in antidromic latencies from the two levels plus the axon's refractory period.

Using a single, movable stimulating electrode we found that an individual Deiters' neuron could be activated from several discrete foci within the grey matter and that the effective range of a 50μA monopolar stimulus was 0.5mm or less. In another 7 experiments we studied 72 Deiters' neurons that were activated by 50μA shocks applied within laminae VII or VIII or the adjacent white matter of the cervical enlargement (locations >0.5mm from LVST). 40 of these neurons were also activated from the LVST at L1-4 or from the lumbar enlargement. These data indicate that many lumbar-projecting LVST neurons give off collaterals at one or more higher spinal levels. Work supported in part by Grants NS 02619 and NS 05463 from the NIH.

12.6 DYNAMIC RESPONSE OF BRAINSTEM VESTIBULAR NEURONS. Robert H. Schor. The Rockefeller University, New York, N.Y., 10021.

Tilt-sensitive neurons in the vestibular nuclei are known to have a transient as well as a maintained response to change of tilt. The dynamics of this transient and its peripheral origin are the subject of this investigation. Single unit recordings of vestibular neurons were made in decerebrate, unanesthetized cats with intact cerebellum subjected to small amplitude sinusoidal roll tilt of from 0.01 to 1.0 Hz. The response ratio (the amplitude of spike train modulation divided by the tilt stimulus amplitude) was calculated for tilt-sensitive neurons. Three-fourths of the neurons studied at multiple tilt frequencies showed a general increase in response ratio as the sinusoidal tilt ranged from 0.01 to 1.0 Hz. The slope of response ratio versus frequency was lowest at low frequencies, and averaged one half over the entire population of dynamic neurons. The low frequency response, proportional to the angle of tilt instead of the second derivative, angular acceleration, suggested that these cells were receiving primarily otolith input. To assess the possible role of the semicircular canals in this response, the canals of a series of cats were chronically plugged several weeks before they were used in the acute phase of this experiment. The dynamic responses of vestibular neurons in these animals were substantially the same as in cats with intact canals. A contribution of the canals to the dynamic increase in the response ratio at higher frequencies of tilt can not be ruled out, but these data suggest that such a contribution is a minor one. Thus the otolith organs, which have traditionally been considered static position receptors, can induce dynamic tilt responses in their target brainstem neurons in decerebrate cats. This work was supported in part by NIH Grant NS02619.

12.7 SEMICIRCULAR CANAL INPUT TO CAT NECK MOTONEURONS. V.J. Wilson and M. Maeda*. Rockefeller University, New York, N.Y. 10021.

As part of our investigation of vestibular control of spinal motoneurons, we have stimulated separately individual semicircular canal ampullary nerves and recorded intracellular potentials from neck motoneurons with the aid of computer averaging. Head extensor (dorsal ramus, DR) and lateral flexor (splenius, SP) cells in the C3 and C2 segments were studied in pre-collicularly decerebrated, unanesthetized cats. There is extensive convergence from different ampullae onto motoneurons: a disynaptic potential was evoked in most DR motoneurons by stimulation of 5 ampullae. The typical DR cell was excited by stimulation of the 2 anterior canals, inhibited from the 2 posteriors. Stimulation of the ipsilateral horizontal ampulla usually produced inhibition, while contralateral stimulation produced excitation or no effect. The pattern is somewhat different in SP neurons, where the most consistent actions are ipsilateral inhibition and contralateral excitation from the horizontal canal. To assess the role of the lateral and medial vestibulospinal tracts in these reflexes we have begun a study of the effect of MLF section on potentials evoked in neck motoneurons by ampullary stimulation. Damage to the ipsilateral MVST sharply reduced the incidence of IPSPs evoked in DR cells by ipsilateral horizontal and posterior ampullary nerve stimulation, while incidence of disynaptic EPSPs evoked by anterior canal stimulation was unaffected. Therefore, as expected from previous data (Wilson and Yoshida, Exp. Brain Res. 9:365, 1969) vestibular inhibitory neurons excited by canal stimulation project into the MVST, whereas this tract does not appear to be an important ipsilateral pathway for canal-activated excitatory neurons. Supported in part by N.I.H. grant NS 02619.

12.8 INTRACELLULAR RESPONSES OF SPINAL MOTONEURONS IN THE PIGEON TO STIMULATION OF THE VESTIBULAR SYSTEM. Aaron Rabin. The Rockefeller University, New York, N.Y. 10021.

The reflex regulation of spatial orientation in vertebrates is an important function of the vestibular system. This system is undoubtedly of great importance to flying animals, for flight places great demands on an animal's ability to orient and maintain postural equilibrium. Accordingly, experiments were performed on pigeons to investigate the effects of labyrinthine stimulation on motoneurons innervating neck and limb muscles. Animals were either decerebrated or anesthetized with methoxyflurane. Silver ball stimulating electrodes were implanted in the labyrinth and laminectomies were performed at various levels of the neuraxis. Intracellular recordings from the ventral horn of the spinal cord in the neck revealed that stimulation of the ipsilateral labyrinth (IL) with only a single shock evokes prominent EPSPs and/or IPSPs in the majority of neck motoneurons. Thresholds for effective stimuli were almost always less than 3-4 times the threshold for the labyrinth-evoked N1 potential which was recorded in the ipsilateral vestibular nuclei. In 65% of neck motoneurons, the latencies of the PSPs were short enough so that no more than two synapses could be involved in their transmission. Recordings were also obtained from identified motoneurons which innervate muscles of the wing or the leg. In contrast to the findings in the neck, stimulation of IL, even with multiple stimuli, failed to elicit any observable PSPs in limb motoneurons. PSPs were nevertheless seen in these motoneurons in response to stimulation of peripheral nerves or of the brain stem. Thus the data show that in the pigeon the association of the labyrinth with limb muscles is insignificant when compared to the association of the labyrinth with neck muscles. (Supported in part by NIH Grant NS 02619.)

12.9 CERVICAL EFFECTS ON ABDUCENS MOTONEURONS AND THEIR INTERACTION WITH VESTIBULO-OCULAR REFLEX. M. Maeda* and O. Hikosaka* (SPON: I. Abramov). Dept. of Neurophysiology, Institute of Brain Research, University of Tokyo, Japan.

Since the experiments of Magnus and his collaborators, it has been proposed that the neck proprioceptors play an important role in control of eye position. Effect of neck afferents on abducens motoneurons, and their interaction with the vestibulo-abducens reflex, were examined in chloralose-anesthetized, or unanesthetized decerebrate cats. The test reflex response elicited in the abducens nerve by stimulation of the contralateral vestibular nerve was inhibited by contralateral and facilitated by ipsilateral cervical dorsal root or neck joint stimulation. These reciprocal effects were obtained by stimulation at the level of C2 and C3, but not from C5 or lower. Contralateral and ipsilateral cervical stimulation induced IPSPs and EPSPs, respectively, in the abducens motoneurons (latency range 2.8-6.0 msec). The labyrinthine-induced disynaptic IPSP or EPSP was facilitated by conditioning stimulation of the contralateral and ipsilateral cervical dorsal root, respectively. It is thus postulated that the cervico-abducens and vestibulo-abducens reflex pathways converge upon common inhibitory or excitatory interneurons in the vestibular nuclei. Labyrinthine- and cervical-induced responses of presumed interneurons in the vestibular nuclei or those of their axons recorded in the abducens nuclei were consistent with the above view. Lesion experiments in the brain stem indicated that afferent volleys from the neck joints ascend ipsilaterally in the spinal cord, cross to the contralateral side in the brain stem, and eventually project to the vestibular nuclei. This cervico-ocular reflex pathway may function jointly with the vestibulo-ocular reflex in coordination of head and eye movement.

12.10 PROJECTIONS FROM SPECIFIC LABYRINTHINE RECEPTORS TO TROCHLEAR MOTONEURONS. R. Baker, W. Precht* and A. Berthoz*. Div. Neurobiol., Dept. Physiol. & Biophys., Univ. Iowa, Iowa City; Dept. Neurobiol., Max-Planck Inst. for Brain Res., Frankfurt, GFR; Lab. de Physiol. du Travail, Paris, France.

In the anesthetized cat, individual vestibular nerve branches were stimulated peripherally under direct visual observation and synaptic responses recorded from the ipsi- and contralateral trochlear nuclei (TN). Stimulation of the anterior canal nerve produced an early presynaptic positive-negative field potential (latency of 1 msec) followed by a later postsynaptic positive wave in the ipsilateral TN and no response in the contralateral TN. Only IPSPs were found in the ipsilateral trochlear motoneurons (TRO Mns). All other labyrinthine nerve activation was ineffective except when stimulus intensity was ten times larger than threshold for anterior canal stimulation. However, in the contralateral TN, presynaptic positive-negative fields (latency of 1 msec) followed by a postsynaptic negativity were evoked by posterior canal-saccular nerve stimulation. These nerves generated disynaptic EPSPs in contralateral TRO Mns without exhibiting any central convergence between utricular and posterior canal-saccular pathways. All disynaptic EPSPs were mediated through the medial longitudinal fasciculus (MLF) and brachium conjunctivum. Lesions indicate that 80-90% of the response projects through the MLF. A significant polysynaptic excitatory pathway is also present to contralateral TRO Mns through the reticular formation. These results demonstrate a number of direct excitatory pathways from canal and otolithic receptors to contralateral TRO Mns, but only a single inhibitory one to ipsilateral TRO Mns. In addition, they emphasize the reciprocal nature of the anterior-posterior canal control of TRO Mns via the MLF pathway. (Supported by the Max-Planck Society and USPHS research grant NS09916 from NINDS)

12.11 POSTURAL RESPONSES TO GALVANIC STIMULI, MODULATION BY HEAD POSITION AND BY PROPRIOCEPTIVE CUES FROM THE FEET. Lewis M. Nashner. Lab. of Neurophysiology, Good Samaritan Hospital & Med. Cntr., Portland, Oregon 97210.

The study focuses on defining quantitatively the effects of galvanic stimulation of the labyrinths on the posture control system in humans. The galvanic technique is then applied to study how vestibular information is used to control posture under a variety of conditions. With eyes closed a transient EMG response was found in gastrocnemius muscles beginning 100 msec after the onset of a bipolar current of as little as 75 μa. The duration of this response was 300-400 msec, independent of the duration of the current beyond a 75 msec minimum. Continuous currents produced in addition a steady state offset in body sway angle. These responses were modulated by position of the head. Rotating the head 180° from the left to the right shoulder transferred an excitatory response into an inhibitory one, while a 90° rotation to face forward completely suppressed the response. A two degree-of-freedom platform enabled the ankle joints of subjects to be maintained at fixed angles relative to antero-posterior sway; thus making vestibular cues critical when eyes were closed. With the platform servodriven to make vestibular cues critical, the "gain" of the steady state offset was significantly increased over that seen in the rigid platform, although the initial transient response was unchanged. Dynamics of postural responses were tested using galvanic and motion stimuli, both with the platform base rigid and servodriven to fix the ankles. Models of these data suggested three properties associated with vestibular initiated postural responses: (1) a strong effect on the vestibular response by proprioceptive and cutaneous cues from the feet and lower legs, (2) a variable "gain" for the response, depending on the task, and (3) a linear summation of vestibular responses to motion and to current stimuli.

13.1 RAPID INTRACELLULAR MOVEMENTS OF PARTICLES IN CULTURED CEREBELLAR NEURONS. David S. Forman, George R. Siggins, and Robert S. Lasher. Lab. of Neuropharmacology, NIMH, St. Elizabeths Hosp., Washington, D.C. 20032 and Dept. Anat., Univ. of Colorado Sch. of Med., Denver, Colo. 80220.

Rapid movements of intracellular particles can be seen inside neurites of cultured rat cerebellar neurons. Dissociated cerebellar cells from 2 day old rats were cultured in a modified Ham's F-12 medium containing high (24.5 mM) potassium (Lasher and Zagon, Brain Res. 41: 842, 1972) and examined after 3 to 40 days in vitro. Intracellular particles were visualized by phase microscopy and photographed with time-lapse microcinematography. Computer based methods were used to analyze the particle movements. At one frame every 2 seconds, rapid saltatory movements of particles inside neurites are evident. The rates of movement are consistent with rapid axonal transport. Particle movement is bidirectional, but most individual particles were observed moving in only one direction. The particles also exhibit other types of movement such as rapid back-and-forth oscillations. At one frame every 8 seconds, slower movements of particles or of bulges in the neurites were seen; these might represent slow axonal transport.

13.2 COLD BLOCK OF FAST AXOPLASMIC TRANSPORT: REVERSIBILITY AND EFFECTS OF COLCHICINE AND VINBLASTINE. Sidney Ochs. Dept. Physiol. Ind. Univ. Med. Center, Indianapolis, In., 46202

A Q_{10} of 2-2.3 was found for the temperature dependence of fast axoplasmic transport in vitro as shown by the outflow of labeled proteins in cat sciatic nerves following injection of their L7 ganglia with ^{3}H-leucine (Ochs and Smith, Fed. Proc. 30, 665, 1971). In subsequent studies, a complete block of transport was found at temperatures of 11°C and below. The block could be due to a cold dissociation of microtubules (Echandia and Piezzi, J. Cell Biol. 39, 491, 1968). By returning nerves after cold-block to 38°C, reversibility could be tested. Transport at the usual rate quickly resumed, implying a rapid reassembly. To further test disaggregation, colchicine and vinblastine, which are believed to block transport by binding to microtubular protein subunits, were studied. Only a moderate effect on transport in vitro was seen even with high levels of colchicine (50 mM) and a more effective block with slope change was seen with vinblastine (1-2 mM). If during cold-block there is disassembly of microtubules, these agents combining with microtubule subunits should then prevent reassembly when the nerve is rewarmed and produce a marked block of transport. A few such cases of augmented block were seen, but in a large number of experiments only a relatively small additional block of transport was seen using colchicine. Vinblastine was a little more effective than colchicine in this respect. Cold-block may therefore not be due to disaggregation, or colchicine and vinblastine may not readily combine with microtubule subunits to prevent their reaggregation. Most likely these agents block transport in a more subtle manner, possibly by acting at the cross-bridges carrying the transport filaments in the model proposed to explain fast axoplasmic transport. (Ochs, Science, 176, 252, 1972). Supported by NIH NS 8706, NSF GB28664 and the John A. Hartford Foundation, Inc.

13.3 REVERSIBILITY OF FAST AXOPLASMIC TRANSPORT FOLLOWING DIFFERING DURATIONS OF ANOXIC BLOCK IN VITRO AND IN VIVO. John Leone* and Sidney Ochs. Dept. Physiol. Ind. Univ. Med. Center, Indianapolis, In., 46202

Fast axoplasmic transport in cat sciatic nerve shown by a crest of outflow of labeled protein after L7 dorsal root ganglion injection with ^{3}H-leucine, is maintained in vitro at the usual rate of 410 mm/day in chambers containing 95% O_2 + 5% CO_2. Action potentials and transport are both blocked within 10-30 min when N_2 replaces O_2 (Ochs, Science, 176, 252, 1972). In the present study, recovery was tested after varying periods of N_2 anoxia. Both transport and responses recovered fully after periods of anoxia lasting up to 1-1/2 hr. After periods of anoxia lasting 1-3/4 to 2-1/2 hr, a partial failure of transport was seen, indicated by slope changes of the crest and a slower rate of fast transport. Responses, however, showed full recovery and the ~P level (ATP + creatine phosphate) returned to control levels (ca. 1.2 uM/gm). After 3 to 4 hr of anoxia an apparent block of fast transport was seen with again a good return of responses and ~ P. The apparent dissociation of fast axoplasmic transport and electrical responses appears to be due to a delay in the recovery of fast axoplasmic transport from anoxia. The time of in vitro observation is limited and recovery after longer times of anoxia was studied in vivo using limb compression to produce sciatic nerve anoxia and then examining fast axoplasmic transport some 16-20 hr later. As usual, the L7 ganglia were injected with ^{3}H-leucine and the crest positions in nerves on compressed and control sides compared after 6-7 hrs of downflow. Recovery of fast transport at the usual fast rate was found after periods of compression lasting as long as 5 hr, while compression times of 6 hr led to an irreversible block. Supported by NIH NS 8706, NSF GB28664 and the John A. Hartford Foundation, Inc.

13.4 INTERACTION OF LOCAL ANESTHETICS WITH MICROTUBULES DURING IN VITRO REPOLYMERIZATION. Richard H. Haschke*, Margaret R. Byers*, and B. Raymond Fink, Dept. Anesth, Sch. Med., Univ. Washington, Seattle, 98195

Lidocaine causes reversible disappearance of microtubules and reversible inhibition of rapid axonal transport in rabbit vagus nerve, (Byers, et al, J. Neurobiol, 4:125-144, 1973). Therefore, it is of interest to determine what effect lidocaine and other local anesthetics have on microtubules in a cell-free system. Microtubules were repolymerized from a crude supernatant obtained from a rabbit brain. Electron micrographs were prepared and the number of microtubules present counted. Addition of 34.6 mM (1%) - 17.3 mM lidocaine to the crude extract prevented entirely the repolymerization of microtubules, 8.7 mM - 3.5 mM concentrations were strongly inhibitory and 1.8 mM had no significant effect. At the higher drug concentrations the tubule length was also decreased by 50-90%. If tubules were first allowed to repolymerize and then exposed to the anesthetic, lidocaine concentrations up to 17.3 mM caused no significant breakdown. Procaine and etidocaine (which differ in anesthetic potency and lipid solubility by a factor of 1000) also prevented microtubule repolymerization to approximately the same extent as did lidocaine.

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13.5 DYNAMICS OF AXOPLASMIC TRANSPORT IN THE OPTIC SYSTEM OF THE RAT. Doris J. Schlichter* and William O. McClure. Department of Biochemistry, University of Illinois, Urbana, Illinois 61801.

Labeled protein synthesized in the retina of the rat after an intraocular injection of ^{3}H-l-proline is carried by axoplasmic transport to the terminals of the optic nerve in the superior colliculus (SC). Using subcellular fractionation, the characteristics of this material have been examined both during the course of transport down the nerve and after arrival at the SC. Transported material isolated from the nerve is largely (37.2%) found in the microsomal fraction. During passage down the axon changes in the physical properties of the transported material are observed. Vesicular material with a density of 1.04 in the nerve is replaced in the tract by material having a density of 1.02. In contrast to material actually being transported, radioactive material which has accumulated in the SC is primarily found in the synaptosomal fraction. Lysis of synaptosomes from the SC releases a labeled fraction which has a sedimentation coefficient of about 2S. This material yields only a small number of bands upon disc gel electrophoresis. The fractionation characteristics of the transported material were not dependent upon the time which had elapsed after the intraocular injection, or upon the time of day at which the injection was made. Further characterization of material at all stages of transport is underway.

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13.6 PROJECTION OF NORADRENERGIC NEURONS OF LOCUS COERULEUS TO TELENCEPHALON. Robert Y. Moore, Barbara E. Jones and Angelos E. Halaris. Depts. Peds, Med., Anat. and Psychiat., Univ. Chicago, Chicago 60637

Projection of locus coeruleus neurons to the telencephalon was investigated by injection of labelled amino acid into the nucleus and determination of the amount of label transported to the telencephalon, and also by destruction of the nucleus and assay of endogeneous telencephalic noradrenaline. Labelled amino acids have been shown to be selectively taken up by cell bodies, incorporated into protein, and axonally transported to terminals. In the present study the transport of radioactive label following unilateral injection of 25 μCi ^{3}H-leucine (in 1 μl saline) into cell bodies of locus coeruleus was compared to that following the unilateral injection into fibers of the restiform body. After injection of locus coeruleus, total radioactivity per mg tissue was approximately two times greater in ipsilateral than in contralateral telencephalic structures and at least two times greater than after injection of restiform body (which produced an homogeneous distribution of radioactivity) in all telencephalic structures including frontal, temporal and occipital cortex, olfactory bulb and tubercle, amygdala, hippocampus, striatum and septum with the highest concentration in the latter structure. These results suggest that labelled protein is transported from the locus coeruleus to terminals in the telencephalon. In a complementary study, lesions of locus coeruleus produced an almost complete depletion of noradrenaline in whole telencephalon. The sum of these results indicate that neurons of locus coeruleus project directly to telencephalon and that this innervation is the primary contribution of noradrenergic terminals to this region.

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13.7 TRACING OF THE NIGRO-STRIATAL PROJECTION BY ELECTRON MICROSCOPIC AUTORADIOGRAPHY. T. Hattori*, H. C. Fibiger and P. L. McGeer. Div. Neurological Sciences, Dept. Psychiatry, Univ. British Columbia, Vancouver, Canada

The nigro-striatal projection was traced by stereotaxic injection of [^{3}H]leucine into the zona compacta of the substantia nigra and subsequent electron microscopic autoradiography of labelled protein in the caudate-putamen (CP). One day after the injection synaptic terminals in the CP were preferentially labelled. Labelling of axons and dendrites in the CP increased between one and four days. Two morphologically distinct types of nerve ending were labelled: seventy-five percent had an asymmetrical synapse with moderately pleomorphic vesicles, while the remaining twenty-five percent had symmetrical synapses with highly pleomorphic vesicles. Only the former type of nerve ending was destroyed by intraventricular 6-hydroxydopamine. Degeneration in small unmyelinated axons was also observed after 6-hydroxydopamine. In animals where intraventricular 6-hydroxydopamine was administered 4 days after nigral injections of [^{3}H]leucine, degeneration of labelled terminals was observed. These experiments indicate that dopaminergic nigro-striatal boutons in the CP contain moderately pleomorphic vesicles and make asymmetrical synaptic contacts. The exact source and nature of the nerve endings with symmetrical synapses and highly pleomorphic vesicles is presently unknown.

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13.8 CONNECTIONS OF THE MAMILLARY BODY IN THE RAT. J.A.F.Cruce and Ruth Bleier. Laboratory of Neurophysiology, University of Wisconsin Medical School, Madison, Wisconsin, 53706.

Efferent connections of the mamillary body were investigated using the autoradiographic tracing method. By using slow pressure on a microsyringe, an injection of 0.4 microliters or less of tritiated leucine was made into one of the mamillary bodies of a rat. The injection time was fifteen to thirty minutes, and the needle was left in the brain for another ten minutes. The concentration of H-3 leucine was 20 to 50 microcuries per microliter. The animals were sacrificed thirty minutes to one week after injection. Either paraffin embedding or freezing was used to section the brains; the exposure time was two to six weeks. With a survival time as short as one hour and forty minutes, grains (presumably terminal labeling) could be seen in the anterior thalamus. The mamillothalamic tract was labelled throughout its course. When the injection site was primarily in the lateral mamillary nucleus, label was restricted to the anterodorsal nucleus bilaterally. Injections including the medial and posterior mamillary nuclei resulted in labeling in the anteromedial and anteroventral thalamic nuclei. The results suggest a topographic relationship between the posterior mamillary nucleus and the anteroventral nucleus. In addition, label was demonstrated in the ventral and dorsal tegmental nuclei, although it was difficult to follow the fibers of the mamillotegmental tract.

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13.9 EFFERENT CONNECTIONS OF THE VENTRAL LATERAL GENICULATE NUCLEUS (LGNv). L. W. Swanson and W. M. Cowan. Dept. Anat., Sch. Med., Washington Univ., St. Louis, Mo., 63110.

The efferent connections of the LGNv of the rat have been studied autoradiographically following the stereotaxic injection of small volumes of ^{3}H-leucine, or ^{3}H-proline, into the lateral geniculate complex. From injection sites involving the LGNv grains were followed to the ipsilateral superior colliculus to specific subdivisions of the pretectal area on both sides, and to the lateral terminal nucleus of the accessory optic tract and suprachiasmatic nucleus of the hypothalamus (SC) on both sides. The projection to the SC is of particular interest in light of recent demonstrations of a direct retinal input to this nucleus. Both the retino- and geniculo-hypothalamic fibers end in the same (ventral) portion of the SC, although the projection to the nucleus on the side of the labeled LGNv is approximately twice as heavy as that to the contralateral side. This apparent duplication of the retinal projections by the efferents of the LGNv suggests that this nucleus is important for the centrifugal control of most subcortical centers receiving direct visual input.

13.10 AN AUTORADIOGRAPHIC STUDY OF THE THALAMIC AND CORTICAL PROJECTIONS OF THE AMYGDALA IN THE RAT. John E. Krettek* and Joseph L. Price. Dept. Anat., Wash. Univ. Sch. Med., St. Louis, Mo. 63110.

Previous attempts to determine the specific origin of the efferent connections of individual nuclei of the amygdaloid complex have been hampered by the interruption of fibers arising in adjacent structures, and by the difficulty of reliably demonstrating degenerating axons after very small lesions. In order to overcome these problems, the connections of the amygdala have been studied with the autoradiographic method for tracing axonal connections. Stereotaxic injections of H^3-Leucine or H^3-Proline (5 to 10 μCi in 0.05 to 0.1 μl) have been made into each of the constituent amygdaloid nuclei in the rat. In addition to demonstrating a number of previously described pathways, such as those from the medial and posterior cortical amygdaloid nuclei to the "core" and "shell", respectively, of the ventromedial hypothalamic nucleus (de Olmos, J. Comp. Neur. 146: 303, 1972), these experiments have confirmed the previously questioned projection from the lateral and basal amygdaloid nuclei to the mediodorsal nucleus of the thalamus. The basolateral nucleus has also been shown to project to part of the cortex on the medial side of the frontal pole of the hemisphere which constitutes the projection field of the medio-dorsal thalamic nucleus (Leonard, Brain Res., 12: 321, 1969), while the lateral amygdaloid nucleus has been found to project to a cortical area immediately dorsal to the lateral or sulcal portion of the medio-dorsal projection area. In addition, projections have been demonstrated from the amygdala to more posterior cortical areas within the rhinal sulcus, and to the subiculum and adjacent portions of the hippocampal formation.

13.11 MEDIODORSAL NUCLEUS PROJECTION TO MACAQUE PREFRONTAL CORTEX: AN ORTHOGRADE STUDY. Thomas J. Tobias*. (SPON: E. Stellar). Anat. Dept., Sch. Med., Univ. of Pa., Phila., Pa., 19174

Afferents to primate prefrontal cortex (PFC) from the thalamic mediodorsal nucleus (MD) have been described previously by examining degenerative changes in the thalamus after removing portions of the frontal lobe. However, to assess the contribution of thalamocortical afferents in relation to the organization of this "association" neocortex, it is necessary to leave the PFC intact. Moreover, recent observations following cortical ablations have substantiated the existence of chromatolytic changes of transneuronal origin, thereby questioning the validity of interpretations of connectivity based upon ostensible retrograde changes. For both of these reasons, an attempt was made to ascertain the laminar distribution of thalamic axonal termination within the granular prefrontal neocortex using an orthograde approach. Anterograde degeneration, scintillation spectroscopy, and autoradiographic techniques have been employed in verifying the topographic pattern established in numerous earlier studies (e.g. Clark and Boggon, Philos. Trans. 224 (1935) 313-359). The projection to the midprincipalis region of PFC terminates in layers III and IV, while the more caudal area 8 (frontal eye fields), receiving synaptic input from the lateral, paralamellar portion of MD, displays terminals primarily in layer III, conforming to the pattern typical of Motor cortex.

14.1 COMPARISON OF CEREBELLAR UNIT AND FOCAL ACTIVITY ELICITED BY GRADED INTENSITY SOUND. R.J. Shofer and A. Newman*. Dept. Anat., Albert Einstein College of Medicine, Bronx, N.Y. 10461

In an earlier study of single units in the teleceptive region of the cerebellum graded-intensity tone bursts gave rise to exponentially increasing numbers of unit discharges, as a function of tone frequency. More recently, similar graded effects in the peak to peak amplitude of averaged evoked focal potentials have been observed and used in further evaluation of tonally specific responses. Closed system stimulation of one or both auditory canals with 100 msec tone or noise bursts was carried out in encephale isole cats. Extracellular single unit activity was selectively filtered to separate underlying slow-waves from concomitant action potentials. For certain tones the number of spikes represented in successive PST histograms at different intensity levels and the slow wave activities both significantly increased with stimuli ranging from 40-95 db. Irregular and considerably reduced response gradients were elicited by other less effective tones. Focal and/or surface-recorded amplitude changes generally showed a greater dynamic range than that found for nearby units. Regional differences in slow wave responses to various tones could be noted though topological boundaries did not appear sharply defined or systematic. In contrast, marked differences in response gradients were often found within a few mm. along the same folium. Further effects have been noted following use of modulated and non-modulated tone bursts as well as the local application of drugs or locally induced lesions. Such results possibly reflect fundamental regional differences in the density and distribution of auditory projections to the cerebellum.

14.2 TRIGGER FEATURES FOR THE VISUAL CLIMBING FIBER INPUT TO RABBIT VESTIBULOCEREBELLUM. J. I. Simpson* and K. E. Alley* (SPON: D.E.Hillman). Div. Neurobiol., Dept. Physiol. & Biophys., Univ. Iowa, Iowa City 52242.

The visual system has been shown to project as a climbing fiber (CF) afferent system to the vestibulo-cerebellum (nodulus and flocculus) of rabbit (Maekawa & Simpson, Brain Res. 39: 245, 1972). The types of visual stimuli conveyed through this pathway were determined by field potential and single unit recording of CF activation of Purkinje cells in the nodulus of albino rabbit. Animals were anesthetized with urethane—α-chloralose, immobilized with Flaxedil and respirated artificially. Presentation of a variety of visual stimuli to one eye revealed that the trigger features for this pathway are On and Direction-Selective. Step changes in light level (5-15° spots) evoked CF field potentials at On but not at Off throughout large receptive fields (up to 40°). Antagonistic effects were not seen upon increasing the size of the illuminated field; turning on the room lights was often an effective stimulus. However, no obvious changes occurred in background CF activation of Purkinje cells with widely differing whole field light levels; thus the CF activity does not reflect steady-state light level. Movement of a large field (100°) target, comprised of a collection of small (<5°) irregular white shapes on a black card, resulted in a marked increase of CF activity for motion in a preferred direction and a suppression of CF activity for motion in the opposite direction. Unitary activity increased 2-3 times over background during slow target movements (<5°/sec for 5 sec) in the preferred direction. The preferred direction was from posterior to anterior for most units. The trigger features found for the visual CF input to the nodulus suggest that this pathway is related to optokinetic responses in rabbit (Oyster et al., Vision Res. 12: 183, 1972). (Supported by USPHS grants NS05748 and DE53223 from NIH)

14.3 RESPONSES OF DENTATE NEURONS TO INPUTS FROM CEREBRAL CORTEX. Gary I. Allen and Tadao Ohno*. Dept. of Physiology, State Univ. of New York at Buffalo, N. Y. 14226

The dentate nucleus is part of a cerebro-cerebello-cerebral circuit which has been implicated in the control of skilled movements. The present study was designed to determine the response patterns of dentate neurons and the input patterns from sensorimotor and association areas of the cerebral cortex. The responses of dentate neurons following cortical stimulation were studied in cats under nitrous oxide or light thiopental anesthesia. The response patterns of dentate neurons consist of combinations of the following components: early inhibition, excitation, and later inhibition. Both inhibitions are mediated by Purkyně cells, and are due to the short-latency mossy fiber and later climbing fiber inputs, respectively. Excitatory collaterals of climbing fibers contribute to the excitation of dentate neurons. Collaterals of the early mossy input to the hemisphere via the pons were relatively ineffective in activating dentate neurons. Each dentate neuron receives inputs from various regions of the sensorimotor cortex, as well as motor and sensory association areas. The combination of effective areas varies from one neuron to another. However, the inputs from the association areas are often the strongest. Since the dentate nucleus projects to the motor cortex, the neuronal circuitry is available for a pathway from motor and sensory association areas to the motor cortex via the cerebellar hemisphere. In the normal initiation of skilled movements, the cerebellar hemisphere could exert an influence on the movement at a relatively early stage by affecting pyramidal tract neurons before their discharge.

14.4 MUSCLE AFFERENT PATHWAYS TO THE INTERPOSITUS NUCLEUS. William A. MacKay*, and John T. Murphy. Dept. Physiol., Univ. of Toronto., Toronto, Can., M5S 1A8.

The pathway for excitatory input from forelimb muscles to the cerebellar nuclei is slower in the cat than the pathway to the cerebellar cortex. As a result, afferent excitation and Purkinje cell inhibition converge upon the nuclear cells at about the same time. We have investigated in regionally anesthetized cats the two most likely sources of the excitatory input to interpositus neurons elicited by controlled forelimb muscle stretch. Firstly, extracellular unit recordings from the caudal, lateral part of the ipsilateral lateral reticular nucleus (LRN) showed that many of the neurons were readily activated by stretch of a single muscle. Of these, a significant proportion could be excited antidromically from the interpositus nucleus. The minimal latency however, of the stretch-evoked excitation was 20±6 msec (19±3 msec for antidromically-activated cells), which is longer than the latency for interpositus excitation from the same muscle (15±2 msec). Secondly, in recordings from single rostral spino-cerebellar tract (RSCT) fibers in the ipsilateral lateral funiculus of the cervical cord, we have also seen excitatory responses to stretch of a single muscle. The threshold is quite high (0.4-0.5 mm) in both instances, as it is for interpositus neurons. We conclude from the latency of RSCT fiber responses (11±2 msec) that this pathway may be the fastest major afferent route to the interpositus nucleus from muscles. Input from LRN evidently can act to sustain the early excitation induced by the RSCT pathway. (Supported by the MRC of Canada).

14.5 POSSIBLE SOURCES OF PREFERRED CENTRIPETAL CONDUCTION OF DENDRITIC SPIKES IN ALLIGATOR PURKINJE CELLS: A COMPARTMENTAL NEURON MODEL. James A. Mortimer and Erik W. Pottala*. Lab. Appl. Studies, Div. Comput. Res. and Tech., Nat. Inst. of Health, Bethesda, Md. 20014.

Field potential studies of alligator cerebellar cortex have disclosed that spikes initiated in the peripheral dendritic tree of Purkinje cells are propagated preferentially toward the soma. It has been suggested that this tendency results from the higher threshold and increased electrical load seen by a spike ascending the dendritic tree (Llinas et al., SCIENCE 163: 184, 1969). To test this hypothesis as well as to examine other sources of preferred conduction direction in the dendrites, a hardware model of a single alligator Purkinje cell was constructed. This model consisted of a branched dendritic tree with 19 passive and 3 active compartments and a soma/initial segment compartment capable of spike generation. In the active dendritic compartments, spikes with a time course similar to those recorded intradendritically were simulated by triggered depolarizing and hyperpolarizing conductance changes. The interaction of active compartments by electrotonic spread led to a saltatory conduction of spikes in the dendritic tree. With realistic geometric and membrane parameters, the model showed a tendency for preferred conduction of spikes toward the soma and for relative independence of spike generators in different dendritic branches. Investigation of the source of this tendency indicated that, in addition to the increased electrical load, the longer time course of dendritic (vs. somatic) spikes was important in determining the direction of preferred spike conduction. It was not necessary to postulate higher spike thresholds in the dendrites to acheive this effect.

14.6 MODULATION OF PRIMARY SPINDLE AFFERENTS FROM THE REGION OF THE RED NUCLEUS. Harvey B. Nudelman,*Gyan Agarwal*, Jerold Brodkey. Prog. in Psychiatry, Univ.Tx.Med.Sch. at Houston, Houston, 77025.

Frequency modulated pulse trains were injected into the "region of the red nucleus" (RRN) of a cat while recording from a primary muscle spindle afferent, isolated from thin dorsal root segments in the contralateral gastrocnemius muscle held under constant tension. This was done to see if time dependent "demand lengths" could be sent to an alpha motor neuron via the gamma-spindle loop as is required by many current theories of reflex motor control. The results showed that this could be done and that the shape of the modulation wave from injected into the RRN was reflected in the shape of the output modulation of the primary spindle afferent for modulation frequencies up to 3Hz. The firing rate of the primary ending going as high as 250 pulses per second. The primary endings could be modulated up to 10Hz responding with 2-3 action potentials per cycle. The delay time from RRN to primary afferent was measured and found to decrease to a constant value as a function of modulation frequency. This can be explained in terms of a length threshold for primary endings and the mechanical dynamics of the intrafusal muscle fibers.

14.7 THE SPINAL ACTION OF THE DENDATE OUTPUT PROJECTING VIA THE "EXTRAPYRAMIDAL" NUCLEI. James R. Bloedel. Depts. Neurosurg. and Physiol., Sch. Med., U. of Minn., Minneapolis, 55455

Experiments were performed on Rhesus and squirrel monkeys in order to determine the action of pathways involving both the dendate nucleus and the nuclei of the "extrapyramidal" system on segmental reflexes activated by afferents from muscle spindles and Golgi tendon organs. To demonstrate the significance of the projections via these nuclei, the effect of dentate stimulation on the reflexes activated by group Ia and Ib afferents from hind limb muscles was studied in monkeys whose primary motor and sensory cortices as well as area 6 were ablated. Intracellular recording from alpha motor neurons showed that the most predominant effect of a conditioning dentate stimulus was an increase in the inhibitory action of Ib afferents on motoneurons innervating the homonomous muscles. It was concluded that the interaction between the dentate nucleus and "extrapyramidal" nuclei is indeed significant in regulating segmental reflexes involving proprioceptive afferents and that the effect of this interaction is primarily on the inhibitory pathway from Golgi tendon afferents onto homonomous alpha motoneurons. This research was supported by NIH grant NS09447.

14.8 CEREBELLAR DENTATE NUCLEUS PRECEDES MOTOR CORTEX IN THE INITIATION OF A PROMPT VOLITIONAL MOVEMENT. W.T. Thach, Department of Physiology, Yale Medical School, New Haven, Conn. 06510

Two contradictory hypotheses on the function of the dentate nucleus and the parts of the brain to which it is connected propose different timing: 1) a command for movement originates in motor cortex and goes not only to inter- and motor neurons but also (via pons) to dentate which feeds back (via thalamus) to motor cortex and there maintains or modifies the command; 2) a command for movement originates in the parietal "association" cortex and (via pons) feeds through dentate to thalamus to motor cortex to inter- and motor neurons. In the one hypothesis, dentate changes after motor cortex; in the second, before.

Rhesus monkeys are being trained to move the wrist (and elbow and shoulder) promptly in response to a light signal. Their reaction time is a consistent 220-260 msec from light to first detected change in force exerted by the hand ("onset of movement"); in two monkeys studied, the muscles that angulate the wrist changed before the muscles that angulate the elbow or shoulder. Single unit discharge during performance of the task is then recorded in dentate and the "hand area" of motor cortex in alternate penetrations on alternate days. In the one monkey so far studied completely, the discharge of single neurons underwent marked significant changes ($p=.001\%$) before the onset of movement in both areas. Distribution of the time-of-change relative to movement was computed both for dentate (48 neurons in 13 penetrations) and for motor cortex (34 neurons in 10 penetrations). The two distributions overlapped but that of dentate preceded that of motor cortex. The time difference was clearly visible in the two distribution histograms (for dentate 19% of the changes preceded any change in motor cortex, and the peak was 20-30 msec and the mean 26 msec earlier), and was significant by the X^2 test ($p=.1\%$).

These preliminary results favor the second hypothesis and suggest that changes in dentate help to initiate the first changes in motor cortex.

14.9 ELECTRICAL TRANSMISSION BETWEEN CELLS IN THE INFERIOR OLIVE OF THE CAT. R. Llinás, R. Baker and C. Sotelo*. Div. Neurobiol., Dept. Physiol. & Biophys., Univ. Iowa, Iowa City 52242; Lab. d'Histol. Normale et Pathol. du Système Nerveux, INSERM, Hôpital de Port-Royal, Paris 14°, France.

Intracellular recordings were obtained from inferior olive (IO) neurons (main, medial and lateral nuclei). Electrical stimulation of the olivo-cerebellar pathway, at the cerebellar white matter, evoked antidromic invasion of IO neurons - the identification criteria being location, latency and intracellular staining with Procion yellow dye. Intracellular records demonstrated a short latency depolarization (SLD) having a latency from 0 to 300 μsec with respect to arrival of the antidromic volley at IO. This SLD was found in a large percentage of IO cells and had a graded amplitude with a short time course. Its amplitude in a large percentage of neurons was sufficient to reach firing level; thus true antidromic invasion in these cells must be differentiated from "orthodromic" activation via SLD. Collision between outgoing action potentials (direct stimulation through a Wheatstone bridge) and the antidromic volley into the IO differentiated SLDs from M spikes. Ultrastructural studies demonstrated the presence of gap junctions between IO cells.

Antidromic invasion also generated long lasting IPSPs in IO cells. The IPSPs were graded and had a time course of 30-50 msec. Units responding in a repetitive manner following antidromic invasion of the olive were observed in the vicinity of the nucleus. Since a direct relationship was found between the amplitude of the antidromic volley, the amplitude of the IPSP and the number of spikes generated by these cells or axons, it is inferred that IO cells exercise a feedback inhibition through collateral excitation of recurrent inhibitory interneurons. No inhibitory interneuron candidates have been found in the IO itself. (Supported by an INSERM grant and USPHS research grant NS09916 from NINDS)

14.10 TWO PRENATALLY INDUCED CEREBELLAR MALFORMATIONS IN THE CAT WITH CONTRASTING SYMPTOMATOLOGY. R. K. Haddad, William E. Lawson*, Ruth M. Dumas* and Ausma Rabe. Neuroteratology Laboratory, New York Institute for Basic Research in Mental Retardation, 1050 Forest Hill Road, Staten Island, New York, New York 10314

Treatment of pregnant cats on gestation day 59 with 15 mg of methylazoxymethanol acetate (MAM Ac) per kg of body weight resulted in marked cerebellar hypoplasia in the progeny. The cerebellar hemispheres were markedly hypoplastic although close to normal in their external configuration. The vermis, however, was strikingly dysplastic and lacked the typical vermal shape seen in cats. Despite the very evident cerebellar pathology produced in these animals, their clinical symptomatology was minimal. Other than a stiffness in the use of their hind legs, no motor symptoms were observed. In contrast, treatment of the pregnant cat on day 49 of gestation with the same dose of MAM Ac resulted in kittens that were severely ataxic. They were unable to walk or even to stand. Although they were hyperactive, they could not move about at all without falling. They showed intention tremor, dysmetria, and cerebellar rebound. All of these symptoms were readily apparent in their feeding behavior. Functional impairment of their hind limbs was so severe as to render them useless, but control of their forelimbs appeared unaffected. They played readily and actively and followed moving objects with appropriate head movements, though their vision was impaired. Their affective responses, both positive and negative, were vigorous, perhaps excessively so. Body conformation and weight gains were normal. The cerebellar pathology seen in these animals was severe. Not only the vermis, but the cerebellar hemispheres, showed dysraphia, as well as hypoplasia. Some hydrocephaly was apparent in the temporal regions, which were rather lissencephalic.

14.11 PREDATORY ATTACK, GROOMING AND CONSUMMATORY BEHAVIORS EVOKED BY ELECTRICAL STIMULATION OF CEREBELLAR NUCLEI IN CAT. Donald J. Reis, Nobutaka Doba* and Marc A. Nathan*. Dept. Neurol., Lab. Neurobiol., Cornell University Medical College, New York, 10021.

Electrical stimulation ventro-medially in the rostral fastigial nucleus (FN) of anesthetized cat evokes a profound rise of blood pressure and tachycardia (Miura & Reis, Am. J. Physiol. 219: 1330 1970), the fastigial pressor response (FPR). To examine if the FPR is associated with behavioral changes, stimulating electrodes were chronically implanted in FN of cat along with an indwelling cannula in the carotid artery. Electrical stimulation restricted to FN (50cps for 30-60 sec) in awake cat at intensities just above threshold for hypertension most commonly elicited alerting and vocalization. At slightly higher intensities the cats exhibited a range of stimulus-locked behaviors including intense grooming, predatory (biting) attack on rats, eating or drinking. The behavioral responses were stereotyped, coordinated and characteristic for each animal. No abnormalities of posture or movement were noted. Lesions at electrode tips abolished the behavior and pressor responses without producing motor deficits or impairment of defensive responses to attack or pain. We conclude that the rostral fastigial nucleus can modulate behaviors such as aggression, feeding and drinking heretofore considered as preponderantly organized in upper brainstem and limbic system. (Supported by NIH grant 04876-08 and NASA grant 33-010-179).

15.1 INVERTEBRATE SYNAPSE: POSTSYNAPTIC MORPHOLOGY FOLLOWING DEGENERATION OF PRESYNAPTIC STRUCTURES. Jeffrey J. Wine, Dept. of Psychology, Stanford University, Stanford, CA. 94305.

Does the geometry of dendrites depend on the presence of synaptic structures? The abdominal nerve cord of the crayfish contains 4 giant axons that contact identified motoneurons via large, electrical, 'axo-axonal' synapses. Although the synapse is characterized as axoaxonal, the postsynaptic motoneuron sends out fine dendritic branches at the junction site; contacts are made exclusively with these branches (Stirling, Z. Zellforsch. Mikrosk. Anat. 131, 31, 1972). The branches can be visualized by injecting cobaltous chloride into the motoneuron (Mittenthal & Wine, Science, 179, 182, 1973). In some ganglia the dendrites contact only the medial pair of giant axons, which arise from somata in the supraesophageal ganglion and run the entire length of the nerve cord. When the medial axons are transected midway along their length, the distal portions show anterograde degeneration. However, the degeneration rate is exceedingly slow: it requires approximately 4-6 months for conduction loss and complete collapse of the axon profile to occur (Wine, Exp. Neurol. 38, 157, 1973).

Dendrites of identified motoneurons were examined with the light microscope up to 18 months following transection of the medial axons. No obvious signs of altered morphology could be detected; dendrites that formerly contacted the medial axons had not retracted, and there was no indication of newly formed contacts with neighboring axons (collateral sprouting). The animals used in these studies were immature, hence these structures in the crayfish motor system appear to illustrate an extreme example of anatomical rigidity.

15.2 RENEWAL AND REGENERATION OF OLFACTORY NEURONS IN ADULT MICE. Joseph F. Metcalf* (Spon: P. P. C. Graziadei). Fla. State Univ., Tallahassee, 32306.

For well over a hundred years experimentalists have attempted to study the effect of various treatments on degeneration and regeneration of the olfactory epithelium. These experiments have indicated that olfactory neurons degenerate following olfactory nerve section, bulb removal, or $ZnSO_4$ applications. A few authors, however, have reported that olfactory neurons also regenerate following these treatments. (S. F. Takagi, Hb. Sen. Physiol. IV). These reports of regeneration of olfactory neurons are opposed to the long-held view that neurogenesis, at least in adult mammals, is a pre-natal phenomenon.

The presence of mitotic cells in the olfactory epithelium of mammals has been demonstrated (K. H. Andres, 1965, Naturwissenschaften 17: 500), and Moulton et al. (Ciba Foundation Symposium, 1970) have shown that H^3-thymidine labeled cells migrate from the basal zone of the epithelium into the mid-zone occupied by neurons. These authors suggested that olfactory neurons represent a renewing cell population in adult mammals.

In the present study H^3-thymidine was injected into adult mice 3 x daily for 14 days. The animals were sacrificed at various times during and after isotope administration, and autoradiography was used to determine the time course of olfactory receptor cell turnover.

Following olfactory bulb ablation, degenerative changes were observed in the neurons within 24 hours, and all of the receptors had degenerated after 5-7 days. On the third day after bulb ablation, a burst of mitotic activity was observed among progenitor cells in the basal zone of the epithelium. These cells produced olfactory neuroblasts which differentiated into mature olfactory neurons within 10-14 days.

A model for the control of renewal and regeneration of olfactory neurons in adult mammals is proposed.

15.3 MYELIN FORMATION: EFFECT OF VINBLASTINE SULFATE ON SCIATIC NERVE DEVELOPMENT IN CHICK EMBRYOS. Betty Geren Uzman, Gloria M. Villegas* and Frank A. Rawlins*. Sparks Regional Medical Center, Fort Smith, Arkansas, 72901, and Instituto Venezolano de Investigaciones Cientificas, Caracas.

Vinblastine sulfate (Velban, VB) was administered by chorio-allantoic inoculation to chick embryos at Hamilton-Hamburger (H-H) Stages 35-37 in doses of 0.5-8 micrograms/gram chick embryo weight. Effects on Schwann cell proliferation, emergence of "pro-myelinating" axons, and appearance of myelin have been studied in surviving embryos compared to H-H Staged and weight-matched saline injected controls. Unexpected acceleration of nerve development has been observed with respect to axonal individualization by Schwann cells and appearance of myelin. Evidence is sought concerning the possibility that VB acts by affecting axonal microtubules.

15.4 SYNAPTOGENESIS IN RAT CEREBELLUM. Mark J. West and Manuel del Cerro. Dept. Anat., Ctr. Brain Research and Dept. Neurol., Univ. Rochester, Sch. of Med. and Dent., Roch., N.Y. 14642

In an attempt to determine the age at which the first synaptic contacts appear in the vermis of the rat cerebellum, material was studied from 20, 21 and 22 day embryos and from newborn pups. Tissue was prepared by block staining with ethanolic phosphotungstic acid (E-PTA) and also by conventional E.M. techniques. At embryonic day 20 the individual presynaptic dense projections, the intersynaptic cleft material and the post-synaptic thickening of mature synaptic contacts are recognizable in the molecular layer of E-PTA stained tissue. Other profiles with dense post-synaptic thickenings and presynaptic dense projections of varying density can be seen. Numerous structures resembling post-synaptic thickenings, without adjacent presynaptic dense projections and intersynaptic cleft material, are visible on the faint outlines of perikaria and dendrites. From embryonic day 21 to postnatal day 1, progressively fewer post-synaptic thickenings without presynaptic dense projections can be seen. By postnatal day 1 more synaptic contacts approach the appearance of the mature contact in which the intensity of staining is equal in the pre- and post-synaptic structures. This suggests that during maturation of the synaptic contact there is a gradual build-up of the presynaptic material that stains with E-PTA. Synaptic contacts at all the ages studied were asymetrical with respect to pre- and post-synaptic structures. The more mature synaptic contacts often appeared on or near perikaria. Maturation of the synaptic contacts as seen with E-PTA correlates with that shown by conventional E.M. techniques.

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15.5 METHYLAZOXYMETHANOL-INDUCED ULTRASTRUCTURAL LESIONS IN THE POSTNATAL MOUSE CEREBELLUM. Margaret Z. Jones, Elizabeth Gardner and Modesto Yang, Department of Pathology, Michigan State University, East Lansing, Michigan 48823

Administration of Methylazoxymethanol to the postnatal mouse shortly after birth regularly produces cellular necrosis in differentiating cells of the central nervous system and causes granuloprival cerebellar hypoplasia. (Jones, Yang and Mickelson, Fed Proc. 31:1508, 1972) (Hirano & Jones, Fed Proc. 31:1517, 1972, Hirano, Dembitzer & Jones, J. Neuropath, Exp Neurol 31:113, 1972).

The present study was initiated to clarify the pathogenesis of early lesions at the ultrastructural level. Swiss albino mice were sacrificed by perfusion fixation at 6 hours, 2, 3 and 5 days after the administration of methylazoxymethanol within 24 hours of birth. A wide variety of nuclear and cytoplasmic alterations were demonstrated in undifferentiated cells of the cerebellum. Necrosis of nuclei was marked. Although many necrotic elements were surrounded by pale cytoplasm, some were clearly engulfed by microglial cells. The rapid resolution of lesions was partially attributed to the macrophage response. Purkinje cell alterations were not observed and some granule cell - Purkinje cell synaptic contacts were demonstrated at 2, 3 and 5 days postnatal.

15.6 FINE STRUCTURE OF A DEVELOPING LEPIDOPTERAN NERVOUS SYSTEM AND ITS ACCESSIBILITY TO LANTHANUM AND HORSERADISH PEROXIDASE. Barbara J. McLaughlin. A.R.C., Dept. Zool., Univ. of Cambridge, Cambridge, England.

Changes in the neural lamella and perineurium of the abdominal connective of Manduca sexta were studied from late larval stages through metamorphosis. The larval connective is enclosed by a multi-layered sheath of tracheoles, tracholasts, and fibrous lamella overlying a flattened interdigitating perineurial cell layer. During the early stages of metamorphosis, the perineurial cells greatly increase in size and the lamella is broken down by invading blood cells. In the final stages of development, the lamella is restored and the perineurium has become a flattened interdigitating cell layer. The apical borders of the perineurium are attached to each other by desmosomes and gap and tight junctions are occasionally seen between the basal borders. When the lamella is intact, horseradish peroxidase does not penetrate below the apical borders. When the lamella degenerates, peroxidase penetrates further but not beyond the basal borders and there is increased pinocytotic uptake of peroxidase by the perineurium. Lanthanum, in contrast, penetrates freely between perineurial cells at all stages of development and passes below the basal borders where it is stopped by a bracelet of two cells, which adhere to the overlying perineurium by desmosomes and are clasped together by extensive gap and tight junctions. This cell layer appears to constitute the blood brain barrier of this developing system.

15.7 THE INFLUENCE OF ESTROGEN ADMINISTERED DURING VARIOUS TIMES OF PREPUBERAL LIFE ON THE SEXUAL BEHAVIOR OF RATS. Shelton E. Hendricks and Mary Weltin*. Dept. Psychol., University of Nebraska at Omaha, Omaha, 68101

Male and female rats gonadectomized on the day of birth received injections of estradiol benzoate (EB), (1 µg/10 gm body wt.) every other day for 10 days beginning at 2,12,22 or 32 days of age. Females were further divided as to whether, at 3 days of age, they were injected with oil vehicle, 5 µg testosterone propionate (TP) or 50 µg TP. Subjects received sham injections throughout the prepuberal period whenever they were not being injected with EB or TP. Further, one group of males and three groups of females received oil injections only except on Day 3 when one of these female groups was injected with 5 µg TP and another with 50 µg TP. Female behavior was evaluated in response to injected EB and progesterone beginning at 100 days of age and male behavior was evaluated in response to TP injections beginning at 150 days of age. As frequently reported TP injected during neonatal life significantly suppressed female behavior in both females and neonatally castrated males and potentiated some components of masculine behavior. EB given during prepuberal life was found to complexly influence sexual behavior at adulthood. Administered during the first 10 days of life EB all but abolished female sexual behavior and enhanced male behavior. However, during later periods EB injections were found to be facilitative to female behavior particularly for those groups of females who received TP at Day 3. These data are consistent with findings relative to the role of the ovary in the development of sexual behavior patterns during prepuberal life.

15.8 ENHANCED AVOIDANCE CONDITIONING IN RATS AFTER NEONATAL INJECTION OF TESTOSTERONE. Anthony G. Phillips and Gurcharn Deol.* Dept. Psychology, U.B.C., Vancouver 8, B.C., Canada.

Recent clinical observations of superior intelligence in individuals exposed to excessive amounts of androgen during prenatal development suggest a possible androgen involvement in the determination of learning ability. In an attempt to establish an animal model of this phenomenon, male Wistar rats were injected with either 1.25 mg of testosterone proprionate (TP) on the day of birth, or daily injections of 100 ug TP for the first five days of life. Control animals received oil injection on the same regimen. When tested for acquisition of a one-way active-avoidance task at 25 days of age, the TP injected animals learned the response significantly faster than the oil injected control subjects. Similar results were obtained with both schedules of hormone administration. Immediately following completion of the learning task, all subjects were tested for reactivity to footshock and no significant group differences were observed. On the basis of these preliminary findings, it appears as though elevation of neonatal androgen levels results in enhanced acquisition of a simple avoidance response.

15.9 DENDRITIC BRANCHING: ATTEMPT TO MIMIC COMPLEX ENVIRONMENT EFFECTS BY LONG-TERM TRAINING. W. T. Greenough, J. M. Juraska*, D. Flood*, F. R. Volkmar, and T. DeVoogd. Dept. Psychology and Neural & Behavioral Biology Program, University of Illinois, Urbana-Champaign, 61820, and School of Medicine, Stanford University, Stanford, California 94305.

Previous work indicates that rats reared in complex environments (EC) show increased higher-order branching of dendrites in some cortical areas. Sizeable branching differences have been seen in visual cortex; smaller differences were seen in temporal (auditory) cortex; and no differences were found in frontolateral cortex. Several authors have suggested that similar changes may be associated with more specific types of experience. As a preliminary test of such a possibility, we trained 35 day old male hooded rats on a series of appetitive visual pattern discriminations over a 40 day period, while littermates were handled but not trained. Brains were rapid Golgi stained and layer 2, 4, and 5 pyramidal neurons were drawn at 500X with the aid of a camera lucida. Ten neurons of each type were drawn from the visual cortex of each of 9 littermate pairs. The number of branches at each order away from the cell body was analyzed (For detailed techniques, see Volkmar & Greenough, Science, 176:1445, 1972). The results indicated essentially no main effects of training on the pattern of apical or basal dendritic branching. However, sizeable interactions between litter and treatment were evident. Further analyses of these data and of other cortical areas is in progress. (Supported by NIH grant HD 6862 and PHS grant PHFR 07030)

15.10 GENETIC VARIATION IN THE STATUS OF POSTNATAL DEVELOPMENT OF BRAIN AND BEHAVIOUR OF THE MOUSE. Douglas Wahlsten. Dept. Psychol., Univ. of Waterloo, Waterloo, Ontario, Canada, N2L 3G1.

A time scale for postnatal development was first derived for a single strain and was then used to measure developmental status of several other inbred and hybrid strains of identical gestation ages. Phenotypes measured for all mice included several motor reflexes, simple visual and auditory functioning, body weight, brain weight, myelination of 80 fibre tracts, and thickness of the external granular layer of the cerebellum. These phenotypes were assessed for separate litters of an F_2 cross (from C57BL/6J X DBA/2J) on each of 10 consecutive days starting at 27 days gestation age (about 8 days after birth). Using these data, developmental ages of six inbred and three hybrid strains were calculated at a chronological age of 32 gestation days. Significant differences between developmental status of inbred strains were detected. Hybrid mice were generally more advanced in development than either of their inbred parent strains. The degree of development was also related to the size of the litter and hence to the amount of available nutrition. However, genetic differences in developmental status could not be attributed in large part simply to differences in nutrition. Work currently is being done to make possible the precise calculation of developmental status of the postnatal mouse in order to compare quantitatively the degrees of variation in developmental rate produced by genetic and environmental differences.

15.11 THE NEONATAL SPLIT-BRAIN KITTEN AS AN ANIMAL MODEL FOR MINIMAL BRAIN DYSFUNCTION. Jeri A. Sechzer. Dept. Psychiat., Cornell Med. Coll., White Plains, N.Y. 10605.

Symptoms of minimal brain dysfunction (MBD): hyperactivity, impaired learning and retention, and decreased attention span are shown by kittens whose brains were split at birth. Hyperactivity and impaired learning ability, the predominant deficits, can be reversed by d-amphetamine. Neonatal split-brain kittens show a similar paradoxical response to d-amphetamine as MBD children: hyperactivity diminishes and there is a 33% improvement in learning.

Because these symptoms are present from birth, mimic those of MBD children and can be treated by amphetamine, the neonatal split-brain kitten appears to be an appropriate animal model to study minimal brain dysfunction. These experimental results suggest that MBD may be related to early brain damage and that children with this disorder, like split-brain animals, have less neurons available for complex learning tasks. The effect of amphetamine on hyperactivity and learning implies that catecholaminergic systems may be damaged at birth in minimal brain dysfunction.

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15.12 NEURAL LATERALIZATION OF VOCAL CONTROL IN SONGBIRDS. I. HYPOGLOSSAL ROLE. F. Nottebohm. Rockefeller University, New York, N.Y. 10021.
Bird vocalizations are produced by the syrinx. In songbirds this structure consists of two sound sources, one lodged in each bronchus. Each of these sound sources has its own complement of muscles innervated by the tracheosyringealis branch of the ipsilateral hypoglossus. In canaries, chaffinches, and white-crowned sparrows most or all song components are under left hypoglossal control. On this basis ($n > 40$), the left hypoglossus is described as dominant for vocal behavior, without any exception encountered so far. The right hypoglossus can be made dominant by sectioning its left counterpart before the onset of song learning. A chaffinch'es ability to reverse hypoglossal dominance decreases and ends as song learning reaches completion. In canaries it is possible to influence the extent of right or left hypoglossal dominance as follows: the left hypoglossus is sectioned during the first month of life, an operation that is followed by nerve regrowth. Canaries operated up to 14 days after hatching develop exclussive right hypoglossal dominance. Canaries operated on days 17 and 19 retain to an increasing extent the left hypoglossal dominance normally found in adults. Complexity of song repertoire, lack of access to auditory feedback, and unilateral or bilateral deafening do not influence extent of left hypoglossal dominance. Results on finches will be compared with observations made in parrots. It is suggested that hypoglossal dominance in birds will provide suitable material for testing basic theories of neural growth and lateralization of function.

16.1 CURRENT SOURCE DENSITY (CSD) ANALYSIS IN THE CENTRAL NERVOUS SYSTEM: THEORETICAL CONSIDERATIONS. Charles Nicholson and John A. Freeman*. Div. Neurobiol., Dept. Physiol. & Biophys., Univ. Iowa, Iowa City 52242, and Dept. Anat., Vanderbilt Univ. Med. School, Nashville, Tenn. 37232.

CSD analysis provides a more precise spatial localization of the origins of synaptic currents or action currents than does inspection of extracellular field potential records. CSD analysis derives location of sources and sinks of current, with respect to extracellular space, from measurements of the potential distribution (Howland et al., J. Neurophysiol. 18: 1, 1955). Analysis is based on the equation $\mathrm{Im}(\bar{x}) = -\nabla.(\sigma(\bar{x})\nabla\phi(\bar{x}))$ where Im is CSD at the point $\bar{x} = x,y,z$, σ is the conductivity tensor for the tissue, ϕ is the field potential and ∇ is the 3-dimensional gradient operator. We have investigated the following theoretical and technical obstacles impeding practical CSD analysis: a) conditions under which one dimensional potential sampling can substitute for 3-dimensional sampling, b) effect of measurements in coordinate axes rotated with respect to the principal axes defined by the conductivity tensor, c) anisotropy and inhomogeneity in the conductivity tensor, d) noise reducing algorithms for numerical estimation of derivatives, e) sensitivity of technique to observational errors. We find that, generally, potentials must be sampled in 3 dimensions; that measurements involving non-principal axes and inhomogeneity are feasible but complex and that error bounds can be defined. In rectangular Cartesian principal axes, conductive anisotropy is defined by just three values. Some types of neuronal tissue, e.g. the cerebellum, have such an intrinsic geometry and are thus highly suitable for CSD analysis. We conclude that CSD analysis can be implemented with a laboratory computer and significantly improves resolution of physiological events compared with that achieved by conventional field potential analysis.
(Supported by USPHS grants NS09916 from NINDS and E40117 from NIH)

16.2 OPTIMIZATION OF EXPERIMENTAL TECHNIQUE FOR CURRENT SOURCE DENSITY (CSD) ANALYSIS IN THE CENTRAL NERVOUS SYSTEM: APPLICATION TO AMPHIBIAN CEREBELLUM. John A. Freeman* and Charles Nicholson. Dept. Anat., Vanderbilt Univ. Med. School, Nashville, Tenn. 37232, and Div. Neurobiol., Dept. Physiol. & Biophys., Univ. Iowa, Iowa City 52242.

CSD analysis is a potentially powerful tool for elucidating neuronal relationships and functional interactions. The technique is based on the quantitative analysis of spatial variation in extracellular field potentials within a neuronal tissue. We attempted to optimize the experimental implementation of the technique, using laboratory computers, in terms of accuracy and ease of application. Direct demonstration that the technique provides greater accuracy than conventional field potential analysis was obtained using artificial current sources and sinks introduced into amphibian cerebellum. A method for computing the conductivity tensor in 3 dimensions using a multi-electrode array was developed. Potential dependence of tissue conductivity was measured with a lock-in amplifier and shown to be minimal. Several smoothing and differentiating computational formulae were examined: use of a 3-point formula provides best results in terms of accuracy, signal-to-noise ratio and simplicity. Best electrode spacing was determined from computations of spatial energy distribution for typical laminar field potentials, using a new fast algorithm. A spacing of 50μm was found optimal for analyzing cerebellar electrical activity evoked by stimulation of parallel fibers and Purkinje cell axons. Position of the recording electrode was determined by iontophoretic injection of Alcian blue dye which remained localized at injection site. CSD analysis was used to investigate synaptic interactions in toad cerebellum. Conclusions were checked by intracellular recording, Procion yellow dye injection and electron microscopy. (Supported by USPHS grants E40117 and NS09916 from NIH)

16.3 REVERBERATIONS OF PULSES IN REAL AND SIMULATED NEURON POOLS. R. J. MacGregor and R. L. Palasek*. Dept. EDEE, Univ. Colo., Boulder, 80302.

In a previous paper we suggested that the peak and decay pheonomenon observed in autocorrelation histograms from neurons in the rat mesencephalic reticular formation might reflect reverberations of pulses through many recurrent pathways. The present paper describes computer simulation studies on neuron pools undertaken to help elucidate this prediction. The network model is based on a three state-variable model for single-cell activity, developed particularly to describe plastic repetitive firing characteristics of neurons. We find that autocorrelation histograms for simulated neurons within appropriately interconnected networks do indeed exhibit a peak and decay phenomenon which can be made to match that observed in the real data with reasonable values for cell parameters. Second, we examined in some detail the firing properties of neurons in randomly connected pools of hundreds of cells wherein the number of connections per neuron, the strengths of the synapses and the accommodative and refractory properties of individual neurons could be varied. We found the main characteristic of such mutually exciting pools of neurons is that the spikes tend to come in waves distributed over all the cells and that the waves tend to occur more or less regularly. Network parameters (number of connections per cell and synaptic strength) determine the number of spikes per burst and the width of the burst, whereas background input level and cell refractory and accommodative parameters determine the rate of burst recurrence. Auto-and cross-correlation histograms show the rhythmic character and interdependence implied by this pattern.

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16.4 STOCHASTIC PROPERTIES OF AN INTENSITY CONTINUUM IN TWO NEURONAL MODELS. R. J. Sclabassi*, E. Lábos*, B. Magalhães-Castro*, B. E. Stein* and L. Kruger. Depts. Anat. & Neurol., Sch. Med., UCLA, Los Angeles, 90024

The sensitivity of neurons to stimulus level changes has been investigated in two neuronal models. Recent investigations, using the framework of information theory, have formulated this question as a problem in the determination of channel capacity, but the determination of the maximum number of distinguishable stimulus levels has remained elusive. The determination of cell sensitivity to external stimulus has been reformulated as a problem in Bayesian decision theory. This involves an explicit recognition of the implicit stochastic nature of neuronal cell firing, together with the concomitant problems of variable definition, level of sampling, and estimation of distribution functions. The a-posteriori probability of a particular stimulus level having caused a response is calculated and probabilistic statements concerning the stimulus level responsible for a given firing pattern can be stated. The stochastic properties of impulse discharges elicited by intracellular current pulses in esophageal ganglion cells of Helix pommatia and first order neurons for slowly adapting cutaneous mechanoreceptor (types I & II) of cats excited by mechanical displacement have been investigated. The observed changes in firing patterns across a wide intensity continuum display several parameters of variance, which can be precisely defined. The number of impulses increases and the interspike intervals decrease systematically with increasing stimulus levels of $<10^{-10}$ A for Helix neurons and $<10^{-6}$ m for both types of mechanoreceptors. Probability distribution functions of both the number of impulses and of interspike intervals reveal a non-linear sensitivity. These measures can be employed in comparing sensitivity as determined by application of decision and information theory and classical Weber function analyses. (Supported by USPHS grants NS-5685 and NS-2501.)

16.5 DIFFUSION PROCESSES MODELING SINGLE NEURON'S ACTIVITY. Luigi M. Ricciardi. Dept. Theoret. Biol., University of Chicago, Chicago, 60637.

Use of continuous Markov processes (CMP) has been made by some authors for describing the variability and randomness observed in most intracellular recordings. A critical review of existing papers on this subject is presented, aiming to overcome some conceptual difficulties and to correct some errors therein present. A CMP described by a singular diffusion equation is proposed, to account for burst activity of neurons, and its solution is discussed. Finally a general heuristic procedure to achieve acceptable phenomenological descriptions of membrane potential fluctuations is outlined. It consists in interpolating interspike histograms to construct firing probability distributions, and in determining the CMP's, if any, admitting of those disdributions as first passage time distributions through the neuron's threshold value.

16.6 THEORETICAL AND COMPUTER SIMULATION STUDIES OF RHYTHMIC ACTIVITY IN THE HIPPOCAMPUS. Thomas W. Calvert and K-C Yang*, Kinesiology Department, Simon Fraser University, Burnaby 2, B.C., Canada

There is considerable interest in the functional significance of rhythmic electrical activity in the brain in general and of the theta rhythm in the hippocampus in particular. It is known that hippocampal theta activity correlates with the activity of septal pacemaker neurons, but it is not known whether the hippocampus itself is also capable of oscillation or how the rhythmic input from the septum interacts with other inputs to the hippocampus. We have studied these questions both theoretically with nonlinear differential equations and by digital computer simulation of a portion of CA3/CA4. The equations represented the gross activity of populations of excitatory and inhibitory neurons while the digital simulation accounted for many of the spatio-temporal properties of a sheet of 48 excitatory pyramidal cells and 4 inhibitory interneurons. As a result of these studies we conclude that:

1. Regions CA3 and CA4 of the hippocampus exhibit an intrinsic rhythmicity which apparently has a natural frequency of 10 - 12 Hz - i.e. rather higher than the theta rhythm.
2. The rhythmic input from the septum can effectively change the gain of pyramidal cells for other inputs (e.g. from the entorhinal area).

16.7 SPATIAL FILTERING PROPERTIES PREDICTED FOR CORTICAL NEURON POPULATIONS. S. M. Ahn*, Walter J. Freeman. Dept. Physio.-Anat., UC Berkeley, Berkeley, 94720

A theoretical model for a neuron population has been obtained. A neuron population is defined as follows: excitatory neurons and inhibitory neurons group together to form excitatory subpopulations and inhibitory subpopulations of neurons, respectively. A subpopulation is a dynamical system whose input-output reaction satisfies certain properties. These subpopulations are uniformly distributed along a given spatial domain $[0,\ell] \subset \mathbb{R}$. We call a collection of these distributed subpopulations a neuron population. It is assumed that at a fixed time, t, a subpopulation is composed of two non-intersecting subsets--a receiving subset and a transmitting subset. That is to say, those neurons which are transmitting pulses are in the refractory period and are thus unable to receive from others. All those which are not transmitting are receiving. It is further assumed that the class at $x = x$ gives input to a class at $x = \xi$ with a gain, $K d \exp(-d|x - \xi|)$. If $h(t)$, the impulse response of a subpopulation, K and d are known, the model cast in the form of two coupled integro-differential equations shows that the system has the spatial filtering property. That is, the solution can be represented by the eigenfunctions of the spatial variable of the differential operator of the system, and changes in K and d make possible the filtering for certain input components corresponding to certain eigenfunctions of the neuron population. Therefore, if the information which arrives at the neuron population is encoded by the spatial patterns, then the neuron population is capable of discriminating different information. This model also shows a way to obtain $h(t)$ experimentally, by using a particular eigenfunction of the space variable. Supported by a grant (MH06686) to WJF and a postdoctoral Fellowship (5 ROI NS 09520) to SMA.

16.8 AN EEG MODEL FROM RANDOMLY CONNECTED NEURAL NETS
Photios A. Anninos and V.K. Murthy*. Depts. of Biomathematics and Anat., Scho. Med., UCLA, Los Angeles, 90024

In our previous work we have explored in a model the dynamics of a large number of interconnected neurons proceeding from isolated netlets to the treatment of interacting ones. However, unlike most of the earlier investigators, our research involved study of the properties of large neuronal populations as a function of the parameters of the individual neurons. In addition our model attempts explanation of the behavior of the brain in terms of the capabilities and limitations of individuals neurons. In the dynamics of neuronal nets the activity of any single neuron is in principle observable. On the other hand, the simultaneous monitoring of more than a few neurons presents great difficult problem as far as the observability of the individual neurons firing pattern is concerned. These firing records of a large number of neurons during a time interval we are taken to be the microstates of the system. However, the EEG, which can be considered as the sum of all potentials in the cell population at any instant of time, could in principle be taken to define a set of macrostates. Therefore our effort in this research is to study the simulated EEG from statistical point of view via a model which incorporates some physiological and anatomical characteristics of brain structure and function. From such statistical analysis we are able to obtain, under certain parameters of the model, all known rhythmic activities which characterize a particular brain function.

17.1 DIFFERENTIAL DEVELOPMENT OF TETRODOTOXIN BINDING IN REGIONS OF CHICK AND MOUSE BRAIN.
Dennis R. Hafemann and Brian R. Unsworth*. Dept. Biol., Marquette Univ., Milwaukee, Wis. 53233

Preliminary experiments (J. Neurochem. 20:613, 1973) have shown that the binding of tritium-labelled tetrodotoxin (TTX) increases as the nervous system develops. There are significant differences between mice and chicks in the rate of maturation of TTX binding, and these differences correlate with behavioral differences between the young of the two species.

In chickens the brainstem and optic tecta begin to develop TTX binding at 12 days before hatching, and are at 25% of the adult level at hatching. By contrast, the telencephalon and cerebellum do not develop TTX binding until 5 days before hatching, and are at only 10% of the adult level at hatching. The difference in TTX binding between these two classes of structures is maintained through the first 30 days posthatch.

In the mouse, the TTX binding of the brainstem is 20% of the adult level at birth, but the telencephalon is only 3% of the adult level, and the cerebellum shows no detectable binding. During the first week after birth the telencephalon develops TTX binding rapidly, but development of TTX binding in the cerebellum does not really begin until the animal is 12 days old.

The cerebellum is the last structure to develop in both species, but it is much slower to develop in the helpless young mouse than in the relatively independent chick.

17.2 MUSCLE PLASMA MEMBRANES: AN IN VITRO APPROACH TO EVALUATION OF THEIR GENERAL FUNCTIONS AND JUNCTIONAL RECEPTOR PROPERTIES. B.W. FESTOFF, J. SCIABBARRASI* AND W.K. ENGEL. MEDICAL NEUROLOGY BRANCH, NINDS, NIH BETHESDA, MD 20014

Purified mammalian sarcolemmal fragments (SLF) were prepared by a modification of the method of Boegman et al. (BBA 203:506, 1970). Electron microscopy reveals large and small vesicular membranes without contaminating mitochondria or myofibrillar material. SLF, isolated from a continuous sucrose gradient, are found in the region corresponding to 0.96-1.16M sucrose (D_4^{20} 1.12-1.15). Discontinous sucrose gradient centrifugation produces SLF at the 0.8-1.0M and 1.0-1.2M sucrose interfaces. The fraction is enriched for oubain-inhibitable, NaK stimulated-ATPase (NaKATPase), acetylcholinesterase (AChE) and has acetylcholinergic-receptor (AChR) activity as measured by the binding of I-125, and specific-antibody-tagged, alpha-bungarotoxin (αBT). SDS polyacrylamide gel electrophoresis demonstrates 4 major protein bands and at least 8 minor ones. At least 3 of these bands are glycoprotein in nature. αBT binding was found in 3 bands at approximate molecular weights of 22,000, 30,000 and 35,000 in order of decreasing radioactivity. AChE activity has been tentatively located to 2 of the higher molecular weight bands. SLF have been solubilized with Lubrol-WX. This treatment releases into the supernatant 70% of the pre-Lubrol protein, 85% AChE, 75% NaKATPase, and 80% AChR activities. Characterization of these solubilized membrane functions is continuing with a view toward applying this approach to seek plasma membrane abnormalities in various neuromuscular disorders.

17.3 DEVELOPMENTALLY-REGULATED AGGLUTININS OF FORMALINIZED ERYTHROCYTES: POTENTIAL ROLE IN INTERCELLULAR INTERACTIONS. Steven D. Rosen*, David L. Simpson*, John Kafka*, and Samuel H. Barondes. Dept. of Psychiatry, Sch. Med., Univ. California, San Diego, La Jolla, California 92037

Soluble crude extracts of the cellular slime mold, Dictyostelium discoideum and embryonic chick brain contain factors which agglutinate formalinized red blood cells. These are present in varying concentrations as a function of the development of the systems. The factor from D.discoideum is absent in the nonassociating vegetative cells and in cells which have been deprived of food for three hours but is present at very high concentrations in cells which have been deprived of food for nine hours at which time the cells are highly cohesive. The factor from embryonic chick brain is abundant between 6 and 10 days of incubation but its concentration decreased approximately 75% by 17 days. The factor from D. discoideum has been characterized more extensively than that from embryonic chick brain. The D. discoideum factor has the following properties: (1) its agglutination of formalinized sheep erythrocytes is inhibited by N-acetyl-D-galactosamine, D-galactose and L-fucose but not by other monosaccharides; (2)it binds quantitatively to a Sephrose 4B column and can be eluted from this column with D-galactose; (3) the protein eluted from the Sephrose column is pure by electrophoretic criteria and its properties will be reported;(4) it is present on the surface of cohesive but not vegetative cells. The factor from embryonic chick brain has the following properties: (1) its activity in agglutinating formalinized chicken erythrocytes is not antagonized by simple monosaccharides but is antagonized by glycopeptides derived by proteolytic digestion of embryonic chick brain;(2)it can be sedimented by high speed centrifugation. The possibility that these developmentally-regulated agglutinins of formalinized erythrocytes play a role in intercellular recognition will be considered.

17.4 THE ROLE OF MEMBRANE LIPIDS IN NEUROBLASTOMA DIFFERENTIATION. Richard M. Arneson, William G. Struve,* Charles K. Cartwright,* and Peter D. Jones.* Brain Research Institute and Departments of Biochemistry and Neurology, University of Tennessee Medical Units, Memphis, Tennessee, 38103.

Logarithmically growing clone N18 mouse neuroblastoma C 1300 cells (log cells) were transformed to nondividing axonated cells by removal of fetal bovine serum from the culture medium. This differentiation process is accompanied by changes in membrane structure as determined by studies with spin labels. The hydrophobic spin label 2,2,6,6-tetramethylpipirdin-1-oxyl partitions more into transformed cells than log cells. This result may be due to an increase in the fraction of lipids in the fluid state. Preliminary gas chromatographic data indicate a change in the fatty acid composition of the membrane phospholipids after transformation. This change may be responsible for the spin labeling results. A factor or factors which inhibit lipid peroxidation are produced when log cells are transformed to axonated cells. Freeze-thawed axonated cells do not produce lipid peroxides upon incubation in 0.05 M KH_2PO_4, 0.1 M KCl, pH 7.0, at 37° in the presence of 1×10^{-6} M $FeCl_2$ and 2×10^{-4} M ascorbate, and axonated cells will inhibit the peroxidation of rat liver mitochondria under these conditions. When homogenates of axonated cells are separated into a supernatant fraction and a pellet fraction by centrifugation at 100,000 x g for 90 minutes, the antioxidant capacity of these two fractions is approximately equal.

17.5 **REGULATION OF BRAIN MEMBRANE LIPIDS BY DIETARY DEFICIENCY.** **Grace Y. Sun, J. Go,* H. Winniczek* and T. M. Yau.* Lab. Neurochem., Cleveland Psychiat. Inst., Cleveland, Ohio 44109**

A fatty acid deficient diet was imposed on C57BL/10 mice at various stages during development and maturation. The acyl group composition of phospholipids was determined from microsomal, myelin and synaptosomal-rich fractions isolated from the brain homogenates. Fatty acid deficiency in brain was expressed by the ratio of 20:3(n-9) to 20:4(n-6) of diacyl-sn-glycero-3-phosphorylethanolamine in the microsomal fraction. When a deficient diet was initiated with the pregnant mice one week prior to delivery and then continued after birth, brain deficiency ratios for the mice at 3 weeks, 4.5 and 7 months of age were 0.2, 1.1 and 1.5, respectively. Mice given the deficient diet for 3 months starting at 1 month of age gave a ratio of 0.5 while mice given the deficient diet for 7 months starting at 4 months of age gave a ratio of 1.4. Brain deficiency symptoms can be alleviated after switching to a normal control diet. Thus, when the deficient diet was limited only to the mother during the nursing period, the decrease in ratio indicated a half-life of less than two weeks for the recovery. When mice given the deficient diet after being weaned up to 3 months of age, a longer half-life of 3 weeks was obtained for the recovery. Consequently, brain membrane fatty acids can be regulated by dietary means at various stages during development and maturation. The reversible process further allows the system to be a good model for subsequent studies involving membrane structure and function in brain. **(Supported in part by U.S. Public Health Service Research Grant NS-09338 from NINDS).**

17.6 NODAL, PARANODAL AND INTERNODAL MEMBRANES OF CEREBELLAR MYELINATED FIBERS VISUALIZED BY FREEZE-ETCHING AND ELECTRON MICROSCOPY. Bruce Schnapp* and Enrico Mugnaini. Laboratory of Neuromorphology, Dept. of Biobehavioral Sciences, U-154, University of Connecticut, Storrs, 06268

The nodal and paranodal regions of myelinated axons have been identified for the first time in replicas of freeze-etched preparations from chick cerebellar cortex. The fractured axonal Face A at the nodal and paranodal regions has been recognized in three different types of Ranvier nodes, provisionally named simple, branching site and synaptic. The nodal region is provided with numerous, evenly distributed particles, 80-120 Å in diameter. In the scalloped paranodal region the particles are scanty and are prevalently distributed in correspondence to the gap between neighboring lateral loops. The axonal B Face matches the A Face and, in addition, at the paranodal region, presents a peculiar pattern of grooves and double rows of small particles at an angle with the longitudinal axis of the nerve fiber. The glial B Face of the fractured lateral loop membrane has a spiral row of particles 120 Å in diameter (sometimes cleaving with the A Face), presumably related to the special axo-glial junction present in this region. These particles are different from those observed on fractured faces of internodal myelin. Supported by NIH Grant NS 09904-02.

17.7 CHANGES OF SURFACE CHARGE ON THE AXON MEMBRANE DURING THE DEVELOPMENT OF NERVOUS TISSUE. Riley C. Yu* and Walther Hild, Dept. Anat., Univ. Texas Med. Br., Galveston, Texas 77550

The presence of a signal that initiates myelin production by myelin-forming cells around particular axons has been postulated, but the nature of the signal is not known. In order to be effective this signal must act at the level of the surfaces of the cells involved. It is possible that a change in the chemistry and/or structure of these surfaces occurs when a glial process begins to approach a nerve fiber. Mouse cerebellum cultures at various stages of development were fixed with glutaraldehyde and stained with positively charged ferric colloid as an electron stain which marks negatively charged sites on cell surfaces. Electron micrographs revealed uniform and dense deposition of positive iron particles on the surfaces of individually outgrowing fibers as well as on glial cell surfaces. Axons with an approaching glial process, however, showed a marked reduction of charged iron deposits scattered along the surfaces of the axolemma while the distribution of iron particles on the surfaces of the approaching glial process remained unchanged. The chemical nature of the molecules responsible for these negatively charged sites was shown to be neuraminic acid because preincubation of the cultures with pure neuraminidase before staining prevented iron particle deposition on cell surfaces. The change of negative charges on the cell surface indicates that these alterations might well be involved in the basic chemical structure of cell membrane since neuraminic acid has been found to be an integral part of the surface structure bound to glycoprotein. The alteration of axolemmal surface charge may be a direct signal to an advancing glial process to indicate whether the axon is prepared to establish a functional relationship with that process.

17.8 SYNAPTOSOME MEMBRANE POTENTIAL CHANGES MONITORED WITH A FLUORESCENT PROBE. J.M. Goldring* and M.P. Blaustein* (SPON: R.P. Bunge). Department of Physiology & Biophysics, Washington Univ. School of Med., St. Louis, Missouri 63110.

Metabolically-dependent accumulation of K^+ against a concentration gradient (Bradford, J. Neurochem. 16: 675, 1969), and a K^+/Na^+ permeability ratio of about 20 (Keen & White, J. Neurochem. 18: 1097, 1971) may indicate the presence of a K^+ diffusion potential across the surface membrane of presynaptic terminals (synaptosomes) isolated from rat brain. Since the small diameter of synaptosomes (< 1 μ) precludes microelectrode measurements, fluorescence changes of the fluorochrome, 1,1'-dipentyl-2,2'-oxacarbocyanine (from A. Waggoner) was used to monitor membrane potential changes (Davila et al., Nature New Biol. 241: 159, 1973; Laris & Hoffman, Fed. Proc. 32: 271 Abs., 1973). Synaptosome fluorescence (SynFl) increased when Na_o from the standard medium (including 132 mM NaCl + 5 mM KCl) was replaced by K^+ or Rb^+, but not by Li^+ or $choline^+$. SynFl was directly proportional to log ($[K]_o$ + 0.05 $[Na]_o$). Replacement of Cl^- by methylsulfate$^-$ did not affect the SynFl increase due to increased $[K]_o$. Veratridine (10^{-4} M) or gramicidin D (10 μg/ml), both of which enhance Na^+ permeability, increased SynFl when added to the standard medium; this effect was greatly reduced when $choline^+$ replaced Na^+ in the medium. The veratridine effect was also inhibited by 3 x 10^{-7} M tetrodotoxin, which blocks the depolarizing action of veratridine in intact nerve (Ohta et al., J. Pharm. Exp. Therap. 184: 143, 1973). SynFl also increased when synaptosomes were treated with 1 mM ouabain to decrease $[K]_i$. These observations support the view that synaptosomes incubated in physiological saline may have resting membrane potentials similar to those of intact neurons. (Supported by NIH grant NS08442).

17.9 THRESHOLD CHANGES IN SINGLE FIBERS OF FROG SCIATIC NERVE FOLLOWING NERVE IMPULSE DISCHARGES. Stephen A. Raymond* (SPON: Gerald E. Schneider). Dept. of Biology, M.I.T., Cambridge, Mass. 02139

Non-synaptic, activity-related processes have important effects on the threshold of nerve axon membrane in the time zone ranging from a few milliseconds to more than 15 minutes after activity. Threshold curves measured following various trains of nerve impulses have three distinct phases:

i) the refractory phase lasts only a few milliseconds.

ii) the supernormal phase, when threshold drops below the threshold of a "rested" axon, may last as long as 1 second. The supernormal phase is briefer after a long train of many closely spaced impulses; but the minimum threshold value, occurring about 15 milliseconds after each impulse, remains the same as in a rested nerve.

iii) the depression phase, when threshold is raised, is generated by impulse rates ranging from 2 impulses/sec to more than 100 impulses/sec. Such rates are commonly observed physiologically. During the supernormal phase, depression is momentarily abolished, but the threshold rises again to its maximum value within a second. A nerve may require more than 15 minutes to recover from depression even if no impulses are conducted during the recovery period.

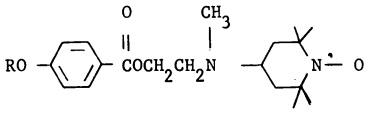
In axon terminals, where conduction of action potentials is chancy, these activity dependent threshold changes are partly responsible for determining the pathway each impulse will follow as it travels through the teledendron. The coupling of each impulse to postsynaptic elements thus depends on the pulse interval pattern in the main axon.

17.10 EXCITABILITIES IN MEMBRANOUS MICROSPHERES PRODUCED FROM PROTEINOID AND PHOSPHOLIPID. Yoshio Ishima* and Sidney W. Fox. Inst. Molec. Cell. Evoln, University of Miami, Coral Gables, FL 33134

Excitabilities are observed in microspherical membranes assembled from synthetic thermal proteinoids (leucine-rich variety especially) and lecithin. This membrane displays osmotic activities in mannitol solutions. When the ionicity of the external medium is decreased, various patterns of spontaneous electrical activity are observed. Calcium ions stabilize the membrane and less activity is observed. With 1 mM external calcium ion concentration, the membrane is induced to display all-or-none responses by currents passed in either the hyperpolarizing or the depolarizing direction. These results are similar to those obtained from the excitable droplets produced from the protoplasm of the Nitellas.

17.11 BINDING OF SPIN LABELED LOCAL ANESTHETICS TO BIOLOGICAL MEMBRANES. Howard H. Wang, Gregory J. Giotta*, Donald D. Koblin* and Robert J. Gargiulo*. Division of Natural Sciences, Univ. Calif., Santa Cruz, Calif. 95064

A series of spin labeled analogs of tertiary amine local anesthetics 2-(N,N-diethylamino) ethyl p-alkoxybenzoates were synthesized for studying membrane mechanisms involved in excitation. Pharmacological testing of these compounds showed that they are effective local anesthetics, and that their anesthetic durations were dependent upon the length of the alkoxy group. Electron spin resonance studies revealed that the binding and immobilization of local anesthetics by membranes is correlated with the length of the alkoxy group. Hyperfine measurements indicated a hydrophobic environment for the nitroxide group. Other experiments, using the quenching of 1,8 ANS fluorescence by the nitroxide radical, suggested that the nitroxide group of the spin labeled anesthetic is near the polar-apolar interface of the membrane. (This research is supported by a grant from the USPHS.)



R = CH_2CH_3

= $(CH_2)_3CH_3$

= $(CH_2)_5CH_3$

18.1 A METHOD TO PREPARE SUSPENSIONS OF TASTE BUD CELLS.

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The few biochemical studies of taste that have been reported have utilized preparations derived either from entire taste papillae, only a small proportion of which are taste buds, or tongue epithelium. Using bovine circumvallate papillae, we have developed a procedure to prepare suspensions of whole taste bud cells. The papillae are partially dissected and then excised from the tongue. They are incubated for up to 1 hour at 37°C in a collagenase-containing medium. By subsequent teasing with a microforceps, the epidermis containing the taste buds of the papilla is separated from the inner gelatinous dermis. Dispersion is accomplished by gentle homogenization of this epidermal tissue. The resulting suspension in 2% (w/w) Ficoll is fractionated on a discontinuous Ficoll gradient [8, 10, and 12% (w/w)]. The low density band (2-8% interface) is a suspension greatly enriched in cells that on a morphological basis appear to be derived from taste buds. Control preparations using lingual epithelium devoid of taste buds yield no cells of the slender morphology that appear when taste papillae are used. These preparations may be useful for biochemical studies of the preneural events in taste sensation.

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18.2 Spatial, Qualitative, and Quantitative Integration in Rat Chorda Tympani Taste Fibers. Inglis J. Miller, Jr., Department of Anatomy, Bowman Gray School of Medicine of Wake Forest University, Winston-Salem, North Carolina 27103.

The response of a single rat chorda tympani nerve fiber is derived from 1 - 12 taste buds spread over an area of 2 - 5 square millimeters of the rat tongue. This report brings current anatomical evidence derived from FitzGerald silver stained preparations of the chorda tympani innervation of fungiform papillae together with electrophysiological observation derived from recording from single chorda tympani nerve fibers in response to chemical and electrical stimulation of single taste buds. In 407 papillae in 9 Sprague-Dawley rats, 79% showed morphological branching of fiber bundles beneath the papillae. It has been demonstrated previously that single chorda tympani nerve fibers respond to stimulation of more than one taste bud and that the response differs quantitatively among the innervated taste buds. Whether the inputs from the several taste buds are integrated as generator currents at a common locus of spike impulse initiation or, alternatively, remotely initiated spike trains can be modified at branch points in a single fiber; two observations suggest that input from stimuli which do not initate spike potentials in the fiber are capable of modulating the single fiber response. These observations are that either electrical stimulation by cathodal current or chemical stimulation with compounds containing a large organic anion such as benzoate depress the response generated by NaCl stimulation in a different taste bud. These inputs to a single taste fiber from several taste buds respond as elements in series, while other fibers receiving input from the same set of taste buds, and from other sets of taste buds, respond as elements in parallel. From a standpoint of peripheral coding, the specificity of single receptor cells or of single taste buds may be much less important to the message than the result of their interactions.

(Supported by NS 10389)

18.3 TIME COURSE OF THE RAT CHORDA TYMPANI RESPONSE TO CONSTANT DEPOLARIZING CURRENT. David V. Smith and Steven L. Bealer*. Dept. Psychol., Univ. Wyoming, Laramie, 82071.

The integrated response of the rat chorda tympani nerve was recorded following stimulation of the ipsilateral anterior tongue with constant depolarizing current. An investigation of the effects of current intensity (1-250 μA) showed that the response of the chorda tympani to depolarizing current followed a time course similar to that of the response to chemical stimulation of the tongue. An initial phasic discharge was followed by a slowly declining tonic level of activity, the magnitude of both being a function of current intensity. Faull & Halpern (Science, 1972, 178, 73-75) previously demonstrated that the time course of the gustatory neural discharge to NaCl stimulation could not be accounted for by theories of taste stimulation which dealt with the dynamics of the stimulus-receptor site binding process. The present data suggest that the decline of the chorda tympani discharge over time is due to adaptive mechanisms of the taste receptor cells or chorda tympani fibers rather than to the dynamics of the chemical-receptor site interaction.

18.4 DISTENTION-EVOKED DIFFERENTIAL MODULATION OF MEMBRANE DEPOLARISATION CHARACTERISTICS OF LINGUAL CHEMORECEPTORS. K. N. Sharma*, S. Dua-Sharma, M. J. K. Doss*, and H. L. Jacobs*. St. John's Medical College, Bangalore, India and U. S. Army Laboratories, Natick, Massachusetts 01760.

Intracellular recording of gustatory receptors in frog's tongue show -10 to -25 mv resting membrane potential. These gustatory receptors are electrically excitable, and 1-3 nA pulses of 4 msec dur. were sufficient to produce a stable depolarisation response of 40 - 60 mv. The electronic potentials generated had characteristic exponential waveform from which time constants were calculated for rising phase and also membrane resistances and capacitances. Gastric distention in well-fed (Type I) animals produced inhibition of the receptor potential : slow rate of rise and lower amplitude of depolarisation. The inhibition depended on the amount and mode of gastric distention. By contrast, identical gastric distention in chronically food-deprived (Type II) animals, facilitates rather than inhibits the receptor potential. The distention-evoked inhibition in Type I animals is potentially minimised by gastric vagotomy and sectioning of glossopharyngeal nerves, while the facilitation obtained in Type II animals is lost after sympathectomy and severing of hypoglossal nerves. Thus, the differential modulation of gustatory receptor potential is biased by the nutritional state of the animal, the inhibitory influence of the control system being mediated via vago-glossopharyngeal nerves and facilitation being brought about via sympathetic and hypoglossal nerves.

18.5 RESPONSE OF CAT GENICULATE GANGLION TONGUE UNITS TO AMINO ACIDS, NUCLEOTIDES AND OTHER BIOCHEMICAL SUBSTANCES. James C. Boudreau. University of Texas at Houston, Graduate School of Biomedical Sciences, Neural Sciences, Houston, Texas 77025

Single unit spike recordings were taken from chemoresponsive cells of the cat geniculate ganglion while the tongue was stimulated with a variety of chemical substances. The three different neural groups responded to different types of substances. Group I units discharged to practically all solutions with a pH less than 4.0. In addition they discharged to some nonacidic solutions, the most stimulating being L-histidine, taurine, L-histidinol phosphate, fructose -6- phosphate, o-phosphorylethanolamine and L-carnosine. Group II units were maximally discharged by the di-and tri-phosphate nucleotides and by certain amino acids such as L-proline, L-cysteine and L-histidine. Certain amino acids such as L-isoleucine, L-tryptophan and L-phenylalanine inhibited Group II units. Group III units were divisable into two groups on the basis of stimulus-response measures. Group IIIA units responded to di-, tri-, and monophosphate nucleotides. Group IIIb units responded to relatively few substances, among them butyryl choline chloride, phytic acid and quinine. Group III units showed no appreciable response to amino acids. Neither group II nor group III units exhibited marked response to low pH solutions. (Supported in part by NIH Grant)

18.6 TASTE RESPONSES OF GERBILS TO INORGANIC SALTS[1]. William Jakinovich, Jr. and Bruce Oakley. Department of Zoology, Univ. of Michigan, Ann Arbor, Mich. 48104.

Summated taste responses of the chorda tympani nerve were recorded from four species of gerbils and compared with responses from rat, hamster and guinea pig. Gerbils resemble the hamster and guinea pig in response to the four classical taste qualities whereas the laboratory rat is anamolous in having a large NaCl and a weak sucrose response. North African gerbils, in contrast to other rodents, have excellent responses to divalent cations and weaker responses to Na^+ and Li^+. A complete absence of the "water response" was found in the gerbil species adapted to the most arid desert. Summated taste responses were obtained for a series of NaCl concentrations. In a reciprocal plot, the NaCl data was best described by two straight lines. Similar results have been obtained for rat and hamster. The results suggest that there are two types of sodium chloride receptors in rodents.

[1]Supported in part by NINDS Grant #07072.

18.7 MULTIPLE SENSITIVITY TO CHEMICAL STIMULI IN SINGLE HUMAN TASTE PAPILLAE
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The sensitivities of 10 human fungiform papillae were tested using a 5-alternative forced-choice procedure. Ss were asked to recognize which of the following stimuli was presented to a papilla on each of 250 trials: 5.0 M NaCl, 0.5 M citric acid, 0.1 M quinine hydrochloride, 1.0 M sucrose, and distilled H_2O. Solution droplets were delivered to individual papillae from 1 mm. diameter platinum wire loops. Based on each S's responses to distilled H_2O, corrections were made for individual response biases. Of the papillae tested 40% responded to all four compounds, 20% to three, none to only two, 20% to only one, and 20% to none of the chemical stimuli. These results did not confirm the earlier work of von Bekesy (J. appl. Physiol., 1966, 21, 1-9), in which it was suggested that taste quality is encoded by chemically specific papillae, but were consistent with the electrophysiological data suggesting multiple sensitivity of mammallian gustatory receptor cells and first-order fibers. The data suggested that the narrow range of sensitivity reported by von Bekesy (1966) was determined by the reciprocal relationship between area of stimulation and the concentration necessary to elicit a threshold sensation.

18.8 ODOR EVOKED SLOW POTENTIALS IN THE TURTLE OLFACTORY BULB.
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A slow potential response can be evoked in the olfactory bulbs of the box turtle, Terrapenne carolina, and the gopher tortoise, Gopherus polyphemus, by odorous stimulation of the nose. Three potential components of this odor evoked response are: (1) a monophasic potential of some 160-220 msec. in duration, (2) a change in the DC level often more than 1 sec. in duration, on which are superimposed, (3) the induced oscillations. Potential reversal of these components depended on the anatomical layering of the bulb in both the longitudinal and vertical bulbar axes. Potential one and the induced oscillations reversed polarity at the mitral cell layer; the DC potential reversal occurred in the external plexiform layer. Odorant responses in olfactory nerve twigs and the odor evoked response of the bulb were compared in gopher tortoise preparations. Oscillatory activity in the nerve twigs were shown not to be confused with the induced oscillations of the bulb. Continuous response measures were obtained for the potential components of the odor evoked response to three odorants, amyl acetate, high purity geraniol (97%, donated by Givaudan Corp.) and technical geraniol (50%) using a specified nasal flow rate and concentration range of 10^{0}-$10^{-2.5}$ of saturation at 20°C. Amyl acetate was the most stimulatory, followed by technical geraniol and high purity geraniol, in that order. It is suggested that the odor evoked response of the bulb is a useful measure of the activity of bulbar neuronal elements in response to odor stimuli.
(Supported in part by NS08943, NS07468 and NS08814.)

18.9 SINGLE UNIT DISCRIMINATION OF FISH ODORS RELEASED BY SALMON POPULATIONS.[1] Bruce Oakley, Kjell B. Døving* and Hans Nordeng*
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In a study of electrophysiological correlates of homing in salmonids we examined the physiological capacity of artic char (Salvelinus alpinus) to detect and distinguish among odors from 4 different geographic populations of artic char, which were kept without food in 120 liter tanks at 9°C with a fresh water flow of 2.4-6 lit/min. We recorded from olfactory bulb single units in MS-222 anesthetized char and found that 87% of the cells responded to tank water from the different char groups. 39 of the 45 cells studied in detail gave reliable differential responses, as defined by excitation to some and inhibition to other char odors. As stimulants, tank water and diluted body surface mucous produced closely similar neural responses. Two of our char populations are found in the same river system, yet have completely different spawning sites and migratory behavior. Odors from these two populations elicited differential responses in approximately half of the responsive single units. We suggest that char olfactory neurons are sufficiently discriminating to permit fish odors released by young char remaining at the spawning site to be used as pheromones which assist in homing.

[1]Supported by NS-07072 to B.O. and the Norwegian Research Coun.

18.10 A NEUROANATOMICAL INVESTIGATION OF THE OLFACTORY PROJECTION FIELD IN THE PIGEON (COLUMBA LIVIA). G. K. Rieke* and B. M. Wenzel. Dept. Physiol. and Brain Research Institute, Sch. Med., UCLA, Los Angeles, 90024

The Fink-Heimer I method was used for the detection of axonal and terminal degeneration in a series of 22 mature pigeons of either sex, after unilateral partial ablation of one olfactory bulb. The postoperative survival periods ranged from 18 hours to 3 days for 14 birds, and from 6 hrs. to 8 days for 8 birds. Fine degenerating axons were traced from the olfactory bulb in three loosely organized homolateral groups: one to the cortex prepiriformis (CPP), a second to the rostral portion of the hyperstriatum ventrale (HV), and the third to the lobus parolfactorius (LPO) and possibly to the tuberculum olfactorium (TO). Terminal degeneration, dense argyrophilic granules on cell soma and initial processes, was observed in the CPP, HV, and LPO. A temporal sequence of degeneration was apparent. The earliest degeneration was seen after 6 hours in the CPP. As survival time increased, so did the extent of degeneration, reaching a maximum of two to three days. Since the pigeon does not have an accessory olfactory bulb, and the anterior olfactory nucleus is reduced and protrudes only slightly into the postero-dorsal portion of the bulb, the lesions did not involve these structures. In conclusion, the observations show that the primary olfactory projection field, i.e., the axons of mitral cells of the olfactory bulb, projects to and terminates in at least the homolateral cortex prepiriformis, the rostral portion of the hyperstriatum ventrale, and the lobus parolfactorius.

18.11 ODOR DETECTION CURVES FOR α-IONONE IN DOG AND MAN. D. A. Marshall* and D. G. Moulton. Dept. of Animal Biology and Monell Chemical Senses Center, Univ. of Pennsylvania and V. A. Hospital, Philadelphia, Pa. 19104.

Reported differences in odor detection thresholds between dog and man show discrepancies of up to 5 or 6 orders of magnitude. Such comparisons are difficult to evaluate because these data were obtained by different investigators and generally given without detection curves. (Detection curves define the dynamic range of performance, allow evaluation of response stability, and provide a broad basis for assessing individual differences). We have therefore compared detection performances of dog and man over a range of concentrations of α-ionone using the same procedures and automated testing apparatus for both. This compound, a "floral", is detected by dog and man in relatively low concentrations and has no known biological importance for either. We used a restricted operant procedure employing an approach-avoidance discrimination between odor and purified air. Detection thresholds for 4 dogs and 6 humans differ by 3 ± 4 $\log_{10}$ concentration units. For dogs, the threshold range is 8.1×10^7 to 8.1×10^6 molecules/ml; one dog showed a lower threshold between 8.1×10^5 and $8.1 \times 10^{4.5}$ molec./ml. In man, threshold values range from $8.1 \times 10^{9.5}$ to $8.1 \times 10^{8.5}$ molec./ml. In dogs, stable performances could be achieved only by using small decrements in a descending concentration series. Discontinuities in dog detection curves are similar to those reported in curves derived behaviorally and electrophysiologically for other odorant compounds. In our data, discontinuities fall at relatively high performance levels. Below these, performances decline to chance over $\frac{1}{2}$ - 1 log unit of concentration; above, asymtotes are reached gradually over $2\frac{1}{2}$ to 3 $\log_{10}$ units. Such breaks in odor detection curves, although of an unknown origin, may imply a dual process at the receptor level.(Supported by AFOSR Grant No. 73-2425)

18.12 OLFACTORY CONTINUOUS RECOGNITION TASK IN THE ASSESSMENT OF FUNCTIONAL BRAIN DEFICITS. Richard G. Davis. Psychology Service, Veterans Administration Hospital, Knoxville, Iowa, 50138.

Elsberg (1935) has established that certain quantitative measures of olfactory sense performance do reflect general locus and extent of brain lesions. Olfactory tests given by a clinical neurologist are typically designed merely to confirm that the first nerve is intact. Thus, Elsberg's or similar procedures, burdensome in the clinical setting, are not popular.

Several considerations in an efficient clinical olfactory test go largely unnoticed; although the significance of such factors as verbal loading have been identified (Sumner 1962). The olfactory continuous recognition (OCR) task has been selected for study as a test instrument which can provide a powerful clinical technique with modest demands on the test administrator. The OCR task is expected to provide broad spectrum detection of partial olfactory deficits which may then be elaborated by more precise techniques.

A consideration of the functional attributes of olfactory perception and inferences based on a comparative study of olfactory neuroanatomy point to the prospect of a broader use of the OCR task. Examination of olfactory based behavior may reveal functional brain deficits in telencephalon and rhinencephalon regions which are not detected by any other clinical techniques currently in use.

This report details the basic nature of the OCR task and presents some preliminary normative data. Additional work supporting the rationale of the test is presented.

19.1 Synaptic and neuroependymal contacts in "visual" cortex of the turtle. Ford F. Ebner and Marc Colonnier. Neurosciences Section, Brown Univ., Prov. R.I. and Dept. Anat., Univ. of Ottawa, Ontario.

The cortex that receives axons from cells of the dorsal lateral geniculate nucleus in turtle consists of one lamina of neuronal cell bodies with their apical dendrites ascending towards the pial surface and with their basal dendrites in a subcellular zone. In electron microscopy, it has been seen that synaptic contacts in this cortex are similar to those of mammalian neocortex. Both round-asymmetrical and flat-symmetrical synapses are found on dendritic shafts, dendritic spines, and cell bodies. Numerous samples from this area were analyzed to determine the density of each type of synaptic contact as a function of distance from the pial surface. Spines containing mitochondria and membranous sacs form the predominant postsynaptic element from 0-100 microns. Small spines without organelles are most numerous from 100-250 microns, while dendritic shafts are most frequently seen as postsynaptic elements in the subcellular zone. After thalamic removal, degenerating thalamic terminals are seen only in the outer 100 microns of cortex, with the greatest density in the outer 50 microns, where they constitute 23% of all contacts; they mainly form asymmetrical synaptic contacts on spines containing mitochondria and/or sacs. Two types of unusual contacts are also found in this cortex. One is a membranous invagination of dendrites by axon terminals, glia, or other dendrites. The other consists in a differentiation of the two apposed membranes of axon terminals and ependymal profiles. Some of these features of synaptic organization are also seen in mammals, but they are more striking in turtle, suggesting that the patterns observed in the latter's "visual" cortex may be useful as a model and guide in the study of mammalian neocortex.
(Supported by PHS NS-06551 and MRC.MA-3735)

19.2 RECEPTIVE FIELD PROPERTIES OF VISUAL CORTICAL NEURONS IN THE TREE SHREW (TUPAIA GLIS). P. Kaufman, E. Wallingford*, R. Ostdahl* and G. Somjen. Dept. of Physiol. Pharmacol. Duke Univ., Durham, N.C. 27710

The receptive field properties of neurons in the striate cortex (area 17) and the peristriate belt (area 18) of adult tree shrews were examined. The cells were classified as simple, complex, or non-oriented (Hubel and Wiesel, J. Physiol. 160:106, 1962; Pettigrew et al., Exp. Brain Res., 6: 373, 1968). More than half of the neurons examined in the striate area were simple and about one fourth were non-oriented. Complex cells were least prevalent. About one third of the cells in the peristriate belt were simple, one half were complex, and non-oriented cells were least prevalent. Only a few cells were suspected of being hypercomplex. The finding of simple cells in area 18 has not previously been reported in the cat or monkey. The finding of simple cells outside area 17 may be related to the unusual degree of retention of visual discrimination after ablation of the striate cortex in these animals (Snyder and Diamond, Brain, Beh. Evol. 1: 244, 1968). A few cells responded only to stimulation of the ipsilateral eye, or to simultaneous binocular stimulation, but the majority of the cells were activated from either eye (50% in area 17, 82% in area 18) or by contralateral stimulation only (44% in area 17, 18% in area 18). Some cells responded to very narrow stimuli (0.05° in width) and others to very rapid movement (approximately 500°/sec.). (Supported by PHS Grant NS10507.)

19.3 CORTICAL VISUAL AREAS OF THE RABBIT. Clinton N. Woolsey, Chitr Sitthi-amorn*, U. Tulunay Keesey and Richard A. Holub*. Depts. Neurophysiol. and Ophthalmology, Sch. Med., Univ. Wis., Madison, Wis., 53706.

Visual areas I and II of the cerebral cortex of the rabbit were mapped with the evoked potential method by Thompson, Woolsey and Talbot (J. Neurophysiol., 13:277, 1950). In the present study, maps determined by evoked potential and by unit-cluster methods are compared. The arrangement of the field representation in visual areas I and II as defined by the two methods is similar, although a much more detailed picture is provided by the cluster method. In addition, it has been possible to define at least one other visual representation anterolaterally in the cortex where the visual, auditory and somatic sensory areas approach one another. This area is tentatively referred to as the anterolateral (AL) visual area. Representation of the upper visual field is located anterolaterally on the cortex, while the lower visual field is represented medially and caudally adjacent to visual area II. The horizontal meridian projects upon the cortex as a curved line concaved in an anterolateral direction, enclosing within it the representation of the upper visual field. Center of gaze (20^{o} on the horizontal meridian) is represented medially in the area, while the temporal field (180^{o}) projects laterally in the area. (Supported by NIH grants NS-06225 and EY-00308).

19.4 EFFECT OF INTERACTION OF TWO MOVING LINES ON THE RESPONSES OF SINGLE UNITS IN THE CAT'S VISUAL CORTEX. Robert W. Phelps* (SPON: Karl H. Pribram). Dept. of Psychiatry, Stanford Medical School, Stanford, CA 94305

The responses of single units in the visual cortex were recorded with extracellular microelectrodes from immobilized cats lightly anesthetized with N_2O (70%) and O_2 (30%). Stimuli consisted of two narrow ($<0.1^{o}$) lines displayed on the face of an oscilloscope moved about in any orientation and direction by a computer. Receptive fields and directional preference were established by hand held displays and computer mapping. Response histograms were then collected as one or both stimulus lines were moved through a neuron's receptive field in either the preferred or non-preferred direction with a variety of separations. Many units showed a clear decrease in both peak and total response when the separation of the stimulating lines averaged about 0.5^{o}. Occasionally, units showed a slight enhancement in their response at separations less than or greater than this. Enhancement was usually correlated with a bimodal excitatory response to a single line. The inhibitory effects of certain separations was interpreted to mean that the excitatory area of the receptive field was flanked by inhibitory regions. Stimulation with two lines moving in opposite directions appear at present to indicate that these flanking inhibitory regions, like the center excitatory region, are induced by movement in the preferred direction, and not by any other characteristics of the stimulation. This receptive field organization can act to selectively 'tune' the response of the unit to more specific characteristics of the stimulus.

19.5 ANALYSIS OF MOTION SELECTIVITY IN VISUAL CORTEX NEURONS OF THE CAT. Leo Ganz* and Arthur F. Lange* (SPON: K. H. Pribram). Stanford Univ., Stanford, CA. 94305.

Moving edges of varying velocity and contrast and gratings of varying velocity and spatial frequency were employed to analyze the receptive field properties of visual cortex neurons, recorded using an extracellular microelectrode. We examined particularly how these properties changed during dark adaptation. (1) We found neurons which were selective with respect to velocity and motion direction of stimuli in the visual field, (2) The peak of the velocity function, relating rate of cell firing to the velocity of the moving stimulus, shifts in the direction of slower velocities during dark adaptation. This shift reflects, we believe, the shift in temporal properties of the retina during dark adaptation, (3) Gratings of lower spatial frequency (wider stripes) yield velocity functions that peak at proportionately faster velocities, in the same neuron, (4) Bimodal velocity functions are often obtained, suggesting the motion-sensitive cell is being activated by a temporal wave having a sequence of excitation-inhibition-excitation. These findings parallel the perception of motion by human subjects; some of these parallels will be discussed.

19.6 STRUCTURAL AND FUNCTIONAL PROPERTIES OF INDIVIDUAL NEURONS IN THE STRIATE CORTEX OF THE CAT. J. P. Kelly* and D. C. Van Essen* (SPON: T.N. Wiesel). Dept. Neurobiol., Harvard Med. Sch., Boston, Mass. 02115

Most neurons in the striate cortex of the cat can be classified as stellate or pyramidal on morphological grounds and as simple, complex, or hypercomplex on the basis of their responses to visual stimuli. We have used the technique of intracellular dye injection to study the relationship between the anatomy and physiology of these cells. Microelectrodes filled with Procion yellow were used to stain single neurons whose receptive fields were mapped with spots and slits of light. Forty-eight cells have been successfully injected and identified. Most of the simple units were stellate (8 of 13), while pyramidal cells constituted the majority of complex cells (19 of 28) and hypercomplex cells (5 of 7). One cell with intermediate functional properties was pyramidal. Several of the injected complex cells were neither stellate nor pyramidal, but belonged to more infrequently occurring neuronal types such as multiform and double bouquet cells. Simple cells occurred most frequently in layer IV of the cortex, complex units were aggregated in both superficial and deep laminae, and hypercomplex cells were concentrated in layers II and III. These results indicate that there is a close correlation between the structure and function of individual neurons in the visual cortex.

19.7 NEURONAL VARIABILITY: POPULATION RESPONSES OF VISUAL CORTICAL NEURONS IN NORMAL CAT. G.J. Tomko* and D.R. Crapper* (SPON: J. T. Scott) Dept. Physiol., Faculty of Medicine, University of Toronto, Toronto, Canada.

Simultaneous recordings (two electrodes) were obtained from visual cortex of cats randomly presented with a patterned stimulus. The average 'hit probability' associated with a sample of 150 neurons responding to the stimulus was found to be 0.55. In an interval encompassing the averaged response the spike statistics of 50% of the units approached a poisson process with 35% demonstrating no significant difference from equal-interval samples of spontaneous activity. The occurrence of stimulus-locked cross-correlations was found to be inversely related to the physical separation of the neurons. The probabilities associated with cross-correlations were always less than 0.4. These facts lead to the postulate that a responsive ensemble of neurons exists in which a randomly shifting sub-set discharges to any single stimulus presentation. It is further postulated that stimulus information is conveyed by a function of the pulse density from the ensemble during an interval. Presentation of a stimulus does not statistically alter the output of an already spontaneously active cell but alters the probability of an output at a time subsequent to the presentation.

19.8 EFFECT OF STRIATE AND EXTRA STRIATE VISUAL CORTICAL LESIONS ON LEARNING AND RETENTION OF FORM DISCRIMINATIONS. J. M. Sprague, J. Levy*, A. Di Berardino* and J. Conomy*. Dept. Anat., Sch. Med. Univ. Pennsylvania, Philadelphia, Pa. 19174

This study was undertaken to evaluate and compare contributions of geniculocortical and pretectal-superior collicular cortical systems in flux and form discriminations in cat. Total, bilateral removal of area 17 (2 cats) and areas 17+18 (2 cats) resulted in no deficit in retention of several preoperatively learned form discriminations, and modest deficit in one but with marked savings in reaching 90% criterion. Original postoperative learning was normal in a flux and in 2 form discriminations; slowed learning was present in one other pattern task, but criterion was achieved. Three cats had lesions in area 19, suprasylvian gyrus and lateral suprasylvian area. Original learning was normal in simple flux and form discriminations, was prolonged in two additional form tests and lacking in a third. Retention was perfect in the flux and one form discrimination, but was lacking in two other form tests, both relearned at preoperative rate. Reversal tests were prolonged with perseveration. Subsequent ablation of superior colliculi resulted in loss of retention of two form tests: one, learned normally after the cortical lesion, was relearned at normal rate; the second which showed prolonged learning after cortical lesion, again was prolonged without achieving stable criterion. The geniculocortical system appears to be little involved in either original learning or retention of perception and discrimination of forms. These functions are severely impaired by lesions which destroy much of the cortical target of the pretectum and and superior colliculus (supported by NIH grant Ey-00577).

19.9 VISUAL PERIMETRY OF CATS WITH VISUAL CORTEX ABLATIONS. S. Murray Sherman. Dept. Physiol., Univ. Va. Sch. Med., Charlottesville, Va. 22901

By use of a visual perimetry test it has been shown that with either eye a normal cat can see a region bounded approximately from 100° ipsilateral (to the open eye) to 45° contralateral. The binocular field is a composite of the above (i.e., from 100° left-lateral to 100° right-lateral). The present study measured the perimetry subserved by the midbrain in cats which had bilateral removal of lateral, suprasylvian, and ectosylvian gyri (including all of areas 17, 18, & 19) plus a midsagittal transection of the commissure of the superior colliculus. Following a 2-6 week recovery period, the visually guided behavior of these cats was surprisingly good despite the extensive decortication. One major deficit was seen in monocular perimetry testing: the responses were only to objects in the ipsilateral hemifield; the 45° of contralateral hemifield seemed lost to these cats during monocular testing. Binocular testing revealed much less of a deficit. Other cats which had similar visual cortical lesions but no collicular commisurectomy remained blind throughout the several month postoperative period. These findings confirm and extend those of Sprague (Science 153: 1544, 1966). The visually guided behavior and extent of visual perimetry for these cats is nearly the same as that previously described for cats reared with binocular deprivation (Sherman, Brain Res. 49: 25, 1973). These data strengthen the tentative suggestion that such visually deprived cats do not develop geniculocortical control of visually guided behavior, but rather do this via retinotectal pathways.

19.10 PARALLEL PROCESSING OF COLOR, SHAPE, AND DIRECTIONAL INFORMATION BY CELLS IN RHESUS MONKEY FOVEAL STRIATE CORTEX. Bruce M. Dow. Laboratory of Vision Research, National Eye Institute, NIH, Bethesda, Md. 20014.

Recordings obtained with glass micropipettes from 236 units in foveal striate cortex (area 17) of anesthetized rhesus monkeys indicate that most cells in this region are specialized for the detection of a single stimulus feature (color, orientation, direction of movement) at the expense of other features. The majority of color sensitive cells respond without regard to orientation or direction of movement. The most precisely orientation specific cells show no specificity for color or direction. Directional cells tend to have loose orientation and chromatic requirements. A small number of cells show specificity for both orientation and color. Another group shows no specificity for orientation, direction, or color. Recordings in a region of prestriate cortex (area 18) receiving direct projections from striate cortex reveal cells with color but not orientation specificity and other cells with the converse properties, indicating that the parallel processing of separate stimulus features which begins in area 17 is being maintained at least as far as area 18.

19.11 EXTRAGENICULOSTRIATE VISION IN THE MONKEY: EFFECT OF OPTIC CHIASM SECTION AND ACCESSORY OPTIC SYSTEM LESIONS. Tauba Pasik and Pedro Pasik. Dept. of Neurology, Mount Sinai Sch. of Med., CUNY, New York, N.Y. 10029.

Bilateral destruction of the accessory optic system (A.O.S.) abolishes a light vs no-light discrimination habit which had been reacquired after total bilateral removal of the striate cortex in monkeys (Pasik and Pasik, J. Neurophysiol., 1973, 36). The nucleus of the accessory optic tract has been shown to receive retinal afferents from both the contralateral and the ipsilateral eye (Pasik, Pasik, Hámori and Szentágothai, Soc. for Neurosc., 1972, 231). In the present study, 4 monkeys (Macaca mulatta) were trained on a light vs no-light discrimination before and after serial surgical procedures involving the occipital lobes, the optic chiasm and the A.O.S. All lesions were histologically verified. Results: Preoperatively, all animals reached the criterion level of performance (90% correct responses in 300 consecutive trials) in 600 mean trials. After bilateral removal of the occipital lobes, which included the entirety of area 17 plus partial damage to 18 and 19, monkeys showed a significant deficit ($p < 0.02$) but all relearned the problem, reaching criterion in a mean of 1300 trials. Following additional midline section of the optic chiasm there was an almost perfect retention of the habit, the animals mastering the test in a mean of 425 trials. Bilateral destruction of the A.O.S., made in two of these monkeys as a third stage procedure, abolished the habit which was not regained to the established criterion level in 6000 trials of postoperative testing. Conclusions: Findings confirmed that the A.O.S. is critical for the ability of monkeys to perform a light vs no-light discrimination in the absence of striate cortex. Ipsilateral input through the A.O.S. appears to be sufficient for the retention of such capacity. (Aided by U.S.P.H.S. Grants # MH-02261 and K3-EY-16,865).

19.12 PSYCHOPHYSICS OF ELECTRICAL STIMULATION OF STRIATE CORTEX IN MACAQUES. B.B. Lee, R.W. Doty, J.R. Bartlett* and N. Negrão*. Center for Brain Research, University of Rochester, Rochester, N.Y. 14642.

To provide information relevant to electrical stimulation of human cortex for prosthetic purposes, several Macaca nemestrina have been tested extensively for their ability to discriminate various features of cortical stimulation. Threshold for detection of 50 Hz, 0.5-msec monophasic pulses is 0.05-0.10 mA for 80 μ diameter electrodes penetrating striate cortex, and 5-8 times greater for electrodes ~1 mm diameter placed on the pia mater. Intact macaques invariably display interhemispheric generalization for striate cortical stimulation, but three macaques with one hemisphere blinded by cutting optic tract did not generalize initially from the sighted to the blind hemisphere. However, in one macaque tested, thresholds were lower after bilateral blinding. The intact macaque can detect the following: 1) Elimination of 1-? pulses in a steady suprathreshold pulse train at 50 Hz. 2) Onset of stimulation at an electrode surrounded by four concurrently stimulated electrodes each 3 mm distant. Threshold at the central electrode is doubled when the surround is at 4 times threshold. 3) Changes of 5-10% in frequency (10-80 Hz) or amplitude (twice threshold) of continuing stimulation. 4) Whether pulses 2-10 times threshold are applied simultaneously or sequentially (>?0 msec separation) at loci 1-?0 mm apart. -- A single pulse decreases the threshold for detection of subsequent pulses for up to 200 msec. Stimulation for a few hours at 50 Hz, even at subthreshold currents with isometric biphasic pulses, can cause permanent threshold increases. Thus, although striate cortex is exquisitely sensitive to variation in temporal and intensive parameters of such artificial input, it may prove difficult to avoid deleterious effects from the protracted stimulation required for feasible prosthetic use. (Supported by NIH Contract No. 70-2279)

22.1 AFFERENT CONNECTIONS OF THE SUBSTANTIA NIGRA IN THE RAT. Ronald L. Smith, Eugene H. Strayhorn* and William R. Mehler*. Dept. of Anat., Sch. of Med., Univ. of Calif., San Francisco, CA 94122 and Neurosciences Branch, NASA Ames Research Center, Moffett Field, CA 94035

Stereotaxic lesions of the corpus striatum were placed in 25 rats sacrificed at intervals of 2 to 7 days. Striatal projections to substantia nigra (SN) were initially studied with Nauta variations and Fink and Heimer ('67) (F&H) techniques. A medial-lateral topology of the striato-SN projections comparable to that reported to exist in cat (Vonieda, '60) and monkey (Szabo, '62) is confirmed. Optimal F&H impregnation results were obtained at 4 days. In regions of terminal degeneration, dendrites of SN pars reticulata are literally outlined by degenerating bouton-like argyrophilic structures. Few axosomatic-like terminals appear. No terminal degeneration is evident in the pars compacta from our light microscopic studies. In some cases with or without cortical damage the pars compacta appears as an isolated clear zone without even degenerating passage fibers. Rat Golgi sections indicate that some dendrites of compacta cells extend into the pars reticulata, but the majority of dendrites, and the somata, of compacta cells are oriented horizontally and confined to the pars compacta.

Unilateral lesions of the corpus striatum were created in another series of rats surviving 2-6 days. They were perfused with glutaraldehyde and paraformaldehyde in cacodylate buffer. EM examination of normal SN contralateral to a lesion revealed that most synapses there are axodendritic, while only a small number of axosomatic synapses can be found. Rounded synaptic vesicles are most prevalent, but some synaptic profiles do contain elongated vesicles. EM evaluation still in progress of various stages of degeneration in SN on the lesion side has provided ultrastructural details confirming and supporting most of the conclusions from light microscopy studies. The source of afferent fiber input to the pars compacta remains to be established.

22.2 STRIATO-NIGRAL AND SENSORY INTERACTIONS IN CENTRUM MEDIANUM. G. Krauthamer and M. Dalsass*. Department of Anatomy, C.M.D.N.J. Rutgers Medical School, Piscataway, New Jersey 08854.

Cats, anesthetized with chloralose and immobilized with Flaxedil were used to study the modulation of polysensory neurons of Centrum medianum-Parafascicular complex (CM-Pfc) by caudate nucleus (Cd) and substantia nigra (SN). Stimulation of the lateral Cd generated a 300 msec. long postsynaptic inhibition of CM-Pfc neurons displaying sensory convergence properties. By contrast, stimulation of the medial Cd excited these same thalamic neurons at a mean latency of 25 msec. A mutual blocking interaction between somatosensory and medial Cd inputs was established by means of conditioning-test stimulus procedures. Stimulation of medial Cd generated maximal field potentials in the topographically corresponding nigral projection zones. Stimulation of this SN zone, like stimulation of medial Cd, also excited the polysensory neurons of CM-Pfc. Similarly, combined peripheral and nigral stimulation generated prolonged mutual blocking interactions. These results suggest a functional heterogeneity within the striato-nigral system. Medial Cd, SN, and sensory inputs compete for excitatory synaptic activation of CM-Pfc in contrast to the inhibitory input from lateral Cd.

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22.3 STRIATAL INPUTS TO PALLIDAL NEURONS. N.A. Buchwald, C.D. Hull, M.S. Levine* and D.R.G. Fuller*. Depts. Anat. & Psychiat., Mental Retardation Res. Ctr., NPI, University of California, Los Angeles 90024.

Analysis of intracellular records of caudate neurons indicates that the great majority of inputs to this structure are excitatory. Recent anatomical data provide a base for these findings. While the caudate receives direct inputs from cortex, thalamus and brain stem, the morphological data show that striatal outputs are few in number and restricted in site of termination. About 3% of striatal neurons are long axoned and these seem to terminate entirely in pallidum and substantia nigra. We have been interested in determining the characteristics of these output axons and their effects on pallidal neurons. Intracellular recordings in caudate neurons in response to antidromic stimulation of pallidum or nigra confirm the anatomical data for the low percentage of striatal efferents. Less than 5% of Cd cells penetrated gave secure evidence of antidromic invasion. On the other hand, stimulation of the caudate nucleus regularly evokes synaptic potentials in intracellularly recorded pallidal and entopeduncular cells (n=200) in cats; initial EPSP or EPSP-IPSP sequences in 70%; initial IPSPs in the other 30%. Thus, the excitatory caudatopetal inputs are converted into a spectrum of excitatory and inhibitory inputs at the pallidal level. These same pallidal neurons respond (with much longer latencies) to a variety of sensory inputs. Such interactions between striatal and sensory influences suggest a prime integrative role of the strio-pallidal system. Whether the caudate evokes IPSPs and EPSPs in the pallidum via separate striatal efferents or whether IPSPs evoked in pallidal neurons by caudate stimulation are induced by other mechanisms (e.g., excitation of the impaled neuron by a pallidal interneuron) cannot be answered as yet.

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22.4 ALTERATIONS IN SPONTANEOUS FIRING RATES OF CAUDATE NEURONS. M.S. Levine*, N.A. Buchwald, and J.R. Villablanca* (SPON: J.D. French). Depts. of Anat. & Psychiat., Mental Retardation Res. Cntr., NPI and Brain Research Inst., University of California, Los Angeles 90024.

Bilateral recordings of spontaneous firing patterns of single units in the caudate nuclei (Cd), precruciate cortices (PC) and ventrolateral nuclei of the thalamus (VL) were made in acute paralyzed cats. Mean interspike intervals (ISIs) computed for these units were averaged to produce a grand mean for all units. The mean ISIs were: 1353 msec for the Cds, 725 msec for the PCs, and 517 msec for the VLs. Unilateral surgical ablation of one caudate nucleus produced a significant slowing of the spontaneous firing rates of units in the remaining caudate (mean ISI = 6563 msec) when compared to values derived from intact cats. This asymmetry was specific to the caudate nucleus as there were no alterations in firing rates of PC (mean ISI = 1156 msec) or of VL (mean ISI = 525 msec) units. Previously, we reported that unilateral lesions in and around the nigrostriatal pathway resulted in a similar asymmetry; units in the caudate contralateral to the lesion fired more slowly (mean ISI = 4868 msec) than units in the ipsilateral caudate (mean ISI = 1211 msec). We have recently found that this asymmetry in caudate unit firing rates was abolished when the lesion in the nigrostriatal pathway was combined with an ipsilateral thalamic lesion. (Mean ISIs for units in two caudates were 3201 msec and 3244 msec.) Large unilateral thalamic lesions alone, however, produced no significant change in firing rates of caudate nuclei units (mean ISI = 2203 msec). These results provide data concerning possible neurophysiological alterations occurring during basal ganglionic diseases.

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22.5 THE INTERRELATIONSHIP OF DOPAMINERGIC AND CHOLINERGIC INFLUENCES IN THE EXTRAPYRAMIDAL SYSTEM OF THE SQUIRREL MONKEY. H.Warren Goldman, David Lehr*, Elliot Frank*, and Paul Casner*. Dept. Pharmacol., NY Medical College, Valhalla, N.Y. 10595.

The dense concentration of cholinergic neurons in extrapyramidal nuclei points to their importance in the physiological function of this system. Present concepts imply that cholinergic and dopaminergic neurons act antagonistically with acetylcholine stimulating and dopamine-supressing single unit discharge. In the present investigation, the acetylcholine-dopamine interrelationship was studied in intact, unrestrained squirrel monkeys which had been stereotaxically implanted with chronic cannulae with the tip directed at various basal ganglia nuclei. The introduction of carbachol (10ug) into the striatum caused abnormal movements contralateral to the site of drug application consisting of fine resting tremor, clonic seizure activity, tonic neck posturing and circling behavior. In addition, tonic deviation of the eyes and chewing and licking movements were frequently observed. Sialorrhea was seen in over 90% of the experiments. This entire spectrum of effects could be prevented by the prior intracerebral injection of atropine sulphate through the same cannula. In an attempt to intensify the effects of central cholinergic stimulation by selectively modifying dopaminergic influences, striatal dopamine was antagonized by synthesis inhibition and receptor blockade. Unexpectedly, pretreatment with either alpha-methyl-para tyrosine or haloperidol prevented the abnormal movements induced by carbachol without effecting the excessive salivation. These findings suggest that in the extrapyramidal system, cholinergic and dopaminergic stimulation may not necessarily exert antagonistic effects.

22.6 ACTIVITY OF BASAL GANGLIA, MOTOR CORTEX, AND CEREBELLAR NEURONS DURING SLOW AND RAPID LIMB MOVEMENTS. Mahlon R. DeLong and Peter L. Strick, Lab. Neurophysiology, NIMH, Bethesda, Md. 20014.

In monkeys trained to execute both slow and rapid arm movements, it was found (Science 179: 1240-1242, 1973) that more than half of the movement-related units recorded in the putamen discharged preferentially in relation to slow movements while only a few units discharged preferentially in relation to rapid movements. These findings were interpreted as lending experimental support to the view of Kornhuber (Kybernetic 8: 157, 1971) that the basal ganglia function primarily in the generation of slow movements. In the present study unit activity was recorded from the globus pallidus as well as the putamen, in order to determine whether the preferential relationship of units for slow movements is also found in this nucleus, which gives rise to the major output from the basal ganglia. Confirming the earlier observation, the majority of movement-related cells in putamen discharged preferentially during slow movements. In the globus pallidus, also, nearly half of all movement-related units (n=86) discharged preferentially during slow movements, and only a small number preferentially during rapid movements. A second aim of this study was to contrast basal ganglia activity with that in cerebellum and motor cortex in relation to slow and rapid movements. Nearly all of the movement-related units in the motor cortex (n=130) and cerebellar cortex (n=60) discharged in relation to both slow and rapid limb movements. Taken together, these findings lend further support to the hypothesis of a preferential role of the basal ganglia in the control of slow movements.

23.1 PHENTOLAMINE - AN ANTAGONIST OF CYCLIC AMP REGULATION OF NARCOSIS. Major L. Cohn and Marthe Cohn*. Dept. Anes., Univ. Pgh. Sch. Med., Pittsburgh, 15213

It is increasingly clear that cyclic AMP plays a specific role in the regulation of the duration of narcosis in vivo. Cyclic AMP has a dose-related regulatory effect on the duration of amobarbital-induced narcosis (Cohn et al., Neuropharm., in press). Furthermore, cyclic AMP regulates, in a dose-related manner, the duration of narcosis induced with other sedative, hypnotic, tranquilizer and anesthetic agents. The purpose of this research was to determine if the regulatory control of cyclic AMP may be altered by the administration of other agents. Sprague-Dawley male rats weighing 80-125.g were injected intraperitoneally amobarbital, 80 mg/kg. Upon the loss of the righting reflex, groups of rats were treated by intracerebroventricular (ICV) injections into the right ventricle. The ICV administration of catecholamines, biogenic amines, acetylcholine, γ-amino butyric acid, atropine, and histamine were without effect on the shortening of the duration of amobarbital-induced narcosis. The central administration of the analeptic drugs d-amphetamine, pentylenetetrazol, caffeine, theophylline, strychnine, and doxapram similarly failed to lessen the duration of narcosis, with the exception of picrotoxin. However, the antianesthetic effect of picrotoxin was associated at all dose levels with marked toxicity, including moderate-to-severe convulsions. Whereas propranolol did not alter the duration of amobarbital-induced narcosis, the central administration of the α-adrenergic blocking agent, phentolamine, prolonged the duration of amobarbital-induced narcosis and antagonized the antianesthetic effect of exogenously administered cyclic AMP in a dose-related manner. Further research is required to explain the mechanism of the inhibition of the antianesthetic effect of cyclic AMP by phentolamine.

23.2 OPPOSITE EFFECTS OF INTRAVENTRICULARLY INFUSED DOPAMINE AND NOREPINEPHRINE ON SHOCK-INDUCED FIGHTING. Mark A. Geyer* and David S. Segal. Dept. Psychiatry, Sch. Med., UCSD, La Jolla, 92037

Shock-induced fighting (SIF) between pairs of male rats was elicited by 1.0 mA scrambled shocks (0.5 sec every 7.5 sec). The number of attacks per 50 shocks was scored on 2 baseline days and 1 test day. One member of each pair, previously implanted with a cannula in the lateral ventricle, was infused intraventricularly for 1 hr at 20 µl/hr with 0.9% saline, 1.0, 3.0, or 6.0 µg/µl dopamine HCl (DA), or 0.5 or 2.0 µg/µl dl-norepinephrine HCl (NE) immediately before testing. At these doses, both DA and NE increase locomotor activity. Relative to saline-infused rats or baseline scores, animals infused with either dose of NE made significantly fewer attacks and often displayed supine submissive postures. In contrast, the central infusion of the lower doses of DA increased SIF.

Previous work indicated that DA-induced hyperactivity is mediated by the effects of DA at NE terminals (Physiol. Behav. 8:653, 1972). That 6.0 µg/µl DA produced no change may be attributable to the opposite effects of the direct and indirect actions of infused DA. After 5.0 mg/kg imipramine, which limits the indirect action by reducing uptake of DA into NE cells, 6.0 µg/µl DA increased SIF, while 2.0 µg/µl NE still reduced attacks. In rats pretreated with 250 µg 6-hydroxydopamine, which markedly increased SIF, NE, but not DA, reduced attack posturing. These findings suggest that SIF is mediated by a balance between dopaminergic and noradrenergic systems.

23.3 DIRECT ROLE OF DOPA IN THE CENTRAL NERVOUS SYSTEM. A. J. Vazquez, W. J. Giardina, Liliana Madrid-Pedemonte*, A. D. Mosnaim*, and H. C. Sabelli. Dept. of Pharm. The Chicago Medical School, Chicago, Illinois 60612.

In rabbits, L-DOPA (100 mg/Kg) reduced the amplitude of the slow component of visual evoked responses; this effect was reversed by pretreatment with α-methyldopa (MeDOPA). DOPA (150 mg/Kg) first (30 min) reduced and later (180 min) increased the exploration (single mouse) and the spontaneous activity of rats. In grouped mice, DOPA (150 mg/Kg) induced hyperactivity and reversed the sedation induced by Δ^9-tetrahydrocannabinol (Δ^9-THC) into aggressive excitement. DOPA (500 mg/Kg) also induced aggressive excitement. The peripheral decarboxylase inhibitor MK 486 (200-500 mg/Kg) blocked DOPA-induced reduction of exploration (single mouse), aggressiveness and jumping (grouped mice) and hyperactivity (rats). Thus, these DOPA effects are either due to peripheral formation of catecholamines (CA) or are prevented by excessive CA synthesis in brain. The central and peripheral decarboxylase inhibitor MeDOPA (500 mg/Kg) blocked DOPA-induced increase in exploration (single mouse) (indicating mediation by central or peripheral CA) and enhanced the aggressive excitement of grouped mice treated with DOPA or with DOPA + Δ^9-THC (suggesting that this effect is not mediated by CA). Since DOPA (150 mg/Kg) induced aggressive excitement in mice treated with reserpine, or with both MK 486 and MeDOPA, or with both reserpine and MeDOPA (but not in untreated or in MK 486 treated mice), this effect appears to be a direct central action of DOPA which is counteracted by central CA. The aggressive excitement induced by DOPA or by DOPA + Δ^9-THC was enhanced by 2-phenylethylamine (PEA) and reduced by atropine. DOPA (200 mg/Kg) increases PEA brain levels. These results suggest that some central effects of DOPA are not mediated by CA, and that DOPA interacts with endogenous PEA and acetylcholine.
(Supported by NIMH Grant MH-14110.)

23.4 RATS DO NOT EXPLORE AN OPEN FIELD BUT ARE ACTIVE IN HOME CAGES AFTER HYPOTHALAMIC INJECTIONS OF 6-HYDROXYDOPAMINE (6-OHDA). R.C.Young* and G.P.Smith. E.W.Bourne Behav. Res. Lab., Dept. of Psychiatry, N.Y. Hosp.-Cornell Med. Ctr., White Plains, New York 10605

6-OHDA was microinjected bilaterally into the anterior hypothalamus at the caudal edge of the optic chiasm at lateral or medial sites. Such injections decreased hypothalamic and forebrain norepinephrine but did not change striatal dopamine (Smith et al., Soc. for Neuroscience 10.4, 1972). Open field exploration was markedly decreased on days 1-9 postoperatively (p.o.) in 9 of 9 rats receiving anterolateral 6-OHDA and in 6 of 8 rats receiving anteromedial 6-OHDA. Vehicle injections at these sites did not reproduce this effect. Decreased open field activity was not the result of recent surgery because anterolateral 6-OHDA markedly decreased exploration in 7 of 7 rats first tested 30 days p.o. and in 4 of 7 rats first tested 70 days p.o.. In contrast, home cage photocell beam crossings/ 24 hours had returned to preoperative values by day 4 p.o. in 6-OHDA injected rats. D-amphetamine (2 mg./kg., i.p.) increased open field exploration in 6-OHDA injected rats. These data suggest that: (1) the deficit in open field exploration is related to hypothalamic or forebrain catecholaminergic damage by 6-OHDA because it was not produced by vehicle injection; (2) this hypokinesia occurs despite an intact nigrostriatal dopaminergic pathway; and (3) this hypokinesia, like previously reported deficits in motor performance of visual placing and active avoidance training, is critically dependent on stimulus conditions.

23.5 SURVIVAL OF FREE-RANGING PRIMATES AFTER 6-HYDROXYDOPAMINE. D.E.Redmond,Jr.* and J.W.Maas. Caribbean Primate Center, NIMH, Bethesda, 20014, and Yale College of Medicine, New Haven, Conn.

Intraventricular 6-hydroxydopamine (6-OH-DA) or vehicle was administered to eight free-ranging Macaca mulatta to study the effect of monoamine depletion on the social behavior and relationships of primates exposed to natural social and environmental stresses. 30 mgs. were injected in divided doses through implanted cannulae. (Previous studies of another Macaque species in the laboratory had confirmed significant norepinephrine depletions of 70% or more in 9 of 14 brain areas with sacrifices 16 days after 31 mgs.) The animals were released after treatment on the 80 acre island where they had lived for many years before a three week captivity. Intensive social observations during the first 14 days after treatment revealed slowness in returning to the social group, deficits in social and self-grooming, threats, attacks, and total social initiatives by the treated vs. the sham-treated or "field" controls. Failures by 6-OH-DA treated animals to avoid punishment from other animals were noted as well as significant deficits in positive approach behaviors. All animals have now survived 14 months in this setting. Intermittent behavioral and monthly census observations have revealed no gross abnormalities in behavior after one year, with definite recovery from most changes observed initially. Primates treated with intraventricular 6-OH-DA appear to show more initial deficits in social behavior in a free-ranging setting than in a small enclosure, but compensate thereafter biochemically or behaviorally for any monoamine deficits which remain.

23.6 EATING INDUCED BY DIAZEPAM IN RATS. Roy A. Wise and Vivien Dawson*. Dept. Psychol., Sir George Williams Univ.,Montreal.

Diazepam is a minor tranquilizer thought to act centrally on monoamine systems. Two actions of the drug have been reported in rats. First, it causes sedation, presumably by an action on a nor-adrenergic arousal system, and second, it causes disinhibition of punished behavior, apparently by an action on a serotonergic substrate. We have studied a third action of the drug: the arousal of eating in sated rats. Low doses (0.5-5.0 mg/kg) cause dose-related eating which lasts on the order of 20 min. The eating is motivated and not stereotyped; the animals will perform learned responses for food if food is not readily available. The response is specific to eating: drinking is not induced, and lever press is not sustained by water reward. The eating is terminated by feedback and not by passive drug metabolism: stomach loads of food but not water inhibit the eating, but delays in food availability do not decrease meal size or duration. It seems that the eating cannot be attributed to disinhibition from some form of emotional control: familiar foods are eaten, in both home and test cages and in both day and night. Amount eaten is not predictable from emotionality scores in open field tests. Diazepam-induced eating does not undergo tolerance as do effects linked with nor-adrenergic actions of the drug, however, 6-OHDA treatment which caused major depletion of nor-adrenaline and dopamine (but did not disrupt normal eating) eliminated diazepam-induced eating. Large lesions of the medial and dorsal raphe nuclei did not alter the diazepam-induced eating.

23.7 TEMPORAL SUMMATION AND THE NEUROPHARMACOLOGY OF THE REWARD EFFECT IN SELF-STIMULATING RATS. C. R. Gallistel and Don Edmonds.* Dept. Psychol.,Univ. of Penn., Phila. 19104.

Rats ran a runway for a single train of brain stimulation reward. Running speed was plotted as either a function of the number of pulses in the train or as a function of the current intensity. Running speed rose from nothing to asymptote in 0.1-0.6 log units. When the interval between pulses was increased, the point at which this rise occurred shifted systematically toward higher values. The magnitude of this shift provides an index of the decrease in synaptic summation produced by the increase in the interval between pulses. A variety of variables (priming; hurdles; curare; disease) that reduce the rat's ability or inclination to run produced no shift toward higher values--only a decrease in asymptotic running speed. AMPT also produced a decrease in asymptotic running speed but no shift toward higher values, suggesting that the effect of this catecholamine synthesis inhibitor on self-stimulation performance is not mediated by an effect on synaptic processes in the reward system. The paradigm is suggested as an approach to the problem of distinguishing between drug effects on a specific system and drug-induced impairments of ability or willingness to perform.

23.8 EFFECT OF SEROTONIN MANIPULATIONS ON ACTIVITY OF RATS. Barry L. Jacobs, Edwin E. Eubanks* and William D. Wise*. Dept. Psychol., Princeton Univ., Princeton, NJ 08540.

The notion that serotonin, acting as a mammalian CNS neurotransmitter, has sedative or sleep-inducing properties derives primarily from studies utilizing systemic injections of the serotonin precursor, 5-hydroxytryptophan, or the tryptophan hydroxylase inhibitor, p-chlorophenylalanine. In the present study, the effects of various other pharmacological manipulations of the serotonergic system were investigated in relation to tilt cage activity of adult male albino rats. Injections of methiothepin, a presumed serotonin receptor blocker, in doses as low as 1 mg/kg i.p. significantly decreased activity, whereas the fast-acting tryptophan hydroxylase inhibitor, 6-fluorotryptophan (115 mg/kg i.p.) had no significant effect on tilt cage activity. When dietary l-tryptophan content was varied in animals deprived of food for 2 or 9 days, moderate amounts of tryptophan (20-40 mg/kg) produced no change in activity, whereas larger amounts (90-160 mg/kg) consistently resulted in small increases in activity. When l-tryptophan was injected (25 & 150 mg/kg i.p.) it produced no significant effect, however, in animals pretreated with a MAO inhibitor (50 mg/kg pargyline) l-tryptophan produced a 15 fold increase in activity. This latter effect could be blocked by pretreating with p-chlorophenylalanine. In conclusion, these data provide no support for the notion that serotonin has sedative or sleep-producing effects, and indicate that under certain circumstances, serotonin may exert an excitatory effect on gross behavior.

23.9 EFFECTS OF Δ^9-TETRAHYDROCANNABINOL (THC) ON SOCIAL BEHAVIOR OF GROUP-CAGED MACAQUES. E.N. Sassenrath, J.D. Cowen* and G.P. Goo*. Dept. Behav. Biol., Sch. Med., Univ. Calif., Davis, 95616.

Δ^9-THC was given orally in preferred food to individual members of pre-established cage groups of M. mulatta and M. irus at levels of 0.6, 1.2, and 2.4 mg/kg. Spontaneous and elicited group social interaction was assessed at 1, 3, 5 and 24 hours after drugging via a repertoire of 64 behaviors. Drug effects varied among the 15 Ss tested, reflecting individual differences in social roles and normative behavioral profiles.

In M. mulatta cage groups, drugged subordinates received more aggression, responding with more avoidance or mild submission but decreased intense submission or fear behaviors: M. irus subordinates showed increased anxiety behaviors when drugged. Drugged dominant group members showed less aggression and competition for preferred food. All subjects showed marked increases in passive affiliation (huddling, embracing) with favorite cagemates, though active affiliation (play, grooming) was eliminated in most drugged Ss. Stereotypy (pacing, flipping) was greatly increased in Ss which normally showed these behaviors alternating with periods of sleep, or inactive withdrawal. One S showed apparent hallucinatory attack behavior. Chronic daily drugging over a ten-day period increased withdrawal, with a delayed increase in disturbance behaviors (exploration, pacing, self-biting) in some Ss. The observed effects of Δ^9-THC on social behavior are consistent with neuroendocrine effects of the drug, particularly on pituitary-adrenocortical activity and catecholamine metabolism.

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23.10 MURICIDAL BLOCK PRODUCED BY DELTA-9-TETRAHYDROCANNABINOL. Paul D'Encarnacao and Rod Bowers*. Dept. of Psych., Memphis State Univ., Memphis, TN 38152.

Muricide, mouse killing, has been reported as being an aggressive type of behavior (Karli, 1956). It is also known that the selective action of antidepressants, amphetamines, and some antihistaminics block the killing response (Harovitz, Piala, High, Burke, and Leaf, 1966). The study was designed to show that 1) THC will produce a blockade of muricidal aggression, 2) THC could possibly be associated with the antidepressant class of drugs. Male albino rats, which were known mouse killers, were tested for five trials on three consecutive days to demonstrate consistent attack and kill latencies. The animals were then injected with a single dose of delta-9-THC, 1, 2, 3, or 4 mg/kg. The results of the study indicate that THC in low dosages produces no blockade whatsoever; medium dosages may produce a partial effect; high dosages, 4 mg/kg, produces a complete blockade for 15 minutes. One of the more interesting features of the study was the residual effects of the THC on mouse killing which lasted for several days after. It would be interesting to associate THC's effect as being an antidepressant one, but the evidence is not conclusive, at present.

23.11 BEHAVIORAL AND NEUROPHYSIOLOGICAL EFFECTS OF METHIONINE AND ITS METABOLITES. J. M. Beaton*, G. V. Pegram*, R. J. Bradley*, and J. R. Smythies* (SPON: E.C. Crosby). Neurosciences Program and Dept. of Psychiatry, Univ. of Ala. in Birmingham, Alabama 35294.

Pollin et al (Science, 133: 104,1961) reported that the administration of l-methionine plus a monoamine oxidase inhibitor (MAOI) induced an acute florid psychotic reaction in 40% of schizophrenics tested. This finding has been repeated and confirmed by several other groups using methionine alone and with a MAOI. The mode of action of l-methionine in brain is unknown, but may be via one or more of three mechanisms: the excess methionine (1) may lead to the production by transmethylation of some psychotomimetic methylated derivative of dopamine or serotonin or (2) could result in an increase in the levels of a metabolite of methionine (e.g. homocysteine, cystathionine or cysteine) or (3) may affect the cellular uptake of other amino acids. In order to test the first two hypotheses betaine (another methyl donor), l-methionine, l-methionine plus l-serine, l-cysteine, l-serine and saline have been examined on a discriminated Sidman avoidance schedule in rats and on the electroencephalogram of mice. Daily injections of 250 mg/kg of these compounds were administered for at least 21 consecutive days. Schedule performance in the rat and sleep/wake cycles in the mouse were monitored during this period and compared to controls. The results indicated that only methionine had significant behavior disrupting effects. This disruption was removed by the addition of serine, suggesting that the methionine effects may have been due to the metabolite homocysteine.

23.12 RAT SCOTOPHOBIN CAUSES TEMPORARY DARK AVOIDANCE IN ROACHES. Helene N. Guttman and Michael Hoffman*. Dept. Biolog. Sci., Univ. Illinois at Chicago Circle, Chicago, 60680

Scotophobin is a pentadecapeptide produced in dark-preferring rodents and goldfish concomitant with acquisition of dark avoidance. Synthetic rat scotophobin (=SRS gift of Prof. G. Ungar) has been shown by our group, and others, to induce temporary dark avoidance in rodents and fish. We now show that SRS induced temporary dark avoidance in the roach, Leucophaea maderae. Roaches from a departmental colony were kept in darkened cages at 20-23°C. Larvae of different stages were segregated according to size and winged adults segregated according to sex. The roach shuttle box consisted of a central light compartment (64 mm long) which, on one end terminated in a dark compartment (70 mm) and on the other in a starting compartment (35 mm) which was not open for free traverse after the roach undergoing test emerged into the light compartment. Each test consisted of two 180 sec. trials during which we measured latency (traverse time from starting to dark compartment) and total dark time/trial. Roaches were tested 6, 24 and 48 hrs. after 40 µl injections of SRS of 0.001-1.0 µg. The last larval stage is most susceptible to the effects of SRS: striking dark avoidance is observed when one measures either latency or total dark time/trial is evaluated. The effective dose range is the same as for rodents. Our observation of a difference in sensitivity of various larval stages suggests that SRS action in roaches involves stage-dependent insect hormones. That an invertebrate reacts to an exogenously-supplied mammalian behavioral effector suggests an early evolution of this learning-related property.

23.13 EFFECT OF BEHAVIORAL TRAINING ON TRANSFER RNAs OF GOLDFISH BRAIN. B.B. Kaplan, J.C. Dyer and J.L. Sirlin. Dept. Anat., Cornell Univ. Med. Coll., New York, N.Y. 10021.

Goldfish were trained in a new swimming skill by attaching a polystyrene float to their venter (Shashoua, Nature 217:238, 1968). Transfer RNA (tRNA) was extracted from whole brains from 0-8 hr after a 4 hr training session. Total amino acid acceptor capacity measured in vitro with ^{3}H- or ^{14}C-protein hydrolysates showed no appreciable change in tRNA from trained fish (T) compared with free-swimming (FS) controls. However, of 13 individual amino acid acceptor activities tested, leucyl-tRNA from T increased progressively from 2-8 hr post-training. No changes were observed in leucyl-tRNA from FS, sham-operated (SO) or whirlpool-stressed (WS) controls. Kinetics of aminoacylation for these 13 activities showed a corresponding increase only in leucyl-tRNA from T but not from SO or WS controls. Methylated albumin column co-chromatography of ^{3}H- and ^{14}C- leucyl -tRNA of T and SO indicated that the increased activity of T was confined to late eluting fractions. Reversing the label gave identical results. Higher resolution co-chromatography of these samples using a reversed-phase system (RPC-5) then showed that the increase was in 2 minor isoaccepting species. No changes were observed between leucyl-tRNAs obtained from livers of T and SO. The data suggest that this tRNA species may limit the rate of brain translation and implicate protein synthesis in the molecular events that follow training. (Supported by PHS grants MH-45139 and 5 SO1 RR05396-11).

23.14 **NEURAL PROCESSES INVOLVED IN THE ALTERATION OF BRAIN COMPOSITION BY ENVIRONMENTAL SENSORY STIMULATION.** **Roger N. Walsh, Robert A. Cummins* and Otto Budtz-Olsen*. Dept. Psychiat, Sch. Med., Stanford, 94305 and Dept. Physiol, Queensland Univ., Australia.**

An ever growing number of brain changes following exposure to an enriched as opposed to a stimulus deprived environment are being identified but as yet no mechanism capable of satisfactorily explaining the mediation of these changes has been advanced. A major mechanism may be arousal since it is particularly elicited by environmental complexity and its properties are such as might offer an explanation of several hitherto puzzling findings. The arousal reaction is characterized initially by extreme generalized cortical activity but with repeated presentation of an initially novel stimulus habituation occurs and the general activity is replaced by a more localized discrete cortical analysis. Thus exposure to a complex environment might be expected to result in habituation both within and across days and this has been observed behaviorally. This may explain the finding that brief daily exposures are as effective as exposure throughout the whole 24 hour period and that whereas the whole cortex shows initial biochemical and anatomical responses these are maintained only in the occipital region. As might be predicted enrichment effects occur in dark reared and blind subjects and factors other than enrichment which elicit arousal, e.g. amphetamines, social grouping and the dark phase of the diurnal rhythm have been found to induce brain changes similar to, and to augment those of, environmental complexity.

Several methods of testing the arousal hypothesis will be discussed.

Futhermore arousal may be important for several other forms of environmental sensory stimulation e.g. light versus dark rearing, social grouping, handling; suggesting that a common mechanism may mediate the effects of what have previously been thought of as several seperate and discrete fields of research.

24.1 EFFECTS OF PENTYLENETETRAZOL ON APLYSIA NEURONS: INDUCED OSCILLATIONS AND ALTERED CURRENT-VOLTAGE RELATION UNDER VOLTAGE CLAMP. R.J.David* and W.A. Wilson* (SPON: G.G.Somjen) Epilepsy Ctr.,VA Hosp., Durham, NC.

Certain Aplysia neurons normally exhibit slow membrane potential oscillations which give rise to bursts of action potentials. Voltage clamp studies have shown these bursting neurons to exhibit a region of negative slope resistance in their current-voltage (I-V) curves which, like the bursting firing pattern, is abolished by cooling. Other studies have shown that silent Aplysia cells can be made to exhibit bursting by treatment with pentylenetetrazol (PTZ). We studied the interaction of PTZ and temperature on bursting and non-bursting neurons using the voltage clamp technique to obtain I-V curves. The giant cell R2 is normally silent at 15°-20°C. Warming the cell to 23°-28° induced bursting accompanied by appearance of negative resistance in the I-V curve. Application of 25 mM PTZ to cell R2 at 16° induced bursting, again accompanied by appearance of negative resistance. Cooling the cell to 6° did not diminish either of these PTZ-induced effects, but 10 minutes washing with normal seawater did reverse both effects. Cell L2, normally a bursting neuron with a negative resistance region in its I-V curve, was silenced and the negative resistance abolished by cooling from room temperature to 10°. Subsequent application of 25 mM PTZ returned the cell to an autoactive state; it fired steadily, or, when a steady 3nA hyperpolarizing current was injected, fired in bursts. At this point the neuron again displayed negative resistance; this I-V curve effect and the bursting behavior were reversed by washing. Previous work has demonstrated a voltage sensitive current source responsible for negative resistance in warm bursting cells. Our results strongly suggest that this same current source can be activated in some normally silent cells by warming or by treatment with PTZ; similarly, when this current source is inactivated by cooling in bursting cells, it can be reactivated by PTZ.

24.2 VOLTAGE CLAMP ANALYSIS OF PENTYLENETETRAZOL EFFECTS UPON EXCITABILITY IN MOLLUSKAN NEURONS. T. L. Williamson* and W.E. Crill. Depts. of Medicine and Physiology & Biophysics. Univ. of Washington, Seattle, 98195.

The effects of the convulsant drug pentylenetetrazol (PTZ) were studied in molluskan neurons using both current and voltage clamp techniques. PTZ was selected because it causes changes in the intracellularly recorded responses similar to those recorded from cat motoneurons during penicillin induced segmental myoclonus. Isolated circumesophageal ganglia of Archidoris monteryensis were bathed in artificial sea water at 10°C and pH 7.3. Single neurons were impaled with two microelectrodes. When the perfusate contained 110-140 mM PTZ episodic prolonged depolarizations with superimposed high-frequency spikes appeared within a few minutes. These effects of PTZ are a direct action on the neuron membrane since the response could be evoked by intracellular stimulation and was recorded in cell bodies isolated from their synaptic input by a ligature. Voltage clamp data were obtained from the same cells before and after perfusion with sea water containing PTZ. The major changes induced by PTZ were in g_K and the g_A of Connor and Stevens (1971). PTZ causes a 50-70% decrease in peak g_A; a shortening of the time constant for inactivation of g_A; a 15-20 mV depolarizing shift in the equilibrium potential for g_A and a 10-15 mV depolarizing shift in the curve relating the steady state inactivation of g_A to membrane potential. PTZ also caused a 33-66% decrease in $\bar{g}_K$ and a 20-25 mV depolarizing shift in the equilibrium potential for g_K. The smaller and more rapid inactivation of A currents is one factor that could be responsible for the PTZ induced bursting. Supported by USPHS Grants NS 07987; NS 05082 and GM 02103.

24.3 EFFECT OF DIPHENYLHYDANTOIN ON THE ACTIVITY OF SELECTED ENZYMES IN CHRONIC ISOLATED CEREBRAL CORTEX OF CAT AND ENZYME ACTIVITIES AND HYPEREXCITABILITY IN THE CHRONIC ISOLATED CEREBRAL CORTEX OF MONKEY. John R. Green, Lawrence M. Halpern and Jeffrey A. Amick-Corkill*. Dept. Neurosurgery, Dept. Pharm., Sch. Med. UW, Seattle, 98195

The effect of diphenylhydantoin on enzyme activities related to transmitter functions (monoamine oxide (MAO), acetylcholine esterase and choline acetylase; a membrane-related enzyme sodium-potassium dependent adenosine triphosphotase and an energy process-related enzyme succinic dehydrogenase) on hyperexcitability monitored physiologically is to attenuate the overshoot of MAO activity and the hyperexcitability normally found in these preparations. The above enzymes were also evaluated in the chronic undercut cerebral cortex of monkey, and only MAO was found to be significantly increased over control values. The increased MAO activity when compared to that of tyrosine hydroxylase activity, where no activity changes between control and undercut cortex was detected, suggests a net deficit in cortical inhibitory substances which could be causally related to the hyperexcitable state.

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24.4 ASTROGLIA IN ALUMINA EPILEPTIC FOCI. A. Basil Harris. Dept. Neurol. Surg., Sch. Med., Univ. Wash., Seattle, Wash., 98195

Astrocytes show the most marked change of all cells in the alumina epileptic focus. This gliosis was studied for comparison with non-epileptic scars. Light and electron-microscopic studies were done in the Macaca mulatta at intervals after the onset of seizures following intracortical alumina injection. The presence of experimentally induced foci, or absence in controls, was established by transdural electrocorticography under anesthesia. Fixation was performed either with formalin ammonium bromide, Cajal stains, or buffered aldehyde intervascularly followed by osmium immersion for electron microscopic studies. In control scars, Cajal stains showed a small rim of reactive astrocytes, but in animals with alumina foci, the gliotic reaction extended far beyond the cortical injection site. Ultrastructural alterations consisted of increased astrocytic cytoplasm containing filaments and increased numbers of filament attachment plaques to the inner aspect of the plasma membrane, glycogen and microtubules. Connections to other astrocytes by tight junctions, electrotonic, and dense desmosome junctions were profuse in the experimental groups. These were also seen in controls, but less often. Astrocytic membrane connections of the desmosome type of junction to dendrites were also observed. These contacts, astrocyte to astrocyte and astrocyte to neural elements, may represent the anatomical counterpart for the electrical syncytium proposed by some physiologic studies.

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24.5 CORTICAL EFFECTS OF DISCRETE EXTRADURAL COBALT IMPLANTATIONS IN THE CAT. G. R. Hanna and L. F. Stewart*, Dept. of Neurology, University of Virginia School of Medicine, Charlottesville, Virginia 22901.

By means of an extradurally-implanted recording electrode fabricated with cobalt wire, we have developed a method of causing discrete reproducible cortical epileptic lesions, and simultaneously recording their electrical activity. The contact point is the smooth cross-sectional "end" of the fine cobalt wire, which produces prompt focal epileptic effects when implanted over pericruciate cortex. Typically, the first day post-operatively, there are seen motor movements consisting of repeated series of multiple jerks associated with stereotyped polyspike discharges on electrocorticogram. These effects are unlike the repetitive single jerks or corticographic events seen after comparable areas of cortex have been frozen (Stalmaster and Hanna, Epilepsia, 1972, 13:313). Histologically, in such lesions the superficial cortical layers are relatively spared, with necrosis spreading laterally through the middle layers. The lesions resemble an inverted mushroom, rather than the simple craters produced by freezing. These results suggest a physiologic difference between the epilepsy of freezing and that of cobalt, and the character of the lesions suggests a selective toxic effect, the nature of which remains to be elucidated.

24.6 SPONTANEOUS SEIZURES PRODUCED BY LONGTERM REPETITIVE AMYGDALOID STIMULATION IN RATS. John P.J. Pinel, A. G. Phillips, R.F. Mucha* and G. Deol*. Dept. of Psychology, Univ. of British Columbia, Vancouver 8, B. C.

Daily amygdaloid stimulation administered to rats at current levels initially too low to produce a motor response but high enough to produce an after discharge (AD) resulted in the progressive development and intensification of stimulus-induced epileptic activity (kindling). In contrast to previous studies, however, stimulation was continued long after the point where the exacerbation of motor seizures (MSs) seemed complete. After the appearance of full MSs (about 10 days), there was a gradual decrease in the day-to-day variability of MS patterns and of MS and AD durations until the within subject variability was negligible for most subjects (about 35 days). Furthermore, both the establishment of stability and the initial kindling of full MSs was found to be more rapid and more complete in subjects receiving high levels of stimulation (1 sec, 60 Hz, 500 μA) as opposed to those subjects receiving stimulation at current levels just above the AD threshold. We have stimulated several animals for up to seven months and found that with continued stimulation there was a development of interictal spiking which was associated with a decrease in the day-to-day stability of MSs and ADs. Two of these animals eventually developed spontaneous MSs which were present a month after cessation of stimulation. Thus, the kindling paradigm not only produces a valuable technique for seizure research where stable baselines are essential, but it also provides a model for studying the step-by-step development of a genuine epileptic syndrome characterized by spontaneous, recurrent behavioral seizures.

24.7 DETERMINATION OF CRITICAL MASS FOR ACETYLCHOLINE INDUCED SEIZURE ACTIVITY. John H. Ferguson, David R. Cornblath*, and Pamela A. Havre*. Division of Neurology, Case Western Reserve U. Sch. Med., Cleveland, Ohio 44106.

A study was carried out to determine the minimum surface area of intact and undercut cat suprasylvian gyrus activated by acetylcholine(Ach) necessary to produce seizure activity. It was hypothesized from other studies that this area should be 2x2mm or greater. Pieces of filter paper 1x1mm, 2x2mm or 4x4mm were wetted with 0.125ul,0.5ul or 2ul respectively of from 0.5 to 4% Ach in neostigminized Elliotts solution. In any experiment, each filter paper had the same amount of Ach/mm^2 (3.4 to 27.2 nanomoles/mm^2). The results showed that:1. The probability of seizure occurring does not depend on which portion of suprasylvian gyrus is activated(arbitrarily divided into posterior, middle and anterior thirds). 2. There is a greater probability for seizure with a 4x4 than with a 2x2 and with a 2x2 than with a 1x1 mm area. 3. As the time after undercutting increases, the probability for seizure with a smaller area of activation increases. 4. In intact preparations, the probability of seizure increases for small areas of activation as the percentage of Ach increases. 5. No lower limit of area for surface activation has been determined in these experiments. Seizure will occur with 1x1 activation in intact preparations if percentage of Ach is sufficient(4%) or with 1% in undercut preparations if time after undercut is long enough(40 days). It is concluded that the critical mass for Ach induced seizure is inversely proportional both to percentage of applied Ach and to time after undercutting. No absolute minimum mass could be determined in these studies and the original hypothesis is disproved.

24.8 CHOLINERGIC MECHANISMS OF HIPPOCAMPAL EPILEPSY IN CATS. Thomas L. Babb, Carlos A. Ottino and Paul H. Crandall*. Dept. Neurosurg., Sch. Med., UCLA, Los Angeles, 90024

Acute focal epilepsy with behavioral components similar to psychomotor epilepsy was established in unanesthetized cats by inducing changes in acetylcholine (ACh) activity in ventral hippocampus. Field potentials were recorded with macroelectrodes or 30 micron diameter wire microelectrodes which also detected extracellular action potentials from hippocampus near an implanted injection cannula. Small injections (10 micrograms) of ACh with neostigmine (Neo) or Neo alone induced complex focal seizure discharges within 10 minutes, accompanied by facial twitches, head turning, pupillodilation, and meowing. Neurons initially increased in firing rate but later fired in a pattern often related to the seizure waves. Some neurons were activated while others were inhibited for the duration of a seizure complex. Subsequent injection of the anti-muscarinic, atropine, increased the seizure duration and severity. Atropine alone (80 micrograms) produced focal spiking (latency 8 minutes) and clinical seizures (latency 12 minutes). The anti-nicotinic, d-tubocurarine, did not appear to affect ACh-induced seizures. Comparable or greater doses of l-arterenol or normal saline were ineffective. The lack of post-synaptic competition of ACh by atropine or curare suggests a pre-synaptic action by ACh. Possibly excess levels of ACh result in depolarization block of the terminals of recurrent collaterals of pyramidal cells, which would prevent excitation of basket cells in the recurrent collateral inhibitory circuit.

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24.9 THE ROLE OF CHOLINERGIC PATHWAYS IN PETIT MAL EPILEPSY. Jay D. Glass, Gerhard H. Fromm*. Dept. Pharmacology, Neurology, U. of Pittsburgh, School of Medicine, Pittsburgh, Pa. 15261

A conditioning stimulus to the coronal gyrus in the chloralose anesthetized cat is known to inhibit the response of some cells in the trigeminal nucleus to maxillary nerve stimulation. This corticofugal inhibitory effect upon the trigeminal nucleus is reduced by anti-petit mal drugs such as trimethadione (Tridione) and ethosuximide (Zarontin). Imipramine (Tofranil), a drug previously used in the treatment of depression and enuresis, was found to have a similar effect. Initial clinical trials have shown that imipramine also lowers the incidence of petit mal and minor motor seizures in some patients as predicted by the animal experiments. These results confirm the validity of using the corticofugal inhibition of the trigeminal nucleus as a model for examining the mechanisms that might be involved in the production and control of petit mal seizures. We have now found that atropine has a biphasic effect upon this corticofugal inhibition. One to five minutes after the i.v. injection of 0.04 mg of atropine, the inhibition of the trigeminal unit response was reduced, similar to the effect produced by the anticonvulsant drugs previously studied. However, 15-20 minutes following the atropine administration, the corticofugal inhibition had not only returned, but was actually enhanced. In subsequent experiments, a 1-2% solution of atropine was applied topically to the coronal gyrus and the initial reduction in corticofugal inhibition did not occur; although the subsequent enhancement was present. The results indicate that the anti-petit mal drugs may be exerting their effect subcortically on structures that receive cholinergic corticofugal inhibitory projections.

24.10 URIDINE CONTROL OF NUCLEOSIDE INCORPORATION IN PENICILLIN INDUCED EXPERIMENTAL EPILEPSY (RANA CATESBIANA). Charles A. Roberts, Norman R. Kreisman, and Mary Waltman*. Depts. of Anatomy and Physiology, School of Medicine, Tulane University, New Orleans, La. 70112

Recent studies indicate that uridine behaves as an anticonvulsant and is selectively incorporated into nuclear neuronal RNA of primary and mirror foci in penicillin induced epilepsy (Brain Research, in press). The present study was designed to evaluate potential anticonvulsant effects and selective incorporation of other nucleosides (H^3-adenosine, H^3-guanosine, H^3-cytidine and H^3-thymidine) into epileptic regions of the frog cortex (3 hr. in vivo labelling) using ECoG and autoradiographic techniques. None of these nucleosides induced appreciable ECoG changes in either control or experimental animals. No change was observed in autoradiographic localization patterns or grain intensity in relation to epileptogenic regions. In contrast, nucleosides injected in combination with non-radioactive uridine (which has an anticonvulsant effect) resulted in marked alterations in their incorporation into neuronal nuclei of epileptic regions as compared to control regions. RNase and DNase digestion procedures indicate that H^3-nucleosides (including H^3-thymidine) injected in combination with uridine were incorporated totally into nuclear neuronal RNA of both control and epileptic regions. These results and other studies (anticonvulsant drugs and antimetabolite studies) in our laboratory suggest that uridine plays a central role in the control of nucleoside metabolism and subsequent brain function in normal and epileptic animals.

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24.11 CAN LOCALIZED SEIZURE ACTIVITY BE A CONDITIONED SIGNAL? AN EXPERIMENTAL STUDY OF EPILEPTIC AURA. Emil C. Zuckermann and Martha E. Wolski.* Dept. of Neurology Yale Univ. School of Medicine. New Haven, 06510.

Focal sensorial seizures perceived by patients as "auras" suggest that the brain possesses the ability to integrate localized cortical paroxysmal discharges; but the important disorganization of neuronal circuitry generated by seizure argues against this possibility. In order to assess this experimentally, cats were prepared with chronic electrodes implanted in muscles of the fore legs in specific thalamic nuclei and primary neocortical receiving areas. Conditioned reflexes either classical or operational were obtained to rhythmic flashes or cliks - and then the animals were trained to respond in the same way to direct electrical stimulation of thalamus or neocortex. When the intensity of the stimulation was increased till a threshold for focal seizures - after a slightly longer training - similar effects were obtained. In each animal, differentiation and extinction proved that local seizure activity had indeed a signaling value independent from the electrical stimulation which preceded it. The facts suggest that seizure activity limited to neocortex or specific thalamus does not disturb memory printing and retrieval or learning ability. The brain uses the "paroxysmal" messages in a similar fashion to normal messages, but can clearly distinguish between seizure and non-seizure stimulations of the same points.

24.12 **IMMUNOLOGICALLY INDUCED EFFECTS ON EEG AND CONDITIONED BEHAVIOR IN RATS.** **Stephen E. Karpiak, Florry P. Bowen, and Maurice M. Rapport. Depts. of Neurology and Biochemistry, Columbia University College of Physicians and Surgeons, and Division of Neuroscience, N. Y. State Psychiatric Institute, New York, N. Y. 10032.**

In a previous study intraventricular injection into rabbits of antiserum to rat synaptosome membrane fraction (Anti-SMF) produced recurrent epileptiform activity bilaterally in the caudate nucleus (Karpiak, Bowen and Rapport, 1973). We have now tested this antiserum in rats by monitoring: a) electrophysiological changes and b) behavioral effects. Baseline EEG recordings were taken from electrodes implanted bilaterally into the calvarium as well as from depth electrodes in the caudate and hippocampus. Twenty rats were injected with 25 μl of Anti-SMF on each of two consecutive days. Beginning on Day 2, groups were tested on 3 behavioral tasks: 2 caudate-mediated tasks involving body orientation (spontaneous and conditioned alternation) and one control task (reported to be unaltered by caudate lesions). It was found that rats injected with Anti-SMF developed recurrent spiking bilaterally in the caudate and showed alterations only on the caudate-mediated tasks. Rats either injected with anti-erythrocyte serum or uninjected had normal EEGs and behavioral responses. It is concluded that antibodies directed against the synaptosome membrane fraction are capable of producing behavioral alterations as well as relatively long-lasting epileptiform activity in rats.

This work was supported in part by grants from the NIH (NS 05184; MH-10315) and the Epilepsy Foundation.

24.13 THE ANTICONVULSANT CARBAMAZEPINE (TEGRETOL®)-A PILOT STUDY. Allan S. Troupin*, John R. Green. Dept. Neurosurgery, UW, Seattle, 98195

In preparation for a large double blind crossover study of the anticonvulsant properties of Carbamazepine (Tegretol®) a pilot study was performed on 12 patients with partial seizures. The principle aims of the pilot study were: 1. to establish dosage equivalency between Carbamazepine and DPH; 2. to develop a successful crossover routine for Carbamazepine to DPH and vice versa; and 3. to estimate the gross effectiveness of the agent as an anticonvulsant. The patients were all on DPH alone at the beginning and all were hospitalized for one week for study of the crossover to Carbamazepine. This was monitored with multiple determinations of serum levels of both agents. The patients were then followed for 4 months as outpatients on Carbamazepine, after which the reverse crossover was again performed in the hospital. The results were: 1. Dose equivalency for similar anticonvulsant effect was 3:1 for Carbamazepine to DPH. 2. A successful crossover routine was developed and will be illustrated. 3. Carbamazepine is a successful anticonvulsant when administered alone in that 10 patients showed an improvement in seizure frequency in comparison to DPH. 2 showed no improvement and none showed a deterioration. One patient was removed from the study because of a rash. 3 patients were not able to continue on Carbamazepine because of side-effects - unsteadiness, eye movement disturbances, etc. despite adequate or improved seizure control. Carbamazepine is clearly an effective anticonvulsant of the same order of magnitude as DPH, but a further definition of its value awaits the full double blind study now in progress.

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24.14 EFFECTS OF DIAZEPAM AND PHENOBARBITAL ON SPONTANEOUS ELECTRICAL ACTIVITY OF THE LIMBIC SYSTEM AND CORTEX IN MAN. Jeffrey P. Lieb*, Mary A. B. Brazier and Paul H. Crandall+. Div. Neurosurg. & Dept. Anat., Sch. Med., UCLA, Los Angeles, 90024.

Ongoing studies comparing the anticonvulsive actions of diazepam with those of phenobarbital are being carried out on patients with intractable temporal lobe epilepsy who are clinically resistant to medication and are therefore candidates for diagnostic and therapeutic surgery. Electrodes are implanted stereotactically and left in place for a period of 3-4 weeks. The EEG is recorded bilaterally from many deep sites including the amygdala, hippocampus, and hippocampal gyrus as well as from dural leads. After a period of withdrawal from previous medication, i.v. diazepam 20 mg is administered on a single occasion and its action studied. Next day, the same drug is given p.o. (20 mg) for 3 days. A similar program is followed with phenobarbital each patient receiving both as the test drug, the sequence being randomly alternated across patients. In general it appears that diazepam may have its maximal effect in the limbic system in contrast to phenobarbital with its preferential action on the cortex. The tests in use include spectral analysis with distribution of power across frequencies, with a standard statistical test of changes at each frequency band as well as across the total spectrum. Diazepam has a more marked effect on the power at all frequencies than phenobarbital whether given i.v. or orally. Spike rate is also counted and appears more effectively depressed by diazepam than by phenobarbital. Diazepam i.v. has an immediate but shorter lasting anticonvulsant effect than phenobarbital although its tranquillizing action persists for a longer time.

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25.1 RESPONSES OF SLOWLY AND RAPIDLY ADAPTING MECHANOSENSITIVE AFFERENTS ASSOCIATED WITH STIFF HAIRS ON THE MONKEY'S FACE.
S. Starkman*, R. Sumino*, B. Munger*, and R. Dubner. (Spon: R.E. Beitel). NIDR, NIH, Bethesda, and M. S. Hershey Medical Center, Hershey, Pa.

The responses of stiff facial hairs to mechanical and thermal stimuli were studied in anesthetized monkeys by dissecting fine strands of the infraorbital nerve. Slowly adapting (SA) responses were histologically verified to be associated with (1) one or two non-sinus hairs located above the lip, and (2) single sinus hairs located above the lip and lateral to the nose and lip. No touch domes were found in association with any of these hairs. Sinus hairs associated with SA units were found to have only intraepithelial and palisade endings. The mean conduction velocity (C.V.) of SA units was 36.5±8.4 m/sec and they exhibited either regular(10-35/sec), irregular (0.1-5/sec) or no spontaneous activity. In response to maintained displacement of the hair or adjacent skin,SA units usually had very regular firing rates >20/sec which persisted for more than 90 sec. Von Frey thresholds to mechanical displacement were never higher to hair movement than to stretching or displacement of the area adjacent to the hair follicle. SA units were directionally-sensitive; vertical movement of the hair into the skin and deflection in one direction evoked the best responses. SA units responded weakly and variably to rapid cooling steps and their activity was suppressed by noxious heat (>45°C) stimulation. Rapidly adapting units sometimes were associated with one or two stiff hairs and mean C.V. was 43.0±9.1 m/sec. They exhibited on and off responses only during movement of the hair and their von Frey thresholds were >50 mg. We conclude that (1) slowly adapting responses are associated with non-sinus hairs in addition to sinus hairs located above the lip; (2) palisade and intraepithelial endings in sinus hairs are the terminals of rapidly adapting and regular firing, slowing adapting mechanosensitive fibers, respectively; and (3) the intraepithelial endings probably innervate Merkel cell-neurite complexes.

25.2 DISCHARGE VARIABILITY OF SLOWLY ADAPTING MECHANORECEPTIVE AFFERENT FIBERS INNERVATING GLABROUS SKIN OF SQUIRREL MONKEY AND RACCOON HAND. Lillian M. Pubols and Benjamin H. Pubols, Jr. Dept. of Anatomy, Hershey Medical Center, Pennsylvania State University, Hershey, Penna. 17033

Discharge properties of slowly adapting cutaneous mechanoreceptors innervating the glabrous skin of the hand of the squirrel monkey and raccoon have been examined by single unit recording from fibers of the median and ulnar nerves, and the spinal dorsal columns. Modality specificity, absolute indentation thresholds, receptive field areas, and relationships between mechanical stimulus onset velocity and discharge rate in single fibers of the squirrel monkey are all similar to those reported previously for the raccoon (Pubols, Pubols, & Munger, Exp. Neurol., 1971, 31, 165-182). In the squirrel monkey, however, 95% of units are very slowly adapting (VSA, discharge to static displacement continues at a high rate for > 60 sec.), whereas in the raccoon 95% of units are moderately slowly adapting (MSA, discharge ceases within 10 sec.). No units displayed a resting discharge, and all have single, spot-like receptive fields. Using the coefficient of variation as an index of interspike interval variability, it was found that raccoon MSA show significantly greater variability (Mdn ≃ .80) than do raccoon VSA (Mdn ≃ .25). Squirrel monkey VSA showed a homogeneous population with Mdn ≃ .40, and a range of ≃ .10 to .95. The few squirrel monkey MSA fell within the distribution of the VSA. It does not appear possible, in terms of interspike interval variability, or of any other criteria which have been proposed, to dichotomize squirrel monkey glabrous skin VSA into types analogous to the slowly adapting Types I and II of mammalian hairy skin (Chambers, Andres, Duering, and Iggo, Quart, J. Exp. Physiol., 1972, 57, 417-445). (Supported by USPHS grants NS-06371 and NS-38,829)

25.3 CODING OF MECHANICAL STIMULUS VELOCITY AND INDENTATION DEPTH DURING STATIC DISPLACEMENT OF SQUIRREL MONKEY AND RACCOON SLOWLY ADAPTING MECHANORECEPTORS IN GLABROUS SKIN. Benjamin H. Pubols, Jr. and Lillian M. Pubols. Dept. of Anatomy, Hershey Medical Center, Pennsylvania State University, Hershey, Pennsylvania 17033.

First-order afferent fiber discharge rate during static displacement of slowly adapting cutaneous mechanoreceptors in glabrous skin of squirrel monkey and raccoon hand is a monotonic, increasing function of depth of skin indentation. Analyses of the total numbers of impulses per trial indicate that depth of skin indentation, up to 960 μ, is coded with the greatest reliability within the first 1000 msec. The nature of the best fitting function (highest r), however, varies (a) from unit to unit, (b) with the length and temporal locus of the measurement period, and (c) with prior onset ramp velocity. Using a set of standard conditions (msecs. 100-500 of static displacement, following 100 μ/msec. onset velocity), the ratio of units for which linear, as opposed to logarithmic functions provided the best fit was 3:2 for squirrel monkeys, and 1:3 for raccoons. Few units had power functions as best fits in either species. Differences between r's for different functions within the same unit, however, were often trivial. Response rate during static indentation is strongly influenced by onset velocity. For at least the first 500 msec., discharge rate is positively related to onset velocity. After 3-5 sec., however, the relationship becomes an inverse one in some units. These findings may call for re-interpretation of results of previous investigations in which stimulus rise time was held constant, thus completely confounding indentation depth and velocity. (Supported by USPHS grants NS-06371 and NS-38,829)

25.4 CAPACITY OF HUMANS AND MONKEYS FOR DISCRIMINATION AND IDENTIFICATION OF VIBRATORY STIMULI DELIVERED TO THE HAND. Robert H. LaMotte. Dept. Physiol., Sch. Med., The Johns Hopkins University, Baltimore, Maryland 21205

Human and monkey subjects were trained to make a successive discrimination between vibratory stimuli differing in either frequency or amplitude. At 30 Hz, the Weber fraction for amplitude was constant at about 0.10, for amplitude standards ranging from 35 to 154 microns. Subjective amplitude matches between 30 Hz and various test frequencies were obtained. The frequency difference limen (DL) at 30 Hz, with test frequencies subjectively matched for amplitude, was 1.5 to 2.5 Hz. Random variations in amplitude of test frequencies 20% above and below the point of subjective amplitude equality had little effect on the frequency DL. Lowering the amplitude of all frequency stimuli in equal proportion to levels as low as two or three times detection threshold also had little or no effect on the frequency DL. These results were identical for both monkey and human subjects.

The frequency DL remained the same with or without the presence of a standard, indicating the excellent capacity of both monkey and human to make a two-category identification of sine-wave frequencies from memory. In order to study this capacity further, subjects were trained to identify frequency-without a standard-in a three-, four- or five-category choice task with the requirement that the subject select the correct response key corresponding to each test frequency. Within the frequency range from 10 to 50 Hz, the maximum number of stimulus categories which could be perfectly discriminated was four or less.

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25.5 RESPONSES OF FACIAL CUTANEOUS THERMOSENSITIVE AFFERENTS IN THE MONKEY TO NOXIOUS HEAT STIMULATION. R. Sumino*, S. Starkman*, and R. Dubner. National Institute of Dental Research, NIH, Bethesda, 20014.

The responses of cold and warm fibers to noxious heat stimulation (>45°C) were studied by recording discharges from fine dissected strands of the infraorbital nerve in anesthetized rhesus monkeys. Cold fibers (mean conduction velocity (C.V.) ±S.D.=8.7±3.7 m/sec, n=74) whose firing rates were increased during cooling and suppressed during warming, often responded initially to thermal stimuli above 55°C. Repeated noxious heat stimulation sensitized these fibers and lowered their thresholds to below 50°C. Limited noxious heat stimulation did not alter the linear response curves to rapid cooling steps. Repeated stimulation, however, reduced the linear response range by suppressing the initial transient response to larger cooling steps. In some cases, repeated noxious heat stimulation ultimately suppressed completely the response to cooling even though consistent, repeatable firing rates to noxious heating persisted. Warm fibers (C.V.±S.D.=3.3±1.9 m/sec, n=26) whose firing rates were increased during warming and suppressed during cooling, often responded to temperatures above 45°C. The response profiles to noxious heat displayed higher frequency initial transients than those to warming, although firing rates were reduced or suppressed completely after 2-3 sec of stimulation. Repeated noxious thermal stimuli raised the threshold to constant temperature stimuli from 30° to 40°C and depressed the responses to rapid warming steps in the same temperature range; responses to noxious thermal stimuli above 45°C were not changed. The data suggests that warm fibers conducting in the A delta range transmit impulses centrally during the presence of noxious thermal stimuli while cold fibers initially are inactive in the critical temperature range of 45-50°C.

25.6 DEPRESSION OF Na+-K+ PUMP AS A TRANSDUCTION MECHANISM OF THERMORECEPTORS. David C. Spray* (SPON: F.A. King). Depts. Physiology and Neuroscience, U.F. Coll Med, Gainesville, Fla. 32601.

Frog cold receptor activity is modified by sympathetic stimulation, adrenergic and cholinergic agonists, and cold acclimation. The sensitivity of the receptors and the modulation of this sensitivity by these agents might be explained on the basis of a very large surface area-to-volume ratio in a very small nerve ending. Frog skin contains freely ending receptors which meet these criteria. Oubain applied to the inner skin surface in concentrations as low as 10^{-8} g/ml caused a marked discharge of thermoreceptors, followed by a depressed sensitivity to thermal stimuli. Furthermore, current applied across the skin could be correlated with the magnitude of cooling necessary to produce the same discharge in the receptors. A plot of $-1/\Delta T$ vs. ln i was linear, with a slope corresponding to the temperature coefficient traditionally assigned to the metabolic sodium-potassium pump. These findings constitute evidence in favor of a reduction in pump activity as a mechanism for thermoreceptor stimulation. (Supported by NIMH training grant).

25.7 DIFFERENT EFFECTS OF OUABAIN ON RAT CUTANEOUS MECHANO- AND THERMORECEPTORS. Fr.-K. Pierau* and D. Carpenter. Neurobiology Department, Armed Forces Radiobiology Research Institute, Bethesda, Md. 20014

In Aplysia neurons a ouabain-sensitive electrogenic Na^+ pump tends to make each cell more excitable on cooling, whereas a greater temperature dependence of $g_{Na}+$ than g_K+ acts to increase excitability with warming. In cat motoneurons, excitability is decreased on warming as a result of a greater temperature dependence of g_K+ than $g_{Na}+$. In an attempt to determine which, if any, of these mechanisms operates in specific thermosensitive afferents, we have studied the effects of local ouabain infiltration on temperature dependent activity of afferents isolated from the rat pudendal nerve. The temperature of scrotal skin was controlled using a metal thermode containing circulating water at different temperatures. Three types of fibers were identified. 1. Mechanoreceptors showed no change in maintained discharge but a marked decrease in the transient discharge on cooling after ouabain. 2. Warm sensitive afferents showed an increase in both transient and maintained discharge on warming after ouabain. 3. Cold sensitive afferents became, if anything, more transiently responsive to cooling after ouabain, although occasionally the steady discharge in the warm increased. These results suggest that the transient discharge on cooling of mechanoreceptors reflects the temperature dependence of an electrogenic Na^+ pump. Furthermore, it appears that an electrogenic pump modulates the sensitivity of warm receptors. However, an electrogenic pump does not appear to be the mechanism imparting cold sensitivity to specific thermoreceptors.

25.8 SPINAL CORD DORSAL HORN CELLS SUBSERVING PERIPHERAL NERVE STIMULATION IN GALLUS DOMESTICUS. J.A. Holloway. Department Physiol., Sch. Med., Howard Univ., Wash., D.C. 20001

Dorsal horn cell (DHC) response patterns to electrical stimulation of the lateral femoral cutaneous (LFCN) and peroneal nerves (PN) were studied in lightly nembutalized chickens. Some units were observed that did not respond to electrical stimulation at intensities up to 40V with pulse frequencies below 30/sec. At pulse frequencies of 30/sec, unit response was evoked. Fifteen percent of the units studied were both excited and inhibited ipsilaterally, whereas only five percent were contralaterally excited and inhibited. Fifty six percent of the DHC studied were driven by single shock stimulation at threshold for both the LFCN and PN. As the stimulus activated more of the A and finally the C fibers, the train of spikes increased in duration, but the frequency in the initial burst remained the same. The firing frequency that occurred in the early part of the burst ranged between 120 and 400/sec. A silent period and prolonged discharge were not seen even following unmyelinated fiber stimulation. The minimum latency of response ranged from 10 to 30 msec with a mean of 18.2 msec. Conduction velocities of the largest fibers were calculated to be 26-32 m/sec with a mean of 29 m/sec. (Supported in part by NSF Grant GB 34294)

25.9 ORGANIZATION OF THE DORSAL SPINAL GRAY OF CAT AS STUDIED BY QUANTITATIVE STIMULATION OF THE TYPE I RECEPTOR SYSTEM. Daniel N. Tapper and Paul B. Brown. Cornell University, Ithaca, New York 14850.

In anesthetic-free decerebrate-low spinal (lumbar-1 transection) animals many spinal neurons in laminae III-VI of the first sacral segment discharge in response to single action potentials evoked exclusively in single Type I axons. Afferent inflow was controlled by using just-threshold mechanical stimulation of single Haarscheiben (Hs) in the skin receptive field, by carefully monitoring evoked activity in the intact cutaneous nerve (the posterior femoral cutaneous nerve), and by average response computing of activity occurring in the first sacral dorsal rootlets. As judged by poststimulus time histograms of one hundred stimuli spaced at least 3 seconds apart, a variety of evoked discharge patterns were produced ranging from: (a) a simple short latency impulse with or without postresponse inhibition; (b) prolonged inhibition of ongoing activity; (c) a bursting discharge; and, (d) long latency bursting activity preceded or followed by inhibition. This variety of response patterns can be elicited from the same cell depending upon which Type I axon is used to introduce the single spike into the central network. These discharges reflect interactions within the network of which the recorded cell is a member and the specific connectivity of the afferent channel with the network. Although many of these neurons have monosynaptic contact with at least some Type I fibers of their cutaneous receptive fields, central delay measurements from many single fibers reveal that each neuron is connected to the periphery by way of multiple, serial and parallel pathways.

The work was supported principally by U.S.P.H.S. Grant NS-07505.

25.10 RESPONSES OF DORSAL HORN CELLS TO GRADED NOXIOUS AND NON-NOXIOUS STIMULI. Andrew C. Browe* and Donald D. Price. Dept. Physiol., Medical College of Virginia, Virginia Commonwealth Univ., Rich. Va. 23298.

Over 150 units within L-7 dorsal horn layers IV-VI were studied in unanesthetized spinal cats. Each cell was characterized in terms of its responses to electrical stimulation of cutaneous A and C fibers, graded intensities of radiant heat, and 3 types of mechanical stimuli - touch, pressure (compressing skin with flattened forceps), and pinch (with serrated forceps). This analysis yielded 5 classes of units distinguished by the range of mechanical stimuli over which they responded: (1) touch, (2) touch-pressure, (3) touch-pressure-pinch, (4) pressure-pinch, (5) pinch only. Cells in (1) and (2) were usually insensitive to heat or responded to non-noxious skin temps. (35-42°C). These cells typically had only A fiber input and were found primarily in layer IV. Cells in (3) responded over temperature ranges of 40-47° C, had both A and C fiber input and were located in layers IV-VI, but primarily V. Cells in (4) and (5) responded between 44-48°C, many had both A and C input, and most were found in layers V-VI. No cells were found that responded to heat and not mechanical stimuli. Heat sensitive cells had a 4-8°C range of response and response thresholds that were independent of rate of heat transfer (mcal/cm^2/sec) as indicated by their strength-duration curves. Response thresholds were distributed continuously over a 36-50°C range with 2 modes, one in the warming and the other in the nociceptive range. As skin temperature increased from pain threshold (43°C) to 48°C there was a progressive recruitment of higher threshold units as well as increased firing in lower threshold layer V-VI cells. Some units responding to warming and others responding to noxious heat projected in DLC. These results indicate an important recruitment principle related to nociception. (Supported by NIH grant NS 10251-01.)

25.11 Somatotopic Representation of Hindlimb Skin in Dorsal Horn of Cat. Paul B. Brown and Jannon L. Fuchs* Neurological Unit, Boston State Hospital, Boston, Mass. 02124

Cats were decerebrated and spinalized at T_{12} under halothane anesthesia, and anesthetic was subsequently discontinued. Initial anatomical identification of spinal segments was verified by mapping the dermatomes of their dorsal roots. Single units responding to light touch were recorded from segments L_4-S_2 inclusive, using stainless steel microelectrodes. Most units were found in laminae IV-VI, although some were located in laminae I-III. Cutaneous projection maps revealed an orderly shift of receptive fields along the known dermatomal trajectory from L_4 through S_2: from lateral flank, down the lateral hindlimb, to foot, up the medial leg, across the perineum and onto the proximal tail. The area of skin represented in a single dorsal horn segment is larger than the dermatome of that segment's dorsal root. At a given antero-posterior level in segments L_4-S_1, more proximal leg areas are represented in the lateral dorsal horn and more distal leg areas are represented medially. Toe projections are limited to L_6 through S_1. Segment S_2 is devoted to perineal and tail regions. At a given antero-posterior level, cells located along lines normal to the dorsal surface of the dorsal horn have similar receptive field locations.

25.12 SOMATOTOPIC ORGANIZATION OF EXTERNAL CUNEATE NUCLEUS IN ALBINO RATS. T.D. Parker*, S.R. Campbell* and W.I. Welker. Lab. of Neurophysiology, Univ. of Wisconsin, Madison, Wis., 53706.

Sensory circuits from muscles and tendons to the cerebellum are essential for motor control. Yet, information about details of patterns of projections within these circuits is limited. We mapped the sensory projections from individual muscles of the forequarter to the external cuneate nucleus (EC). Activity of single units in EC was recorded by tungsten-ball microelectrodes in rats anesthetized with sodium pentobarbital. Musculature of the arm, shoulder, neck and thorax was exposed. Individual muscles were stimulated by punctate pressure with fine wires, or by stretching them by moving limbs or pulling tendons. Only stretch-activated units from ipsilateral forequarter muscles were found in EC. No units were activated by cutaneous stimulation. Every unit in EC responded tonically as long as its activating muscle was stretched. Of 244 units recorded in EC, 149 (61%) were activated by gentle natural stimulation of only a single muscle. Remaining units (N=95) had receptive fields only identified by general location (i.e., neck, shoulder) and were usually, but not always, small, deep-lying or inaccessible muscles. The pattern of projections of individual forequarter muscles in EC was somatotopically organized, with the neck represented rostrolaterally, the thorax laterally, the shoulder, arm and forearm successively more caudomedially, and the wrist and hand muscles most caudoventromedially. There was no overlap of projections from these several body segments. Adjacent cells recorded from a single electrode location in EC were activated from different muscles. Histological reconstruction revealed that when the electrode passed from EC into adjacent trigeminal, cuneate or gracile nuclei, receptive fields shifted from muscle bellies to either cutaneous, or deep non-muscular tissues (N=298). (Supported by USPHS grants 5326, 6625 and 46,838.

25.13 RESPONSE PROPERTIES OF NEURONS IN THE TRIGEMINAL NUCLEUS EXCITED BY THE LINGUAL NERVE. M.A. Biedenbach. Dept. of Physiology, University of Washington, Seattle, Washington 98195

The aim of this study was to determine how sensory input, evoked by both weak and noxious (intense) mechanical stimulation of the tongue, is processed in subregions of the trigeminal nucleus (TN). In cats, paralyzed and anesthetized with chloralose, the brain stem was exposed dorsally for unit recording. TN units responsive to electrical stimulation of the lingual nerve (LN) were tested for mechanosensitivity. Units responsive to light tactile stimuli were further tested with mechanically generated sine wave and step functions. The unit population was divided into those caudal and those rostral to the obex. Both populations contained units responding to 1) light tactile tongue stimulation, 2) intense to noxious mechanical stimulation but not to light touch, 3) electrical LN excitation but not mechanical tongue stimulation (although some of these last had tactile fields on the external face). Unit types showed overlapping response latencies, but short latencies predominated for tactile tongue receptors, and long latencies for units excitable only electrically. Only a fraction of the tactile receptors entrained to 1-100 Hz sine wave stimulation, and these were located in the rostral population. Units requiring intense tongue stimulation were more frequent in the caudal population. The effect on the rostral population of tractotomy near the obex will be described. (Supported by DE 02152).

25.14 ABSOLUTE AND DIFFERENTIAL SENSITIVITIES TO TOUCH STIMULI AFTER SPINAL CORD LESIONS IN MONKEYS. Charles J. Vierck, Jr., Dept. of Neuroscience, University of Florida College of Medicine and Veterans Administration Hospital, Gainesville, FLA. 32601.

Concurrent two-choice and go-no-go procedures were used to measure difference thresholds (DLs) for discrimination of touch intensities and absolute thresholds (RLs) for detection of light tactile stimuli. Macaca speciosa monkeys were trained to push a manipulandum with their left hand if touched on the sole of either foot with a von Frey hair calibrated at 7.1 grams (the standard stimulus); if a lighter hair was applied to either foot (the comparison stimulus), the animals received food reward for responding to the manipulandum on the right. DLs were tracked by varying the intensity of the lighter stimulus in blocks of 50 trials so that threshold performance (75% correct responses) was bracketed as frequently as possible. RLs were determined by the method of limits, interspersing trials with very light hairs (starting at 2 mg), and increasing the intensity on successive RL trials until the animal responded to either manipulandum within 2 sec of contact; threshold was defined as 50% correct responses.

In 3 animals, RLs were not affected, even transiently, by ipsilateral dorsal column lesions or subsequent dorsolateral column lesions on the same side. DLs were elevated significantly by dorsal column lesions but recovered to control levels after months of testing. Additional dorsolateral column section reinstated the DL deficits, but recovery was seen again with extensive testing. (Supported by NIH grants NS 07261 and FR 00421).

26.1 FLUOROMETRIC ASSAY OF DOPAMINE WITH FLUORESCAMINE. Kazuhiro Imai*, Stanley Stein*, Peter Böhlen*, and Sidney Udenfriend. Roche Institute of Molecular Biology, Nutley, New Jersey, 07110.

A new fluorometric assay for dopamine is presented based on the reaction with fluorescamine, a reagent which forms intensely fluorescent products with primary amines. The reaction proceeds within seconds at alkaline pH and excess reagent is hydrolyzed within a minute. Both the reagent and its hydrolysis products are nonfluorescent. Assay of dopamine in brain was carried out as follows. Tissue homogenate was extracted with 0.4 N perchloric acid. Catecholamines were adsorbed onto alumina and eluted with 0.2 N acetic acid. An aliquot was applied to a 0.6x8 cm column of Aminex AG 50W-X2 equilibrated with 0.15 M phosphate buffer, pH 6.5. Stepwise elution was performed with 10 ml of equilibration buffer, 1 ml of water and 20 ml of 2 N hydrochloric acid. Dopamine appeared after norepinephrine in a 4 ml fraction. A 0.2 ml aliquot was added to 1.3 ml of 0.15 M sodium phosphate buffer, pH 8.5. Fluorescamine dissolved in acetone (15 mg/100 ml) was added and mixed immediately. Fluorescence was measured at 390 nm excitation and 475 nm emission. The sensitivity of this procedure is 100 picomoles/ml. This compares favorably with the trihydroxyindole (THI) method, in which the lower detection limit is about 500 picomoles/ml. The fluorescamine technique is faster and simpler than the THI method. By concentrating the hydrochloric acid extract and performing the fluorescamine reaction in smaller volumes, it should be possible to measure less than 100 picomoles of dopamine in a single sample of tissue. When the fluorescamine and THI procedures were compared on tissue extracts, dopamine gave values about 20% higher by the fluorescamine technique. Preliminary attempts have been made to automate the final detection step.

26.2 REGULATION OF CATECHOLAMINE SYNTHESIS IN RAT BRAIN SYNAPTOSOMES. Robert L. Patrick* and Jack Barchas, Department of Psychiatry, School of Medicine, Stanford, California, 94305.

Catecholamine synthesis in synaptosomal preparations of rat striatum, cortex and brain stem was investigated. The striatum had the highest activity and cortex the lowest. ^{3}H-Tyrosine equilibration between tissue and incubation medium was completed within two minutes at 37°. The apparent K_m for tyrosine of tyrosine hydroxylase and of the overall catecholamine synthetic pathway were both approximately 5 x 10^{-6} M. The following amines were found to inhibit striatal dopamine synthesis: dopamine, 50% inhibition at 10^{-6} M; noradrenaline, 50% inhibition at 10^{-5} M; and serotonin, 30% inhibition at 10^{-5} M. Increasing the potassium concentration in the medium from 5 to 55 mM caused a release of amines into the medium, but did not affect synthesis. No increase in dopamine synthesis could be demonstrated with the addition of the synthetic tyrosine hydroxylase cofactor, $DMPH_4$ (2-amino-6,7-dimethyl-4-hydroxy-5,6,7,8-tetrahydropteridine). At $DMPH_4$ concentrations above 0.1 mM synthesis was inhibited, with 50% inhibition occurring at 6 x 10^{-4} M. These results suggest that even though exogenously added amines can inhibit catecholamine synthesis, the basal synthesis rate in isolated striatal synaptosomal preparations may not be regulated by end-product inhibition.

26.3 CNS INHIBITORS OF DOPAMINE-β-HYDROXYLASE. F. Christine Brown and Marie DeFoor.* Brain Research Institute, University of Tennessee, Memphis, Tennessee, 38105

Using a recently developed assay procedure [Molinoff et al., J. Pharmacol. Exp. Ther., 178:425, 1971: Bonnay et al., Fed. Proc., 29: 278, 1970], we have studied the properties of dopamine-β-hydroxylase (DBH) in rat brain extracts. In aqueous or buffered extracts, the enzyme is inhibited by an endogenous inhibitor(s). These inhibitors appear to have properties similar to those described for an analogous inhibitor isolated from bovine adrenals (Duchs and Kirshner, Biochim., Biophys. Acta. 236:628, 1971). They are heat stable, but lose activity upon dialysis apparently because protein has a stabilizing effect. Inhibitory potency is lost if preparations are allowed to stand longer than 48 hours, even at -20°. Preliminary experiments suggest that brain contains at least two kinds of inhibitors, one of which is copper sensitive and one which does not respond to copper. Partially purified DBH from bovine adrenals is not inhibited by dilute brain extracts. In any case, an activity overshoot occurs when the CNS inhibitor of the partially purified enzyme is nullified by dilution or by copper.

26.4 DOPAMINE -B- HYDROXYLASE FROM ADRENAL CHROMAFFIN GRANULES: EVIDENCE FOR A COMMON GLYCO-PROTEIN SUBUNIT STRUCTURE FOR SOLUBLE AND MEMBRANE-BOUND FORMS. Haryey B. Pollard, Nina M. Chace*, and Joseph T. Coyle* National Institutes of Health, Bethesda, Maryland, 20014

Dopamine-B-hydroxylase (DBH) catalyzes the biosynthesis of noradrenalin in chromaffin granules and adrenergic synaptic vesicles . Following hypotonic lysis of intact granules approximately half of the DBH activity is released in a soluble form. The remainder , bound to the granule membrane, can be released only by detergents. The molecular basis for the existence of two enzyme forms is not known, though it might be anticipated that either the enzymes are different, or than binding could be a membrane property. To examine the first alternative we have compared some physical and chemical properties of soluble and membrane-associated DBH by disc electrophoresis in SDS. Purified, soluble DBH is found to be a PAS-positive glycoprotein with a subunit molecular weight of 62,500. Purified chromaffin granule membranes, prepared by cycles of hypo-and hyper-tonic shock and equilibrium banding at density 1.12 g cm^{-3} , were found to have a glyco-protein component which co-electrophoresed with purified DBH at several gel concentrations. The membrane was found to contain at least 9 other protein components, as well as at least 3 other glycoprotein components. These findings were unaffected by delipidation to remove glycolipids from membranes. These data suggest that both membrane-bound and soluble forms of DBH have similar glyco-protein subunit structures when compared by electrophoresis in SDS. It is therefore likely that binding of DBH to membranes may depend on other membrane components.

26.5 THE RELATIONSHIP AMONG MULTIPLE FORMS OF MONOAMINE OXIDASE. Jean C. Shih* and S. Eiduson. Dept. Psychiat. and Biol. Chem., NPI, UCLA, Los Angeles, Calif. 90024.

Previous reports from our laboratory indicated that rat brain mitochondrial monoamine oxidase (MAO) can be solubilized and separated into several forms. By agarose column (Bio-Gel A 1.5 m) chromatography, 2 fractions A and B were separated (J. Neurochem., in press). Upon rechromatographing A on an agarose column, no dissociation occurred. If B is rechromatographed on an agarose column, it aggregated to A and also dissociated to D. The mol. weight of A was approximately 1.5×10^6. B was 400,000. D was 40,000 or smaller, Using Sephadex-electrophoresis, 2 fractions (I and II) were obtained. If fraction I is put on an agarose column, IA and IB are obtained; IA had mol. wt. of 1.5×10^6, IB was about 40,000 or smaller. If II is rechromatographed on an Agarose column, depending on the concentration of the sample, different fractions of MAO possessing different mol. weights were obtained.

IIA and IIC were obtained if a concentrated sample was used; IIA had molecular weight of 1.5×10^6 and IIC had molecular weight of 400,000. If a diluted sample was used, IIA and IIB was obtained. IIA had molecular weight of 1.5×10^6, whereas IIB was 40,000 or smaller. If an MAO active fraction is run in the presence of 8 M urea or 6 M Guanidine chloride, 2 fractions A and D were obtained, A had mol. wt. of 1.5×10^6 and D had molecular weight of 40,000 or smaller. This result indicated that A was not an aggregate of B. From these results, we concluded that B is an intermediate form of MAO which can either aggregate or dissociate. It would appear that A is an aggregate of B. However, since Sephadex-electrophoresis showed that A consisted of at least 2 species, and also that A was still observed in the presence of 8 M urea and 6 M Guanidine chloride, we concluded that A may also contain a separate form of MAO.

26.6 EFFECT OF AMANTADINE ON THE STIMULATION INDUCED RELEASE OF H^3-NOREPINEPHRINE BY THE SYMPATHETIC NERVE TERMINALS OF THE RAT IRIS. Catherine Mytilineou* and Robert E. Barrett. Columbia University, New York, N.Y. 10032.

Preganglionic stimulation of the superior cervical ganglion of the rat resulted in release of previously administered H^3-norepinephrine (NE) from the iris of the stimulated side. When a high dose of amantadine HCl (50 mg/kg., i.v.) was injected 15 min. prior to the stimulation, the release of H^3-NE was completely prevented. A lower dose of amantadine (10 mg/kg, i.v.), on the other hand, resulted in a more pronounced release. Similar results were obtained with a high and low dose of desmethylimipramine (DMI, 20 mg/kg and 2 mg/kg, i.v.). The greater release after low doses of amantadine and DMI can be explained by blockade of reuptake of H^3-NE released by the adrenergic nerve terminals of the iris. In separate experiments amantadine in a high dose did not inhibit the normal release of H^3-NE over a period of 4 hours, but it did significantly inhibit the uptake of H^3-NE in the iris and the heart. The preganglionic fibers synapse in the superior cervical ganglion with both principal neurons and the inhibitory interneurons. The interneurons are known to be very resistant to various adrenergic drugs. To determine whether the high doses of amantadine and DMI blocked the reuptake of dopamine (DA) released by the interneuron during stimulation (and thus made more DA available at the receptor sites), we blocked the DA receptor with phentolamine (15 mg/kg, i.v.). When the DA receptor was blocked the release of H^3-NE by preganglionic stimulation after a high dose of amantadine was greater than in control animals. We suggest that uptake blockers, such as amantadine and DMI in high concentrations, inhibit the uptake of DA released by the interneuron. This can result in continued inhibition of the principal neuron, thereby preventing the stimulation induced release of NE. (Supported by PHS Grant NS 05184).

26.7 EXOCYTOSIS AND ENDOCYTOSIS IN THE ISOLATED ADRENAL PERFUSED WITH HORSERADISH PEROXIDASE. J.A. Thomas*, N.B. Thoa*, J.L. Costa* and I.J. Kopin. Lab. of Clinical Science, NIMH, Bethesda, Maryland 20014.

Isolated adrenal glands were perfused retrogradely with either normal Krebs-Ringer solution (KR), 15 mM carbachol (Cch) or 8 mg/ml horseradish peroxidase (HRP). Effluents were collected and each gland analyzed by subcellular fractionation and sucrose density gradient centrifugation according to a modified method of Winkler et al. (Naunyn-Schmiedebergs Arch. Pharm. 273: 43-61, 1972). Gradient fractions were analyzed for dopamine-beta-hydroxylase (DBH), catecholamines (CAs), HRP and total protein. Electron microscopy was performed on selected gradient fractions. The effluents of the Cch-perfused glands gave peak release of CAs and DBH at three minutes, with subsequent decrease up to 60 minutes. HRP-perfused glands gave a peak CA and DBH output at five minutes which was twice that seen with Cch, with a slower decrease over the next 60 minutes. Subcellular fractionation showed uptake of HRP selectively into vesicles migrating at 1.2 M sucrose, both by biochemical analysis and by electron microscopy. There was a two-fold increase in total protein of the 1.2 M fraction of the HRP-perfused glands, as compared to the KR- or Cch-perfused glands. These data suggest that HRP is or contains a secretagogue and that HRP is selectively taken up (presumably by endocytosis) into vesicles migrating at 1.2 M sucrose. The increase in total protein in this fraction, often accompanied by a decrease in protein in the 1.45 M fraction, suggest that this 1.2 M fraction might represent a post-exocytotic population of secretory vesicles which acquired HRP during exocytosis.

26.8 NOREPINEPHRINE (NE) TURNOVER IN THE CENTRAL NERVOUS SYSTEM (CNS) - ESTIMATED IN THE RAT FROM URINARY 3-METHOXY-4-HYDROXYPHENYLGLYCOL (MHPG) EXCRETION. F. Karoum*, R. Wyatt, and E. Costa. Labs. Clin. Psychopharmacol. and Preclin. Pharmacol., NIMH, St. Elizabeths Hosp., Washington, D.C., 20032

There is an important need for a nontraumatic method of measuring CNS turnover of putative neurotransmitters. The method presented here for rat CNS-NE turnover can presumably be applied to other species. Rats were injected i.v. with 5 μc L 7^3H NE and 17 hours later urines collected for 7 hours (0 to 7 hours). At 0 and 3 hours, 1 ml normal saline was injected i.p. The experiment was repeated 3 days later but this time rats were injected with 5 mg/kg debrisoquine i.p. at 0 and 3 hours. Debrisoquine (Hoffman La Roche, Inc.) was found to be an ideal drug to perturb the function of peripheral noreadrenergic axons by selectively reducing the catecholamine output from peripheral neurons and limiting catecholamine metabolism by intraneuronal MAO; it does not pass the blood-brain barrier and it accumulates in peripheral noradrenergic axons. The 7-hour urine collections were hydrolyzed by glusalase and extracted with ether and the radioactivity of the deaminated metabolites of H^3 NE and the MHPG measured as previously described (Karoum et al., Clin. Chim. Acta. 43: 127, 1973). The radioactivity of deaminated H^3 NE before (RO) and after (RD) divided by that of MHPG before (HO) and after (HD) debrisoquine is equal to the fractional contribution of the peripheral sympathetic neurons to the total excreted MHPG. The fractional contribution of the CNS is, therefore, equal to (1- the peripheral fractional contribution). The CNS 24-hour production of MHPG (Mean $\pm$ SEM) for 5 normal rats injected intraventricularly (Int. V.) with saline and 5 rats injected Int. V. with 6-hydroxydopamine (300 μg of the hydrobromide salt) were respectively: 6.3 $\pm$ 0.1; 7.1 μg $\pm$ 1.5; and 1.4 μg $\pm$ 0.30. The CNS contribution of MHPG was significantly reduced after Int. V. 6HD ($p<0.01$).

26.9 EFFECT OF TRYPSIN ON NOREPINEPHRINE (NE) UPTAKE IN CORTICAL HOMOGENATES AND NERVE ENDING PARTICLES (NEP). Barbara A. Hitzemann*, Robert J. Hitzemann* and Horace H. Loh* (SPON: Mike Herz). Langley Porter Neuropsychiatric Institute and Dept. of Pharmacology, Univ. of Calif., San Francisco, Calif. 94122.

The uptake of NE into rat brain homogenates or NEP is an energy and Na+ dependent process. In agreement with White and Paton (Biochim. Biophys. Acta 266:116, 1972), Na+ was found to effect only the velocity of NE uptake. Prior digestion of homogenates or NEP with trypsin (15 min x 2,000 units) was found to noncompetitively inhibit the uptake of NE but this treatment did not effect the uptake of γ-aminobutyric acid, dopamine, serotonin or choline. In homogenates prepared from the caudate nucleus, trypsin treatment was found to effect only the uptake of NE but not dopamine. Equilibrium dialysis experiments indicated trypsin does not bind to NE. Phospholipase C and α-chymotrypsin were not found to alter NE uptake. However, phospholipase A was extremely potent in blocking the uptake process. The decrease in NE uptake caused by trypsin was not the result of an increase in NE efflux nor did it appear to be the result of a change in the morphology of the NEP as evidenced by electron micrographs. In a low Na+ (56 mM) incubation mixture, trypsin did not alter NE uptake suggesting that perhaps trypsin interferes with the binding of Na+ to the carrier molecule. It is concluded that the system in NEP responsible for NE uptake contains labeled basic amino acid residues and these residues may be located in the synaptic apparatus.
(This work was supported in part by MH-24036. HHL is a recipient of NIMH Research Scientist Development Award K2-DA-70554).

26.10 ONTOGENY OF CATECHOLAMINE RECEPTORS IN THE BRAIN. C. Kellogg and G. Wennerström*. Dept. Psychol., Univ. of Rochester, Rochester, N.Y. 14627.

Ontogenic development of receptors in the brain sensitive to catecholamines was studied by examining the ability of catecholamine receptor-stimulating agents to attenuate the decrease of noradrenaline (NA) and dopamine (DA), in the brain, following synthesis inhibition of NA and DA. Analysis was done in rats at 4, 14, and 28 days postnatal age. NA and DA synthesis was inhibited by α-methyl-p-tyrosine methyl ester (α-MT, 250 mg/kg). Apomorphine (1 mg/kg) and clonidine (1 2-(2,6-dichlorphenylamine)-2-imidazoline hydrochloride, 2 mg/kg) were utilized as DA and NA receptor-stimulating agents respectively and were injected 30 min. before administration of α-MT. The brains were removed 2 hrs. later and dissected into 4 regions: hemispheres, neostriatum, diencephalon, and midbrain-brainstem. The data indicate that at 4 days of age, functional NA receptors with feedback control over NA synthesis in presynaptic neurons are apparent in the cortex and brain stem. In these regions, clonidine significantly retarded the decrease of NA following α-MT. With increasing age, the effectiveness of this feedback control increases in these regions. According to these criteria, functional NA receptors appear in the diencephalon at 14 days. Although functional DA-containing neurons are apparent in the striatum and diencephalon at 4 and 14 days, control from postsynaptic receptors over the synthesis of DA in these neurons does not become marked until after 14 days since apomorphine was ineffective before this age in altering significantly the decrease of DA following α-MT. The ontogeny of postsynaptic receptor sensitivity to NA and DA respectively appears to occur at different ages in agreement with other aspects of the development of these transmitter systems. Also, it appears that synthesis of the two neurotransmitters may be controlled by different mechanisms at certain stages of development. (Supported by ONR Grant No. N00014-68-A-0091 and local GSRG Funds.

26.11 CYCLIC ADENOSINE 3',5'-MONOPHOSPHATE: SELECTIVE INCREASE IN THE RAT STRIATUM FOLLOWING THE ADMINISTRATION OF L-DOPA. E. Garelis* and N. H. Neff* (SPON: E. Costa), Lab. Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, D.C. 20032.

Dopamine activates a specific adenylate cyclase in homogenates of sympathetic ganglion or caudate nucleus (Kebabian and Greengard, Science 174: 1346, 1971; Kebabian et al., Proc. Nat. Acad. Sci. USA 69: 2145, 1972). Apparently activation by dopamine only occurs in tissues that normally contain dopaminergic nerve endings. For example, the adenylate cyclase in homogenates of cerebellum is not activated by dopamine and there are almost no dopaminergic neurons to be found in the cerebellum. Dopamine is formed throughout the brain following the administration of L-DOPA. We have measured the concentration of cyclic adenosine 3',5'-monophosphate (cAMP) in the caudate and cerebellum to determine if endogenously formed dopamine only activates a specific adenylate cyclase. Rats were injected intraperitonally with L-DOPA (100 mg/Kg) or the vehicle. The animals were killed with a microwave oven and the caudate nuclei and cerebellums were assayed for cAMP using a protein binding procedure. The concentration of cAMP increased in the caudate and reached concentrations of up to 2.5 times control values in about 5 minutes. cAMP was still elevated 15 minutes after the injection and approached normal values in about 30 minutes. There was no significant change of cAMP in the cerebellum. A dose-response curve was rather narrow with maximal increases occurring at about 100 mg/Kg L-DOPA. We propose that dopamine formed endogenously from injected L-DOPA activates a specific adenylate cyclase of brain and that this activation may be a useful model for studying the biochemistry of post-synaptic events in brain.

26.12 PHENYLETHYLAMINE AND PHENYLETHANOLAMINE IN RAT BRAIN. J. Willner*, H. LeFevre* and E. Costa, Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, D.C. 20032.

Phenylethylamine and phenylethanolamine have been identified and quantified in specific regions of the rat brain by the technique of mass fragmentography. Pentafluoropropionic acid anhydride derivatives of these amines and appropriate internal standards were prepared after extracting parts of the rat brain with acidified methanol. The compounds were then separated in a gas chromatograph on a 9' OV1 column and identified and quantified in a Finnigan 3000 mass spectrometer. The criteria used to specifically identify these amines in the rat brain were that they had the same gas chromatographic retention times as authentic compounds and that their fragments possessed the same mass/charge ratios and ion densities as the authentic compounds. High concentrations of these amines occur in the pineal, hypothalamus, pituitary and colliculi. The current evidence for phenylethylamine and phenylethanolamine being neurotransmitters will be discussed.

26.13 DIFFERENTIAL EFFECTS OF TWO PUTATIVE NEUROMODULATORS: 2-PHENYLETHYLAMINE AND PHENYLETHANOLAMINE. H. C. Sabelli, A. J. Vazquez, and Dana F. Flavin*
Dept. of Pharm., The Chicago Medical School, Chicago, Illinois 60612.

We postulated that 2-phenylethylamine (PEA) is an alerting neuromodulator (Fischer et al., Acta Physiol. Lat. Amer., 1967) and that its metabolite phenylethanolamine (OHPEA) is a possible neurotransmitter (Giardina et al., Life Sci., 1973). We have identified both compounds in mammalian brain (Inwang et al., Soc. Biol. Psychiat., 1972; J. Neurochem., 1973). Saavedra and Axelrod (Proc. Nat. Acad. Sci., 1973) confirmed the presence of OHPEA in brain and postulated that PEA acts as a precursor for OHPEA. Behavioral studies were conducted in mice pretreated with pargyline, isocarboxazid, or nialamide. PEA and OHPEA increased activity at low doses (2-10 mg/Kg); fighting and jumping were observed with higher doses. In the maximal electroshock test, PEA (50 mg/Kg) abolished tonic extension whereas OHPEA was only mildly anticonvulsant. PEA (6 mg/Kg) enhanced the stimulatory effects of Δ^9-tetrahydrocannabinol (5 mg/Kg) whereas OHPEA did not. The stimulant and anticonvulsant effects of PEA were not prevented by reserpine or by FLA-63. Electrophysiological studies were conducted in non-anesthetized rabbits pretreated with nialamide or with pargyline. PEA (2.5 to 10 mg/Kg) and OHPEA (10 mg/Kg) induced behavioral and EEG arousal, and long lasting hypertension. Reserpine abolished the hypertensive effect without preventing behavioral and EEG arousal. FLA-63 enhanced the motor effects of PEA and did not prevent EEG arousal. PEA (10 mg/Kg) induced a marked reduction of the slow component of visual evoked potentials (which was not prevented by FLA-63). OHPEA (10 mg/Kg) only altered the fast components of the evoked responses. We conclude that the central effects of PEA are not mediated by OHPEA or by norepinephrine.

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26.14 FURTHER EVIDENCE FOR A ROLE OF 2-PHENYLETHYLAMINE AS A MEDIATOR FOR THE STIMULANT ACTION OF Δ^9-TETRAHYDROCANNABINOL. A. D. Mosnaim*, C. Whalley*, W. A. Pedemonte*, A. J. Vazquez, and H. C. Sabelli (SPON: R. Greenberg)
Chicago Med. Sch. and Univ. of Illinois, Chicago, Illinois 60612.

We have previously reported that the sedative effect of Δ^9-tetrahydrocannabinol (Δ^9-THC) (5 mg/Kg) in mice is changed into a pattern of excitement and aggressiveness by pretreatment with monoamine oxidase inhibitors (MAOI) pargyline, isocarboxazid or nialamide. This Δ^9-THC stimulation is mimicked by PEA (50 mg/Kg) and potentiated by PEA (6 mg/Kg) (after MAOI) and it is not prevented by α-methyl-p-tyrosine or by p-chlorophenylalanine. Δ^9-THC (3 mg/Kg) increased 4-fold the rabbit brain levels of PEA (method of Mosnaim and Inwang, Anal. Biochem., 1973). Δ^9 -THC (0.3 mg/Kg, once daily for 8 days) doubles PEA brain levels. Measuring the recovery of labelled PEA after intraventricular injection of trace amounts of labelled L-phenylalanine, we found that rabbit brain synthetizes PEA: Δ^9-THC (3 mg/Kg) doubles newly synthetized PEA in both untreated and pargyline-treated rabbits. In MAOI treated rabbits, PEA (10 mg/Kg, iv) reduces the amplitude of the slow component of the visual evoked responses. Δ^9-THC (2.5 mg/Kg) induces a biphasic change in evoked responses and enhances or does not modify PEA effects. Δ^9-THC (3 mg/Kg, iv) slows the rate of firing of optic cortex neurons (extracellular microelectrode recordings) and increases the excitatory effect of iontophoretic injections of PEA in all cells. We conclude that endogenous PEA may mediate the mood-lifting effects of marihuana. Endogenous PEA appears to modulate affective behavior because PEA urinary output is decreased in endogenous depression (Fischer et al., Arz.-Forsch., 1968; Mosnaim et al., Biol. Psychiat., 1973) whereas the mouse brain levels of PEA are increased by antidepressive drugs (Mosnaim and Sabelli, Pharmacologist, 1971).

(Supported by Grants from the St. of Ill. Dept. of Mental Health 310-11-RD and 316-11-RD.)

27.1 RESPONSES OF NEURONS IN NUCLEUS ANGULARIS IN THE DOMESTIC CHICKEN TO PURE TONE STIMULI. Ralph E. Beitel, Mary Morton Gibson and Michael C. Vivion*. Laboratory of Neurophysiology, University of Wisconsin, Madison, Wisconsin, 53706.

Responses of neurons in the cochlear nucleus angularis (NA) were studied to determine whether frequency information is transmitted by phase-locked discharges in a brain stem auditory nucleus in birds. Action potentials were recorded extracellularly with glass coated microelectrodes from single neurons in chickens anesthetized with urethan. Pure tone stimuli were delivered to the ear via a short tube connected to an earphone. NA was found to be organized tonotopically as indicated by the orderly sequence of best frequencies obtained within a penetration. Best frequencies ranged from 0.1 to 5.2 kHz. Threshold intensities ranged from 10 to 90 dB SPL. Frequency-intensity response areas were centered near the best frequency of the neuron. Discharge rates were monotonically decreasing functions of distance from best frequency and were related monotonically to stimulus intensity up to the level of response saturation. Discharges of the majority of neurons were phase-locked below 1.2 kHz. Phase-locked discharges were not obtained with stimuli above 2.8 kHz. For other neurons, phase-locked discharges did not occur at any frequency to which the neuron was responsive. Compared to recent work in the pigeon which indicates that discharges in cochlear nerve fibers are phase-locked to stimulus frequencies below 4.0 kHz (Sachs et al. J. acoust. soc. Amer., 1972), our results suggest that neurons in NA relay frequency information by phase-locked discharges only at lower frequencies of the stimulating tone. (Supported by USPHS Grants 5326 and 6225.)

27.2 FIRST SPIKE LATENCY IN THE ANTEROVENTRAL AND POSTEROVENTRAL NUCLEI OF THE CAT IN RESPONSE TO PURE TONES. Leonard Kitzes*, Mary Morton Gibson, Jerzy Rose* and J.E. Hind* (SPON: J.M. Gibson). Lab. Neurophysiol., Univ. Wis., Med. Sch., Madison, Wis. 53706

The pertinence of time in auditory function is well known at the behavioral level and in the temporal structure of responses of certain neurons in the auditory system. We studied, in the ventral cochlear nuclei of anesthetized cats, the latency of unit discharge. The mean latency was calculated on the basis of 10, 20, or 30 repetitions of pure tone stimuli. Rise-time was 6 msec.. Stimulus frequency and intensity were systematically varied over the response area of each unit. Unit activity was recorded extracellularly with indium filled glass microelectrodes. The first spike latencies of low frequency units that exhibit phase-locked responses occur at intervals equal to the period of the stimulus and diminish in interval steps as SPL is increased. For low and high best frequency units that exhibit monotonic spike-count functions with increasing SPL, the latency of the first spike is an orderly function of frequency and SPL, being usually symmetrical about best frequency. Latency is minimal at best frequency for near-threshold SPL values and, at all SPL values, increases monotonically as the stimulus departs from the best frequency. For a small sample of non-monotonic units, the latency functions do not display such regularities. The latency of the first spike, therefore, should be considered a highly pertinent temporal parameter of unit activity in processing acoustic stimuli. (Supported by Grants USPHS 5326 and 6225; and Fellowship NS 30, 897).

27.3 DISCHARGE PATTERN OF CAT LATERAL SUPERIOR OLIVARY NEURONS TO TONE BURST STIMULI. Chiyeko Tsuchitani, Division of Neuroscience., GSBS, University of Texas at Houston, 77025

Single unit activity was recorded extracellulary with stainless steel microelectrodes from auditory neurons located in the lateral superior olive. The discharge pattern of LSO neurons with characteristic frequency (CF) greater than 2.0 kHz were studied. The post-stimulus time (PST) and interspike interval time (ISI) histograms produced by discharges elicted with tone bursts at unit CF were examined. Stimulation of the ipsilateral ear with stimuli 20 to 30 dB above CF threshold produced 3 types of PST histograms: Several units produced pause-type histograms characterized by a peak of activity near stimulus onset that was followed by a period of low discharge that recovers to a higher level lasting the duration of the stimulus. The discharges of other neurons generated "short-chopper" type histograms. The discharges occurring in the first 5 to 20 msec. of the spike train were time-locked to stimulus onset with the remainder of the train occurring at irregular intervals for the duration of the stimulus. The majority of LSO neurons produced discharges that were time-locked to stimulus onset for a longer period of time; often for the duration of the tone bursts. The PST histograms of these "long-chopper" type neurons had wider peaks and longer inter-peak intervals than the "short-chopper" type histograms. The ISI histograms of discharges to CF tone bursts produced by pause-type neurons were usually unimodal and asymmetrical in shape. The ISI histograms of "short-chopper" type neurons were often bimodal with a short, narrow peak at an interval equal to the inter-peak distance of the chopper portion of the response. ISI histograms of "long-chopper" type neurons were unimodal and usually symmetrical in shape. The effects of monaural stimulus level and binaural stimulation were also examined. This research supported in part by an NINDS grant.

27.4 PLASTIC PROPERTIES OF VOCALIZATION DETECTOR CELLS IN MONKEY AUDITORY CORTEX: AROUSAL LEVEL AND RETICULAR STIMULATION. John D. Newman and David Symmes.* Nat. Inst. Hlth., NICHD, Bethesda, Md. 20014

Prior studies have demonstrated that most cells isolated in auditory cortex of awake restrained squirrel monkey respond to species-specific vocalizations and that some cells do so selectively. In the present study spontaneous fluctuations in arousal and electrical stimulation of the mesencephalic reticular formation have been correlated with such responses. Arousal level was inferred from a zero crossing vs. amplitude analysis of surface EEG. It was found that most cells, including those of high selectivity, were arousal independent over the range studied. A minority (about 40%) were either directly driven by stimulation or showed long lasting changes in firing rate following stimulation but retained original response patterns. A small number (less than 10%) of cells exhibited altered response patterns. These effects included both bringing out responses to previously ineffective vocalizations and weakening existing responses with concurrent reticular stimulation.

27.5 ELECTROPHYSIOLOGICAL EVIDENCE OF PATTERN REVERSALS DURING AUDITORY PERCEPTION. L. T. Andrews and M. L. Pinheiro. Dept. Neurosciences, Med. Col. Ohio, Toledo, O. 43614

The averaged evoked responses (AERs) to auditory patterns were studied in order to further investigate the phenomenon of perceptual reversals reported in earlier behavioral research. Six binary pattern triads were made up of 100 msec. SOFT and LOUD noise bursts with an interburst interval of 120 msec. Patterns were randomly generated by the PDP-12 computer and presented binaurally. The EEG was recorded from an active scalp electrode at vertex with reference electrodes on the earlobes. The sampled evoked responses (ERs) were sorted according to the subject's manual response. For each pattern the ERs for the correct responses were averaged separately from the ERs for reversed responses. Results showed the AERs for correct perceptions of a pattern stimulus were significantly different from AERs for reversed perceptions of the same pattern. Therefore, it was concluded that a relationship existed between the brain's electrophysiological activity and the subject's perception of the auditory pattern stimulus, since the same stimulus evoked different cortical responses when it evoked different perceptions.

27.6 DISTRIBUTION OF VOLUME-CONDUCTED AUDITORY-EVOKED FAR FIELD POTENTIALS ON THE HEADS OF MAN, CAT, AND RAT. John S. Williston, Robert J. Plantz, and Don L. Jewett. Dept. Physiol., Univ. of Calif., San Francisco, 94132

Very short latency (1-5.0 msec) auditory "click" evoked responses were systematically recorded from many locations on the heads of humans, cats, and rats using distant parts of the body for reference placements. A series of 4 to 5 waves with very similar peak latencies were seen at almost all recording points in the three species. The size, shape, and polarity of the individual waves varied according to species, position on head, and between individuals. The largest interspecies differences in response was between rat and the other two although presumably homologous individual components were clearly identifiable in all three. At least part of the difference may be due to skull configuration. The exact shape of the multiple-wave far field response also depended upon the location of the recording electrode. The first two waves showed the greatest variability, being of maximal size and of negative polarity near the stimulated ear and changing to positive as the electrode is moved forward and dorsally. The first two waves were also different from each other in their distribution on the head, suggesting different brainstem generators. The last two waves were much more uniformly distributed on the head, and are probably from deeper brainstem generator locations. This data, together with our previous reports, supports the view that the individual waves represent sequential activation of brainstem components of the auditory pathways and show that "optimal" positions for the recording of the auditory far field do exist on the head.

28.1 ADRENOCORTICAL HORMONE AS A MEDIATING FACTOR IN ETHANOL-INDUCED INCREASE OF BRAIN RIBOSOMAL PROTEIN SYNTHESIS. Paul Y. Sze and Jonathan L. Hess.* Dept. Biobehavioral Sciences, Univ. Connecticut, Storrs, Conn. 06268

After continuous administration of ethanol to mice for two weeks using liquid diet containing 6% ethanol, incorporation of C^{14}-leucine into protein by ribosomes isolated from brain was shown to be markedly increased (Kuriyama, Sze and Rauscher, Life Sci., 10:181, 1971). This increase of brain ribosomal protein synthesis was accompanied by persistent elevation of plasma corticosterone levels. In the present study, it was found that similar chronic administration of ethanol to adrenalectomized mice did not lead to the increase of brain ribosomal protein synthesis. These results indicate that ethanol-induced increase of brain ribosomal protein synthesis may be mediated by adrenocortical hormone. Incorporation of H^3-uridine triphosphate into RNA by brain nuclei remained unchanged after chronic ethanol administration, either in intact or in adrenalectomized mice. It suggests that ethanol may act on brain protein synthesis by a steroid-mediated mechanism at the translational level. Current work (Sze, Yanai and Ginsburg) has further shown that corticosterone is required in the ethanol-induced behavioral change (development of susceptibility to seizures) in mice. Both the neurochemical and behavioral findings are consistent with our hypothesis that adrenocortical hormone may be a necessary factor in the induction of neural changes during chronic ethanol administration. (Supported by PHS Grant MH 20760).

28.2 STIMULATORY EFFECT OF ETHANOL ON IN VITRO PREPARATION OF RAT BRAIN CHOLINE ACETYLTRANSFERASE ACTIVITY. Ruth B. Reisberg* and Joseph J. Noval* (Spon: A. Gelperin). Neurochem. Sect., Bur. of Research, N.J. Neuropsychiatric Inst., Princeton, N.J. 08540.

In electrophysiological studies at the neuromuscular junction, Gage (JPET, 150:236, 1965), and others have shown that physiological concentrations of ethanol increase the quantal content of the end plate potential (e.p.p.), implying an increase in released acetylcholine (ACh). This could involve an ethanol stimulated increase in the rate of synthesis of ACh, mediated by choline acetyltransferase (ChAc). An investigation of the effect of ethanol on this enzyme by Kalant, et al. (CJPP, 45:172, 1967) in mitochondria gave inconclusive results. In experiments on ChAc activity, in whole homogenates or partially purified KCl extracts of rat cerebrum, incubated at 38° with ^{14}C-acetylcoenzyme A and choline chloride, an 11-37% stimulation of ACh synthesis was found when 0.17 M to 1 M ethanol was added to the incubation mixture (IM). The ester was assayed by passing the IM through a Dowex-1 anion exchange column, and measuring the ^{14}C ACh formed in a scintillation counter. In preincubation experiments with ethanol and the enzyme fraction, the inactivation of the enzyme by the alcohol, which occurs at incubation times longer than 20', could be at least partially prevented by the addition of one of the substrates to the preincubation mixture.

28.3 INCREASED DOPAMINE LEVEL OF CAUDATE NUCLEUS ASSOCIATED WITH CHRONIC ALCOHOL ADMINISTRATION. Albert Y. Sun. Lab. Neurochem., Cleveland Psychiat. Inst., Cleveland, Ohio 44109

Evidence has been presented suggesting that alcohol may effect synaptic transmission by altering the reuptake and storage capacity of neurotransmitters at the synaptic level (Sun, 1973; Post, Samorajski and Sun, 1973). Alcohol dependence was induced in guinea pigs by intubation of alcohol solution with a daily increasing dose of 4 to 8 g of ethanol per kg of body weight over a period of 16 days. At the end of this time, the animals were sacrificed by decapitation. The hypothalamus and caudate nucleus were rapidly removed for analysis of catecholamine content. There is no significant difference in the content of norepinephrine (NE) of hypothalamus between control and alcohol groups. However, dopamine (DA) content of the caudate nucleus in the alcohol group is 2 1/2 times higher than that of the control group (5.69 $\pm$ 2.47 μg/g and 14.10 $\pm$ 4.26 μg/g for the control and alcohol groups, respectively; $P<0.005$). In the same study, we have also observed that the membrane-dependent synaptosomal Na-K ATPase was also altered after chronic alcohol administration (1.485 $\pm$ 0.077 μmoles Pi/mg/10 min for control group as compared with 1.870 $\pm$ 0.249 μmoles Pi/mg/10 min for alcohol group, $P<0.025$). Since the reuptake of DA, like NE, may also be related to the membrane-dependent, active transport process, the increase in DA after chronic alcohol ingestion may indicate that the alcohol inhibits the DA-reuptake process causing an activation of DA-biosynthesis in dopaminergic neurons through a feedback control mechanism. The abnormal behavior observed in alcohol addiction may be due to an excessive accumulation of DA in certain dopamine-containing neuronal pathways.

28.4 REGIONAL DIFFERENCES IN NERVE IMPULSE ACTIVITY IN RESPONSE TO ALCOHOL. W. R. Klemm and R. E. Stevens III*. Dept. Biol., Texas A&M Univ., College Station, Texas 77843.

These experiments tested the hypothesis that alcohol affects various brain regions differentially. Numerous brain areas of rats were monitored simultaneously in sets of 7 for the effect of alcohol on nerve impulse activity (multiple-unit activity - MUA). Recordings were obtained before and after remotely controlled administration of 20% alcohol, in unanesthetized rats that were paralyzed with tubocurarine and artificially respired. Of the brain areas that were sampled on numerous occasions, 4 appeared to be relatively resistant to alcohol effects over the dose range of 200 to 1000 mg/kg: amygdala, olfactory tubercle, substantia nigra, and superior colliculus. On the other hand, neurons in 5 brain areas responded to these doses of alcohol with statistical significance, and these are presumed to be leading candidates for primary target sites of alcohol action: cerebral cortex, cerebellar cortex, hippocampus, medial forebrain bundle, and septum. We conclude that the recording of MUA is a useful way to screen large numbers of brain areas in search of primary target sites for alcohol action. This approach may prove useful for the study of other psychoactive drugs as well.

28.5 ETHANOL WITHDRAWAL SYNDROME IN RATS: BEHAVIORAL AND ELECTROGRAPHIC CORRELATES. Bruce E. Hunter*, Don W. Walker, Carl A. Boast*, and Steven F. Zornetzer. Dept. of Neuroscience, Col. of Med., Univ. of Florida and VA Hospital, Gainesville, Fla. 32610.

Rats, chronically implanted with electrodes bilaterally in the ventral hippocampus, amygdala, and frontal cortex, were maintained on liquid diets as their only source of calories and fluid for fifteen days. The diet consisted of 35-40% of the calories in the form of ethanol while a control group received identical diets with sucrose isocalorically substituted for ethanol. The mean daily consumption of ethanol for each rat was 15.2 g/kg. On the sixteenth day the ethanol was removed and the rats were observed for behavioral and electrographic abnormalities for eight hours. The removal of ethanol resulted in behavioral symptoms including tremors, piloerection, tail stiffening, severe ataxia and spontaneous vocalizations. Auditory-induced behavioral convulsions and electrographic seizure activity were elicited 6-8 hours following withdrawal from alcohol. Electrographic abnormalities which appeared in close association with the onset of behavioral symptoms, consisted of intermittent high amplitude slow-wave activity and transient spiking. Taken together, these results suggest that a state of latent brain hyperexcitability develops upon removal of ethanol following prolonged consumption. Supported by PHS Grant # AA 00200, and the Veterans Administration.

28.6 ALCOHOL EFFECTS ON ACQUISITION, RETENTION, AND SPONTANEOUS LOCOMOTOR ACTIVITY IN THE COMMON GOLDFISH. Rodney C. Bryant, Frederick Petty, Judith Warren,* and William L. Byrne. Brain Research Institute and Department of Biochemistry, University of Tennessee Medical Units, Memphis, TN 38103.

Fish were immersed in water solutions of ethyl alcohol (428, 628, or 856 mg/100 ml) for 3 hours before receiving 20 trials of active dark-avoidance training in individual shuttleboxes containing the same concentrations of alcohol as that of pretraining immersion. A dose-related facilitation of performance was found in fish treated with alcohol compared to fish treated similarly but not exposed to alcohol. Additional experimentation demonstrated that this effect cannot be attributed to increased non-directional shuttling activity during the CS period of the active avoidance conditioning procedure. In other experiments, fish treated with alcohol or only water were run in the following conditions: CS alone; US alone; backward pairing; no stimuli. The dose-related increase in general locomotor activity over periods up to 24 hours in alcohol-treated fish, was explored in additional work, using two different methods to estimate activity. The activity level in alcohol-treated fish was correlated with blood-alcohol levels over 24 hours. Finally, alcohol effects on retention were examined in several learning and control conditions. A 2x2 design allowed estimation of the effects of alcohol during training, during testing, and their interaction. An optimum (intermediate) dose was found for demonstration of state-dependence in goldfish in our procedure.

29.1 DEVELOPMENT OF RETINAL RECEPTIVE FIELDS IN THE NEONATAL RABBIT. Richard H. Masland. Neurosurgical Service, Mass. General Hospital, Boston, MA 02114

The rabbit retina at birth has just begun its final differentiation into 3 cellular layers and the cells of the outer layers are immature in form, although the ganglion cells already appear adult. During the succeeding days the plexiform layers become distinct, and at roughly 10 days the gross structure of the retina approximates that of adults, with the photoreceptor outer segments the last cellular elements to develop (Noell, Arch. Ophthal. 60:702-733, 1958). I have recorded from ganglion cells of the peripheral retina in rabbits aged 1 to 15 days. The retinas were maintained with an *in vitro* system (Ames and Pollen, J.Neurophysiol. 32:424-443, 1969) which eliminates the problem of clouding of the eye in young animals. Receptive fields were plotted by moving spots of light on a tangent screen focussed on the retina. The first responses to light were found at 8 days, and by 10 days all of the types of receptive field found in the peripheral retina of adult animals could be identified. Responses to light were limited in the younger animals by the development of the outer retina or its synapses on the ganglion cell, since the ganglion cells of animals 1 day old had some spontaneous activity and produced trains of spikes when the extracellular potassium concentration was increased.

29.2 DEVELOPMENT OF RECEPTIVE FIELD CHARACTERISTICS OF NEURONS IN THE DORSAL LATERAL GENICULATE NUCLEUS OF RABBITS. Salvatore C. Rapisardi*, Lawrence H. Mathers and Kao Liang Chow. Dept. of Neurology, Stanford Univ., Stanford, Ca. 94305

The development of receptive field characteristics of single neurons in the dorsal lateral geniculate nucleus of newborn, dutch-belted rabbits was studied. Extracellular recordings were made with tungsten microelectrodes in acute preparations. Units in the dorsal lateral geniculate nucleus were driven by electrical stimulation of the optic nerve as early as two days after birth. Neurons with receptive fields similar to those in the dorsal lateral geniculate of the adult were found in neonatal animals before eye opening. On the other hand, a significant number of cells are present several days after eye opening whose receptive fields are poorly defined. This latter type of cell is not present in the adult. Relationships between this work and the development of receptive field characteristics in the visual cortex of the rabbit will be discussed.

29.3 SPECIFICITY OF RETINO-TECTAL PROJECTION IN THE CHICK AS STUDIED BY PARTIAL LESIONS OF THE OPTIC CUP. W. J. Crossland*, W. M. Cowan, L. A. Rogers* and J. P. Kelly*. Dept. Anat., Sch. Med., Wash. Univ., St. Louis, Mo., 63110, and Dept. Neurobiol., Harvard Med. Sch., Boston, Mass., 02115.

The topographic specification of retino-tectal connections has been studied in the chick by making partial ablations of the optic cup during the third day of incubation at Stage 17, which is about 2½ days before the axons of the retinal ganglion cells normally invade the optic tectum. Towards the end of the incubation period (Stage 45) the resulting small eyes were injected with ^{3}H-proline and the distribution of the axonally transported proteins to the optic tectum was determined autoradiographically. In addition to reconstructing the eyes and both optic tecta, the nucleus of origin of the centrifugal fibers to the retina (the isthmo-optic nucleus) was examined in order to monitor which portion of the retina had survived the earlier optic cup lesion. The site of termination of the axons from the remaining retinal segment could be distinguished by the presence of silver grains over the outer layers of the optic tectum and by the cytoarchitectonic appearance of the innervated and non-innervated regions of the tectum. In every case examined the persisting retinal tissue had innervated a localized area of the optic tectum and, so far as can be determined, the area involved is that to which the surviving ganglion cells would normally have sent their axons. Significantly, in several animals the rostro-ventral portion of the tectum (which is the first area invaded by the ingrowing optic nerve fibers) was not innervated and the ingrowing axons had passed over a non-innervated area of the tectum before reaching its dorso-caudal region where they terminated. This result implied that the destination of the axons of the ganglion cells is determined well before they establish contact with the tectum, and indeed before the majority of the ganglion cells have undergone their final mitoses.

29.4 POSTNATAL DEVELOPMENT OF VISUAL ACUITY, CYTOARCHITECTURAL AND CHEMICAL ORGANIZATION OF THE STRIATE CORTEX AND GROWTH OF THE BRAIN, PITUITARY AND ADRENALS IN THE SQUIRREL MONKEY (SAIMIRI SCIUREUS). J. M. Ordy, K. R. Brizzee* and T. Samorajski*. Delta Regional Primate Res. Ctr., Tulane Univ., New Orleans, La., 70433 and Cleveland Psych. Inst., Cleveland, Ohio 44109

The squirrel monkey is rapidly becoming one of the more widely used primate species for the study of brain mechanisms and behavior. One of the more singular advantages for using the squirrel monkey for brain-behavior research is the extensive behavioral capacity and the very large size and weight of the adult brain (26 g) relative to the body weight (700 g). Due in part to this unique brain/body ratio, increasing interest has been directed towards the possibility of using the squirrel monkey as a primate "model" for studying the effects of drugs, ionizing radiation, and malnutrition on the pre- and postnatal development of the brain. The aims of this study were to examine the postnatal development of behavior in relation to neurochemical and morphological changes in specific cortical and subcortical regions of the infant squirrel monkey brain. Observations on behavioral development indicated a progressive increase in sensory, learning and motor capacity from the 2nd month to relatively mature levels by the end of the 1st year. Brain weight increased from 15 g. at birth to adult levels of 26 g. by the end of 12 months. Brain weight, DNA, RNA, protein and lipids increased rapidly during the perinatal period encompassed by the "brain growth-spurt". Observations on the maturation of the cerebral cortex indicated isocortical stratification during perinatal development, increasing synaptic and neuropil density, and a relatively mature cytoarchitectural organization of the neocortex by the end of the 1st postnatal year. It was concluded that detailed neurochemical and morphological analyses can be made in more discrete anatomical areas of the primate brain.

29.5 VISUAL SYSTEM IN EARLY AND LATE INFANCY. D. Nico Spinelli, Jacqueline Metzler* and Robert W. Phelps*. Dept. Psychiatry, Stanford Univ. Sch. Med., Stanford, Ca. 94305.

The receptive field shapes of single nerve cells in the visual cortex of kittens, who have viewed only one stimulus during development, are almost completely determined by that stimulus (Spinelli and Hirsch, 1971). After the kittens reached adulthood in a normal environment (Spinelli et al, 1972), further plastic changes occurred. However, the modifications generated by the first experience remain as permanently acquired characteristics for some visual cortex cells. The above work is being continued to investigate the time course of the plastic changes and their possible reversibility. Kittens are raised in the dark, but available to them is a feeding station. Whenever a kitten goes to feed, a picture window lights up which displays 3 horizontal bars at a distance of 25 cm. After 13 weeks of exposure, we recorded from single cells in their primary visual cortex: all receptive fields were horizontally oriented. Some receptive fields consisted of 3 excitatory bars separated by the same number of degrees of visual angle as the bars in the stimulus. The direct relationship between the shape of the stimulus and the shape of the receptive field is striking: indeed, an unbiased observer can tell what it was the kitten saw months ago, just by looking at a receptive field map. Further, there was no binocular disparity between cells, i.e. all receptive fields had perfect correspondence. Binocular disparity is believed to be the physiological basis for stereoscopy. This experiment is being continued by adding a second stimulus which is being displayed every time the kittens enter a drinking station. These results indicate that the basic machinery for vision has to be either built up or exercised very early in life for normal function to be possible in the adult.

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29.6 A DEVELOPMENTAL MODEL FOR STRIATE CORTEX. Bernard Kripke, Depts. of Neurology and Physiology, University of Utah College of Medicine, Salt Lake City, Utah 84112.

How are the specific connections in cat striate cortex laid down during development? Many of the observed specificities can be explained by a model that takes into account the influence of early postnatal experience. The model supposes that: (1) Y cells establish synapses in the cortex before X cells. (2) Excitatory connections from ON- and OFF-center Y cells are initially formed at random in small numbers on a population of first-order cortical neurons. (3) A first-order neuron drives a column of second-order neurons vertically above and below it in the cortex. This explains why a column of cells in a visually inexperienced animal may share a common preference for a direction of movement. (4) During the first few postnatal weeks, some follower cells also receive direct input X and Y cells in the lateral geniculate body. The formation of these additional synapses is subject to control by visual experience. (5) During the first few postnatal weeks, there is a finite probability that an established synapse will be functionally disconnected. (6) The probability of disconnection of an excitatory synapse is increased whenever the presynaptic fiber fails to fire within a few milliseconds of a spike in the postsynaptic cell. (7) The probability of disconnection of an inhibitory synapse is increased whenever the presynaptic fiber fires within a few milliseconds of a spike in the postsynaptic cell. This model predicts the development of orientation preferences in cells that initially are specific only for directions of movement, the organization of cells having a common orientation preference into columns, and the similarity in structure of the two monocular receptive fields of a binocularly driven cortical cell. It also predicts that animals with congenital squint will lack binocularly driven cortical cells, while animals subjected to binocular lid closure be less severely affected.

30.1 EFFECTS OF PRIOR MORPHINE DEPENDENCE ON SINGLE ALTERNATION LEARNING. Khalil A. Khavari and Thomas C. Peters. Dept. Psychol., Univ. Wisconsin-Milwaukee, Milwaukee, 53201.

Rats were placed on a morphine ingestion regimen (4 mg morphine HCl/gm of food and 1 mg morphine HCl/ml of 10% sucrose) for 6 days. On day 7 the ingestion regimen was switched to plain food and water. The rats showed severe withdrawal signs upon change of regimen and after recovery (day 24) they were trained to bar press for water, then tested for acquisition and performance of a temporal single alternation task. A matched body weight control group was treated similarly except that the controls were not given morphine. The morphine group's acquisition and performance was significantly inferior as compared to controls. Specifically, the morphine pre-treated group persevered in responding to non-reinforced trials and during intertrial intervals. It is concluded that prior morphine dependence adversely affects subsequent acquisition and performance of a temporal single alternation learning task.
(Supported by NSF Grants B023365 and P2B0349)

30.2 EFFECT OF REPEATED HEROIN ADMINISTRATION ON AD LIB SELF-STIMULATION, EATING, AND DRINKING. George F. Koob, N. Herbert Spector and James L. Meyerhoff*. Dept. Neurophysiology, Walter Reed Inst. Res., Wash. D.C., 20012.

Male, albino, Walter Reed strain rats[1] were implanted with bipolar electrodes aimed at the medial forebrain bundle dorsal to the mammillary bodies. Following recovery from surgery each rat was allowed to bar-press for intracranial self-stimulation (ICSS) and then placed in an experimental chamber where it had ad lib access to 3 separate levers for ICSS, food and water. Three days after stable baseline rates of ICSS were established, each rat (n=8) received 0.5 cc of saline intraperitoneally (i.p.) followed by 5 consecutive daily injections at the same time each day of heroin hydrochloride (5mg/kg i.p.). ICSS in 7 rats was augmented 2-6 hours post administration of heroin, but had no significant effect on food and water intake. This facilatory effect increased with successive daily administrations, reaching 300% of the saline control level by the fifth drug day. The latency of the onset of this drug effect decreased from 2-hrs on day 1 to 1-hr on day 5. Pretreatment with 5 mg/kg of naloxone hydrochloride (i.p.) attenuated by 75% the facilatory effect of heroin on ICSS, and food and water intake remained at control levels. An eighth rat showed complete inhibition of ICSS following heroin administration. This inhibition of ICSS was also blocked by naloxone pretreatment. Generally, these results are consistent with other studies demonstrating a facilatory effect of morphine on ICSS and suggest that the effect of heroin is specific to ICSS and is not due to a general increase in locomotor activity.

[1]In conducting this research, the investigators adhered to the "Guide for Laboratory Animal Facilitities and Care," of the Institute of Laboratory Animals Resources, National Academy of Sciences - National Research Council.

30.3 EVOKED EEG RESPONSE CHARACTERISTICS OF INFANTS BORN TO METHADONE-TREATED MOTHERS. Ann Lodge and Marilyn M. Marcus*. Infant Development Res. Lab., Children's Hosp. San Francisco; Brain-Behavior Res. Ctr., Sonoma State Hosp., Eldridge, Calif. 95431.

Computer-averaged electroencephalographic potentials to auditory and visual stimuli were recorded on a longitudinal basis beginning in the neonatal period from 15 infants whose mothers received methadone treatment for narcotic addiction during pregnancy. Responses obtained during the early months of life tended to be of low voltage, dysynchronous, had a rippled appearance suggestive of CNS irritability and frequently displayed inertia in building up a response to the repeated stimulus. Nevertheless, the majority of records appeared to contain short latency response components rarely found with normal infants at this age. While the origin of these response characteristics has not yet been determined, the findings suggest the possibility that prenatal exposure to methadone may affect electrocortical response patterns to sensory stimulation in the infant and at least temporarily alter the normal course of electrophysiological maturation. However, the possible contribution of muscle tension, activity level and state of arousal to evoked response wave forms found with methadone-addicted infants requires further investigation.

During the neonatal period most of the infants manifested clinical symptoms of withdrawal including hypertonicity, irritability, hyperactivity, tremulousness and gastrointestinal distress. Although some infants continued to display a tendency toward excitable behavior, subsequent developmental evaluations were indicative of at least average progress in behavioral development during the first year of life.

30.4 PERIOD ANALYTIC DESCRIPTORS OF THE EFFECTS OF PSYCHOTROPIC DRUGS IN THE SUBHUMAN PRIMATE. L. P. Gonzalez*, H. L. Altshuler and N. R. Burch* (SPON: Mary K. Roach). Texas Research Institute of Mental Sciences, Houston, Texas 77025

Period analysis of the electroencephalogram (EEG) has been used to evaluate the human EEG (Burch, et al, Ann. N. Y. Acad. Sci., 115: 827, 1964), but only to a limited degree in animal experiments (Straw, R. N. and Sauer, R. A. Fed. Proc. 32: 793, 1973). These studies were designed to establish its efficacy as a means to evaluate the effects of centrally active drugs on the electrical activity of the brain and behavior. Three rhesus monkeys were used in this study. They were restrained in monkey chairs and placed in a quiet, shielded room for the experiments. Intravenous saline injections were used for control studies. Intravenous doses of pentobarbitol (2.0-20.0 mg/kg), morphine sulfate (0.5-5.0 mg/kg) or chlorpromazine (1.0-10.0 mg/kg) were administered to each animal according to a modified Latin Square design. The EEG was continuously recorded for two hours after each dose and the analogue data base reduced by computer-based period analysis. Major emphasis was placed on the changes observed in the minor period. All three compounds decreased the major and intermediate period counts below saline controls in a dose-related fashion. All three drugs induced substantial and distinctive changes in the second derivative function, the minor period. Minor period counts were generally reduced for the higher doses of each drug, and lower doses occasionally increased minor period counts at upper frequency bands. The data demonstrate the efficacy of the period analysis technique in distinguishing between different psychoactive drugs and serve to provide data base for studies of the EEG correlates of the behavioral changes induced by these and similar compounds.

30.5 PUPILLARY RESPONSIVITY DURING ACUTE HEROIN WITHDRAWAL IN VIET NAM. Malcolm G. Robinson*, John G. Varni, Richard C. Howe*, and Frederick W. Hegge*, Dept. of Exp. Psychophysiology, Walter Reed Army Institute of Research, Washington, D.C. 20012

During the recent conflict in Viet Nam, American military personnel were exposed to very inexpensive heroin of extreme purity. Taken predominately by the nasopulmonary route, and administered in uniquely large quantities, this heroin produced tolerance without many of the usual signs of dependence. As part of a larger study of abstinence syndrome in Viet Nam (manuscript in preparation), pupil diameters were measured under conditions of constant lighting and with light stimulation of the contralateral eye. Ten heroin using patients and five concurrent drug-free controls were evaluated with macro-camera pupillometry by the method of Jasinski and Martin (Clin. Pharm. and Therap. 8:271, 1967) for five days following the last doses of heroin. Measurements were made at 0600, 1000, and 2200 hours on each day along with other procedures allowing definition of clinical abstinence syndrome. Miosis present during acute heroin intoxication was clinically unresponsive to light and accommodation. Mydriasis gradually developed during the first 12-18 drug-free hours and persisted throughout the five days of measurement. Although the dilated pupils of heroin abstinence responded to light-stimulation with some constriction, the divergence from controls similarly stimulated also persisted for five days. A Lindquist Type VI ANOVA indicates a significant circadian effect in pupil sizes of both heroin users and controls. Abnormalities in pupil diameter following withdrawal from heroin persisted beyond other gross indices of abstinence syndrome in this population.

30.6 THE RAPID DEVELOPMENT OF TOLERANCE TO BARBITURATES BY PELLET IMPLANTATION. I. K. Ho, V. C. Sutherland* and H. H. Loh*. Langley Porter Neuropsychiatric Institute and Dept. of Pharmacology, Univ. of Calif., San Francisco 94122.

Subcutaneous implantation of a 6.4 mg tablet of sodium pentobarbital or a 16 mg tablet of barbital in the back of a mouse results in measurable tolerance within 24-48 hrs. The rate and degree of tolerance development can be measured by the decrease in anesthetic response to sodium pentobarbital as estimated by sleeping time. In mice receiving one barbital pellet for 2 days, the sleeping time of pentobarbital was decreased 80% after challenge with 75 mg/kg i.p. sodium pentobarbital. In a group of mice receiving a sodium pentobarbital pellet every 24 hrs for 2 days, the degree of tolerance development is about the same as those implanted with one barbital pellet for 2 days. However, in mice receiving 75 mg/kg i.p. sodium pentobarbital daily, the sleeping time of pentobarbital was decreased 40% only at the fourth day. Although the experiment was carried for an additional 6 days, these animals failed to show any greater decrease. Physical dependence was demonstrated by determining the median effective dose (ED50) of pentylenetetrazol (PTZ) needed to induce seizures. The median effective dose (ED50) of pentylenetetrazol in barbital pellet implanted mice after 48 hrs was 47 mg/kg as compared to 72 mg/kg in those mice receiving placebo implantation for the same period of time. With this substantial methodological improvement in producing a high degree of barbiturate tolerance in a short period of time, we hope to facilitate further research regarding barbiturate tolerance and physical dependence. (H.H. Loh is a recipient of a NIMH Research Scientist Development Award, #K2-DA-70554).

31.1 FLUORESCENT STAINING OF ACETYLCHOLINE RECEPTORS AT VERTEBRATE NEUROMUSCULAR JUNCTIONS. M.J. Anderson* and M.W. Cohen. Dept. Physiol., McGill University, Montreal, P.Q.

The polypeptide α-bungarotoxin has recently been shown to bind irreversibly to acetylcholine receptors of vertebrate skeletal muscle. We have labeled the toxin with fluorescent dyes in order to achieve a simple and rapid method of visualizing the distribution of these receptors. Several amphibian and mammalian muscles were exposed to the dye-toxin conjugates. The resulting fluorescent stain was found to have a distribution parallel to that of junctional cholinesterase. The fluorescence was prevented by pre-treatment with native toxin and was reduced by nicotinic agents, such as carbamyl choline and curare, which have been shown to inhibit binding of toxin to receptor. It was not affected by atropine or by neostigmine. When viewed at sufficiently high magnification a non-uniformity was observed in the fluorescence on muscle cells known to have junctional folding. Intense bands of fluorescence, occurring at intervals of about one micron, appeared superimposed on a less fluorescent background. This observation indicates that acetylcholine receptors are distributed throughout the junctional membrane, including the junctional folds. (Supported by MRC of Canada).

31.2 THE EFFECTS OF LONG-TERM ADMINISTRATION OF CHOLINESTERASE INHIBITORS ON NEUROMUSCULAR TRANSMISSION AND MORPHOLOGY IN RATS. M. D. Ward, M. S. Forbes† and T. R. Johns, Department of Neurology, University of Virginia, School of Medicine, Charlottesville, Virginia 22901.

Three groups of 200 gm rats were injected sub-cutaneously with neostigimine-methylsulfate 100 μg twice daily for 7, 30 and 100 days. Electrophysiologic changes were assessed in vitro using microelectrode techniques to examine diaphragm muscles of control and treated animals. A reduction in minature end-plate potential (MEPP) amplitude was found in neostigmine-treated preparations. Resting membrane potentials, and the wave form and frequency of MEPP's were similar in treated and untreated preparations. Addition of guanidine-HCl to the bathing solution has been found to enhance transmitter release and increase MEPP frequency in control preparations. All animals treated for 7, 30 and 100 days examined between 6-72 hours after discontinuance of neostigmine revealed an impaired response to the facilitating influence of guanidine. Serial sacrifice revealed recovery of guanidine response between 7-22 days following discontinuance of neostigmine. Recovery time was inversely related to length of treatment with neostigmine. Electronmicroscopic examination of motor end-plates in animals treated for 100 and 180 days revealed ultrastructural changes in the form of smaller, simplified end-plates and, in many fibers, multiple, separate junctional regions. Thus, the long-term administration of neostigmine (1 mg/kg/day) impairs neuromuscular transmission manifest as a decrease in MEPP amplitude and inhibition of the facilitating influence of guanidine. The intensity and reversibility of the physiologic defects are inversely related to length of treatment with neostigmine.

31.3 ACETYLCHOLINE RECEPTORS IN NORMAL AND DENERVATED MUSCLE. Darwin K. Berg* and Zach Hall* (SPON: David Hubel). Dept. Neurobiol., Harvard Medical School, Boston, Mass. 02115.

Acetylcholine receptors of the rat diaphragm were labelled in vivo with ^{125}I-α-bungarotoxin and the kinetics of toxin loss from the muscle determined. In normal rats, 66% of the toxin which was originally bound remained in endplate regions of the muscle after 5 days, and most of the radioactivity could be recovered as a 9 S complex. In contrast, toxin bound to extra-junctional receptors of denervated hemidiaphragms was reduced to less than 40% in 24 hours and was not detectable after 5 days. The rate of toxin loss from the junctional receptors of denervated muscle was close to that found for receptors in normal muscle.

To investigate the difference in toxin loss from junctional and extra-junctional receptors, normal and denervated muscles were transferred to organ culture 3 hours after labelling in vivo. After 24 hours in culture, normal muscles retained 77% of the toxin, while extra-junctional receptors from denervated muscles retained only 19%. No difference was seen in the loss of toxin from junctional receptors of normal and denervated muscle. When denervated muscles were cultured in 10 μg/ml cycloheximide, the amount of radioactivity remaining after 24 hours in non-endplate regions was increased to 72%. Thus the rapid removal of labelled toxin from non-junctional receptors in denervated muscle requires protein synthesis, ruling out simple dissociation of the toxin-receptor complex as the primary mechanism of loss. Although other interpretations are possible, the loss of toxin could reflect a process of receptor turnover which is dependent on protein synthesis.

31.4 ENZYME ACTIVITY CHANGES RELATED TO FORMATION OF NEUROMUSCULAR JUNCTIONS IN CELL CULTURE. B. K. Schrier, E. L. Giller, Jr., A. Shainberg*, H. R. Fisk*, and P. G. Nelson. Behav. Biol. Br., NICHD, NIH, Bethesda, Md. 20014.

Cells dissociated from fetal mouse spinal cord formed functional synapses with myotubes in culture. Associated with neuromuscular junction development there was a marked potentiation of the activity of the neuronal marker enzyme choline acetyltransferase (CAT). Myoblasts from 20-day fetal mice were grown on collagen-coated dishes for 14 days under conditions favorable to myotube formation. Spinal cord cells from 15-day fetal mice were added to the myotubes or to collagen-coated dishes without muscle and grown for up to 21 days with scheduled alterations in serum content of the medium and treatment with fluorodeoxyuridine. The level of CAT activity per dish after 21 days in combined spinal cord-muscle (SC-M) cultures was nearly 10-fold greater than the sum of the activities in control spinal cord (SC) and muscle (M) cultures. In addition to CAT we measured the levels of DNA and protein and the activities of total cholinesterases (ChE), creatine phosphokinase (CPK), myokinase (MK), phosphorylase (PH) and phosphoglucomutase (PGM) at various times in SC, M and SC-M cultures. In contrast to the apparent induction of CAT activity, CPK, ChE, MK, PH and PGM activities in SC-M were approximately equal to the sums of SC and M activities. The data with CAT show that a specific increase of an enzyme activity crucial to neuromuscular transmission accompanied the establishment of functional neuromuscular junctions in culture.

31.5 A COMPARISON OF α-BUNGAROTOXIN BINDING IN FAST AND SLOW MUSCLE

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Increased acetylcholine sensitivity following denervation in fast and slow skeletal muscle has been attributed to an increase in acetylcholine receptors. However, the increased number of receptors, determined by the binding of α-bungarotoxin, has been assessed primarily in mammalian diaphragm, a mixed muscle, and no studies have contrasted the toxin binding properties of slow and fast muscle. In the present experiments the acetylcholine receptors of normal and denervated extensor digitorum longus (fast) and soleus (slow) of the rat were compared. The binding of iodinated α-bungarotoxin to deoxycholate extracted muscle homogenates was assessed by column chromatography on Sephadex G-200. At a toxin concentration of 100 nM fast muscle bound 0.15 p moles/muscle, whereas slow muscle binding was almost 4-fold greater (0.56 p moles/muscle.) Following denervation fast binding increased to 0.54 p moles/muscle, whereas slow actually decreased slightly to 0.47 p moles/muscle. An increase in the number of acetylcholine receptors may therefore be the explanation for the spread of ACH sensitivity along the muscle surface membrane in fast muscles. However, such a spread of sensitivity is not so readily explained in slow muscles where no increase in detergent extractable receptors could be demonstrated. The greater toxin binding of slow muscle and its lack of increase following denervation represent two distinctive characteristics which distinguish it from fast muscle.

31.6 EFFECT OF PREDNISOLONE ON NEUROMUSCULAR TRANSMISSION. R. W. Wilson*, M. D. Ward, and T. R. Johns. Department of Neurology, University of Virginia, School of Medicine, Charlottesville, Virginia 22901.

Intracellular microelectrode recording of miniature end-plate potentials (MEPPS) was used to analyze the effect of prednisolone (U.S.P. Upjohn) on neuromuscular transmission, in vitro, in the rat phrenic nerve-diaphragm preparation. Prednisolone, in concentrations of 0.1 millimolar (mM) in the muscle bath perfusate, had no effect on MEPP frequency or amplitude. At concentrations of 0.5 mM and 1.0 mM there was a two to three fold increase in MEPP frequency above control; and MEPP amplitude, corrected for resting membrane potential, was decreased by 41 to 56 per cent. The capacity of 1.0 mM prednisolone to acclerate the frequency and decrease the amplitude of MEPPS was retained in the presence of either high concentrations of K^+ (10.0 mM) or Mg^{++} (6.0 mM); or low concentrations of Ca^{++} (0.5 mM) in the muscle bath. These data suggest that prednisolone is capable of enhancing the release of acetylcholine pre-synaptically at the neuromuscular junction, as well as altering acetylcholine effect on the post-synaptic membrane.

31.7 Conductance of single acetylcholine receptors in electroplaques from Electrophorus electricus. Henry A. Lester and Jean-Pierre Changeux*, Dept. Biol. Moléculaire, Institut Pasteur, 75015 Paris, France.

With voltage- and current-clamp techniques, we measure the steady-state slope conductance $g = dI/dE$, where I is the current through the innervated membrane and E is the potential across it. An increase (Δg) accompanies bath application of cholinergic agonists. This treatment causes ions to redistribute themselves: Na and K equilibrium potentials, and thus the reversal potential for the synaptic I, approach zero. Desensitization of Δg occurs at rates similar to those reported for neuromuscular junctions. We circumvent the latter two effects and measure Δg as a function of carbamylcholine concentration. A) At all values of E, the dose-response curve is sigmoid with a Hill coefficient of 1.7. B) The apparent dissociation constant is 5×10^{-5} M at E = -180 mV and increases e-fold for each 55 mV depolarization. C) The maximum Δg is constant (0.5 to 1 mho/cm^2 of window area) at E = -180 to -120 mV; it declines 2-fold at -60mV, then more rapidly, e-fold for each 25 mV of depolarization at 0 mV. Effect B probably depends on E; effect C, on synaptic I.

In the same chamber and solutions, 3.5×10^{11} molecules of (^{3}H)α-toxin from *Naja nigricollis* bind irreversibly (1/2-hr incubation at 10^{-7} M, 12-hr wash) per cm^2 (window area) and are prevented from binding by 10^{-3} M carbamylcholine and by 10^{-4} M d-tubocurarine.

Equating bound toxin molecules with acetylcholine receptor sites, we thus find $1 - 3 \times 10^{-12}$ mho as the steady-state Δg under the control of a single receptor site.

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31.8 NEUROMUSCULAR TRANSMISSION OF THE FROG DURING RANDOM AND REGULAR STIMULATION. A. C. Sandersont and D. L. IJpeijt (SPON: T. W. Calvert). Dept. of Biophysics, Delft Univ. of Tech., Delft, The Netherlands, and Physiological Laboratory, State Univ. Leiden, Leiden, The Netherlands.

The effect of stimulation of frog neuromuscular junctions with periodic single stimuli was compared to that of stimulation using random pulse trains and periodically spaced pulse clusters at the same average stimulus frequency. The amplitude of the compound muscle action potential of an indirectly stimulated M. gastrocnemius in vivo was used as a measure of the average synaptic transfer probability. Periodic single stimulation in the range 0.1 to 10 Hz was changed to random or cluster stimulation during the steady state. In general, the application of cluster stimulation caused an abrupt increase in the average transfer probability, which decayed in some minutes to a smaller but still increased steady-state average transfer. This behavior was also found for in vitro intracellular measurements of the end-plate potential. Because the type of cluster stimulation employed approaches natural neuromuscular activity, it is concluded that natural neuromuscular transmission is more effective that that of single periodic pulses. Using the theory of stochastic point processes, an analytical model of transmitter release has been developed, which describes qualitatively the observed dependence of transmitter release on the frequency of stimulation for random, regular, and cluster stimulus patterns. The processes at the neuromuscular junction are described in terms of poststimulus facilitation, expressed as an increased probability of release, and poststimulus depression, related to depletion of transmitter in the immediate releasable store. The model suggests how the characteristics of information transfer through synapses may depend on the interaction between the explicit temporal response of the synapse and the stochastic properties of the incident pulse train.

31.9 LITHIUM AND SODIUM MOVEMENTS IN SHORT-TERM DENERVATED MUSCLE. Norman Robbins, Dept. Anat., Case Western Reserve Sch. Med., Cleveland, Ohio, 44106

The study of early membrane changes in denervated muscle may reveal those parameters of membrane function most closely regulated by innervation in the normal state. One day after denervation, weanling rat Extensor Digitorum Longus muscles take up 29% more Lithium during a two-hour in vitro incubation than do the contralateral control muscles. Muscles denervated 30-34 hours take up 72% more Lithium. The difference cannot be accounted for by cell volume, cell water, or extracellular space. The effect appears to be independent of use and disuse or nerve impulse activity, since the difference is also found between muscles denervated close to or distant from the nerve-entry zone, respectively. Short-term denervation has no effect on Sodium influx measured by Sodium-22 exchange or under conditions in which the Sodium pump is blocked by Ouabain, Potassium-free solution, or both. The most likely conclusion is that the denervated muscle membrane undergoes early and specific alteration in cation permeability.

31.10 HISTOCHEMICAL PROFILES OF INTRAFUSAL FIBERS IN NORMAL, DENERVATED, CORDOTOMIZED AND DENERVATED GUINEA PIG MUSCLES. Alfred Maier* (SPON: D.S. Maxwell). Neuromuscular Research Laboratory, Dept. of Kinesiology, UCLA, Los Angeles, California 90024.

To study the susceptibility of histochemical properties of intrafusal (IF) fibers to conditions of disuse, histochemical profiles of IF fibers were reconstructed from serial cross sections incubated for myofibrillar adenosine triphosphatase (ATPase), nicotinamide adenine dinucleotide diaphorase (NADH-D) and glycogen. In the various normal muscles, based on myofibrillar ATPase activity at polar regions, IF fibers could be sorted into three groups: 1) fibers showing low activity when preincubated in either acid or alkaline medium (ML fibers), 2) fibers demonstrating high activity when preincubated in either acid or alkaline medium (MD fibers) and 3) fibers demonstrating low to moderate activity when preincubated in acid medium, but showing high activity when preincubated in alkaline medium (MR fibers). Fiber groups could be further distinguished by differential NADH-D activity and glycogen content. The activity of all reactions was least at the equatorial regions. Whenever positive identification of morphological features could be made, it was found that both ML and MD fibers were of the nuclear bag type and MR fibers of the nuclear chain type. After four weeks of disuse IF fibers were minimally affected in the tenotomized preparation, but in the cord-sectioned animals a loss of distinction between fiber groups was apparent. In denervated muscles MR fibers showed large cross-sectional area and NADH-D activity decreases, whereas size reduction in ML and MD fibers was less and NADH-D activity was often increased. This differential effect suggests that MR fibers are more dependent on neural innervation than both ML and MD fibers.
Supported by USPH grant NS 10497-01, NS 52927-02 and NS 01143

31.11 EFFECTS OF USE AND DISUSE ON SKELETAL MUSCLE METABOLISM. David H. Rifenberick*, John Carlo* and Stephen R. Max. Dept. Neurol., Univ. of Md. Sch. Med., Baltimore, Md. 21201.

The metabolic properties of skeletal muscle can be altered in response to changes in muscular activity. To study such alterations, we have measured the production of $^{14}CO_2$ from β-hydroxybutyrate-3-^{14}C, pyruvate-2-^{14}C and glucose-U-^{14}C by homogenates of over- and underused rat soleus and plantaris muscles. Overuse hypertrophy was produced by ablation of the gastrocnemius muscle and disuse atrophy was produced by limb immobilization by surgical pinning. Contralateral muscles served as controls. After 10 days of disuse, soleus and plantaris muscles displayed markedly reduced $^{14}CO_2$ production as shown in the following table:

	$^{14}CO_2$ production (% of control)		
Muscle	β-hydroxybutyrate	pyruvate	glucose
Soleus	60	51	25
Plantaris	40	40	33

This impaired oxidative capacity may be a reflection of the loss of respiratory control previously described (BBRC 46:1394, 1972). In overuse hypertrophy no alteration in oxidative capacity was observed. This is in contrast to the increase observed by other workers using models of treadmill running or swimming. Thus the oxidative capacity of skeletal muscle appears to be dependent on the degree and type of activity. (Supported in part by PHS Grant #NS-05077, a grant from the Dysautonomia Foundation, Inc., and by NIH Fellowship #1 F02 NS 54205-01.)

31.12 DYNAMIC AND METABOLIC PROPERTIES OF SLOW-TWITCH MUSCLE AS INFLUENCED BY HYPERINNERVATION AND SYNERGIST-DENERVATION. Jennifer Lee*and V.R. Edgerton, Neuromuscular Res. Lab., Dept. Kinesiology, UCLA, Los Angeles, 90024.

It has been reported that the proximal end of a transected nerve to a fast-twitch muscle, when implanted into a neurally intact rat soleus muscle induces changes in the soleus indicative of speeding. However, more recent experiments have failed to support these results. In ten rats the nerve to the flexor digitorum longus (FDL) was severed and implanted into the normally innervated soleus muscle of one leg. In the contralateral leg, the FDL nerve was implanted into the medial gastrocnemius to prevent reinnervation of the FDL. A second group of rats also underwent FDL nerve implantation into the normal soleus, but the contralateral control leg was left intact. With the two groups of animals it was possible to compare both hyperinnervation and synergist-denervation with normal muscle. This study supports previous evidence that the weight of the muscles with the implanted nerve was greater than that of normal muscles. However, we were unable to support earlier findings of enhanced tension-generating capabilities in the "hyperinnervated" muscle, which is consistent with a lack of change in protein content in this experimental muscle. Histochemical analysis of cholinesterase-stained muscle sections revealed no motor endplates at the site of nerve implantation. We found no increase in contractile speed of either the implanted or the synergist-denervated muscle, as previously reported; nor was there any change in the percentage of fast-twitch fibers as determined histochemically by the myosin adenosine triphosphatase. In conclusion, we have found that the effects of hyperinnervation and synergist-denervation do not differ and only result in an increase in experimental muscle weight. We found no evidence for the earlier proposed "trophic influence" of an implanted nerve on a neurally intact muscle. USPHS Grant NS-10497 and Biomed Research Support Grant.

31.13 CONTRACTILE PROPERTIES OF DOG GASTROCNEMIUS MUSCLE DURING REFLEX RECRUITMENT OF MOTOR UNITS. Dwain J. Reed* (SPON: J. M. Brookhart), Dept. of Physiology, Univ. Oregon Med. Sch., Portland 97201.

Tension and velocity during isometric and isotonic contractions of gastrocnemius muscle were measured at various levels of motor unit recruitment initiated by stimulation of sectioned dorsal roots (L6-S1) in dogs decerebrated at the midcollicular level. Reflex contractions ranged to 75% of tension induced by stimulation of the motor nerve (% recruitment of motor pool). Length-tension and force-velocity relations were determined at various degrees of reflex recruitment. Initial lengths less than L_o were used because the passive tension begins its rapid rise before L_o. At these lengths the force felocity relation depends strongly on length. Therefore the modification of the Hill relation after Abbot and Wilkie (J. Physiol. 120:214, 1953) $(P+a)(V_1+b) = ((P_o)_1 + a)\, b$ was used to generate a family of curves to fit the experimental data at a given reflex level. Vmax was dependent upon the length of the muscle; at a constant initial length the force-velocity relation determined at low reflex recruitment had a lower value of Vmax than that characterizing the maximum reflex response. Thus, direct measurement of speed of contraction confirms the indirect evidence that the "slow" fiber population is recruited first (Henneman et al, J. Neurophysiol. 28:581, 1965). (Supported by grants PHS NB-04744 and GM00538)

31.14 EFFECTS OF INACTIVITY AND PROGRAMMED STIMULATION ON THE PHYSIOLOGY OF A CAT TAIL MUSCLE. Dan A. Riley*. (SPON: H. Yellin) Lab of Neurochemistry, National Institutes of Health, Bethesda, Maryland 20014.

The influence of impulse pattern on the contractile properties of skeletal muscle was investigated. To deliver a known program of impulses, tail muscles were rendered inactive by transecting the spinal cord at S2-3 and cutting dorsal rootlets caudal to this level. The muscles were not denervated because ventral rootlets were left intact. In some of these cats, caudal nerves were stimulated for 1 mo in patterns approximating activity of either tonic motor neurons (10 Hz, given in 40 sec trains, repeated every 200 sec for 6 hr/day) or of phasic neurons (50 Hz, given in 0.8 sec trains, repeated every 200 sec for 6 hr/day). At 1 and 2 mo after surgery, the contraction time of inactive muscles was about 40% prolonged over the control average of 41 msec, but it returned to control level by 4 and 5 mo. Physiological changes were the same for a particular program whether stimulation was begun immediately, 1 mo, or 4 mo after surgery. Tonic stimulation produced a prolongation of contraction time (46%), while phasic stimulation resulted in contraction times not significantly different from controls. Tetanus/twitch ratios declined from 4.6 to 2.0 after 1 mo of inactivity and remained low at all periods thereafter. Stimulation tended to return the ratio toward normal (2.7). In all cases, the decreased tetanus/twitch ratios resulted largely from an increased height of twitch; the maximum tetanic force/cm^2 remained normal. Thus, the contraction time and tetanus/twitch ratio can be modulated by altering the pattern of impulse activation. (U.S.P.H.S. grants HD00277&2T01-GM00723-11)

34.1 DEMONSTRATION OF ADENOSINE TRIPHOSPHATE AND AN ELECTRON DENSE PARTICLE IN CHOLINERGIC SYNAPTIC VESICLES. Alan F. Boyne*, Timothy P. Bohan* and Terence H. Williams. Depts. of Pharmacology and Anatomy, Tulane Med. Sch., New Orleans, La 70112.

Whittaker's group recently reported that cholinergic vesicles isolated from Torpedo marmorata electric organ and purified by zonal density gradient centrifugation contain ATP along with acetylcholine (Bioch. Soc. Symp. 36, 49, 1972). We have confirmed these findings using Narcine brasiliensis electric organ and using swinging bucket density gradients for vesicle isolation. We have also studied the electron microscopic appearance of the nerve terminals in the intact tissue as a function of fixation conditions. We have found that a single electron dense particle is observed within the vesicles both in situ and after density gradient isolation when the following solution is used at 5°C as the primary fixative; 5% glutaraldehyde, 4% paraformaldehyde, 0.09M $CaCl_2$, 0.3 M sodium cacodylate/HCl buffer, pH 7.2. The buffer and salts in this solution are iso-osmotic with elasmobranch body fluids.

The demonstration of an intra-vesicular particle raises the possibility that cholinergic vesicles of elasmobranch electric organ differ from the clear cored vesicles in mammalian cholinergic nerve terminals. This, in turn, raises a question as to the generality of the presence of ATP in cholinergic synaptic vesicles. The possibility that high osmolarity fixation solutions will show up similar cores within mammalian cholinergic vesicles is under investigation.

34.2 THE EFFECT ON IN VIVO ACH RELEASE FROM CAT CAUDATE NUCLEUS OF SURGICAL AND PHARMACOLOGICAL MANIPULATION OF DOPAMINERGIC NIGROSTRIATAL NEURONS. Barbara E. Jones, Patrice Guyunet*, Andre Cheramy*, Christian Gauchy*, and Jacques Glowinski*. Groupe N.B., College de France, Paris.

The interrelationship between dopaminergic and cholinergic neurons of the nigrostriatal system was investigated by observing the effect of surgical and pharmacological manipulation of dopaminergic neurons upon the in vivo ACh release from the caudate nucleus. By modification of the cup technique (Besson et al., 1971), the ventricular surface of the caudate nucleus was superfused with eserinized Ringer Locke solution in the flaxedilized cat. ACh in the superfusate fractions (of 10-15 min) was assayed on dorsal leech muscle. Halothane anesthesia and locally applied tetrodotoxin were both shown to diminish ACh release whereas atropine (iv or local) was shown to greatly enhance spontaneous ACh release (3-4 times) in the awake cat. Drugs which are known to greatly enhance extracellular concentrations of DA including l-DOPA (iv), d-amphetamine (iv and local) and exogeneous DA (local), had no observable effect on the spontaneous release of ACh in the awake animal. Furthermore the administration of alpha-methyl para tyrosine which greatly decreases the release of DA, did not significantly modify the release of ACh. These results suggest that dopaminergic neurons do not directly act upon cholinergic neurons terminating in the caudate nucleus. A partial brain transection at the level of the meso-diencephalic junction which traversed the cortex, midline and lateral thalamic nuclei, and the ventral tegmental area greatly diminished the release of ACh. This effect was shown to be due to the transection of the ventral tegmental area. It was concluded that a non-dopaminergic pathway which ascends through the ventral tegmental area exerts an excitatory influence upon cholinergic neurons of the striatum. (Supported by INSERM, CNRS, DRME, and FFRP.)

34.3 SPECIFIC CHOLINE ACCUMULATING SYNAPTOSOMES IN RAT BRAIN. Henry I. Yamamura and Solomon H. Snyder. Dept. Pharmacology, Johns Hopkins University, School of Medicine, Baltimore, Maryland 21205

An adequate supply of intraneuronal choline is critical for cholinergic nerve function in some systems. Central nervous system tissue, however, appears to be virtually incapable of synthesizing choline de novo. Accordingly, we have sought to demonstrate choline transport systems which might subserve the requirements of cholinergic neurons for choline. The accumulation of [^{3}H]-choline into nuclei-free homogenates of rat corpus striatum, cerebral cortex and cerebellum was studied at varying choline concentrations and was found to be saturable. Two kinetically distinct transport components, a high affinity uptake system with Km values of 1.4 μM (corpus striatum), and 3.1 μM (cerebral cortex) and a low affinity uptake system with Km values of 93 μM and 33 μM respectively, for these two brain regions were demonstrable. In contrast in the cerebellum, choline appeared to be accumulated only by the low affinity system. Subcellular fractionation of nuclei-free homogenates on discontinuous sucrose density gradients into purified synaptosomes and mitochondria indicated that the high affinity component of choline accumulation was localized to the synaptosomal fraction. In addition subcellular fractionation of nuclei-free homogenates on continuous sucrose gradients revealed the existence of a limited subpopulation of synaptosomes that specifically accumulated low concentrations of [^{3}H]-choline (0.5 μM) and sedimented to a more-dense portion of the sucrose gradients than the general population of synaptosomes incubated with high concentrations of [^{14}C]-choline (100 μM). Since we have previously demonstrated (Science 178:626, 1972)that the high affinity uptake system required sodium, was sensitive to metabolic inhibitors and was associated with ACh formation, the present results further support the hypothesis that the high affinity transport represents a selective accumulation of choline by central cholinergic neurons.

34.4 KINETIC STUDY OF CHOLINE IN PLASMA AND BRAIN. John J. Freeman*, R. Leslie Choi* and Donald J. Jenden. Dept. Pharmacol., Sch. Med., UCLA, Los Angeles, Ca. 90024

A gas chromatographic procedure for the simultaneous microestimation of choline (Ch) and acetylcholine (ACh)(Jenden et al., Anal. Chem. 44:1879, 1972)has been modified to incorporate ion-pair extraction of quaternary ammonium compounds utilizing dipicrylamine (2,2',4,4',6,6'-hexanitrodiphenylamine) and subsequent analysis by gas chromatography/mass spectrometry. Deuterium-labelled Ch (D4-Ch) was infused continuously at a rate of 2 μmoles $kg^{-1}min^{-1}$ into the jugular vein of anesthetized rats, and the regulation,transport and metabolism of Ch in the plasma and brain were investigated. The specific activity of carotid Ch rose rapidly and reached a plateau at 70%(mole ratio) within 1 min. The specific activity of the internal jugular Ch reached a plateau of 52%. Concentrations of endogenous Ch (D0-Ch) were higher in the internal jugular than in the carotid, confirming the findings of Dross and Kewitz (N.-S. Arch. Pharmacol. 274:91, 1972). Concentrations of D4-Ch were lower in the internal jugular than in the carotid. Concentrations of D0-Ch in both arterial and venous plasma were not lowered by infusion of D4-Ch. ACh was not found in significant amounts in the plasma. The specific activity of Ch and ACh in the brain rose gradually and approached 10 and 15% respectively following 4 hr of infusion. The infusion of D4-Ch did not appear to affect the total Ch or ACh content of the brain. The results indicate that the supply of Ch to plasma was not subject to feedback inhibition and that plasma Ch was taken up and converted to ACh in the brain. The brain however appears to produce Ch endogenously and to contribute to the observed arterio-venous difference. (Supported by USPHS Grant MH-17691).

34.5 KINETIC PROPERTIES OF THE IMIDAZOLE CATALYSED SYNTHESIS OF ACETYLCHOLINE. Alvin M. Burt. A.R.C. Institute of Animal Physiology, Babraham, Cambridge, England.[1]

Imidazole has been shown to catalyse the synthesis of acetylcholine (ACh) (Burt and Silver, Nature, 1973, in press). Some of the kinetic properties of this non-enzymatic acyl-transfer reaction were studied in detail. The incubation media (110 µl) contained imidazole, 18 or 36 mM, and variable concentrations of choline and (1-^{14}C)acetyl-CoA. Most incubations were for 15 or 30 min. at 39°C with a final pH of 7.5. The reaction was initiated by the addition of (1-^{14}C)acetyl-CoA and terminated by the addition of HCl. An anion exchange resin was used for the complete and separate recovery of the reaction products, (1-^{14}C)ACh and (1-^{14}C)acetate. The transfer of the acetyl group from acetyl-CoA to choline is pH dependent and proportional to both time and imidazole concentration. ACh synthesis increases and acetate formation decreases as a function of choline concentration. The choline K_m for ACh synthesis is the same as the K_i for acetate formation. The K_m values for acetyl-CoA and choline are 4.2 and 62 mM respectively. The qualitative similarity between many of the kinetic properties of this reaction and those of choline acetyltransferase support the idea that an imidazole ring is part of the active center of the enzyme. (Support: a travel grant from the Underwood Fund of the A.R.C., U.S.P.H.S. Research Career Development Award GM-10132 and Grant NS-07441, and the Dysautonomia Foundation).

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34.6 EFFECT OF PREGANGLIONIC DENERVATION ON ENZYMES OF ACETYLCHOLINE METABOLISM IN THE CILIARY GANGLION. Janusz B. Suszkiw*, Hideyuki Uchimura*, Ezio Giacobini* and Guillermo Pilar. Biological Sciences Group and Dept. Biobehavioral Sciences, Univ. of CT., Storrs, CT. 06268

In a previous report (Pilar, Jenden and Campbell, Brain Res. 49: 245, 1973) it was shown that the level of acetylcholine (ACh) in the ciliary ganglion of pigeon is decreased by 85% 5 days after denervation and is not measurable after 10 days. Here we report about the effect of preganglionic denervation on enzymes of acetylcholine metabolism in the ciliary ganglion. Cholinacetylase (ChAc) and acetylcholinesterase (AChE) activities were decreased by 70% and 20% respectively 3 days after denervation; after 6 days ChAc activity was further decreased by 10% and reached a minimum level of 15% of the original activity after 10 days. No further change in AChE activity was observed after 7 days. Monoamine oxidase (MAO) activity was decreased by 20% and 40% at 6 and 12 days, respectively. In contrast to the pronounced changes of ChAc activity, no significant variation was observed in protein content and lactic dehydrogenase (LDH) activity. The apparent discrepancy between the absence of detectable ACh and greatly lowered, but not negligible, ChAc activity at 10-12 days after denervation suggests the possibility that other factors such as levels of AcCoA or choline might be involved in the regulation of ACh metabolism in postsynaptic cells in parasympathetic ganglia.

This investigation was supported by research grants NS-10338 and Univ. of Conn. Research Foundation 35-071.

34.7 TOTAL BRAIN CHOLINE CHANGES DURING THE DEVELOPMENT OF TOLERANCE TO DFP. Virginia G. Carson and Donald J. Jenden. Dept. Pharmacol. Sch. Med., UCLA, Los Angeles, Ca. 90024

Behavioral and physiological tolerance to DFP developed in rats given repeated doses of DFP (1.0 mg/kg im in Arachis oil followed by 0.5 mg/kg every 3 days) (Russell et al., Commun. Behav. Biol. 4:121, 1969) in spite of the fact that the brain cholinesterase activity remained at ~30% and brain acetylcholine levels at ~140% of control values. Biochemical tolerance to DFP was observed when total brain choline levels were measured. Choline levels were determined by gas chromatography. Twenty-four hr after the first injection of DFP brain choline levels in DFP rats (n=23) were significantly less (73%) than choline levels in control rats (n=55; 56.8 ± 1.08 nmoles/g). After ten days on the above DFP regimen brain choline levels of DFP-treated rats (n=19) were still significantly lower than those of controls, but the percentage of control value had increased to 86%. This value was significantly higher than the value at 24 hr. After 22 days on the DFP regimen, rats had become behaviorally and physiologically tolerant to DFP. At this time the choline level of DFP animals (n=18) had risen to 92% of the control value and was no longer significantly different from it. Hence brain choline levels change with the development of behavioral and physiological tolerance to DFP. Furthermore, a number of drugs are known to elevate total brain acetylcholine and choline after an acute injection. However, DFP is the only drug observed thus far that lowers the brain choline level significantly. (Supported by USPHS Postdoctoral Fellowship ES 52513 and USPHS Grant MH 17691).

35.1 AUTOMATIC ENTRAINMENT FOR A CELLULAR LEARNING STUDY. T. Tosney and G. Hoyle. Biol. Dept., Univ. of Oregon, Eugene, OR 97403.

The single excitor innervating the locust coxal adductor fires tonically at 15.2 Hz, S.D. ±4.9. This rate is raised to as high as 41 Hz by operant conditioning in which an electric shock is given to the leg immediately following a spontaneous drift towards the lower ranges of frequencies. Because the neuron soma and those of antecedent interneurons occupy set locations in the ganglion and are large enough to be penetrated by microelectrodes, the possibility of studies on the cellular basis of the learning process has been raised. To facilitate such studies, and to enable exact determinations of the parameters related to the learning, we have developed an automatic entrainment program utilizing an on-line LINC-8 computer. The motor output is analyzed successively in units of 150 pulses to determine whether long intervals are accumulating at faster than average rate, and also whether the mean frequency is below a pre-set demand level. If both are affirmative the computer delivers a correlated shock to the preparation. Following shock, the mean frequency rises. The computer delays 6 sec to permit direct reflex effects of the shock to abate, after which it again analyzes the train. In 68% of our experiments the mean frequency rose, 30% to 300%, after as few as 3 correlated shocks. Maximum rates, achieved by progressive shifts in demand level were achieved by from 10 to not more than 120 shocks. Yoked or random control preparations showed changes of below 10%. The higher rates were retained for from 4 hr to more than 10 hr. A reciprocal computer program was prepared in which the shock was delivered following a trend towards short intervals. This resulted in a fall in the mean frequency in both naive animals and those trained to fire at a higher than normal rate. (Supported by N.S.F. Research Grant GB 16962).

35.2 BULK AS A SIGNAL REGULATING FEEDING BEHAVIOR IN APLYSIA CALIFORNICA. A.J. Susswein* and I. Kupfermann. Depts. of Physiology and Psychiatry, NYU Med. Sch. and Dept. Neurobiol. and Behav., Pub. Health Res. Inst., New York, N.Y., 10016.

Aplysia satiates when fed a large meal. Satiation differs from other forms of behavioral plasticity previously analyzed in Aplysia in that it is an alteration of a motivational state, rather than a form of learning. Before a neural analysis of satiation is possible, it is first necessary to examine the cues that signal satiation. These cues could be provided by (1) the nutritional (chemical) properties of the food, or by (2) the bulk (mechanical) properties of the food. To distinguish between these two possibilities, we determined how much animals ate when fed seaweed diluted with non-nutritional bulk, and when fed undiluted seaweed. If bulk provides a satiation signal, animals should satiate on the same amount of bulk, regardless of its nutritional value. The total quantity of food that was eaten during experimental meals (food diluted with non-nutritional bulk) was found to be virtually identical to the amount of food eaten during control meals (undiluted food). The role of bulk was also examined by filling the gut with non-nutritive bulk via an esophageal cannula. This led to satiation when the amount of bulk injected was comparable to that normally present in the gut of satiated animals. Satiation was not produced when the body wall was stretched by means of injections of bulk into the hemocoelomic cavity. These experiments suggest that passive stretch of the gut is a factor in satiation.

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35.3 CLASSICAL CONDITIONING, SENSITIZATION AND PSEUDOCONDITIONING IN APLYSIA. B. Jahan-Parwar, Clark Univ., Dept. of Biol., Worcester, Mass. 01610.

In several series of classical conditioning experiments with Aplysia, using a flash of light as the conditioned stimulus (CS) and presentation of food as the unconditioned stimulus (US), it was found that the probability of feeding response (CR) to the CS alone was significantly higher in subjects that had received CS,US paired in forward temporal order than in subjects that had received CS,US paired in backward temporal order, or unpaired in random orders indicating that pseudoconditioning was not primarily responsible for the increased responsiveness. The possible effect of sensitization was investigated in several subjects by using the procedures of differential and reversal conditioning. The differential conditioning subjects received two stimuli with the US. One stimulus, the CS^+ (light), was paired (in forward temporal order) with the US, and the other, the CS- (touch), was not. All these subjects developed higher responsiveness to CS^+ with increased training sessions. After reaching the learning criterion with the CS^+, the CS^+ and CS- were reversed during the subsequent sessions. This resulted in the extinction of the CR to the light, now serving as the CS-, and acquisition of the CR to the touch, now serving as the CS^+. These experiments provide adequate controls for the effects of sensitization, pseudoconditioning, and individual differences between subjects and suggest true conditioning of Aplysia. Supported by the PHS Grants NS08868, FR07045-07 and Career Development Award K4-HD-5178.

35.4 FIRING PATTERN CHANGES INDUCED BY LOW INTENSITY MICROWAVE RADIATION OF ISOLATED NEURONS FROM APLYSIA CALIFORNICA. H. Wachtel, W. Joines,* R. Seaman* and C. Walker,* Duke University, Durham, North Carolina 27706.

Current standards for safe exposure to microwave radiation (MWR) are based on the belief that only MWR levels which cause tissue heating are of concern; however, some recent studies suggest the possibility of neural effects at much lower levels. In order to explore such effects, we have exposed isolated ganglia from Aplysia Californica to precisely controlled MW fields. In addition to the usual advantages they offer as prototypical neuronal systems, these ganglia are also ideal from the standpoint of MW dosimetry and thermal measurement. Since these ganglia are far smaller than the wavelength of even our shortest MW's, they cause little or no distortion of the MW field, which allows us to mount the ganglion within a strip line and measure the absorbed power (P_a) along with the temperature. For relatively low level MWR (P_a from 10 to 50 milliwatts/cc) and MW frequencies of 1.5 and 2.45 GHz (the latter being the commercial MW oven frequency), the most pronounced effects were seen on the firing rhythm of pacemaker neurons. The bursting neurons (L_2-L_6) were found to be particularly sensitive to the MWR, which often caused a marked decrease in the interburst interval or even a conversion of the bursting pattern to a steady firing mode. For these values of P_a the temperature was seen to increase somewhat (1 or 2°C), but the changes in neuronal firing pattern induced by MWR could not be mimicked by convectively heating the ganglion to the same, or even higher, temperatures. (Supported by contracts FDA 73-35 and NIEHS 72-2094.)

35.5 **OPERANT MODIFICATION OF UNIT RESPONSES IN VISUAL CORTEX.** **Paul G. Shinkman. Univ. North Carolina, Chapel Hill, N. C. 27514**

Responses to a 25-msec. photic stimulus were studied in visual cortical neurons in Flaxedilized cats. For each cell, peristimulus time histograms (PSTHs) were compiled on-line, showing the cell's temporal pattern of response. Then, reinforcing brain stimulation was made contingent upon a prespecified change in the cell's response pattern, i.e. a rate alteration during a selected segment of the poststimulus interval (the "criterion period"). Usually the criterion period began 300 msec. after the stimulus and lasted 500 msec., although other values were studied in some cells. The brain stimulation was delivered to lateral hypothalamus through previously implanted electrodes; its reinforcing properties had been established ahead of time in testing sessions during which the subject bar-pressed to obtain stimulation.

Conditioned changes in the form of the PSTH were observed in nearly half the cells studied. For some cells, conditioning trials were followed by extinction trials (reinforcement omitted) and then by reconditioning trials. These procedures often, but not always, produced appropriate changes in a cell's response as reflected in the PSTH. Conditioning sometimes took the form of an overall change in rate of firing; usually, however, the change was specific to the criterion period. Cells with modifiable response patterns were encountered much more often in suprasylvian than in posterolateral gyrus.

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35.6 CONDITIONING, EXTINCTION, AND HABITUATION IN THE SPINAL RAT. Suzzette F. Chopin*[1], Marvin H. Bennett[2], and J. Michael Kerrigan*[1]. [1]Dept. Anat. L.S.U. Med. Centr., New Orleans, La., 70112 and Div. Neurol. Surg., Univ. Pitts., Sch. Med., Pittsburgh, Pa., 15213.

The spinal cord of adult female rats was transected at the second lumbar vertebra. One electrode was inserted into the right hip between the greater trochanter and the ilium; a second electrode was inserted beneath the dorsal skin of the right foot. The animal was placed in a restraining cage such that the right limb was allowed to hang free. The animal received electric shocks whenever the foot electrode made contact with an electrolyte bath beneath the restraining cage. Flexion of the limb permitted the animal to escape the shock. Operant conditioning was considered to have occurred when the foot electrode made contact with the electrolyte bath less than 10% of the time over a 5 min. period. Once an animal reached criterion, the foot electrode was adjusted so that the animal could not escape shock, and thus was shocked independently of foot position. The conditioned behavior became extinguished. The animal eventually habituated to the stimulus and could be dishabituated by increasing shock intensity. In a control group of naive spinal rats in which the foot electrode was arranged so that the animal received inescapable shock independent of foot position, the criterion of learning was not obtained. These animals quickly habituated and could easily be dishabituated. Extinction of the conditioned response in trained animals and habituation in the naive animal argue against neuronal sensitization as the cause of the observed behavior. The responses described above are analogous to those observed in classical learning situations. Thus, it would seem that learning, or behavior closely approximating it, is possible in spinal cord deprived of higher control. (Spon. by NIH-T01 DE 00241, CA 13322, Can.Soc. N.O.LA.)

35.7 HABITUATION OF THE FLEXOR REFLEX IN ADRENALECTOMISED RATS. J.A. Pearson* and R.A. Vickars* (SPON: J.J. Miller). Dept. of Physiology, Univ. of British Columbia, Vancouver 8, B. C.

It has been suggested that a common neuronal mechanism is responsible for extinction and habituation (Thompson and Spencer; Psychol. Rev., 73, 16-43, 1966). Since extinction of conditioned avoidance responses is retarded following adrenalectomy it might be expected that habituation also would be impaired by this procedure. Experiments were carried out on the effect of adrenalectomy on habituation of the flexor reflex in conscious rats. Integrated EMG activity, recorded from the caudal head of the right biceps femoris was used as an index of reflex activity. Electrical stimuli (20 V, 10 mA, 1 msec) were applied to the skin of the ipsilateral hind paw (interstimulus interval, 5 sec). In control rats (2 weeks after sham adrenalectomy) the mean response to the 300th stimulus was 48.2 ± S.E. 4.0% of the initial response. In rats which had been adrenalectomised 2 weeks earlier, the mean response to the 300th stimulus was 47.6 ± S.E. 6.2% of the response to the initial stimulus. Thus, habituation of the flexor reflex was shown to be unaffected by adrenalectomy. However, extinction of conditioned avoidance responses, when tested an identical period of time after adrenalectomy, was markedly impaired (Bohus, et al., Int. J. Neuropharmacol., 7, 307-314, 1968). It is suggested that if extinction and habituation are due to a common mechanism, then an additional mechanism which is sensitive to the consequences of adrenalectomy must be postulated for extinction, but not for habituation.

36.1 SIZE, NUMBER AND SPATIAL DISTRIBUTION OF NEURONS IN LAYER IV OF MOUSE S I CORTEX. J. F. Pasternak* and T. A. Woolsey. Dept. Anat., Sch. Med., Washington Univ., St. Louis, Mo., 63110.

The barrel field in layer IV in mouse SI cerebral cortex (Woolsey and Van der Loos, 1970) is an excellent site for quantitative studies. The constancy in the geometric array of these barrels allows similar areas of cortex to be analyzed in many specimens. Such data could be used in two ways: (a) as a measure of the variability of this cortical area in the adult, and (b) as a prerequisite for further quantitative morphological analyses of the barrels. We located barrel C-1 (Van der Loos and Woolsey, 1973) in Golgi-Nissl preparations (Van der Loos) from the brains of 14 white Swiss mice. Each brain was cut serially at 40-50μ in a plane tangential to the pia overlying S I. Using the section in which the barrel C-1 could be optimally visualized, the cross-sectional area of each Nissl and Golgi stained neuron soma was outlined using a camera lucida and measured with the aid of a small computer. In all, over 6,000 neurons have been measured. By extrapolation we estimate the number of neurons in this barrel to be about 2,000. The mean cell size, distribution of cell sizes and the spatial distribution of cells in the barrel are fairly constant. The mean cross-sectional areas of the neurons varied from 60.68 μ^2 to 66.83 μ^2 (S.D. 14-17 μ^2). The distribution of soma areas was unimodal but not normal, with a tail to the right (larger cells). The barrel sides were found to be 1.97-1.42 times more densely populated (cells/μ^3) than the hollows. The Golgi impregnated neurons represent 1.4% of the total population. This study shows that quantitative analyses of barrels are feasible. It also shows that the same area of cortex in different specimens is surprisingly similar and this implies that the mechanisms responsible for the development of at least mouse S I cortex are quite precise. (Supported by NIH Grant NS 10244.)

36.2 ACTION OF TOPICAL STRYCHNINE ON EVOKED POTENTIALS AND SINGLE NEURONS OF POSTCRUCIATE CORTEX OF CATS. Michael D. Mann and Arnold L. Towe. Dept. Physiol. & Biophysics, Sch. Med., Univ. Washington, Seattle 98195.

Both the primary evoked response and the corticofugal reflex discharge evoked by a shock to the contralateral forepaw (CFP) are enhanced by topical application of strychnine sulfate to the postcruciate forepaw focus. Under the same circumstances, there is no change in either cortical potential or the pyramidal tract discharge evoked by off-focus (IFP, CHP or IHP) shock. Neurons in the postcruciate forepaw focus are classed as sa or m, depending on whether they respond to stimulation of the CFP only (sa) or to all four paws (m). Strychnine enhancement of the surface-evoked potential and the corticofugal reflex response occurs when sa neurons are excited by cutaneous stimulation. Most pyramidal tract cells belong to the m class, which is only indirectly affected by topical strychnine. This indirect effect is the result of the known facilitatory influence of sa neurons on m neurons, including pyramidal tract neurons. Single neuron recordings made in this tissue preceding and following application of strychnine show that sa neurons undergo 1) an increase in number of spikes per discharge, 2) no change in first-spike latency, and 3) a marked decrease in threshold to electrical skin stimulation. The indirect effect on m neurons is underscored by the observation that they show: 1) an increase in number of spikes per discharge evoked by CFP stimulation, but no change for off-focus stimulation, 2) a marked decrease in first-spike latency following CFP stimulation, but no change for off-focus stimulation, and 3) a decrease in threshold to CFP stimulation. All effects observed for topical application of limited amounts of strychnine can be understood in terms of these functional sets of neurons, s and m, their relative locations in depth, and their known interconnections. (Supported by USPHS grants NS00396, NS05136 and NS05082.)

36.3 TERMINATION OF THALAMIC AFFERENTS IN THE CAT MOTOR CORTEX. Peter L. Strick. Lab. Neurophysiology, NIMH, Bethesda, Md. 20014

The thalamic projection from the ventrolateral nucleus (VL) to area 4γ of the motor cortex has been studied with experimental electron microscopic techniques. Following VL lesions, degenerating synapses were mainly found in three cortical layers: the upper third of Layer I (18%), Layer III (66%), and Layer VI (13%). Degenerating synapses were not seen in the lower two-thirds of Layer I or in Layer II, and only rarely in Layer V (3%). The density of VL synapses in Layer III varied from 0.36 to 8.2 synapses per 10,000μ^2. The number of VL synapses increased gradually as one proceeded from the top to a point 90μ from the bottom of the layer, where an abrupt decrease occurred. Ninety-one percent of the VL synapses were found on cortical spines and 8% on stellate-type dendritic shafts. Stellate cell bodies rarely (1%) received VL synapses and none occurred on pyramidal or Betz cell bodies and their proximal dendrites. A VL synapse within Layer III was found on two spines of a Betz cell apical dendrite. Thus, part of the VL input to Layer III synapses on the processes of both motor cortex output neurons (Betz cells in Layer V) and cortical interneurons (stellate cells in Layer III). Supported in part by U.S. Public Health Service Grant 2T01-GM00281-11 2-09-010 X1646.

36.4 SIMULTANEOUS AND INDEPENDENT IPSPS IN NEARBY NEURONS IN CAT MOTOR CORTEX. W. Raabe.*(SPON: G.F. Ayala). Neurology Dept., St. Paul-Ramsey Hospital, St. Paul, Minn. 55101.

Simultaneous intracellular recordings from two different neurons were obtained with double-barreled microelectrodes prepared from single microelectrodes. The shanks were attached to each other, and the tip of one barrel was ca. 80 μm remote from the other. All recorded neurons were unidentified neurons. Approximately perpendicular penetration of the cortex by the double-barrel microelectrode suggests that the actually recorded neurons were located in different cortical levels, ca. 80 μm apart, and that the neurons might belong to the same cortical column. No direct relationship between action potentials in one (nearby) neuron and postsynaptic potentials in the other (nearby) neuron was observed. Stimulation of the thalamic ventrolateral nucleus (VL) elicited simultaneous hyperpolarizing potentials in both nearby neurons. On the other hand, spontaneous hyperpolarizing potentials, which prevented cell firing, were seen to occur independently in either nearby neuron. The time course of the hyperpolarizing potentials as well as their occurrence independently of preceding action potentials indicate that they are inhibitory postsynaptic potentials. The following pathways are proposed for the mediation of the simultaneous and independent IPSPs in nearby neurons: the simultaneous (VL-mediated) synaptic inhibition is mediated by common pathways, while the independent synaptic inhibition is mediated by separate pathways. Because of the location of the nearby neurons, pathways for simultaneous and independent synaptic inhibition seem to be present for neurons which belong to the same cortical column.

(The work was done in the Max-Planck Institut f. Psychiatrie, Muenchen, Germany. Supported by Max-Planck-Gesellschaft.)

36.5 INTRACELLULAR RECORDING DURING FOCAL COOLING OF GLIA AND NEURONS IN CAT PERICRUCIATE CORTEX. Arden F. Reynolds, Jr.,* George A. Ojemann and Arthur A. Ward, Jr., Dept. Neurosurg., Univ. Wash., Seattle, 98195.

Intracellular recordings were obtained from cat pericruciate cortex during focal cooling with a Peltier device. Each cooling cycle dropped cortical temperature from 37° to 27° in 5-8 min., maintaining it at 27° for 3-7 min., then rewarming over 5-8 min. to 37°. 28 glia were thus cooled. Membrane potential (Vm) depolarized an average 21 mv from an initial 77 mv resting level. The time course of this depolarization was the mirror image of the temperature curve. Membrane resistance (Rm) was measured in 6 glia and increased in parallel with the Vm. The Q-10 was 2.5. Neurons demonstrated a delayed depolarization after 1.5-3 min. at 27° which lasted as long as the temperature was maintained at 27°. The magnitude of depolarization in 8 cycles in 4 cells averaged 14 mv from an average resting potential of 60 mv. Rm showed a 2-fold increase and the duration of the action potential (AP) increased by a factor of 3 at 27°. The firing frequency increased transiently to 200 Hz at 32° and again after 1.5-3 min. at 27°, on the upramp of depolarization. During the period of maximum depolarization it dropped to 20-40 Hz and AP amplitude decreased to 65% of precool values. On rewarming, Vm hyperpolarized for 2-3 min. As Vm returned toward normal at 34°, bursting activity of 250 Hz was demonstrated. At 37° neuron function was back to precool values except for a slight decrease in AP duration. These findings parallel and extend the extracellular recordings during focal cooling of cat cortex reported by Moseley et al (Exp. Neurol. 37:152, 1972) and suggest that cooling interferes with Na+ pump.
(Supported in part by NIH grants NS 04053 and NS 05211)

36.6 The parietal association areas and immediate extrapersonal space. J. C. Lynch, C. Acuna,* H. Sakata,* A. Georgopoulos * and V. B. Mountcastle, The Johns Hopkins University School of Medicine, Baltimore, Md.

The posterior parietal areas of the monkey cortex have been studied by the method of single unit analysis in 15 waking monkeys trained in behavioral tasks; 929 cells were studied in 67 microelectrode penetrations. We confirm that many area 5 neurons are activated by joint positions and movements, in some cases only by complex postural attitudes; a smaller number is sensitive to muscle stretch. Bilateral receptive fields and directional sensitivity are common characteristics of cutaneous neurons of area 5.

The portions of areas 5 and 7 which line the intraparietal sulcus contain neurons which are active only when the animal projects an arm towards a desired object or a meaningful target, but are not activated by passive stimulation of the arm. Some are active during either projection of the arm or direction of gaze, and their discharge is enhanced during visually guided hand-arm tracking of moving objects.

Neurons of area 7 proper are related to visual phenomena; many are activated when the monkey directs his gaze towards wanted objects within arm's length, and are intensely active as the animal tracks such objects through his (usually contralateral) field of gaze; they are almost always directionally sensitive. Such neurons are inactive during similar eye movements occurring spontaneously. Other cells of area 7 are sensitive to moving objects, and possess large and vaguely defined receptive fields, usually in the contralateral half-field.

Thus neurons of the posterior parietal association areas, neither sensory nor motor in the classical sense, are active before and during the animal's motivated operation within immediate extrapersonal space.
(NINDS, NIH, USPHS Center Grant NSO 6828).

36.7 SCANNING OF CORTICAL NEURONS IN THE EEG: A POSSIBLE MECHANISM OF ATTENTION AND CONSCIOUSNESS. Rafael Elul. Dept.Anat.,UCLA Sch.Med.,Los Angeles 90024

Recent cortical intracellular studies indicate that the wave potentials recorded from any given point on surface of the cerebral cortex originate from synchronized wave activity in a relatively small fraction of the total neuronal population in underlying tissue. Since a consistent correlation cannot be found between spontaneous surface activity and wave potentials in any single neuron, these results imply that the EEG recorded in successive instant in time from the same cortical site results from sequential synchronization of different groups of neurons. Although appearing continuous, the EEG is a sequence of discrete, unconnected waveforms, analogous to 'evoked potentials'(cf. Elul, Internat.Rev.Neurobiol.,1972,15:227). Additionally, local subcortical injections of TTX indicate that inputs from specific thalamic nuclei are essential for maintenance of EEG activity. In contrast, TTX injection in certain non-specific thalamic nuclei has no appreciable effect on cortical EEG activity.

I propose that sequential selective synchronization of discrete groups of cortical neurons mediated through specific thalamocortical pathways provides a means for the non-specific thalamic nuclei, which receive outputs from the entire cortex via corticothalamic pathways, to serially scan selected aspects of cortical processing. The activation at a particular moment in time of the relevant subset of cortical cells, allows non-specific thalamic 'scanners' to discriminate information originating in this same group of cells, from messages arriving over the identical period of time from cortical neurons serving other modalities. In this way the parallel information processing characterizing the cortex may be time-multiplexed and funneled through a unique 'attention channel'. It is perhaps worth while noting that,subjectivly, an important feature of conscious experience is the concentration of attention on different aspects of the external and internal environment in a sequential manner.

37.1 **DIFFERENT PHYSIOLOGICAL PROPERTIES OF NEURONS IN THE ROSTRAL AND VENTRAL PART OF NUCLEUS RETICULARIS THALAMI.** M. Waszak* (SPON: E. G. Keating). VA-Hospital and Dept. Neurosurg., SUNY, Upstate Med. Cent., Syracuse, N.Y. 13210.

Neurons in the rostral and anteroventral portion of n. reticularis thalami underwent changes of opposite polarity during the development of EEG synchronization: In encephale isole cats,the appearance of individual EEG spindle trains in the motor cortex, occurring spontaneously or being "tripped" by single thalamic midline shocks, was accompanied by increased neuronal activity in the rostral pole of the nucleus as compared with inter-spindle intervals. Fast-frequency discharges occurred either in bursts, in phase with the cortical waves, or, more frequently, were tonically sustained throughout the spindle duration, riding on a small (under 5mV) but unusually prolonged (up to 1 sec) membrane depolarization. The i.v. administration of small doses of Brevital was followed by a decrease in the average inter-spindle firing frequency and a break-up of tonic intra-spindle discharge trains into phasic bursts. Neurons in the ventral part of n. reticularis behaved in a fashion similar to that observed in nuclei of the dorsal thalamus, their membranes becoming hyperpolarized to levels in excess of 10 mV for the entire spindle duration. Cortical recruiting responses, in contrast, were accompanied by membrane potential changes of similar configuration in both regions of the nucleus. The data are viewed as lending further support to the concept that different subdivisions of n. reticularis thalami are concerned with different functions.

37.2 EFFECTS OF LOCUS COERULEUS STIMULATION ON RAPHÉ UNIT ACTIVITY. Edward Berman*, Warren Stern and Peter Morgane* (Spon: John R. Bergen). Neurophysiol. Lab., Worcester Fndn. Exp. Biol., Shrewsbury, Mass. 01545.

Many studies have suggested that the raphé nuclei and the locus coeruleus (LC) play a significant role in the sleep-waking cycle. Further, there is histofluorescence evidence of a noradrenergic projection from the LC to the anterior raphé. We examined the possible influence of these LC projections upon raphé unit activity by recording single units from the nucleus raphé dorsalis following electrical stimulation of the LC. Raphé activity was recorded in rats, under chloral hydrate anesthesia, for 2 minutes prior to presentation of unilateral single pulse, monophasic stimulation (0.5 msec, 20 μA). These pulses were given once every 30 seconds via bipolar concentric needle electrodes. To date, a total of 11 raphé units have been recorded (one per rat). Eight units showed inhibition following LC stimulation while 3 showed no effect. The level of inhibition for the first 2 sec. in the 8 cells affected was 30% (baseline spike rate = 1.1 spikes/sec; post stimulation = 0.74 spikes/sec.). A small inhibitory effect was still seen after 15 seconds. Prior to sacrifice 8 raphé units were tested with i.p. LSD (250 μg/kg) and all showed cessation of firing, thereby providing evidence of raphé localization (histology is in progress). Thus, it appears that projections from the LC inhibit the activity of raphé serotonergic units and suggests that one role of the LC is to inhibit serotonin release in terminals of raphé projections. (Supported by NIMH grants 02211 and 01625).

37.3 ROLE OF BIORHYTHM OF SLEEP AND PARADOXICAL SLEEP IN THE PERIODICITY OF GONADOTROPHIN SECRETION IN RATS. Nobuyoshi Hagino and Sadao Yamaoka. Dept. Neurophysiology, Southwest Foundation for Res. and Educ. and Dept. Anatomy, Univ. Texas Health Science Center at San Antonio, San Antonio, Tex. 78284.

Continuously recorded EEG's from chronically implanted rats were converted into circadian distribution of arousal, slow wave sleep (SWS) and paradoxical sleep (PS) for 4 hr. intervals. The female rat is nocturnal and shows a periodic regulation of gonadotrophin (GTH) secretion. Under light-dark (LD) schedule (14 hr. lighting), rats showed a diurnal rhythm of SWS and PS. Rats exposed to constant light (LL) showed an irregular SWS and PS and developed an anovulatory state. One month after return to LD schedule following exposure to LL for five months, a resumption of diurnal rhythm of SWS was seen in these rats, however, PS rhythm was nocturnal, vaginal cycles were irregular. Under LD schedule pinealectomy had no effect on diurnal rhythm of SWS and PS or vaginal cycles. Rats treated neonatally with testosterone developed an anovulatory state and persistent estrus (Barraclough 1961), and showed a diurnal rhythm of SWS with irregular PS under LD schedule. This evidence indicates that the lighting schedule influences rhythmical appearance of SWS and PS and periodical regulation of GTH secretion. Given this situation, correlation may exist between PS rhythm and GTH secretion in rats. The male rat is also nocturnal, but maintains a tonic regulation of GTH secretion. Male rats showed a diurnal rhythm of SWS and PS under LD schedule. When male rats were exposed to LL, irregular SWS and PS was seen. This work suggests that a diurnal regulation of GTH secretion may exist in male rats as well as female rats. (Supported by NSF GB-28871X and AID csd/2821.)

37.4 INDUCTION OF REM SLEEP IN CATS BY GROWTH HORMONE. Warren C. Stern, John E. Jalowiec*, William B. Forbes and Peter J. Morgane*. Neurophysiol. Lab., Worcester Fndn. Exp. Biol., Shrewsbury, Mass. 01545.

In man, growth hormone (GH) is released in large amounts during slow-wave-sleep (SWS), a time period which is often followed by REM sleep. Thus, the possibility exists that REM sleep is induced by the release of GH in the preceding SWS episode. We obtained four 7-hr. baselines of polygraphically recorded sleep-waking cycles (cats bearing chronic electrodes in the neocortex, hippocampus, LGN, neck and eye muscles) and then administered bovine GH, i.p., in doses of 0.05, 0.1, 0.5 and 1.0 mg (n=5 per dose) and recorded sleep-waking patterns for 7hrs. The results showed a significant increase in the percentage of time spent in REM sleep for the first 3 hrs. at all doses--the average REM time increasing to 150-300% of baseline. SWS occurrence was not altered while waking time was decreased to 75% of baseline percentages. From hrs. 4 through 7 after GH injection the opposite results occurred, i.e., a marked diminution of REM sleep and an elevation of waking. One implication of the results obtained in the first 3 hrs. following GH is that the temporal sequencing of REM following SWS may be, in part, mediated by GH release during SWS. Also, these results provide further evidence of an association between the occurrence of REM sleep and periods of elevated protein synthesis in the CNS.

37.5 ONTOGENEY AND CHARACTER OF PARADOXICAL SLEEP IN THE CHICK. C.J. Schlehuber*, D.G. Flaming*, C.E. Spooner, G.D. Lange. Dept. Neurosc., Sch. Med., UCSD, La Jolla, 92037

Paradoxical Sleep (PS) has been found to constitute a significant portion of the sleep phase of higher vertebrate activity. However, some disagreement has arisen over the percentage of time young and adult chickens spend in PS. Published reports of chick sleep time spent in PS have ranged from less than 0.6% (Klein, et al. C.R.Soc.Biol. 158:99,1964) to nearly all (Greenberg, et al. Psychophysiol. 6:226,1969). In the present study on various aged chicks, the states of sleep and wakefulness were classified by computerized monitoring of multiple unit activity, electroencephalographic, and electromyographic recordings. Chicks of one day, one week, one month, and four months of age, were monitored on a 12hr day - 12hr night cycle. No significant differences could be distinguished among the animals one week and older. Day old animals demonstrated mixed electrographic activity for PS, making classification difficult. However, obvious PS periods were both shorter and fewer for the day old animals and total PS appeared to be less than half that of the older animals. Sleep was distributed evenly over the night period. A trend in frequency of PS through the night was evident in the older animals. As the sleep period progressed the duration of PS increased from less than 5% of sleep to nearly 30% of sleep and sometimes more by the conclusion of the night period. The increase was due to an increase in the frequency of the PS periods (mostly 5 to 7 seconds duration) rather than a lengthening of each PS period, as is the case for higher vertebrates. The percentage of total PS in the older chick is similar to that reported for higher vertebrates but the pattern is different. (Supported by USPHS Grants MH 16943 and MH 23209-01.)

37.6 POSSIBLE DIRECT MODULATOR ROLE OF SEROTONIN PRECURSORS AND METABOLITES ON SLEEP MECHANISMS IN NEWLY-HATCHED CHICKS. W. Pedemonte and H. C. Sabelli, Dept. Pharmacol., The Chicago Medical School, Chicago, Illinois 60612.

According to Jouvet and coworkers (Physiol. Rev., 1967), serotonin is the endogenous modulator for slow wave sleep, and one of its deaminated metabolites is the endogenous trigger for REM sleep. We have previously proposed that the MAO-catalyzed products of serotonin (5-hydroxytryptaldehyde) and of tryptamine (tryptaldehyde) are the endogenous modulators of REM sleep (Nature, 1969). We have now studied the effects of inhibitors of enzymes involved in the synthesis and metabolism of indoleethylamines upon the sleep behavior of newly-hatched chicks (which lack blood brain barrier). Sleep was defined by the roosting posture and eyelid closure; drugs were injected i.p. The L-aromatic amino acid decarboxylase inhibitors α-methyldopa (50 and 100 mg/Kg, 4 hr before) and α-methyldopa hydrazine (MK 486) (100 and 200 mg/Kg, 4 hr before) induced drowsiness and did not prevent the lethargic effect of 5-hydroxy-DL-tryptophane (60 mg/Kg). The tryptophane hydroxylase inhibitor p-chlorophenylalanine (150 mg/Kg, 72, 48, 24, and 4 hr before) alerted the animals and reduced the lethargic effect of L-tryptophane (60 mg/Kg). Neither indoleacetic acid nor 5-hydroxyindoleacetic acid induced sleep. After the administration of 5-hydroxytryptophol or of tryptophol (60 mg/Kg), chicks showed periods of drowsiness alternating with phases of excitement. The alcohol reductase inhibitor pyrazole (70 mg/Kg) induced some drowsiness and did not enhance the lethargic effect of tryptophol and 5-hydroxytryptophol. These results suggest that 5-hydroxytryptophane exerts direct effects (not mediated by its conversion to serotonin) and may be one of the endogenous modulators for slow wave sleep, and that the aldehyde derivatives of serotonin and of tryptamine may be the endogenous triggers for REM sleep. (Supported by NIMH Grant MH-14110)

37.7 AROUSAL IN THE FEMALE RAT: THE EFFECT OF STIMULUS RELEVANCE AND MOTIVATIONAL STATE. Stephen R. Zoloth* and Norman T. Adler. Dept. Biol. and Dept. Psychol., Univ. of Penn, Philadelphia, 19104

Paradoxical Sleep (P.S.) has been found to be "deeper" sleep than Slow Wave Sleep (S.W.S.), when arousability is measured by presenting neutral stimuli. In this experiment, we compared arousability from P.S. and S.W.S. using a stimulus and motivational state that normally occur in the experience of the organism: pup's cries were presented to sleeping maternal and virgin rats, and the frequency and quality of behavioral arousal was then measured. The responses of these animals to a "neutral" $3KH_z$ tone was also studied. Although a classical finding is that P.S. sleep is "deep sleep", in this experiment arousability to the pup's cry did not change across sleep states, for a given female. Furthermore, maternal females were much more arousable than virgin females from both P.S. and S.W.S. Maternal females also produced more large body movements and full orienting responses than virgins in arousing from both sleep states. For both motivational conditions behavioral arousal was greater to the pup's cry than to the "neutral" tone. From the analysis of the maternal females' response to pup's cries, we conclude that this natural stimulus presented to a motivationally prepared organism produces high arousability. Furthermore, under these conditions, P.S. is at least as compatible with arousal as is S.W.S.

38.1 LSD-25 INDUCED "HALLUCINATORY" BEHAVIOR IN CATS: RELATIONSHIP TO PGO WAVES. Steven Henriksen, Barry Jacobs, and William C. Dement. Sch. Med., Stanford University, Stanford, 94305.

Cats that have been given LSD-25 exhibit striking hallucinatory behavior. During these periods, the animals are highly aroused and appear to respond to non-existent stimuli. Because of the relationship between behavior in the cats during the occurrence of the ponto-geniculate-occipital cortex (PGO) wave, both during REM sleep and following administration of p-chlorophenylalanine (PCPA), we have studied the relationship of these waves to the hallucinatory behavior which follows administration of LSD-25. Seven cats were monitored for waking behavior as well as EEG, EOG, EMG, and PGO activity as recorded from the LGN. Forty ug/kg of LSD-25 to 100 ug/kg was the dose range used. The following is a summary of our results: 1) Cats that, prior to LSD-25, spontaneously exhibit waking eye movement potentials (EMPs) in the LGN and marginal cortex, exhibit more of these waves following LSD-25. 2) Cats that do not spontaneously exhibit these EMPs in wakefulness prior to LSD-25 do not exhibit any such waves subsequent to LSD-25. In fact, we have never seen an LSD-produced wave in an animal that does not exhibit waking PGO waves, but that does show REM PGO's. This is in contrast to the emergence of these REM PGO's following chronic administration of PCPA in the same cats. 3) The cortical component of the LSD-25 induced EMP is abolished, or greatly attenuated when the animal is placed in the dark; this is not the case for PCPA waves or for REM waves. 4) LSD-25 induced EMPs recorded in the LGN and marginal cortex invariably follow eye movements associated with hallucinatory behavior. This is not true of REM and PCPA-induced waves, which often precede eye movements. 5) The waking PGO waves induced by chronic PCPA administration are attenuated in amplitude and frequency following LSD-25 administration.

38.2 EFFECT OF LYSERGIC ACID DIETHYLAMIDE (LSD-25) ON SEROTONIN CONTENT AND TURNOVER IN SIX DISCRETE AREAS OF RAT BRAIN. Ronald D. Huffman and William W. Morgan*. Depts. of Pharmacology and Anatomy, Univ. Texas Med. Sch., San Antonio, Texas 78284.

The effects of LSD-25 on the content of serotonin (5-HT) and noradrenaline (NA) and the turnover of 5-HT in the medulla-pons, midbrain, diencephalon, striatum, cerebral cortex and cerebellum of male Sprague-Dawley rats (150-200gm) were studied. Rats sacrificed 90 min after the administration of LSD-25 (0.2mg/kg, i.p.) had elevated levels of 5-HT in the medulla-pons ($p<0.05$) and NA levels in the striatum ($p=0.02$), but there was no significant change in five hydroxyindoleacetic acid (5-HIAA) levels in any brain area. Three hours after a cumulative dose of 4mg/kg of LSD-25 (2 mg/kg initially followed by 2mg/kg at 90 min), 5-HT levels were again elevated only in the medulla-pons ($p<0.05$); but 5-HIAA levels were reduced in the medulla-pons ($p<0.02$), striatum ($p<0.01$) and cerebral cortex ($p<0.05$). If the rats were pretreated with LSD-25 (0.2mg/kg) and then given probenecid (200mg/kg, i.p.) and a second dose of LSD-25 (0.4mg/kg total), the probenecid-induced elevation of 5-HIAA at 90 min after probenecid was not significantly reduced. However, if the dose was increased to a cumulative dose of 1mg/kg of LSD-25, the probenecid-induced elevation of 5-HIAA levels in the diencephalon, striatum and cerebral cortex were significantly reduced. In another study, 5-HT turnover in the six brain areas was measured by the probenecid method of Tozer et al., J. Pharmac. 153:177, 1966. Rats initially injected with LSD-25 (0.2mg/kg) or saline were either sacrificed at 90 min or were injected with probenecid (200mg/kg, i.p.) and a second injection of LSD-25, and then the rats were sacrificed at 30, 60 or 90 min following the probenecid injection. 5-HT turnover rates ranged from a high of 0.54µg/gm/hr for the midbrain to a low of 0.07µg/gm/hr for the cerebellum. LSD-25 produced a significant reduction in 5-HT turnover in all brain areas except the diencephalon.

38.3 THE ROLE OF SEROTONIN IN THE ACTION OF PSYCHOTOMIMETIC DRUGS. Daniel X. Freedman and Angelos E. Halaris. Dept. of Psychiatry, Pritzker Sch. Med., Univ. of Chicago, Chicago, Ill., 60637.

Psychotomimetic drugs of the indolealkylamine type raise brain serotonin. In an attempt to understand the physiological significance of this phenomenon, LSD was injected in rats pretreated with drugs that affect the metabolism and disposition of serotonin. Tryptophan hydroxylase was inhibited with p-chlorophenylalanine (p-CPA) methyl ester (400 mg/kg) given 65 h prior to LSD. Central aromatic amino acid decarboxylase was blocked with Ro 4-4602 (800 mg/kg) 30 and 60 min before LSD. Storage of serotonin was impaired with reserpine (5 mg/kg) injected 12, 18, 24 and 48 h prior to LSD. Reuptake was blocked with chlorimipramine (25 mg/kg) given at various intervals before LSD. The serotonin antagonist BOL (2 mg/kg) was given 15 min prior to LSD. P-CPA, Ro 4-4602 and reserpine (in "fully reserpinized" animals) completely abolished the expected rise in serotonin 45 min after LSD. Chlorimipramine, after an increase at 30 min, gradually decreased serotonin; 3 h after the reuptake blocker the LSD effect was abolished. If two doses of chlorimipramine preceded LSD, the abolition of the LSD effect was manifest 90 min earlier. BOL tended to diminish the serotonin increase. All of the above mentioned agents - with the possible exception of BOL - markedly enhanced the gross behavioral response of the animals to LSD. There are previous reports that reserpine and p-CPA prolong the disruptive effect of LSD on fixed-ratio schedules of reinforcement. It appears that the availability of newly synthesized serotonin as well as the binding capacity of storage sites is important for the response of the organism to LSD. It is concluded that serotonin may play a role in modulating or terminating the effects of the psychotomimetic agents. Supported by a FFRP postdoctoral fellowship (to A.E.H.) and USPHS research grant 13, 186-07 from NIMH.

38.4 IS DMPEA HALLUCINOGENIC? Wagner H. Bridger, David M. Stoff* and Irwin J. Mandel*. Dept. Psychiatry, Albert Einstein College of Medicine, Bronx, N.Y. 10461

We have previously reported that the endogenously produced compound, 3,4-dimethoxyphenylethylamine (DMPEA), which has been implicated in schizophrenia has the same excitatory effect as mescaline on classically conditioned behavior in rats. We have also previously reported that LSD and mescaline have excitatory effects on acquisition of shuttlebox avoidance. After chronic injections, there is no tolerance but an increase in this excitatory effect. Two experiments were performed to determine whether these excitatory effects are also true for DMPEA. In Experiment 1, 15 male hooded rats were given 25, 50, or 100 mg/kg DMPEA (ip) before a 200 trial acquisition test in the shuttlebox. In Experiment 2, 15 rats were given 25 or 100 mg/kg DMPEA (ip) daily for 4 days before an acquisition test in the shuttlebox on the fifth day. Results indicated that for both experiments there was no significant difference in mean response latency between any of the DMPEA groups and the comparable saline control on the acquisition test. Thus, the present experiments indicate that acute or chronic DMPEA does not produce the same excitatory effects as LSD or mescaline on acquisition of shuttlebox avoidance which is consistent with the reported absence of an hallucinogenic effect for DMPEA in humans. However, the human studies involved relatively nonstressful situations as does the present work where a coping response was available to avoid shock. Our previous report using unavoidable shock in classical conditioning where a coping response is not available showed that DMPEA has an excitatory effect during this relatively stressful situation. It has been reported that higher than normal levels of brain NE are associated with situations where coping responses are available and lower levels of brain NE with situations which do not permit coping responses. Therefore, stress and catecholamines may be crucially involved with the action of DMPEA and its possible hallucinogenic effects.

38.5 CNS STIMULUS PROPERTIES OF MESCALINE: LACK OF GENERALIZATION BY 3,4,5-TRIMETHOXYPHENYLETHANOL (TMPE). Ronald G. Browne* and Beng T. Ho (SPON: J.H. Perry). Texas Research Institute of Mental Sciences, Houston, Texas 77025

Male Sprague Dawley rats were trained to discriminate between intraperitoneal injections of mescaline hydrochloride (25 mg/kg) and saline in a two lever operant chamber for food reinforcement. Reward was contingent upon responses made greater than 15 sec apart (DRL-15") on the appropriate lever paired with either drug or saline administration. Following the establishment of discriminative response control by mescaline, the subjects were implanted with a chronically indwelling cannula such that injections could be made into the right lateral ventricle of the brain. After recovery from surgery the subjects were run in series of four daily training sessions and tested during extinction on the fifth day immediately following a 10 µl intraventricular injection of either saline, mescaline (10-100 µg) or TMPE (25-100 µg). The results clearly demonstrate that intraventricularly injected mescaline produced a dose dependent generalization to the interoceptive cues produced in intraperitoneal mescaline with a concomitant disruption of DRL-15" responding at doses above 25 µg. However, intraventricular doses of TMPE as high as 100 µg failed to produce either significant disruption of DRL-15" responding or generalization to the mescaline induced state. The results are interpreted as indicating that TMPE, a metabolite of mescaline, does not play a significant role in the CNS stimulus properties of mescaline.

38.6 N-METHYLATION OF TRYPTAMINE AND β-PHENYLETHYLAMINE IN BRAIN IN VITRO WITH N-METHYLTETRAHYDROFOLIC ACID OR S-ADENOSYL-L-METHIONINE AS THE METHYL DONOR. L. L. Hsu* and A. J. Mandell. Dept. Psychiat., Sch. Med., UCSD, La Jolla, Ca. 92037

Since the introduction of the Harley-Mason amine methylation hypothesis of schizophrenia (Osmond & Smythies, J. Mental. Sci. 1952, 98, 309) several groups have approached the problem by searching for an N-methylating enzyme for indole(ethyl)amines or phenylethylamines in the brain. The assay for the enzyme has not been well established, although the existence of the enzyme in the brain has been demonstrated by different authors. We have recently investigated extensively the optimal conditions for the estimation of the activity of the N-methyltransferase in rat brain, using tryptamine or β-Phenylethylamine as the substrate and 5-methyl-^{14}C-tetrahydrofolic acid (5MTHF-^{14}C) or S-adenosyl-L-methionine (SAM-^{3}H) as the methyl donor. The enzyme activity in these studies was assayed with modified methods of Laduron (Nature New Biol. 1972, 238, 223) or Morgan and Mandell (Science 1969, 165, 492). Our results show that the enzyme activity is pH-dependent. The optimal pH range is from 6.5 to 7.0 with 5-MTHF-^{14}C as the methyl donor, under the reaction conditions described by Laduron, while at pH 7.9 very little enzyme activity can be observed. However, with SAM-^{3}H as the methyl donor, the pH optimum is from 7.5 to 8.0. The enzyme activity was purified 4 to 6 fold in the precipitate obtained when the supernate (100,000 x g) was saturated with 40-50% $(NH_4)_2SO_4$. Fractions from a Sephadex G-100 column (1.5 x 20 cm) yielded 15 to 20 fold purifications compared to the whole homogenate. Preliminary studies of Sephadex fractions showed 2 enzyme activity peaks; one was non-specific for the two substrates, while the other was specific for tryptamine when either 5-MTHF-^{14}C or SAM-^{3}H was used as the methyl donor.

38.7 ELECTROENCEPHALOGRAPHIC ALTERATIONS PRODUCED BY KRYPTOPYRROLE.
James L. Walker*. Dept. of Psychology, Brandon University, Brandon, Manitoba Canada. (SPON: E. S. Halas)

The "mauve factor" which has a statistical association with psychosis has been identified by spectrometry as kryptopyrrole. This metabolite has been shown to be toxic and to primarily affect the brain and pleural cavity. (Irvine, et al., Nature. 224: 811, 1969) The present study was designed to investigate the acute and chronic effect of kryptopyrrole on the electroencephalogram (EEG). Standard electrophysiological techniques were used to implant chronic monopolar macroelectrodes at various cortical and subcortical sites in rat brain. After establishing no-drug control recordings for each rat, intraperitoneal injections of kryptopyrrole were administered (10 ul/kg to 40 ul/kg). Marked behavioral and EEG alterations were associated with acute kryptopyrrole injections. The substance induced ataxia, and depression of locomotor activity. Hyperventilation was observed at all dose levels. Several rats exhibited marked "startle" reactions suggesting "Hallucinoid" states. Acute EEG effects included: elimination of hippocampal theta, reduced cortical voltage, subcortical seizure activity at a variety of sites, and desynchronization followed by intermittent periods of hypersynchrony. The kryptopyrrole-induced EEG changes showed the development of rapid tolerance effects. Following two to three successive daily drug injections, most records did not deviate significantly from pre-drug control recordings. (Supported by Brandon University President's Research Grant 2374.)

40 SYMPOSIUM

EFFECTS OF VIRUSES ON NERVE CELLS

Chairman: R. T. Johnson

The diversity of pathological reactions to viral infections of the nervous system.

R. T. Johnson, The Johns Hopkins University School of Medicine, Baltimore, MD

Ultrastructural studies of viral infections of neural cells in vitro and in vivo.

C. S. Raine, Albert Einstein College of Medicine, New York, NY

Latency of virus in neurons.

J. G. Stevens, University of California, Los Angeles, CA

Biochemical correlates of tumorogenic virus transformation.

R. Brady, National Institute of Neurological Diseases and Stroke, Bethesda, MD

Viral infections have recently been associated not only with acute and chronic inflammatory disease of the nervous system but also with degenerative and demyelinating processes, neoplasia, and malformations. This symposium will undertake to explain at a cellular level the mechanisms of selective vulnerability of neural cell populations and how replication of virus within these cells may result in cell lysis, chronic alteration of function, modification of cell membranes, or cell transformation. Ultrastructural, biological, and biochemical correlates of these diverse virus-neural cell relationships will be discussed.

41.1 QUANTITATIVE ANALYSIS OF THE REGENERATIVE PROCESS FOLLOWING SPINAL CORD TRANSECTION IN THE NURSE SHARK (Ginglymostoma cirratum) John B. Gelderd* (SPON: C. H. Narayanan). Dept. Anat. LSU Med. Center, New Orleans, Louisiana 70119

The spinal cord was transected at the mid-thoracic level in 32 nurse sharks and subsequent data compared to unoperated normals. Four animals per group were sacrificed at postoperative intervals of 10,20,30,40,60 and 90 days. Two groups of operated sharks were subjected to a retransection at the same site at 90 days and sacrificed 10 and 20 days later. Three sections of spinal cord were removed from each shark and prepared using: (1) a modified protargol silver stain to assess regeneration across the lesion site, (2) a modified Nauta technique for degenerating, descending nerve fibers and, (3) the Rasmussen stain to demonstrate bouton terminaux on motor horn cells six spinal segments caudal to the lesion. Quantitative behavioral tests were also performed at five-day postoperative intervals.

Regeneration across the lesion site was minimal (9-13% of the normal complement of nerve fibers) and did not occur until 40 to 60 days. Despite this small amount of regeneration, synaptic terminals on motor horn cells caudal to the lesion increased from approximately 50% of normal at 10 days to normal levels by 60 days. Uncontrolled undulatory movements appeared caudal to the lesion immediately upon recovery from anesthesia and increased in strength from 20 to 60 days. Strength of volitional movements caudal to the lesion were severely reduced for the duration of the experiment. The period following the retransection showed negligible changes in behavioral and anatomical parameters when compared to 90 day animals. The increase in postoperative undulatory strength was attributed to the reestablishment of synaptic contacts on motor horn cells caudal to the lesion by local, segmental sprouting. (Supported by NIH grant NS 06 164-07 and NIMH grant MH 10320-70).

41.2 PERSISTENT INCREASES IN SYNAPTIC EFFICACY FOLLOWING BRIEF TETANIC STIMULATION IN ISOLATED FROG SPINAL CORD. Paul B. Farel. Dept. Physiol., Sch. Med., Univ. N. Car., Chapel Hill, 27514

The spinal cord of Rana catesbeiana was removed from the animal and maintained under a constant flow of oxygenated glucose-Ringer's solution. The monosynaptic reflex elicited by stimulation of fibers descending in the lateral column (LC) was recorded from ventral roots. At least one hr was allowed following dissection for the response to stabilize. A tetanus (500/sec for 500 msec) was then applied and the monosynaptic response tested periodically. Maximum potentiation (290% of pretetanus amplitude) was seen 15 sec following the tetanus. This potentiation declined slowly to a value of 179% 120 min following the tetanus (n=10). Preparations in which tetanus was omitted showed no change in reflex amplitude over comparable periods. Application of the tetanus antidromically to ventral root had no effect on orthodromic reflex amplitude. Finally, dorsal root (DR) stimulation excites a set of motoneurons overlapping that excited by LC stimulation. Following tetanus, the ventral root reflex elicited by DR stimulation was slightly increased for less than 2 min. These results show that the increase in reflex amplitude following tetanus is specific to the LC-motoneuron synapse, and thus may be an extended variant of posttetanic potentiation well described in mammalian spinal cord.

41.3 SPINAL CORD REGENERATION IN RATS. E. Feringa, R. Johnson* and J. Wendt*. Depts. Neurol. and Neuropath, VA Hosp. and Univ. of Mich., Ann Arbor, Mich. 48105.

Useful regeneration of long motor tracts in mammals has not been shown either in the laboratory or clinically. Axons will attempt to cross the scar tissue of a transected spinal cord but even with all the many means used to decrease the amount of scar and enhance the regenerative potential, useful long tract function cannot be reliably reproduced.

In immature animals, developing embryos, and less complicated animals regeneration of the spinal cord is well established. In some cases major injuries are followed by complete restoration of form and function. We recognized a correlation between those animals who regenerate spinal cord well after injury and animals who lack a homograph tissue response. This suggested that part of the problem in central nervous system regeneration might be an autoimmune response to the foreign antigens contained in central nervous system tissue of mammals. Our experiments are designed to test whether inhibition of the immune response will enhance the potential for spinal cord regeneration in the rat. Groups of experimental animals included controls and animals whose immunologic response to foreign antigens had been modified by a variety of means.

Electrophysiologic evidence for central nervous system long motor tract regeneration was seen in a small percentage of treated animals. No control animals showed regeneration. Tests demonstrated that the regenerated tracts were capable of producing an impulse in the ipsilateral sciatic nerve. Histologic evaluation showed a very extensive scar remained in the area of transection. Some regenerating axons are seen coursing into the scar but could not be followed in serial sections through the injured area.

41.4 ALTERATION IN SYNAPTIC COMPLIMENT ON NEURONS PROXIMAL TO THE SITE OF SPINAL CORD HEMISECTION IN THE RAT: A MODEL IN NEURONAL PLASTICITY. Jerald J. Bernstein, John B. Gelderd, and Mary E. Bernstein. Depts. of Neuroscience and Ophthalmology, University of Florida College of Medicine, Gainesville, Florida 32601.

Following hemisection new synapses form on motor horn neurons 5 mm proximal to the lesion. The following study was undertaken on 42 Long Evans rats to quantify the synaptic profile of boutons on motor horn neurons. Animals were utilized (normal) 10, 20, 30, 45, 60 and 90 days postlesion. A segment of spinal cord 0-5 mm rostral to the hemisection was processed by the Rasmussen technique for boutons. Boutons were counted (from coded slides) on soma and primary dendrite of 210 motor neurons on the operated and non-operated side. Intra- and intergroup interactions were determined by analysis of variance and Neuman-Keuls analysis. On the operated side, analysis of variance showed a significant overall effect on motor neuron soma ($F=31.31$ d.f. 6, 114, $P<.01$). Ten days postlesion, the number of boutons on soma significantly decreased to 48% of normal. Between 20 and 30 days there was a significant rise in boutons. At day 30 the numbers of boutons were not distinguishable from normal. From 30 to 60 days there was a significant decrease in boutons to 40% of normal. At 90 days the number of boutons was 62% of/and statistically different from normal. There was a significant overall effect, resulting in similar curves, on primary dendrite of operated side and on motor neuron soma and primary dendrite of unoperated side. The secondary degeneration at 30 days has been confirmed by electronmicroscopy and appears to be a system of synaptic remodeling. (Supported by NIH, NINDS, NS-06164).

41.5 AN ANALYSIS OF PYRAMIDAL TRACT SECTION IN TRAINED PRIMATES. R. J. Schwartzman, Dept. of Neurology, University of Miami School of Medicine, Miami, Florida, 33152.

The purpose of this study was to determine the role of the pyramidal tract in monkeys trained to perform specific motor tasks with the upper extremity. Three rhesus macaque monkeys were trained to execute discrete fractionated finger movement, after which they underwent medullary pyramidotomy. The effects of this lesion which cannot be overcome by prolonged retraining are: 1) decrease in speed of movement and weakness of all muscle groups on the affected side; 2) selective increase in tone of the forelimb flexor, hip adductors, ankle extensors and foot invertors; 3) loss of all exploratory tactile movements (evasion, search, contact, and proprioceptive placing); 4) loss of fine postural adjustments dependent on tactile and proprioceptive cues; and 5) more profound weakness of extensor than flexor musculature of the fingers. Fine discrete finger movement and proximal musculature control are well preserved after prolonged motor retraining. The pyramidal tract is a major efferent system in all of the tactile dependent reflexes which enable the extremity to explore and manipulate objects. Its importance in the facilitation of speed and dexterity of distal movements is reaffirmed, but it is evident that other pathways are capable of mediating discrete distal extremity movement.

41.6 EFFECTS OF ABLATION OF MOTOR-SENSORY CORTEX ARE DIFFERENT IN NEWBORN AND MATURE RATS. S. P. Hicks and C. J. D'Amato. Dept. Pathology, University of Michigan, Ann Arbor, 48104.

Rats display tactile placing responses by 1 week, rapidly assume mature walking and running patterns during day 17. A natural function of placing is positioning feet on the ground during locomotion, especially on irregular terrain: unilateral or bilateral ablation of motor-sensory cortex (MSC) in mature rats abolishes contralateral tactile placing responses and the feet slip off the edge of a track. Locomotion on the flat is unimpaired. Unilateral MSC ablation in newborns shows no functional effect until day 17, when contralateral tactile placing responses are lost within hours, permanently. If ablations are bilateral at birth placing responses are never lost (contrast bilateral ablation at maturity), but jumping, initiating motion are impaired....These functional activities parallel development of the corticospinal tract (CST), one outflow of the MSC and a governor of tactile placing responses. Fink-Heimer-Nauta preparations after MSC ablations reveal only pilot CST fibers have reached their medullary terminations and entered the spinal cord at birth. A major portion of the fibers is growing caudalward through the medulla during the 3rd week, including spreading into ipselateral and contralateral rostral and contralateral caudal medullary reticular formations....In one view of the experiments, MSC-CST assume irreversible governance over the immature placing mechanisms on day 17, MSC turning on contralateral, turning off ipselateral responses. For if both MSC's are removed at birth, placing mechanisms still function well.

USPHS NS 10531

41.7 STRUCTURAL CHANGES IN NEURONS OF THE MAMMALIAN CEREBRAL CORTEX ASSOCIATED WITH INCREASED "USE." L. T. Rutledge, Cheryl Wright* and Joyce Duncan*. Dept. Physiol., Med. Sch., Univ. Mich., Ann Arbor, 48104.

Evidence to support the old theory that "use" of a neuronal pathway or system produces morphological changes in participating neurons is meager and indirect. We selected for histological study neurons involved in the transcallosal and interhemispheric delayed response systems in cats. Adult cats with implanted electrodes received 20, 2-sec trains of electrical stimulation to the suprasylvian gyrus daily over a period of several weeks. Cortical tissues ipsi- and contralateral to the chronic stimulation were then removed and prepared with a modified Golgi-Cox method. Contralateral to the chronic stimulation site apical dendrites of layers II and III pyramidal cells (somas 300-450 μ from pial surface) had significantly more branchings in terminal regions, greater lengths, and terminated nearer the pia than they did on the ipsilateral, chronically stimulated side. Studies of apical dendritic spines and pyramidal cell axon collaterals are also being undertaken. Qualitatively, apical dendritic terminals in the contralateral cortex showed various fine branchings, filamentous bare twigs, especially long spines, convolutions with close packing of spines, acute angles of terminals reflecting from the pia, and other changes suggestive of apical dendritic growth. These changes in neuronal structure are interpreted as evidence that increased "use" of specific pathways to the cerebral cortex produces postsynaptic neuronal signs of growth. (Supported in part by NIH grant NS 04119.)

41.8 SENSITIZATION AND HABITUATION OF THE PLANTAR CUSHION REFLEX IN CATS. M. David Egger, Nina R. Adams*, John W. Bishop* and Constance H. Cone*. Dept. Anat., Sch. Med., Yale University, New Haven, Conn. 06510.

Moderate tactile or electrical stimulation of the plantar cushion (PC) in cats elicits a reflex extension of the toes. In cats anesthetized with Nembutal, paralyzed with Flaxedil, and artificially respirated, the magnitude of the PC reflex was monitored by recording from S1 ventral root. In some preparations, the spinal cords were severed at lower thoracic levels. The PC reflex regularly increased in magnitude during 1.0 Hz stimulation, often doubling in size by the twentieth stimulation. The relative magnitude of this sensitization decreased with increasing frequency of stimulation, typically disappearing when the stimulation frequency was increased to 10 Hz. Marked habituation was observed during 5-10 Hz stimulation. E.g., after 75 sec of stimulation at 10 Hz, the PC reflex decreased to less than 35% of prestimulation control values, returning to control values within 1-3 min following cessation of stimulation. Relative magnitudes of habituation decreased with increasing stimulus intensities. That these changes in reflex magnitude occurred within the spinal cord and not in the periphery was demonstrated by recording along the afferent path of the PC reflex and from dorsal root L7 near its entry zone. Interneurons responding to tactile stimuli at or near PC were recorded intraspinally in the medial portion of the dorsal horn, L7 segment. Some interneurons with receptive fields similar to that of the PC reflex itself also showed patterns of sensitization and habituation similar to that of the PC reflex. Interneurons responding to stimuli ineffective in eliciting the PC reflex, such as light brushing of hairs near PC, tended to show only habituation during repeated stimulation.

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41.9 SELECTIVE ACTION OF FACTORS CONTROLLING POST-LESION AXONAL GROWTH. Gary Lynch and Carl W. Cotman. Dept. Psychobiology, UCI, Irvine, 92664

Our studies examine the generality of post-lesion synaptic growth within the rat hippocampus and the parameters controlling its induction. We find that neural reorganization of granule cell afferents in both developing and mature rats is selective: Some fiber systems sprout and others do not. Removal of the entorhinal cortex, the major fiber projection to the outer dendritic field of the granule cell, triggers commissural projections to grow beyond their normal zone of termination on the inner dendritic field of the granule cell and form functional connections within a portion of the overlying entorhinal zone. Fibers from the contralateral entorhinal cortex invade the dennervated zone, and also form functional synapses. In contrast to the results produced by dennervation of the outer granule cell dendritic field, removal of the great majority of afferents within the inner dendritic field do not release synaptic growth in two of the remaining afferents. Entorhinal projections do not grow down into the deafferented zone despite the fact that they lie immediately adjacent to it. Likewise septal projections located immediately below the dennervated area do not expand upwards. Thus on the granule cell, synapses proliferate in one case (dennervation of the outer dendritic field) while in another case (dennervation of the inner dendritic field) synaptic growth is restricted. The selective synaptic reorganizations cannot be accounted for solely by temporal competition between remaining afferents as has sometimes been suggested. Rather, other selective factors involving the dynamics of synapse-dendrite interrelations are involved in establishing the finalized synaptic reorganization. Our results establish that both plasticity and rigidity in post-lesion synaptic growth coexist in the rat hippocampus.

41.10 TRANSLAMINAR GROWTH OF AXONS IN THE KITTEN LGND FOLLOWING REMOVAL OF ONE EYE. T.L. Hickey* and R.W. Guillery. Department of Anatomy, University of Wisconsin, Madison, 53706

Aberrant translaminar growth of retinogeniculate axons occurs in kittens if one eye is removed before the 20th postnatal day. We have confirmed this in cats enucleated on the 1st, 3rd or 5th postnatal day. When the second eye was removed 4-12 months later degeneration of newly grown translaminar axons was demonstrated (Nauta-Gygax and Fink-Heimer) in lamina A contralateral to the first enucleation. While the new fibers reached the dorsal border of lamina A in some regions, they were sparse in regions receiving from area centralis and were absent in the monocular segment. In all animals there was marked cell shrinkage in lamina A. However, some large cells did survive, primarily in areas of new fiber growth.

To extend the above findings H^3-Leucine was injected into the normal eye of cats enucleated before the 7th postnatal day. Injections were also made in adult enucleates and in normal adult cats. In the latter, radioactive label was largely confined to the cell laminae, the interlaminar zones being relatively free of label. Laminae A and C received a contralateral input, A1 and C1 an ipsilateral input. Adult enucleates showed a similar distribution of label. Since ipsilateral to the injection the label ended abruptly at the dorsal border of lamina A1 this method also demonstrates that translaminar growth of axons does not occur in adult animals. In kitten enucleates, however, radioactive label showed the same pattern of aberrant growth as did the degeneration methods.

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41.11 SOME CORTICAL SYNAPTIC EFFECTS OF VISUAL DEPRIVATION DEPEND ON THE COMPLEXITY OF THE REARING ENVIRONMENT. T. Blaise Fleischmann. Biological Laboratories, Harvard University, Cambridge, Massachusetts, 02138.

Quantitative evaluation of synaptic parameters in developing rat visual cortex revealed an interaction between the experience of pattern-vision and the complexity of the post-weaning rearing environment. Eleven littermate pairs of Long-Evans (pigmented) rats were monocularly pattern-deprived before eyelid opening. Each pair was then separated at weaning and reared for 30 days in environments varying in complexity (after West and Greenough, Behav. Biol. 7:280, 1972). At 55 days of age both visual cortical hemispheres of six littermate pairs were coded and prepared for electron microscopic observation. Light microscopic determinations of cortical layering permitted precise electron microscopic localization. The morphology of 14,667 vesicle-filled processes and 3,892 synaptic contacts from neuropil in cortical layers I, III, and IV was examined. In layer IV, comparisons of the densities of asymmetric synaptic contacts and of processes containing round synaptic vesicles revealed significant treatment interactions. Density differences across cortical hemispheres of isolates reversed in direction in their complex-reared littermates. In isolates, visually-experienced hemispheres had significantly more synaptic contacts and processes with synaptic vesicles than contralateral pattern-deprived hemispheres. On the other hand, visually-deprived cortical hemispheres of socially-reared littermates had more contacts and processes than contralateral visually-experienced hemispheres. Thus, some previously reported synaptic effects of visual deprivation during development depend on the complexity of the animal's rearing conditions; and, ideally, several rearing conditions should be utilized in this type of research.

41.12 FORMATION OF RETINOTECTAL PROJECTIONS DURING LIGHT OR DARK DEPRIVATIONS IN GOLDFISH. Myong G. Yoon. Department of Psychology, Dalhousie University, Halifax, Nova Scotia, Canada.

Possible influences of visual inputs on regeneration of optic fibers and on the topographic pattern of neural reconnections between the retina and the optic tectum have been studied in goldfish with neurophysiological mapping methods. In a group of adult goldfish the optic nerves were severed and then allowed to regenerate in complete darkness for about three months. The optic fibers were found to have regenerated in the absence of any visual input and reinnervated the optic tectum in correct retinotopic order. Another group of goldfish were continually exposed to light for about three months after section of their optic nerves. All fish survived the "dark deprivation" and showed restoration of a normal retinotectal projection. In further experiments, an orderly compression of the visual projection from the whole retina onto the rostral half-tectum (Yoon. Exp. Neurol. 35: 565, 1972) has also been induced regardless of whether the animals were kept either in complete darkness or continually exposed to light following excision of the caudal half of the optic tectum. These results suggest that formation of the orderly neural connections and their functional readjustment are endogenous processes which do not depend on external visual inputs.

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42.1 CHARACTERISTICS OF EVOKED POTENTIALS FROM ISOLATED OLFACTORY CORTEX. C.N. Scholfield* and J.A. Harvey. Dept. Psychology, Univ. of Iowa, Iowa City, Iowa 52242.

Sequential surface negative-positive potentials can be recorded in vivo from the olfactory cortex on lateral olfactory tract (LOT) stimulation. Similar potentials were obtained by modifying previous in vitro methods, Yamamoto and McIlwain (J. Neurochem. 13:1333): in particular by using thicker slices (560 mμ) incubated in Krebs' bicarbonate solution containing 2.5 mM Ca^{2+} at ambient temperatures. Such slices were cut from the surface of guinea-pig prepyriform and pyriform cortices. On LOT stimulation an action potential followed by a longer latency (8 msec) surface negative wave were recorded from a unipolar electrode on the LOT and sequential negative-positive waves (17 and 50 msec latencies) were similarly recorded from the pyriform cortex. Similar responses could be recorded from slices 460-780 mμ thick. These slices maintained at 25°C had similar intracellular Na^{+}, K^{+}, and water contents to thinner slices at 37°C indicating adequate oxygenation of the thick slices. All potentials except the action potential were reversibly abolished by either omission of Ca^{2+} from the bathing solution or raised Mg^{2+}, and had similar stimulus parameters to the action potential. Prior removal of the olfactory bulbs led to a rapid loss of the action potential and synaptic potentials of similarly prepared slices between 1.7 and 2.2 days after bulectomy. The loss occurred coincidently over the entire length of the slice and only a small long latency surface negative wave of different stimulus characteristic remained. It is concluded that the predominant activity is synaptically generately from the LOT and that these conditions are more appropriate to the study of synaptic function in this area. Supported by USPHS Grant No. MH-16841-04 and NIMH, KS-MH-21849-05.

42.2 DIFFERENCES IN FACILITATION AND DEPRESSION AT SYNAPSES OF A SENSORY CELL UPON TWO MOTONEURONS IN THE LEECH C.N.S. Kenneth J. Muller* and John G. Nicholls. Dept. Neurobiol., Harvard Med. Sch., Boston, 02115

In leech ganglia a single sensory neuron responding to noxious stimuli makes monosynaptic, excitatory connections with two different motoneurons; one (the annulus erector) raises the skin into ridges and the other (the large longitudinal motoneuron) shortens the animal. A train of impulses at physiological frequencies in the sensory neuron reveals different characteristics of facilitation and depression of e.p.s.p.'s in the two motoneurons. In the annulus erector motoneuron, the synaptic potentials progressively increase in amplitude during a brief train. In contrast the synaptic potentials observed in the large longitudinal motoneuron during similar trains first increase and then decrease with repetitive stimulation of the sensory nerve. The results resemble those found at crustacean neuromuscular junctions and indicate that a single neuron in the C.N.S. can excite different postsynaptic cells with different degrees of effectiveness. Several lines of evidence suggest that these observations can be explained by differences in the release characteristics of the presynaptic terminals, rather than by the properties of the two postsynaptic cells.

42.3 EFFECT OF EXCESS K^+ ON SYNAPTIC TRANSMISSION THROUGH THE CUNEATE NUCLEUS. Mary E. Morris and K. Krnjević. Department of Research in Anaesthesia, McGill Univ. Montreal, Canada.

Extracellular K^+ activity was measured in the cuneate nucleus in decerebrate cats, using K^+-sensitive micro-electrodes (as described by Krnjević & Morris, 1972, Can. J. Physiol. Pharmac., 50, 1214-1217). Stimulation of the afferent fibre terminals through an adjacent attached micro-electrode (tip separation 10-90μ) evoked direct antidromic responses (recorded in forelimb nerves) and synaptically-mediated orthodromic responses (recorded from the medial lemniscus). The input-output relation of the cuneate synapses was estimated by plotting the integrated orthodromic potentials against the integrated antidromic potentials evoked by series of stimuli, regularly varying in intensity. The extracellular K^+ activity (a_K) was raised by superfusion of the nucleus with Ringer's solutions containing excess K^+ or the intranuclear injection of KCl from a fourth micropipette. Afferent fibre terminal excitability was augmented by increases of extracellular a_K > 1-2 mM, but large changes (> 20 mM) led to depolarization block. Although the orthodromic responses evoked by a given presynaptic shock increased, the rise in extracellular a_K caused either no change or a decrease in the efficiency of transmission, as estimated by the slopes of the input-output curves.

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42.4 α-BUNGAROTOXIN AND ACETYLCHOLINE RECEPTOR IN BRAIN. Vesna A. Eterović* and Edward L. Bennett. Lawrence Berkeley Laboratory, Univ. of Calif., Berkeley, 94720

α-Bungarotoxin (αBt) is known to bind specifically to acetylcholine receptor in electric organs of fishes and in the neuromuscular junction [Ann. Rev. Pharmacol. 12, 19 (1972)]. Binding of αBt to crude mitochondrial fraction from rat brain cortex was studied using ^{3}H-acetyl-α-bungarotoxin and ^{125}I-α-bungarotoxin. With ^{3}H-Ac-αBt, the particles bound 0.6 to 1.0 picomoles (pmoles)/g of original tissue at relative toxin concentrations of 0.3 to 0.65 γ/g. Up to 83% of binding was inhibited by d-tubocurarine (d-Tc). However, the saturation value has not yet been determined. With ^{125}IαBt, saturation was reached at a relative toxin concentration of 5 γ/g; the values for this binding were 3 to 4 pmoles/g; up to 40% of binding was inhibited by d-Tc; the extent of inhibition was proportional to toxin/particles ratio. Equilibrium was reached in 10 min (at 14.5 γ/g) and it was not affected by the temperature between 0 and 37°. At higher ^{125}IαBt concentrations (>260 γ/g) up to 4.2 nanomoles/g were bound; this binding was insensitive to d-Tc and it was decreased by increased temperature between 0 and 37°. Another preparation of ^{125}IαBt, which showed highly specific binding in diaphragm, did not compete with d-Tc or carbamylcholine in brain. We conclude that conditions for specific binding of αBt to acetylcholine receptor in brain are more stringent than those in diaphragm. ^{3}HαBt is a more suitable reagent for this study than ^{125}IαBt. Since higher specific activities of ^{3}HαBt are desired for further investigation, we are attempting to tritiate αBt by other methods.
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42.5 TWO TYPES OF INHIBITION ACTIVATED BY PHYSOSTIGMINE IN THE LATERAL GENICULATE NUCLEUS OF THE CAT. Nobuyoshi Iwata*, Kohshi Hatada* and Edward F. Domino, Lafayette Clinic, Detroit 48207 and Univ. of Mich. Ann Arbor 48104.

Chemical studies show that acetylcholine and related enzymes are present in high concentrations in the lateral geniculate nucleus (LGN). The purpose of the present investigation is to study further the role of the cholinergic system in LGN. Adult cats were anesthetized with α-chloralose. Stimulating electrodes were placed stereotaxically in the optic chiasm (OC) and optic radiation. A 2M-NaCl glass microelectrode was inserted into LGN. Another recording electrode was placed in the visual cortex. Unit and field potentials were recorded. By OC stimulation a dominant negative potential about 0.7 msec latency preceded by three phasic potentials was recorded from LGN. Sometimes a small and long lasting (150-300 msec) positive potential was observed following the dominant negative potential. It was confirmed by the double shock test and the high frequency stimulating technique that the field potential of LGN following OC stimulation consisted of two groups of optic fiber action potentials, principal and interneuron discharge, and disynaptically evoked IPSPs. Physostigmine (0.05-0.3 mg/kg i.v.) increased not only the activity of the principal cells but also the interneurons as well. Another effect was the enhancement of the earlier phase of the late positivity. These actions of physostigmine were completely antagonized by atropine (1 mg/kg i.v.). The positivity enhanced by physostigmine was divided into two components. The first phase was blocked by strychnine (0.5 mg/kg i.v.) whereas picrotoxin (0.5-1.0 mg/kg i.v.) blocked the second phase. It is concluded that in addition to the well known "m" cholinergic facilitation of principal neurons, there are two kinds of inhibitory interneurons excited by physostigmine. Of these two inhibitory interneurons, the effect of one is blocked by strychnine and that of the other by picrotoxin. (Supported by grant MH-11846, USPHS.)

42.6 NORADRENERGIC SYNAPSES AND THE EFFECTS OF MICROELECTROPHORETICALLY APPLIED NORADRENALINE IN THE VENTRAL HORN OF THE CAT SPINAL CORD. Larry M. Jordan. Dept. of Physiol., Faculty of Medicine, U. of Manitoba, Winnipeg, Manitoba R3E 0W3, Canada.

Histochemical studies have revealed the presence of nerve terminals containing noradrenaline (NA) in the dorsal and ventral horn of rat spinal cord (Dahlstrom and Fuxe, Acta Physiol. Scand., 64: Suppl. 247, 1965), and some of the terminals are thought to form intimate contacts with alpha-motoneurones. Microelectrophoretic applications of NA onto spinal neurones in the ventral horn of the cat result in depression of motoneurones (Phillis, et al., Eur. J. Pharmacol. 4: 471-475, 1968) and interneurones (c.f., Engberg and Ryall, J. Physiol., 185: 298-322, 1966). Experiments have been conducted to determine which neurones in the ventral horn of the cat spinal cord receive monoamine terminals and to identify the types of interneurones in the ventral horn which are influenced by NA. Fluorescence microscopy revealed NA-containing terminals widely distributed within the ventral horn, but intimate contacts with the somas of alpha-motoneurones were extremely rare. Microelectrophoretic application of monoamines onto neurones in the ventral horn of spinal cats anaesthetized chloralose (80 mg/kg, I.V.) resulted in depression of 38% of the interneurones studied; 59% were not influenced, and 3% were excited. The interneurones which were depressed by NA included units excited monosynaptically or polysynaptically from high threshold muscle afferents and units excited polysynaptically from cutaneous afferents. Type A interneurones (Eccles, et al., J. Physiol., 154: 89-144, 1960) were not influenced by NA. These results suggest that the primary influence of NA in the ventral horn may be on restricted populations of interneurones. (Supported by the Medical Research Council of Canada, grants ME 4879 and ME 4899, and by a Medical Research Council Scholarship.)

42.7 SCORPION TOXIN-INDUCED CATECHOLAMINE RELEASE FROM SYNAPTOSOMES. Jonathan Moss*, Robert W. Colburn and Irwin J. Kopin. Laboratory of Clinical Science, NIMH, Bethesda, Maryland 20014.

A toxin has been purified from the crude venom of the North African scorpion L. quinquestriatus by gel and ion exchange chromatography. In concentrations as low as 0.8 μg/ml, the purified toxin releases ^{3}H-norepinephrine from a preparation of rat brain synaptosomes. The toxin-induced release is dependent on both the duration of exposure and concentration of toxin in the medium. Absence of calcium in the medium diminishes toxin-induced release but does not abolish it. Toxin-induced release is markedly diminished by tetrodotoxin (5×10^{-6}M) and, to a lesser extent, by desmethylimipramine (3 μg/ml). Since the released tritium is present predominantly as amine, it appears that the toxin induces release by a mechanism distinct from that of reserpine. Our results suggest that the toxin can effect the release of catecholamines by direct action on the presynaptic terminal.

42.8 MECHANISM OF ACTION OF A SYMPATHOMIMETIC DRUG, PARA-METHOXYPHENYLETHYLAMINE (PMPEA), IN THE VERTEBRATE CNS. R. Ashkenazi*, B. Haber, J.D. Coulter and W.D. Willis, Jr. Division of Comparative Neurobiology, Marine Biomedical Institute, University of Texas Medical Branch, Galveston, Texas 77550.

The injection of PMPEA in cats produces a short lasting increase in the size of the spinal monosynaptic reflex (Walker et al., Brit. J. Pharmacol., 1970). This action is potentiated by the administration of monoamine precursors (Coulter et al., Ann. Soc. Neurosci., 1972) or by pretreatment with a monoamine oxidase inhibitor, nialamide, and is antagonized by alpha adrenergic or tryptaminergic blocking agents. Therefore, it seems likely that the drug acts at monoaminergic synapses in the spinal cord. In both mice and rats, the intraperitoneal injection of PMPEA (40 mg/kg) results in a transient catatonic state and hyperexcitability to tactile stimuli with no overt changes in brain levels of serotonin or its acid metabolite (5HIAA). In vivo, PMPEA does not appear to alter the turnover of 5HT. In vitro, PMPEA is a competitive inhibitor of monoamine oxidase, using tyramine as substrate. This inhibition explains the short lasting effects of the drug in vivo and the potentiation of its effect by nialamide. The uptake of both norepinephrine and serotonin by isolated synaptosomes is blocked by PMPEA. The inhibition is partly competitive, suggesting that, in part, PMPEA may alter reuptake mechanisms at monoamine synapses. It appears that PMPEA may be an indirectly acting amine, and its interactions with noradrenergic and serotonergic systems is under further investigation, both in vivo and in vitro. (Supported by USPHS grants MH 19502 and NS 09743, USPHS Training Grant NS 05743, a grant from the Robert A. Welch Foundation (H-504), and a grant from the Moody Foundation of Galveston.)

42.9 A CYCLIC AMP-DEPENDENT REPOLARIZATION OF NEURONS (SHORT LATENCY). ISOLATION OF A NEW RECEPTOR FOR CYCLIC AMP. C.Torda, Mt.Sinai School of Medicine and Downstate Medical College, 101 W.12 Street, New York, N.Y., 10011.

In search for a molecular mechanism that may be responsible for repolarization of neurons (with short latency), the effects of cyclic AMP on the enzymatic activity of various postsynaptic enzymes has been first ascertained. Cyclic AMP significantly increased the activity of diphosphoinositide kinase (DPIK). DPIK was fractionated into a regulatory and catalytic subunit (Torda, Biochim.Biophys.Acta, 286, 389 (1972). The regulatory subunit of DPIK has a greater affinity to cyclic AMP than to the catalytic subunit of DPIK. When united with cyclic AMP, the regulatory subunit ceases to inhibit the enzymatic activity of the catalytic subunit, and diphosphoinositide (DPI) is phosphorylated to triphosphoinositide (TPI). Cyclic AMP may have a similar effect in vivo (Torda, Experientia, 28, 1438 (1972). Bioelectric measurements through intracellular microelectrodes revealed that repolarization (short latency) of the postsynaptic neuron usually depends on the enzymatic activity of DPIK, namely, it is inhibited during inhibition of the enzymatic activity of DPIK, and is facilitated by increased enzymatic activity of DPIK. These results led to the conclusion that in neurons that accumulate cyclic AMP during activity (e.g. several known postsynaptic neurons), repolarization may depend on the following molecular chain reaction: Cyclic AMP may use the regulatory subunit of DPIK as one of its postsynaptic specific receptors. When united with cyclic AMP, the regulatory subunit of DPIK ceases to inhibit the enzymatic activity of the catalytic subunit and DPI is phosphorylated to TPI. (The DPI to be phosphorylated has been delivered into the postsynaptic neuron during depolarization (Torda, Neurobiology, 3, 19(1973)). Phosphorylation of DPI to TPI concurs with an increase of membrane-bound Ca^{++} (Hendrickson and Reinertsen, Biochem.Biophys.Res.Communic., 44, 1258 (1971). This movement of Ca^{++} channels the local electric charges towards hyperpolarization (shown by several researchers as quantitatively sufficient).

42.10 EFFECTS OF GLUTAMATE AND GLUTAMATE DIETHYLESTER ON NATURAL CUTANEOUS ACTIVATION OF CAT SPINAL CORD INTERNEURONES. Jonathan O. Dostrovsky and Bruce H. Pomeranz. Dept. of Zoology, University of Toronto, Ontario, Canada.

Glutamate and Glutamate diethylester (GDEE) were applied by iontophoresis to interneurones in the cat lumbar spinal cord while single unit activity was monitored extracellularly and counted on a rate meter. Cats were spinalized at C1 and immobilized with Flaxedil. Glutamate excited 83% of the cells in laminas IV and V of the dorsal horn. GDEE blocked Glutamate excitation in 18 cells, decreased responses to natural cutaneous stimuli in 20 and decreased spontaneous activity in 10. The GDEE results agree with preliminary findings reported by Haldeman and McLennan (Brain Research 45: 393-400, 1972) that GDEE blocked responses of 9 unidentified spinal interneurones which were synaptically evoked by electrical nerve stimulation. Curtis et al. (Brain Research 41: 283-301, 1972) failed to observe this GDEE blockade of electrically evoked synaptic responses but may not have used high enough iontophoretic currents. Our results implicate Glutamate as a transmitter in the touch and nociceptive pathways, and may explain the high concentration of Glutamate in the grey matter of the dorsal horn of cat spinal cord.

42.11 EVIDENCE FOR A RECURRENT COLLATERAL INHIBITORY SYSTEM IN THE SEPTUM. J.J. Miller and H. McLennan*. Dept. Physiology, Univ. British Columbia, Vancouver, Canada.

Unit activity was recorded extracellularly from neurons in the lateral septal (LS) region of the rat with single and seven-barrelled micropipettes. Single pulse stimulation in the ipsilateral fimbria (Fm) and lateral hypothalamus (LH) evoked responses consisting of an excitation followed by inhibition. The latency to activation following Fm stimulation was correlated with the evoked slow potentials which occurred at 4-7 msec in the dorsal region and 12-15 msec in the ventral region of the LS. Activation latencies produced by the LH were more variable and unrelated to any slow potentials, ranging from 2-17 msec. The duration of inhibition following Fm activation ranged from 60-800 msec while that for LH stimulation ranged from 20-350 msec. Bursts of 2-6 small amplitude spikes (400-900 Hz) were frequently observed following antidromic activation from the medial septum (.5-1.0 msec), or following orthodromic activation from the Fm and LH. These discharges were accompanied by inhibition of the large amplitude spikes and are tentatively attributed to inhibitory interneurons. Iontophoretically applied GABA depressed the spontaneous and glutamate-induced discharge of neurons displaying the activation-inhibition sequence, while bicuculline antagonized the GABA mediated inhibition. A similar antagonistic action of bicuculline was observed on the synaptically elicited inhibition produced by the Fm and LH stimulation sites. These results suggest that there is a recurrent collateral inhibitory system, mediated by GABA, within the LS region. This system may act as a gating mechanism for the synchronization of neurons in the medial septal region which serve as pacemakers for hippocampal theta rhythm. (Supported by the Medical Research Council of Canada.)

42.12 PROLONGED INHIBITION OF PYRAMIDAL TRACT NEURONS BY VISCERAL AFFERENT STIMULATION. Fred Rosenthal, Hazel Coleridge,* and J.C.G. Coleridge.* Cardiovascular Research Institute, Univ. of Calif. San Francisco, San Francisco, California, 94122.

We have examined the effects of visceral afferent stimulation on cortical pyramidal tract (PT) neurons in cats anesthetized with α-chloralose (60 mg/kg). Extracellular and intracellular potentials were recorded from PT-cells, which were driven antidromically by stimulating the medullary pyramids, and orthodromically by stimulating peripheral sensory nerves or thalamic nuclei (VL, VPL). Visceral afferent endings were stimulated by injecting 25-100 μg phenyldiguanide into the bloodstream, or by distending the carotid sinus with a small balloon; we also stimulated the central end of the vagus nerve electrically. In about 80% of orthodromically driven PT-cells all three types of visceral afferent stimulation reduced the number of evoked spikes for periods of 100 to 300 seconds. This was much longer than the duration of either the visceral afferent stimulation itself or the reflex cardiovascular and respiratory changes produced by the visceral afferent stimulation. There were also some indications of heightened PT-cell excitability, i.e., the frequency of the remaining spikes was increased, and in about 1/3 of the cells the number of spikes increased briefly before being reduced. During these changes in PT-cell activity there was no evidence of hyperpolarizing PSP's and in some cases the cells were partially depolarized. The results demonstrate that visceral afferent pathways have excitatory and inhibitory effects on PT-cells. However, the most powerful and prolonged influence is inhibitory and this is possibly mediated by a presynaptic mechanism. (Supported by NIH grants NS 05813 and HL 13875.)

43.1 MEMORY IN THE CONTEXT OF THE OPTOMOTOR BEHAVIOR OF CRUSTACEANS. Richard Hirsh and C. A. G. Wiersma. Div. of Biol., Calif. Institute of Technology, Pasadena, California 91109

A crab or crayfish views stationary vertical stripes which then move in the dark. The new stationary position is illuminated. The animal moves its eyes according to the apparent movement. The animal is therefore comparing the stripe positions before and after movement and thus remembering the former.

The activity of the responsible occulomotor neurons was recorded. The size of the memory induced response is a function of the apparent movement. For crabs memory is accurate to within 0.1°. It can last for 8 min. declining gradually. Memory forms immediately gaining in strength as a function of viewing time. Two memories can be present simultaneously.

The preparation is well suited for studies of the biological basis of storage of acquired information. In part the size of the response is a function of the stimulus, part of which is in memory. The nature of the stored information can be determined by systematically varying the stimulus and testing for response variation. Putative storage media can then be so examined. They can also be tested in "dose-response" experiments. All memory can be removed by keeping the animal in the dark with varying viewing times. Longer times should result in more putative storage medium. None of the processes normally attendant upon learning are present. Finally, a paradigm for localizing storage is possible.

43.2 CUE-DEPENDENT AMNESIA: EFFECTS OF CYCLOHEXIMIDE AND THE TRAINING/REINSTATEMENT INTERVAL. Elton E. Quinton, Neuropsychopharmacology Program, Univ. of Louisville, Louisville, Ky. 40208.

Several studies have reported that if electroconvulsive shock is administered to an animal shortly after an established memory is reinstated by exposing the animal to some of the cues of the training apparatus, then the animal will develop amnesia for the task. A recent study has also reported that extinction of a passive avoidance (PA) response is greater if the extinction trial is given shortly after training instead of 24 or 72 hrs. after training. The present study was intended to determine whether cycloheximide (cyc) is an effective amnesic agent in the reinstatement paradigm, and whether the degree of the cyc/reinstatement induced amnesia is a function of the training/reinstatement interval. Mice were trained in a PA task and then given a reinstatement trial 1.5, 24, or 72 hrs. after training. Reinstatement consisted of placing the mouse on the entrance platform for 30 sec.. The mice were given cyc or saline 30 min. before reinstatement, and were tested for retention 72 hrs. after reinstatement. Test performance of both drug groups improved as the training/reinstatement interval increased, but the rate of improvement was considerably greater in the saline treated groups than in the cyc treated groups. Test performance of the cyc treated mice was generally inferior to that of the saline treated mice. These data suggest that cyc is an effective amnesic agent in the reinstatement paradigm, but that reinstatement alone can be amnesic if initiated within 1.5 hrs. after training. Recall without reinforcement (ie reinstatement) may possibly terminate, or at least attenuate, consolidation.

43.3 α-AMANITIN, A POTENT INHIBITOR OF FORM II DNA-DEPENDENT RNA POLYMERASE, AND ITS EFFECTS UPON ACTIVE AND PASSIVE AVOIDANCE RETENTION IN MICE, Paul D. Thut, Robert E. Hruska*, Alexander Kelter*, Joel Mizne*, and Thomas J. Lindell*. Dept. of Pharmacol., Ariz. Med. Center, Tucson, Az., 85724.

α-Amanitin (α-A) (10μg) produced greater than 98% inhibition of form II DNA-dependent RNA polymerase in male HaM/ICR Swiss mouse brains within 2 hr of intracerebroventricular (icv)injection. Mice were given 1 trial passive avoidance training and retested 4 hrs later. Mice given α-A icv either 2 hrs prior to training or immediately after training showed retention deficit on retest relative to saline controls. Active avoidance was trained for 1 hr using a Sidman schedule with a drum-turning response. Responses, % escapes and % avoidances during the last 15 min were compared to those in the first 15 min of a retest session beginning 4 hrs after the start of training. Mice receiving α-A 2 hrs prior to training had fewer responses, % escapes and % avoidances on retest. Mice given α-A immediately after their 1 hr training session had fewer responses and % avoidances on retest. These results occur only with >98% inhibition. Smaller doses yielding lesser inhibition show reduced deficits in retention. To rule out toxicity motor activity (MA) and ability to maintain posture on a rotating drum (rotarod) were measured in donut-shaped cages. α-A did not alter MA after 30 min. Rotarod performance was unaffected by α-A at 2,4, and 6 hrs. To show that previously learned behavior was unaffected by α-A, mice trained in dark avoidance for 3 consecutive days, 3 min/day were given α-A 6 hr prior to being placed in the apparatus on day 4. They showed no significant difference from saline controls. Our data suggest that new mRNA synthesis is required for memory to occur, that it occurs within minutes of the learning experience, and that the inhibition of acquisition of training found in our experiments is the direct result of α-A. Supported by GRS funds (AMC), USPHS Grant No. GM-18764-01 and a gift from Merck, Sharp and Dohme.

43.4 IN VITRO RNA POLYMERASE IN BRAIN CELL NUCLEI AFTER VARIOUS TYPES OF IN VIVO STIMULATION. Pedro A. Ferchmin*, James F. Flood* and Edward L. Bennett. (Spon: M. R. Rosenzweig). Lawrence Berkeley Laboratory, Univ. of Calif., Berkeley, 94720

The synthesis and concentration of brain RNA has been reported to change with learning, stimulation, and convulsions. Male mice injected with radioactive uridine immediately after being trained to avoid shock in a left-right T-maze showed significantly increased incorporation of uridine into the nuclear RNA when compared to cage controls. To study the mechanisms of regulation of RNA synthesis, the incorporation of GMP by purified cell nuclei was studied. Cortical cell nuclei of rats were isolated after injection of convulsive and subconvulsive doses of strychnine. Mn^{++} dependent incorporation of GMP into RNA was decreased about 20% after both convulsive and subconvulsive doses of strychnine. The Mg^{++} dependent incorporation showed a smaller and less consistent decrease. Whole brain nuclei obtained from mice immediately after learning an active avoidance task showed a similar decreased incorporation of GMP when compared to their cage controls. Since the nuclei were purified in an aqueous medium, the reduction of triphosphate nucleotides during the stimulation cannot explain the results.
(Supported by the U.S. Atomic Energy Commission)

43.5 TEMPERATURE SHIFT OR FLUROTHYL ATTENUATE RETROGRADE AMNESIA IN GOLDFISH. Walter H. Riege and Arthur Cherkin. Psychobiology Research Laboratory, VA Hospital, Sepulveda, Ca. 91343 and UCLA School of Medicine, Los Angeles, Ca. 90024.

Memory retention in goldfish can be enhanced by abrupt cooling from 25° to 10°C and rewarming to 25°C. Goldfish (N=1096), trained in one trial to inhibit their spontaneous upstream swimming into a quiet well, significantly increased their avoidance of the well 1 - 4 days later, when the rewarming shift occurred within 12 - 96 min after training. We interpret the increased avoidance as retrograde enhancement of memory. The rewarming shift was also effective in attenuating the retrograde amnesia (RA) induced by carbon dioxide. Trained fish became amnesic after transfer for brief dwell times (4 - 12 min) into water saturated with 80% CO_2;20% O_2, within 2 hr following training; RA increased with dwell time and decreased with Training-CO_2 delays.

In the present experiments, trained fish (N=320) were first subjected to an 8-min dwell in CO_2 solution (starting 8, 32, 128, or 256 min after training), then to temperature shifts from 25° to 5° to 25°C, starting at -16, 4, 16, or 64 min from offset of CO_2 treatment. Retention of avoidance was unimpaired 1 or 4 days later, when the rewarming shift occurred within 16 min before or after the CO_2 treatment; when it was delayed for 64 min, the temperature shift no longer antagonized the CO_2-induced RA. Post-training treatment of goldfish for 16 min in an aqueous solution (566 mg/l) of the convulsant flurothyl (Indoklon®), previously found equally to enhance retention of avoidance (Psychopharmacologia, in press), produced a similar attenuation of CO_2-induced RA. The interaction between enhancing and amnesic treatments may act upon an early, time-limited memory phase that is required for long-term memory formation.

43.6 RETROGRADE ENHANCEMENT OF MEMORY BY MILD FLUROTHYL TREATMENT IN THE CHICK. Arthur Cherkin. Psychobiology Research Laboratory, VA Hospital, Sepulveda, Ca. 91343 and UCLA School of Medicine, Los Angeles, Ca. 90024.

Certain CNS-stimulants (electric current, pentylenetetrazol) or CNS-depressants (pentobarbital, ether) produce either retrograde amnesia (RA) or retrograde enhancement (RE) of memory, depending upon dose. A potent CNS-stimulant, flurothyl ($CF_3CH_2OCH_2CF_3$; Indoklon®, a clinical convulsant) produces marked RA in mice and chicks at vapor concentrations of 0.85% or higher. We have found that 0.2% flurothyl produces RE in our chick model. Chicks were trained in a single 10-sec trial to suppress pecking an attractive microminiature lamp target, by coating the lamp with ethanol, a weak aversant. A control group was "trained" with a non-aversive lamp coating (distilled water). Starting 3 min after training, half the chicks were treated with 0.2% flurothyl vapor for 9 min; the remaining half were untreated. A 10-sec retention trial was given 24 hr later; the measure of retention was the number of pecks at the uncoated target, using the square-root transformation. Flurothyl significantly reduced the peck rate of the ethanol group, reflecting an enhanced memory of the weak aversive training. The RE effect, now demonstrated after mild treatment with five diverse RA-agents, offers heuristic value in memory research.

TRAINING	TREATMENT	(N)	$\sqrt{\text{pecks}}$ ± S.D.	p (t-test)
Control	Untreated	38	3.44 ± 0.92	-
	Flurothyl	38	3.13 ± 0.97	>0.15
Aversive	Untreated	39	2.61 ± 1.48	-
	Flurothyl	37	1.24 ± 1.51	<0.0002

43.7 RETROGRADE AMNESIA PRODUCED BY UNILATERAL AND BILATERAL SUBSEIZURE STIMULATION OF THE AMYGDALA. P. E. Gold and J. L. McGaugh. Department of Psychobiology, School of Biological Sciences, University of California, Irvine, California, 92664.

In a recent series of experiments, we stimulated electrically various brain regions in order to find regions which may be involved in memory disruption. Rats received low-level bilateral electrical stimulation of the amygdala after training on a one-trial inhibitory (passive) avoidance task. The stimulation did not produce brain seizures. Animals which received the stimulation 5 seconds or 1 hour, but not 6 hours, after training had retrograde amnesia as measured on a retention test 24 hours later. The amnesia was permanent over an 8 day period. In addition, unilateral subseizure amygdala stimulation produced RA, although the unilateral stimulation was a less effective amnesia treatment than was bilateral stimulation. Similar subseizure stimulation of the caudate, dorsal hippocampus, cerebellum, preoptic area of the hypothalamus, septum, and dorsal thalamus did not produce RA. These results indicate that 1) retrograde amnesia can be produced without concommitant brain seizures, and 2) the amygdala is a particularly effective brain region for the production of RA with low-level electrical stimulation.

43.8 AMNESIC AND ELECTROGRAPHIC EFFECTS OF AN INTRACRANIAL ELECTROSHOCK IN NEONATAL CHICKS. Lauren K. Gerbrandt, Sylviane E. Herzog, and Arthur Cherkin. (SPON: A. Brunse). Dept. Psych., Calif. State Univ.,Northridge.91324, and Psychobiology Research Lab., V.A. Hospital, Sepulveda. 91343.

This study investigates the amnesic and electrographic effects of an intracranially administered ECS (IECS) in neonatal chicks. The 2-day old chicks were first presented for 10 seconds with a small lamp target coated either with the aversive liquid methyl anthranilate (MeA)(N=225) or with nonaversive distilled water (DW)(N=225). Chicks then received either an IECS, a brain puncture, or a skin puncture treatment at approximately 20 seconds, 4 minutes, or 256 minutes after the end of target presentation The following day, each chick was tested for retention using the square root of the number of pecks in 10 seconds as the dependent variable.

An analysis of variance of the 2x3x3 factorial design indicated a significant main effect (MeA vs DW), and significant 3-way interactions. Follow-up Tukey-studentized range tests indicated that the interactions were due to an amnesic effect produced only by the 20 second-IECS. An assessment of the effectiveness of the IECS in 36 chicks in eliciting electrographic seizures indicated it was asymptotic in number of spikes produced and that IECS is more than 96% as effective as a transcranial mode of ECS delivery. Because the IECS produced only 6% of the number of seizure spikes as a 1.7% v/v vapor concentration of flurothyl for 9 minutes, it is concluded that ECS may produce very short retrograde amnesia gradients because of its inefficiency in producing disturbances in brain functions critical to memory retention.

43.9 COMBINED ELECTROCONVULSIVE SHOCK AND CYCLOHEXIMIDE EFFECTS ON PROTEIN SYNTHESIS AND MEMORY IN MICE. P. T. Kelly*, M. L. Andry*, D. K. Andry* and M. W. Luttges. Univ. Colo., Boulder, Colo. 80302.

We have shown previously that combined electroconvulsive shock (ECS) and cycloheximide (CXM) produced amnesic consequences in mice which neither treatment could produce when used alone. Using a multiple trial, active avoidance task, mice were shown quite resistant to memory deficits produced by either ECS or CXM used alone. Combined ECS-CXM treatments, however, produced almost complete amnesia under appropriate treatment conditions. The amnesic effects were stable for at least a period of one week. Although certain direct reductions in performance were associated with CXM treatments, such effects appear to be unrelated to performance decrements associated with ECS-CXM produced amnesia. The amnesia also appeared unrelated to direct ECS-CXM effects on retrieval. An examination of protein synthesis inhibition revealed that combined ECS-CXM treatments produced no more cerebral protein synthesis inhibition than CXM produced when used alone. In fact, the paired ECS-CXM treatments appear to produce less protein synthesis inhibition than CXM alone. These findings are interpreted as evidence that ECS and CXM exert amnesic effects through different mechanisms. Protein synthesis inhibition in the mouse brain following ECS treatments appears unrelated to the main effects of ECS in producing amnesia.

43.10 MEMORY DEFICITS FOLLOWING INHIBITION OF CATECHOLAMINE BIOSYNTHESIS IN MICE. Rod Van Buskirk,* John W. Haycock* and James L. McGaugh. Dept. Psychobiology, School of Biological Sciences, UCI, Irvine, 92664

These experiments examined the effects, in Ha/ICR mice, of graded doses (100-1350 mg/kg) of diethyldithiocarbamate (DDC), an inhibitor of dopamine-beta-hydroxylase (which converts dopamine to norepinephrine), on (1) the retention of one-trial inhibitory avoidance training, (2) electrographic patterns and (3) catecholamine metabolism. Retention was measured one week following training. Electrocorticographic (ECoG) activity was recorded for two hours after drug administration. The endogenous levels and turnover rates of dopamine, norepinephrine and serotonin were assayed in various brain regions. The findings indicate: (1) 900 mg/kg DDC produced retrograde amnesia if administered up to one hour (but not three hours) following training; (2) This dose of DDC impaired retention if administered up to three hours (but not twenty-four hours) prior to training; (3) At doses above 600 mg/kg, DDC elicited brain seizures in at least fifty percent of the animals. However, the degree of retention impairment produced by these doses was not related to the severity of seizure activity; (4) Endogenous levels and turnover rates of the biogenic amines were related in a complex manner to the retention deficits.

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43.11 EFFECTS OF L-DOPA AND ADENOSINE 3':5'-CYCLIC MONOPHOSPHATE ON LEARNED BEHAVIOR IN GOLDFISH. J.C. Dyer, B.B. Kaplan and J.L. Sirlin. Dept.. Anat., Cornell univ. Med. Coll., New York, N.Y. 10021.

Goldfish were trained for 4 hr to swim with an attached polystyrene float on day 0 (Shashoua, Nature 217:238,1968) and were challenged with identical floats 3 days later (day 3). Group times to reach criterion (100% trained levels) on day 3 were approximately one-half those on day 0. This saving (50%) was reproducible and served as the baseline for assessing drug effects on retention on day 3. Drugs were administered immediately after training (day 0) or 24 hr later (day 1). L-DOPA injected at day 0 (100-200 mg/kg, i.p.) markedly facilitated performance on day 3 ($P < 0.001$), whereas lower doses (50 mg/kg) had only marginal effects. Both L-DOPA injected at day 1 (200 mg/kg, i.p.) and the isomer D-DOPA injected at day 0 (200 mg/kg, i.p.) had no effects on performance. Cyclic AMP, given as the mono- and di-butyryl derivatives (10-30 mg/kg, i.c.) at day 0, also resulted in marked facilitation ($P < 0.001$). Conversely, reserpine (5.0 mg/kg, i.p. at day 0) had an inhibitory effect in that scores on day 3 were similar to those on day 0. Controls injected at day 0 with the diluents for the above drugs behaved normally. Moreover, no peripheral drug effects were observed by day 3. Taken together, these data implicate the biogenic amines in some aspect of the learning process. (Supported by PHS grants MH-45139 and 5 S01 RR05396-11).

43.12 EFFECTS OF ELECTROCONVULSIVE SHOCK ON CONDITIONED AUTONOMIC AND SKELETAL RESPONSES IN RATS[1]. Ralph R. Miller and Alan D. Springer*. Dept. Psychol., Brooklyn College of CUNY, Brooklyn, N.Y. 11210.

Electroconvulsive shock (ECS) administered soon after training is known to induce retrograde amnesia as measured by skeletal responding. Several recent studies have found that memory measured by autonomic indices is not subject to this amnesia thus suggesting that there are different memory processes for autonomic and skeletal responses. However, some researchers report that amnesia can be observed with either type of retention measure. The present study was designed to resolve this contradiction. Using water deprived rats in a lick suppression paradigm, both 45 ma. and 100 ma. ECS were found to produce skeletally indexed amnesia for a single tone-footshock pairing; i.e., relative to animals that had not received ECS, the convulsed animals did not suppress licking when the tone was presented on the 24 hr. retention test trial. Using defecation and bradycardia as measures of conditioning, little or no amnesia was observed after 45 ma. ECS; however, extensive amnesia appeared following 100 ma. ECS. Control groups demonstrated acquisition by all measures when no ECS was administered, and no acquisition by any measure when the tone preceded the footshock and ECS by 1 hr. or when the tone was omitted. These groups indicate that the behavior of the experimental groups reflected memorial differences rather than differences in nonassociative factors. A second study examined memory followed by 180 ma. ECS 0, 3.5, 8, 15, or 60 sec. after footshock. Lick suppression data indicated appreciable memory attenuation up to 15 sec. Heart rate and defecation indices found deficits in memory only up to 8 sec. These data indicate that autonomic and skeletal indices of memory differ in degree of vulnerability to ECS but appear subject to the same kinds of manipulations suggesting that similar memorial processes underlay the different indices.

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44.1 PROFILE ANALYSIS OF ISOTOPE DISTRIBUTIONS ESTABLISHED BY RAPID AXOPLASMIC TRANSPORT IN C-FIBERS. Guenter W. Gross* and Lloyd M. Beidler. Dept. of Biol. Science, Florida State University, Tallahassee, Florida, 32306.

The application of aqueous solutions of tritiated L-leucine to the olfactory epithelium of the longnosed garfish (Lepisosteus osseus) results in the establishment along the nerve of well-defined profiles of labeled proteins. During anterograde transport, these profiles undergo characteristic changes, a quantitative description of which may reveal information about the transport mechanism and its microenvironment. Isotope profiles arrested at various distances along the nerve can be compared quantitatively if the TCA-insoluble activity remaining in the olfactory mucosa is utilized as an incorporation reference factor. At 23°C, the profile displays considerable dispersion. While the base of the wavefront moves at 222 ± 2.4 mm/day, the peak travels at 204 ± 2.7 mm/day, the velocity difference decreasing nonlinearly with temperature. In nerves separated from their cell bodies after a profile is established in the proximal region of the nerve, level plateau regions are produced behind a sharp peak that broadens asymmetrically and decreases exponentially with distance. At least some of the material in the plateau region is still mobile as is revealed by isotope accumulations at local blocks. Profile areas from intact nerves increase with distance reflecting somal release of labeled proteins to the plateau while those from cut nerves decrease, possibly due to tritium exchange and catabolism of some transported macromolecules. The profile variations with distance are believed to be intra-axonal redistributions.

44.2 ANALYSIS OF PROTEINS UNDERGOING AXONAL TRANSPORT IN NIGRO-STRIATAL NEURONS. V. K. Singh*, H. C. Fibiger, E. G. McGeer and P. L. McGeer. Div. Neurological Sciences, Dept. Psychiatry, Univ. British Columbia, Vancouver, Canada

After stereotaxic injections of ^{3}H-leucine into the substantia nigra of rats, a considerable amount of ^{3}H-labelled proteins (trichloroacetic acid-insoluble radioactivity) was found in the caudate-putamen (CP). Chromatographic separation of the radioactive proteins of the CP tissue was carried out at various time intervals. Homogenization of the CP tissue in 0.5% (v/v) Triton X-100, solubilized about 70% of the radioactive proteins which remained in the 100,000 × g/1 hr supernatant. This supernatant fraction, when chromatographed on a DEAE-cellulose column, was resolved into 4 protein peaks (2 major peaks, A and B, and 2 minor peaks, C and D), which were found to be labelled differently as a function of time after the injection of ^{3}H-leucine. Peak A was maximally labelled within 12 hrs, suggesting that the proteins of this peak undergo fast axonal transport. On the other hand, maximal labelling of peak B was observed in about 4-5 days indicating a slower rate of transport. Peaks C and D, also appeared to have slow rates of transport. Peaks A and B contained choline acetylase and tyrosine hydroxylase activities, respectively.

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44.3 CHANGES IN AXOPLASMIC TRANSPORT OF DOPAMINE IN NIGRO-STRIATAL NEURONS AFTER RESERPINE. H. C. Fibiger and E. G. McGeer. Div. Neurological Sciences, Dept. Psychiatry, Univ. British Columbia, Vancouver, Canada

Axonal transport of dopamine in neurons whose cell bodies lie in the substantia nigra and whose projections terminate in the corpus striatum was studied by stereotaxic injection of microlitre quantities of labelled precursor (tyrosine or dopa) into the substantia nigra of tranylcypromine (5 mg/kg) pretreated rats. In accordance with earlier reports, dopamine but not its precursors were shown to undergo axonal transport. Reserpine (10 mg/kg) administered 2 hours before nigral injections of ^{3}H-dopamine produced an 82 percent decrease in the axoplasmic transport of ^{3}H-dopamine suggesting that this process was vesicle dependent. When reserpine (10 mg/kg) was administered 24 hours before the ^{3}H-dopa injections a three fold increase in the amount of transported ^{3}H-dopa was observed. Aromatic L-amino acid decarboxylase activity was not significantly increased in the substantia nigra 24 hours after reserpine. Increased transport was also seen 48 and 72 hours after reserpine pretreatment. Reserpine did not have a significant effect on axonal transport of protein in the nigro-striatal projection suggesting that the effect on dopamine transport was relatively specific.

(Supported by grants from the Medical Research Council of Canada and by a Medical Research Council Scholarship)

44.4 EFFECTS OF CORTICOSTERONE AND PROTEIN SYNTHESIS INHIBITOR ON BRAIN TRYPTOPHAN HYDROXYLASE ACTIVITY. Efrain C. Azmitia, Jr. and Bruce S. McEwen. The Rockefeller University, New York, N. Y. 10021

We have previously shown that systemically administered glucocorticoids can increase tryptophan hydroxylase (TP-H) activity in the midbrain of the rat by a process blocked by intracisternal injection of cycloheximide (Science 1969, 166, 1274). The present study examines the hypothesis that the increase in TP-H activity is the result of de novo synthesis of enzyme and axonal transport to nerve endings. Effects of corticosteroids and protein synthesis inhibitor on whole homogenate TP-H activity were measured in the cell body region (midbrain) and a nerve terminal region (preoptic-septum) at short time intervals after injection. Corticosterone (12 mg/kg) increased TP-H activity in both midbrain and preoptic-septum at 1 hr and 4 hr after i.p. injection in adrenalectomized animals. Intracisternal cycloheximide, 450 μg, decreased TP-H activity in adrenalectomized and normal animals. The effect in normal animals was not apparent 20 min after injection, but was apparent in both midbrain and preoptic-septum at 1 hr. The rapidity of both corticosterone and cycloheximide effects in cell body and terminal regions alike argues against de novo enzyme synthesis and axonal transport of TP-H. These results are similar to published studies on other hydroxylating enzyme systems, such as cerebral tyrosine hydroxylase and the adrenal hydroxylating system. (Supported by NIH grants NS 07080, MH 13189, and GM 01789)

44.5 COLCHICINE BLOCKAGE OF A SYNAPTIC MODIFICATION INDUCED BY HYPERACTIVITY Hugo L. Fernandez and Alejandro L. Donoso.*
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Modification of synaptic permeability leading to an increased probability of transmission along a particular synaptic pathway, can be induced by the exaggerated use of antigravity reflexes in the cockroach (Davidovich, Munoz and Luco-Acta Neurol. Latinoamer. 14, 265, 1968). This synaptic modification is blocked reversibly by the intraganglionic injection of colchicine. Axoplasmic transport is known to be blocked by colchicine. Nerve conduction is not affected under these conditions. These observations are compatible with the concept that the synaptic modification is dependent upon molecules synthesized in the perikaryon and axonally transported to the terminals.

44.6 OLFACTORY MECHANISMS MEDIATING PHEROMONE RESPONSES IN COCKROACHES. Edward F. Block, IV* (SPON: C.R. Wyttenbach). University of Kansas Lawrence, Kansas 66044.

Proteins derived from the membrane surface of the sensory cell dendrites have been implicated in mediating olfaction in insects. This study concerns the role of proteins in responses of cockroaches to aggregation and sex pheromone. Olfactory sensillae which respond to pheromones have been previously identified on the antennae, based on anatomical and neurophysiological studies. Incubating antennae of male cockroaches in solutions of vinca alkaloids (colchicine, vinblastine, vincrystine) reversably inhibits responses to sex pheromone, but does affect responses to aggregation pheromone. Proteins, eluted from antennae, show characteristic band patterns on polyacrylamide electrophoresis which are altered by vinca alkaloid antennae incubation. Exogenously applied H^3-leucine is incorporated into proteins eluted from antennae. Studies are in progress to determine possible correlations between band pattern alterations and changes in behavioral responses to the pheromones.

44.7 AXONAL TRANSPORT OF PHOSPHOLIPID IN THE GOLDFISH VISUAL SYSTEM
Susan C. Specht*, James A. Miller* and Bernice Grafstein.
Dept. Physiol., Cornell Univ. Med. Coll., New York, N.Y. 10021

After ^{3}H-glycerol was injected into one eye of goldfish, labeled material appeared in the contralateral optic tectum. This material, which was soluble in chloroform-methanol (2:1), was presumably phospholipid. Its rate of transport along the optic nerve was calculated, from its initial appearance in the tectum, to be 70-100 mm per day. The amount of labeled phospholipid in the tectum continued to increase for about 8 days, but if the eye was removed 2 days after the injection, the accumulation of the labeled material was rapidly arrested. This suggests that the prolonged period of accumulation was not due to a slow rate of transport but to a slow release of phospholipid into the axons. For 2-3 days after the eye removal the amount of label in the tectum remained constant. Then it declined precipitously as the axons degenerated, which shows that the labeled phospholipid was in the axons rather than in the myelin sheaths which degenerate more slowly. When retinal protein synthesis was inhibited by intraocular injection of cycloheximide, the amount of labeled phospholipid appearing in the tectum was reduced, but this reduction was not so great as the concomitant reduction in the fast component of axonal protein transport (measured with ^{3}H-proline as precursor). It appears likely, therefore, that the phospholipid was synthesized or transported in association with proteins that are part of the fast component of axonal transport.
[Supported by USPHS grant NS-09015 from NINDS.]

44.8 DISTRIBUTION OF LABELED RNA IN THE OPTIC NERVE OF THE RABBIT AFTER INTRAOCULAR INJECTION OF H_3 URIDINE.
P.Gambetti*, L.Autilio-Gambetti*, B.Shafer*(SPON: S.U.Kim) Div. Neuropath., Univ. Penna., Philadelphia, Pa. 19174

After intraocular injection of H_3 uridine, both RNA and precursors are found along the optic nerve and contralateral optic tract. In a previous study (Brain Res. 53: 387-398, 1973) we have recently shown that 70%-80% of the labeled RNA present in the nerve is synthesized locally. The distribution of the labeled RNA in the optic nerve was studied by quantitative ultrastructural radioautography. The highest density of silver grains related to ^{3}H RNA (22-49 grains/100μ^2) was found in glial cell perikarya; a similar or slightly lower density was present in the glial nuclei (19-25 grains/100μ^2). Axons (3-4 grains/100μ^2) and myelin (2-3 grains/100μ^2) had the lowest grain densities. Eighty to eighty-four percent of all counted grains were located outside the axons. By comparing the grain density distribution over the axon with that expected in the case of an exclusive labeling of the surrounding myelin and glial cell processes, it was concluded that the axons contained a number of grains representing ^{3}H RNA significantly higher than that expected to scatter from myelin and glial processes. Most of these grains were concentrated at the periphery of the axon and were not related to axonal mitochondria. These results indicate that RNA is present inside the axons, but its origin is uncertain at the present time.

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44.9 RNA TRANSPORT IN REGENERATING OPTIC NERVES OF GOLDFISH. N.A. Ingoglia and J. Mycek*. Dept. Physiology, New Jersey Medical School, Newark, N.J. 07103.

Recent experiments have shown that RNA may be synthesized in a nerve cell body and then transported along the nerve axon. In the present experiments we have studied RNA transport during regeneration of the optic nerves of goldfish. Both optic nerves were crushed and 17 days (reinnervation of the tectum), 30 days (the maturation phase) or 60 days (regeneration is complete) later, ^{3}H-uridine was injected into the right eye. Fish were sacrificed at time intervals from 12 hrs. to 21 days after the injection of ^{3}H-uridine. ^{14}C-proline was injected into the right eye 1 day prior to sacrificing, the appearance of transported radioactive protein in the tectum serving as a marker of regeneration. Analysis of radioactivity in TCA soluble, RNA, and protein fractions showed an increase of 16 times normal in the amount of RNA transported 17 days after crushing. This increase was still apparent, although greatly reduced, during the maturation phase but was absent 60 days after the crush. Increases in transported TCA soluble material occurred later than the increase in transported RNA, indicating that the change in TCA soluble material is probably secondary to the primary changes in RNA transport. Since levels of transported RNA were significantly greater than 0 as early as 12 hrs. after injection, and since the time to half peak for RNA occurs earlier in regenerating fibers, we have concluded that the rate as well as the amount of RNA transported is increased during reinnervation of the tectum. (Supported by Institutional General Research Grant Funds.)

44.10 THE EXTENT OF AXOPLASMIC MIGRATION OF MATERIALS SYNTHESISED IN THE NERVE CELL BODY. Carol J. Madsen* and Stephen C. Bondy* (SPON: S. K. Sharpless).

Several isotopic precursors have been monocularly injected into chick embryos and into day-old or 15 day-old chicks. After various intervals radioactivity incorporated into distinct chemical species in the retina of the injected eye and into the optic lobes was determined. The lobe contralateral to the injected eye is innervated by this eye while the ipsilateral lobe is not. Thus it is possible to calculate the proportion of a labeled material that migrates distally toward the innervated optic lobe, relative to the label remaining within the retina:

$$\frac{\text{counts in contralateral lobe - counts in ipsilateral lobe}}{\text{counts in retina}}$$

The extent of migration of proteins, glycoproteins and RNA was greater in 15 day embryos and new-hatched chicks than in 15 day-old chicks. Thus there is a quantitative decline of the axoplasmic transport of several macromolecular species during maturation. After monocular injection of a variety of radioactive amino acids into the left eye of new-hatched chicks, the ratio of label in protein of right optic lobes relative to label in the paired left lobes varied widely. However the proportion of synthesised protein that was transported was relatively constant and independent of the amino acid used. Around 30% of retinally synthesised glycoprotein migrated distally and this migrating material appeared to contain very few scialic acid residues. A considerable amount of retinally synthesised gangliosides also appeared rapidly in the distal regions of the optic nerve. (Supported by NIH Grant NS 09603 and the Foundations' Fund for Research in Psychiatry, Grant 70-487. Stephen C. Bondy is recipient of NIH Research Career Development Award NS 49945.)

44.11 PROJECTIONS OF SEROTONIN NEURONS OF THE MIDBRAIN RAPHE. Angelos E. Halaris, Barbara E. Jones and Robert Y. Moore. Univ. of Chicago, Chicago, Ill. 60637.

Serotonin (5-HT) has a nonuniform distribution in the mammalian brain. Studies with the Falck-Hillarp method have shown that the perikarya of 5-HT neurons are in the raphe nuclei of the brain stem but few terminals can be shown reliably with the method. These observations have suggested that ascending axons of the raphe neurons distribute in a selective pattern within the brain. Precise information concerning pathways by which 5-HT axons ascend to diencephalon and telencephalon is lacking as is information on the distribution of terminals within specific nuclear groups of the innervated areas. The present study represents the first step in an analysis of the exact organization of central 5-HT neurons. It compares the effect of lesions in restricted regions of the midbrain raphe on regional 5-HT levels with the distribution of tritium labeled amino acids injected into the same nuclei. The amino acids are incorporated into protein and transported to terminals by the rapid axoplasmic transport (Cowan et al., 1972). Following lesions in the dorsal raphe or the median raphe, the highest depletion of 5-HT occurred in the telencephalon; in decreasing order hypothalamus, thalamus, cerebellum and brain stem were also affected. Tritiated leucine injections into the dorsal raphe and the median raphe was incorporated into protein and transported principally to the basal forebrain structures, the neostriatum, the hypothalamus and the thalamus. No difference was found between 4, 24 and 48 hour survival intervals after the injection. These data are in accord with the view that the cell bodies of serotonin neurons are present both in the dorsal raphe and the median raphe and project to widespread areas of diencephalon and telencephalon. Autoradiographic studies are now underway to determine the precise distribution of the terminals of axons arising from the serotonin neurons of the raphe nuclei.

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45.1 GLYCOGEN HISTOCHEMISTRY IN SPINAL MOTOR NEURONS OF VERTEBRATES. Justiniano F. Campa, Harvey B. Sarnat*, and Judith M. Lloyd*. Dept. Neurol., Sch. Med., UVA, Charlottesville, 22901.

Glycogen and phosphorylase have been demonstrated in large motor neurons and few other neurons of the cat spinal cord (J.F. Campa and W.K. Engel, Neurology 20: 559, 1970). In the present study the previously decribed histochemical methods were uniformly applied to fourteen different species representing six vertebrate classes. Strong reactions for glycogen and phosphorylase were present in the anterior horn neurons of the rhesus monkey, dog, rodents, opossum, pigeon, lizards, shark and tadpole. They were apparently absent in the neurons of the goldfish and frogs despite strongly reacting neuropils. The glycogen rich neurons were mostly large motor neurons but a size related pattern was not as distinctive as in the cat. Outside the anterior horn, glycogen rich neurons were regularly found in Lamina IV and in spinal ganglia of advanced mammals. The size of motor neurons with strong glycogen reactions varied widely from 20 micra in diameter (chameleon) to 100 micra (rhesus monkey). In a given animal a size relation for these histochemical reactions did not apply outside the anterior horn. The presence of glycogen and glycogen enzymes in spinal motor neurons is a common metabolic feature in many vertebrates, regardless of neuronal size. This feature is likely related to the special physiologic and trophic functions of these motor neurons and to tissue and animal variations in ependyma, glia and capillaries (H.B. Sarnat, J.F. Campa and J.M. Lloyd, Neurology 23: 443, 1973).

45.2 MOTONEURON EXCITABILITY DURING SINUSOIDAL FOOT OSCILLATION. William Freedman* and Richard Herman. Dept. Rehab. Med., Temple Univ. Hlth. Scs. Ctr., Philadelphia, 19140

The excitability of the human motoneuron pool has been studied in normal subjects and in patients with specific lesions of the nervous system. One of the prone-lying subject's feet was passively moved through a selected rotational angle (range 1^{o}-10^{o}) at various frequencies of oscillation (range 0.5 Hz-15 Hz). Electromyographic (EMG) signals reflexly generated by the movement were measured using surface electrodes (separation 3 cm) placed over the main ankle flexor (tibialis anterior) and extensors (medial gastrocnemius, soleus). Because of the large inertia involved in the methodology, inertia correction was required so that the torque developed by the ankle musculature could also be measured. The results show that at frequencies above 7 Hz the EMG fires on alternate cycles of the ankle rotation. The ankle torque also alternates in amplitude-low torque for those cycles during which the EMG bursts appear and high torque levels for those cycles during which the EMG is inhibited. By reducing the amplitude of developed ankle torque either by decreasing the amount of ankle rotation or by administering the drug dantrolene sodium which suppresses excitation-coupling reaction of extrafusal muscle fibers, the inhibition of EMG on alternate stretch cycles is removed. Thus it is felt that the EMG inhibition is the result of Golgi Tendon Organ inhibition of the motoneuron pool when torque levels are high.

45.3 EFFECTS OF INHIBITORY INPUTS ON THE RANK-ORDER OF MOTONEURONS. H. P. Clamann and E. Henneman. Department of Physiology, Harvard Medical School, Boston, Mass. 02115.

To measure the precision with which the order of motoneuron recruitment is determined in a single motoneuron pool, brief single shocks were applied to plantaris muscle nerve (Pl) of decerebrate cats. Monosynaptic reflexes were recorded simultaneously from individual Pl motoneurons in filaments of one half of L7 ventral root (L7VR), and from the entire population of responding Pl fibers in the other half of L7VR. The time integral of each population response was fed to a digital voltmeter by means of a sample-and-hold circuit, permitting its measurement with resolution of 0.1%. Individual motoneurons always discharged when the population response was above a certain level, and never discharged below a slightly lower level. This critical firing level (CFL) was constant for a given motoneuron. Pairs of motoneurons whose critical firing levels differed by a known percentage were compared directly. They were excited either monosynaptically or by trains of stimuli to the muscle nerve. The order of recruitment was preserved in 65 pairs, and reversed in 6 pairs whose CFL differed by an average of 2.7%. Stimuli to one of four inhibitory sources (ipsilateral peroneal nerve, contralateral S1 dorsal root, medullary reticular formation, L7VR excited antidromically) were then applied concurrently with excitation. 64 of 68 pairs tested showed no change in rank-order with inhibition. 4 pairs, each of which differed by 1% or less, showed some degree of reversal with inhibition. We conclude that inhibitory inputs are distributed uniformly throughout a motoneuron pool. (Supported by a grant from the NSF).

45.4 SPATIAL AND DIMENSIONAL ORGANIZATION OF HYPOGLOSSAL MOTONEURONS. Philip S. Ulinski. Depts. Anat. and Oral Biol., Loyola Univ., Maywood, Illinois, 60153.

Three sets of muscles produce an invariant sequence of tongue movements in the common boa (Constrictor constrictor). The genioglossus muscles initially protrude the tongue; the intrinsic muscles alternately elevate and lower the tongue; the hyoglossus muscles retract it. Hypoglossal motoneurons must partially "code" this movement pattern. Thus, the spatial distribution of degenerating hypoglossal motoneurons and the sizes of non-degenerating hypoglossal motoneurons were studied following surgical removal of individual muscles with survival times of 7 to 42 days. Distribution functions of non-degenerating motoneuron sizes indicate that genioglossus motoneurons are small with sectional areas less than 240 μ^2 while intrinsic and hyoglossus motoneurons have areas between 240 μ^2 and 720 μ^2. Thus, genioglossus motoneurons should have relatively low thresholds to excitation and be effectively segregated from other hypoglossal motoneurons on a dimensional or threshold basis. Their size is consistent with the initial activity of the genioglossus muscles. Hyoglossus motoneurons innervate only the ipsilateral hyoglossus muscle; genioglossus and intrinsic motoneurons innervate both ipsi- and contralateral muscles. Hyoglossus and genioglossus motoneurons are scattered evenly throughout the nucleus, but intrinsic motoneurons have a gradient distribution being most prevalent in the nucleus' caudal half. Thus, the ratio of hyoglossus to intrinsic motoneurons will decrease as the nucleus' caudal pole is approached so that these two types of large neurons are partially segregated from each other on a spatial basis. These data suggest that a combination of dimensional and spatial factors may allow an excitatory input to the hypoglossal nucleus to activate different sets of motoneurons in the correct sequence. (NIH Grant RO1 NS 101 - 02)

45.5 ORGANIZATION OF SYNAPTIC INPUT TO DEFINED TYPES OF MOTOR UNITS IN CAT MEDIAL GASTROCNEMIUS MUSCLE. R. E. Burke, W. Z. Rymer* and J. V. Walsh. Lab. of Neural Control, NINDS, NIH, Bethesda, Md. 20014.

In the adult cat, the medial gastrocnemius (MG) contains 3 major types of motor units, each type distinguished by having muscle units with a characteristic set of physiological and histochemical attributes (Burke, Levine, Zajac, Tsairis & Engel, Science 174, 709). Synaptic potentials produced by electrical stimulation of peripheral nerves were recorded in MG motoneurons innervating defined types of muscle units, using cats lightly anesthetized with pentobarbital or halothane. Homonymous group Ia EPSPs (MG nerve stimulation with intracellular blockade of antidromic invasion) were, on the average, of large amplitude in type S units (range 5.9 - 12.4mV; mean 9.1mV; n=28), somewhat smaller in FR units (4.5 - 11.3 mV; mean 7.5mV; n=23), and smallest in type FF units (1.2 - 7.4mV; mean 4.1mV; n=58); the few units intermediate between FF and FR units (called "unclassified") exhibited Ia EPSPs of intermediate amplitude (5.6 - 8.0mV; mean 6.7mV; n=10). Heteronymous Ia EPSPs (LG-soleus nerve stimulation), although smaller than the homonymous PSPs, displayed the same correlation between unit type and EPSP amplitudes. In contrast, polysynaptic excitatory PSPs evoked by single volleys in sural nerve tended to be smaller in amplitude and area in type S motoneurons than in most FR and FF motoneurons. The sural PSPs in S cells were dominated by somewhat longer latency inhibitory components which were much less prominent in both FF and FR cells. The excitatory components were evoked by relatively low threshold sural afferents (2X thr.) while inhibitory components were generated by higher threshold fibers (1.5 - 5X thr.). The results suggest an organization of segmental interneurons which may permit differential recruitment of fast-contracting FF and FR motor units with concomitant inhibition of activity in slowly-contracting S units.

45.6 COMPARISON OF TIME AND SPATIAL AVERAGING OF AFFERENT INPUT BY MOTOR NEURONS IN DECEREBRATE CATS. Dale A. Harris. Dept. of Physiol., Harvard Medical School, Boston, Mass. 02115

In order to compare time and spatial averaging by the motor neuron, the coefficient of variation of its firing was compared under various degrees of irregularity and synchrony of its input from muscle afferents. After decerebration and laminectomy, a small filament of L7 ventral root was peeled back and a motor unit to triceps surae was isolated by means of extracellular electrodes. When recruited by ankle flexion, the motor unit was recorded and its coefficient of variation was calculated as a control value. A small dorsal root filament was then peeled back and a primary afferent from triceps surae was isolated and recorded during ankle flexion. The muscle nerve was then crushed and stimulated proximally with a pulse train generated by the previously recorded spindle output. Variability of the motor neuron input was then normal, but input was synchronized making spatial averaging ineffective. Coefficient of variation of the motor unit was found to increase significantly above the control value to an extent dependent on the variability of the recorded afferent; this increase is a measure of spatial averaging by the motor unit. Mean firing rate was approximately unchanged from the control. Further experiments using perfectly regular pulses as stimulation indicated that spatial averaging reduces variability down to a level approximating its minimum. Time averaging was found to be less powerful in reducing variability, but is important in rate limiting of the motor unit. Predominance of spatial averaging is intuitively satisfying since it is capable of increasing signal/noise ratio while preserving the temporal aspects of the signal.

45.7 INFLUENCE OF INTRAMUSCULAR NERVE BRANCHING ON SENSORY-MOTOR ORGANIZATION IN SPINAL α MOTONEURONS. William D. Letbetter and Steven L. Wolf*. Neurophysiology Lab, Regional Rehabilitation Research and Training Center, Emory University, Atlanta, Georgia 30306.

If the medial gastrocnemius (MG) nerve is dissected carefully into the neurovascular hilus, it can be seen to divide naturally into a number of branches which distribute to different parts of the muscle. Since each branch should contain a separate population of afferent and efferent axons, we felt that this might be an appropriate preparation in which to evaluate more explicitly the specificity of muscle afferent-efferent interactions. Nembutalized cats with their spinal cords transected at L_1-L_2 were prepared for intracellular recording from α motoneurons in the L_7-S_1 cord segments. All dorsal and ventral roots were intact. In a given animal we transected as many as six separate intramuscular divisions of the left MG nerve and mounted their cut central ends on individual bipolar stimulating electrodes. Arrangements were also made to stimulate the whole muscle nerve. Ventral horn field potentials produced by α motoneurons antidromically activated in the separate branches of the nerve were not homogeneously arranged within the motor nucleus. Synaptic potentials elicited by orthodromic activation of sensory axons in the separate branches of the nerve showed qualitative and quantitative differences both with respect to the source of stimulation and with respect to the α motoneuron under study. Furthermore, the absence of monosynaptic EPSPs in some MG α motoneurons during stimulation of branches which previously had been shown to produce monosynaptic EPSPs in other MG α motoneurons casts doubt upon the present notion that single Ia spindle afferents project to most of the homonymous α motoneurons (Mendell and Henneman, *J. Neurophysiol.* 34, 171-188, 1971). There may be a more specific organization among spindle afferents and α motoneurons than heretofore thought.

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45.8 *THREE MODES OF MOTONEURON REPETITIVE FIRING AND COMPARISONS TO FIRING PATTERNS OF EPILEPTIC AND DEAFFERENTED CNS NEURONS.* William H. Calvin. University of Washington (Neurological Surgery), Seattle, Washington.

Cat spinal motoneurons seem to exhibit three distinct modes of repetitive firing: 1) an *occasional spike mode*, where depolarizing waves only occasionally cross threshold; 2) a *rhythmic firing mode*, where sustained synaptic currents (often mimicked by injected currents) attempt to keep the membrane potential above threshold somehow resulting in a firing rate proportional to depolarizing current strength; and 3) a *regenerative firing mode*. The regenerative firing arises from large depolarizing afterpotentials; thus an occasional or rhythmic spike may sometimes be followed within 5 msec by an extra spike. This extra spike may itself have a large depolarizing afterpotential, which may evoke yet another extra spike. etc. This regenerative cycle may be self-limited, as when the depolarizing afterpotentials decline in size with successive spikes, finally failing to evoke extra spikes. Patterns of "adaptation" of the depolarizing afterpotentials with successive rhythmic spikes *(J. Neurophysiol. 35:297, 1972)* include a particularly interesting feature: the hump-like afterpotential is sometimes missing after the first rhythmic spike of a train. The spontaneous high-frequency burst firing of some neurons in chronic epileptogenic cortex *(EEG J. 34:337, 1973)* exhibit a "long-first-interval" pattern: Many bursts are quite superposeable following the second spike of the burst, with the first spike standing at various times before this stereotyped event (other bursts are stereotyped from the first spike onwards). A simple explanation would be that the regenerative mode begins after the first or second rhythmic spike evoked by a moderate depolarizing wave, thus "multiplying" a normal response. Stereotyped bursts following chronic deafferentation *(Exp. Neurol. April 1973)* suggest an enhancement of regenerative mode firing.

45.9 SEGMENTAL INFLUENCES OF CUTANEOUS AFFERENTS ON GAMMA MOTOR NEURONS. Mark De Santis. Dept. Anat., Georgetown University Washington, D. C., 20007

Effects of ipsilateral cutaneous nerve stimulation on units identified as gamma efferent axons were studied in adult cats anesthetized with pentobarbital and acutely spinalized. Spontaneous discharge rates of 165 units ranged from 0-98 imp/sec. Sural or posterior femoral cutaneous nerve stimulation most often resulted in an increased firing rate, especially for units having a high spontaneous discharge. Stimulation of each cutaneous nerve usually resulted in a quantitatively different effect for the same unit suggesting some difference in topographical organization. By using graded stimulation of cutaneous nerves or by blocking with procaine, it was evident that gamma firing was influenced by activity in A-β, -γ, -δ afferent fibers. The most rapidly conducting cutaneous afferents alone did not affect gamma firing. Central excitatory delay times calculated for 60 units ranged from 2-10 msec, the majority being from 2-4 msec. This suggests that much of the cutano-fusimotor reflex linkage is di- or trisynaptic and that a monosynaptic linkage is absent. To a single afferent volley gamma units discharge several spikes after which there is a cessation of firing lasting from 25-225 msec. This period of quiescence did not appear to result from recurrent inhibition. It was not abolished by administration of mecamylamine (1.5 mg/kg, iv), nor did ventral root stimulation result in a similar pause in firing. The time course of the cessation of gamma activity did resemble the time course of the dorsal root potential (V of Lloyd) as well as that of primary afferent depolarization.

45.10 IDENTIFICATION AND PERIPHERAL REGULATION OF SINGLE TRIGEMINAL ALPHA AND GAMMA MOTONEURONES IN CAT. L.F. Greenwood* and Barry J. Sessle. Univ. of Toronto, Faculty of Dentistry, Toronto, Canada.

As part of a study aimed at elucidating the functional organization of the trigeminal (V) motor nucleus, extracellular microelectrode recordings were made in decerebrate or anaesthetized (chloralose) cats from single motoneurones innervating jaw-closing (masseter, temporalis) or jaw-opening (digastric) muscles. Recording sites were verified histologically. We have identified gamma as well as alpha motoneurones within the nucleus by utilizing stimuli applied to jaw muscle nerves and to the V mesencephalic nucleus (site of muscle afferent cell bodies). The distinction between a gamma and an alpha motoneurone was based on characteristics such as the latter's monosynaptic input from the V mesencephalic nucleus, it's lower threshold for antidromic activation, and it's faster conduction velocity (although alpha V motoneurones showed slower conduction velocities than those reported for alpha spinal motoneurones). Electronically controlled mechanical stimulation of a tooth produced inhibition of the synaptically or antidromically evoked activity in jaw-closing alpha and gamma motoneurones; many also displayed facilitation or activation as a result of this stimulus. However jaw-opening motoneurones in general showed only facilitation or activation. Regulatory influences on jaw-closing motoneurones were also noted with stimulation of nerves innervating the larynx, oropharynx, face, and jaw muscles, and were predominantly inhibitory on both alpha and gamma motoneurones.

Gamma as well as alpha motoneurones have previously been noted in the spinal cord. Our work indicates their existence in a cranial nerve motor nucleus and also shows some of the regulatory influences on V motoneurone activity which may be used in the reflex control of jaw movements.

Supported by the Canadian Medical Research Council.

46.1 HYPOTHALAMIC MODIFICATION OF DRINKING RESPONSE DYNAMICS. Predrag Vrtunski, Tovi Comet* and Lee R. Wolin*. Laboratory of Neuropsychology, Cleveland Psychiatric Institute, Cleveland, Ohio, 44109

Based on numerous reports on eating and drinking behaviors elicited by hypothalamic stimulation, this study was designed to determine more intimate nature of the information electrical stimulus represents to the hypothalamic structures regulating the drinking response. There were two experiments. In both, the water spout was mounted on a pressure transducer and voltage analog of the licking response was fed into a signal averager. The water-spout was connected to a variable speed infusion pump. Except for the stimulus intensity test, each lick caused the pump to infuse 2.9 µl of water in the spout. In the first experiment, three groups of rats (N=8 each) were tested under various conditions of dipsogenic stimulation. The most pronounced and consistent effect was observed with stimulus intensity test where variation from 0.59 to 9.1 µl of water/lick generated response magnitude changes from 1.9438 to 0.5648 gram-seconds respectively. The second experiment was performed on rats with hypothalamically (N=16) and cortically (N=2) implanted electrodes. In animals where electrical hypothalamic stimulus elicited drinking response and increased the volume of water consumption (N=5), the hypothalamic stimulation also reduced the force emission of the licking response. Reduction ranged from 0.2377 to 0.6077 gram-seconds from corresponding control levels. This was observed both when electrical stimulation preceded drinking test and when stimulus was contingent upon termination of the licking response. The observations are discussed in light of current theories of hypothalamic mechanisms in reinforcement and consumatory behaviors.

46.2 CONDITIONED AGGRESSIVE BEHAVIOR. O.J.Andy, L.Giurintano, and J.W.Laing. Neurosurg. Center for Seizure and Behavior Disorders, University of Miss. Med. Center, Jackson, Mississippi 39216.

Aggressive behavior can be elicited by two basic methods: (1) by externally applied adversive stimulation and (2) by direct hypothalamic stimulation. It is hypothesized that, in both instances, the aggressive behavior represents a response which is generated through the activation of hypothalamic structures.

TECHNIQUE: In six adult male cats, bipolar electrical stimulation in the anterior hypothalamus served as the unconditioned stimulus (UCS) and a tone as the conditioned stimulus (CS). Conditioning trials ranged from 42 to 90 with 2 minute inter-trail intervals. Stimulation parameters were varied by manipulating voltage. Conditioning trials were administered daily in a series of replicated ascending-descending UCS intensities.

RESULTS: Recruitment of various components of the electrically elicited aggressive response was reproduced by the conditioned auditory stimulus. Graded pupillary dilation elicited by direct hypothalamic stimulation was reproduced by a conditioned auditory stimulus. Tapping on the cage during hypothalamic stimulation changed an incomplete aggressive response to a well-directed attack, and similarly, tapping combined with auditory stimulation elicited a well-directed attack, which was not obtained by the conditioned stimulus alone. The observations suggest that conditioned aggesssion is generated and integrated within the hypothalamus.

46.3 A SEARCH FOR THE BRAINSTEM ORIGIN OF TWO HYPOTHALAMIC-HIPPOCAMPAL SYSTEMS MEDIATING HIPPOCAMPAL THETA ACTIVITY AND DESYNCHRONIZATION. Angelica W. Macadar* and Donald B. Lindsley. Depts. Psychol., Physiol., Psychiat., and Brain Res. Inst., UCLA, Los Angeles, 90024

Anchel and Lindsley (Electroenceph. clin. Neurophysiol., 1972, 32, 209-226) identified two pathways in the posterior hypothalamus of the cat, which, when stimulated, caused contrasting hippocampal electrical responses. The medial system caused hippocampal theta activity, the lateral system desynchronization. Either could be blocked rostrally by discrete electrolytic lesion or reversibly blocked cryogenically. Both systems converged in the brainstem at A3, L3-4, HO. The present study sought origins of these systems more caudally in the brainstem by systematic stimulation mapping from frontal planes A5 to P7 and laterally from 0.5 to 5 mm. Particular attention was directed to the raphe nuclei, pontine nuclei pontis oralis and caudalis, nucleus coeruleus and substantia grisea centralis. Operative procedures were under halothane anesthesia; recordings were under N_2O and O_2. The cats were immobilized with gallamine triethiodide and all cut surfaces and pressure points were thoroughly infused with long-lasting procaine (Zyljectin). Four kinds of hippocampal effects were noted: a) no change, b) theta, c) desynchronization, d) mixed. Theta rhythm was obtained mainly from N. reticularis pontis oralis, N. coeruleus, and the ventrolateral margins of the central grey substance. Desynchronization was observed mainly from stimulation of raphe nuclei in the pontine region and N. reticularis pontis caudalis. Hippocampal theta frequency ranged from 2.5 to 6 Hz and was accompanied by cortical desynchronization or slow waves in the theta range depending upon the structure stimulated and the ratio of N_2O to O_2. Supported by USPHS grant NS-8552 to D. B. Lindsley.

46.4 BRAIN PROGRAMED STIMULATION OF THE BRAIN. Calvin C. Turbes*, Gerald T. Schneider* and David L. Jobe*. (SPON: W. A. Himwich). Dept. of Anat., Sch. Med., Creighton University, Omaha, Nebr. 68131.

Extracellular and intracellular unit activity was recorded from the dorsal hippocampus and passed via a discriminator circuit to a triggering circuit which activated a stimulator. The unit activity was used to program the stimulator to emit pulses of 0.3 msec duration at various voltages. The amygdala, lateral geniculate and medial geniculate nuclei were stimulated. Unit activity from the hippocampus and the discriminated unit activity for programing the stimulator was subjected to amplitude discrimination, mean frequency, and interval histogram analysis. The "classical" stimulus was 100 Hz, pulse duration 0.3 msec, for 5 seconds at various voltages. Brain programed stimulation showed variable changes in unit discharge rates. Periodic unit activity was variable. Discriminated large and small units responded differently in periodic activity and unit discharge rates. "Classical" stimulation showed increase or decrease unit discharge rates. Periodic activity was lost and no differential changes in small and large unit activity was apparent.

46.5 FIRING OF HUMAN HIPPOCAMPAL NEURONS DURING MEMORY TESTING. Eric Halgren,* Thomas L. Babb and Paul H. Crandall*. Brain Research Institute, UCLA, Los Angeles, 90024.

Evidence from lesions and stimulations indicate that the hippocampal gyrus and hippocampal pes (Ammon's horn and dentate gyrus) play a necessary role in short term memory in man. We have recorded single units in these structures during delayed response (DR) tests in order to examine the physiology of these roles. The units were recorded from fine wires chronically implanted in temporal lobe epileptics as a part of evaluation for surgery (Babb et al, Electroenceph. clin. Neurophysiol. 34: 247, 1973). The delayed response test used consisted of 3 slides. On the first slide (DR presentation), either a nonsense figure, 3 digits, or 3 letters appeared. The next slide was either a blank (DR delay) or contained 2 stimuli which the patient was asked to identify as the same or different (S/D choice). On the third slide (DR choice), the patient was required to indicate which of 2 stimuli was the same as that presented in the first slide. Responses were indicated by pressing telegraph keys. The slides were advanced either every 3 or 4 seconds by a timer, or by depression of the telegraph key (e.g., when the patient responded). Units were found in the right (nondominant) posterior hippocampal gyrus whose firing rates were depressed before the DR choice ($p < .001$), but were not noticeably affected during DR presentation, DR delay, S/D choice, nor by random pressing of the response keys. This depression was seen to both the verbal and nonverbal stimuli, but was stronger for the nonverbal stimuli. In earlier patients tested with less rigorous controls, units were found in the hippocampal pes and gyrus that showed less specific responses, perhaps related to the response these units show to flash. In conclusion, some units in the hippocampal gyrus are apparently specifically inhibited during a choice involving recent memory.

46.6 A COMPARATIVE NEUROANATOMICAL ANALYSIS OF THE DIFFERENTIAL PROJECTIONS OF THE HIPPOCAMPUS TO THE SEPTUM. Allan Siegel and Henry Edinger. Depts. of Anatomy and Physiology, N.J. Medical School, Newark, N.J. 07103.

The purpose of the present study was to reexamine the projection system from the hippocampus to the septum. Radio frequency lesions or suction ablations of portions of the dorsal or ventral hippocampus were produced in gerbil, rat, rabbit, and cat. Sections were stained principally by the Fink-Heimer I method for demonstrating degenerating axons and their terminals. In each of the species considered lesions involving any of the CA fields of the dorsal hippocampus produced terminal degeneration which was restricted to the medial septum. Following lesions involving any of the CA fields of the ventral hippocampus massive terminal degeneration was limited to the lateral septum and nucleus accumbens. The results demonstrate that the topographical projections to the medial and lateral septum arise from the dorsal and ventral hippocampus, respectively, and not from specific CA fields.

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46.7 EFFECTS OF HIPPOCAMPAL DEAFFERENTATION AND DEEFFERENTATION ON ACTIVITY, NOSE POKE BEHAVIOR AND OPERANT RESPONDING IN THE RAT. Peter W. Bowes* and Richard E. Musty. Department of Psychology, University of Vermont, Burlington, Vermont, 05401.

Groups of rats with lesions of either the hippocampus (H), fornix (F), entorhinal cortex (E), or fornix and entorhinal cortex (FE), and operated (C) and unoperated (N) controls were given a single 1-hr. activity test in an 18 in diameter circular stabilimeter cage. Nose poke behavior was also measured. Subjects were then trained to lever press for water reinforcement until all animals had obtained at least 200 reinforcements. An additional 5 daily crf sessions were given during each of which subjects were allowed 60 reinforcements. Finally, all subjects were placed on a VI 30 sec schedule for four consecutive daily 30 min sessions. It was found that the H, F and FE groups did not differ from one another on any measure, and the E, C and N groups did not differ from each other on any measure. The H, F and FE groups nose poked significantly more often, but had significantly shorter mean nose poke durations than the E, C or N groups. No group differences were found during crf training, but the H, F and FE groups had significantly higher response rates on the VI schedule than the E, C or N groups. The H group was significantly more active than the E, C or N groups, while the F and FE groups did not differ in activity from any of the other groups or from each other. Results indicate the hippocampal influence on both approach behavior (nose pokes) and operant responding is mediated by its connections through the fornix system. Damage to the tempero-ammonic pathways does not appear to affect these behaviors. These data in conjunction with the findings of Van Hoesen et al. (Physiol. & Behav., 8:873, 1972) imply that a unitary concept of hippocampal function is inadequate. Experiments are now in progress to further test the relative behavioral contributions of the fornix and entorhinal systems.

46.8 ARE THERE TWO ASCENDING ACTIVATING SYSTEMS TO NEOCORTEX AND HIPPOCAMPUS WITH DIFFERENT RELATIONS TO BEHAVIOR? C. H. Vanderwolf. Dept. Psychol., Univ. Western Ontario, London, Ontario.

Behavior and hippocampal and neocortical EEG were recorded polygraphically in chronically prepared rats. Atropine SO_4 (25 mg/kg or more, i.p.) produces slow waves (2-6 Hz, amplitude up to 1 mV) throughout the neocortex during immobility, face-washing, scratching, chewing and shivering (Type II behavior), but smaller amplitude faster waves ("activation") always accompany walking, jumping, struggling, and head movement (Type I behavior). Such "activation" is detected by surface-to-depth (transcortical) electrodes, but not by surface-to-surface electrodes. The atropine effect is duplicated by scopolamine but not by atropine methyl nitrate, pentobarbital, phenothiazines, or diethyl ether. In undrugged or atropinized rats, hippocampal RSA (7-12 Hz) was specifically correlated with Type I behavior. There may be two activating systems to neocortex and hippocampus: System I, active only during Type I behavior, produces RSA (7-12 Hz) and atropine resistant cortical activation (ARCA). System II, active during alert Type II behavior, produces atropine sensitive cortical activation and, at times, 5-6 Hz hippocampal RSA. System I and Type I behavior are activated by d-amphetamine and depressed by phenothiazines and FLA-63, a dopamine hydroxylase inhibitor. Eserine activates System II without producing Type I behavior. ARCA, as well as RSA, can be abolished by septal brain lesions, indicating an ascending pathway through the septal nuclei. System I may contain aminergic synapses; System II, cholinergic synapses.

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46.9 PREFRONTAL AND INSULAR PROJECTIONS TO THE ENTORHINAL AREA IN THE MONKEY. J. Astruc and G. R. Leichnetz. Department of Anatomy, Medical College of Virginia, Health Sciences Division, Virginia Commonwealth University, Richmond, Virginia, 23298

In thirty-three old and new world monkeys (Macaca mulatta, Saimiri sciureus, Saguinus oedipus) lesions were made by subpial suction in the granular frontal (medial, convexity and orbital aspects of the frontal lobe) and agranular insular cortices. Four to sixteen days after surgery the animals were sacrificed under Diabutal anesthesia and perfused transcardially with physiological saline followed by ten percent formalin. The Nauta and/or Fink-Heimer selective silver impregnation techniques were used for histological identification of axonal degeneration. The medial aspect of the frontal lobe and the caudal orbitofrontal cortex (Van Hoesen et al. 1972) project to the lateral part of the entorhinal area. The medial part of the entorhinal receives connections from the medial aspect of the prefrontal cortex, the rostral orbitofrontal, and insular cortices. The subicular areas receive projections from the prefrontal convexity (Nauta 1964) and from the medial granular frontal cortex. The major input to the entorhinal and subicular areas appears to come from the prefrontal and insular cortices through the cingulum and/or the uncinate-inferior frontooccipital fascicle. (Partially supported by USPHS NB 08418).

46.10 FIBER DEGENERATION FOLLOWING LESIONS IN THE MEDIAL PREFRONTAL CORTEX OF THE SQUIRREL MONKEY. G. R. Leichnetz and J. Astruc. Department of Anatomy, Medical College of Virginia, Health Sciences Division, Virginia Commonwealth University, Richmond, Virginia 23298

Unilateral partial ablations were made by subpial suction in the granular cortex on the medial aspect of the frontal lobe in six adult squirrel monkeys. Following a survival period of four to fourteen days the brains were removed, and later sectioned and stained with the Nauta and/or Fink-Heimer selective silver impregnation techniques. Corticocortical degeneration was traced to the prefrontal convexity and orbitofrontal areas and was observed to cross to the contralateral hemisphere through the genu of the corpus callosum. Fiber degeneration was traced in three principal directions. A large bundle coursed dorsally to enter the cingulum. This bundle was traced caudally and inferiorly into entorhinal and subicular areas. Preterminal fibers were observed throughout the extent of the cingulate cortex. Another bundle coursed caudally and ventrally in a sublenticular approach to the ventral portion of the internal capsule. In its course, preterminal fibers were seen in the ventromedial caudate and in the putamen. Fibers were observed to leave the internal capsule to join with the inferior thalamic peduncle and terminated in the intralaminar and dorsomedial nuclei of the thalamus. More caudally, fibers of passage were seen traversing the substantia nigra to end in more dorsal tegmental areas. Finally, a bundle was seen to course through the external and extreme capsules, traversing the ventral claustrum, and entering the uncinate fascicle. Preterminal fibers were seen in the rostroventral insular cortex and in the temporal lobe. Fiber degeneration entered the inferior frontooccipital fascicle in the temporal lobe white matter and was followed caudally into the entorhinal cortex. (Partially supported by USPHS Research Grant NB 08418)

46.11 OPERANT CONDITIONING OF 40 HZ ACTIVITY IN THE AMYGDALOID NUCLEI OF THE CAT. T.M. Knapp* and Joel F. Lubar. Dept. of Psychology, Univ. of Houston, Houston, Tx., 77004; Dept. Psych., Univ. of Tenn., Knoxville, Tn.

Although a variety of cortical EEG rhythms have been brought under operant control, relatively little work has been done in trying to condition activity from sub-cortical structures. High frequency activity, such as 40 Hz, in the amygdala has been associated with olfactory functions (Gault and Leaton, Electroenceph. clin. Neurophysiol., 15, 1963), emotional states (Leese, Psychiat. Res. Repts., 12, 1960), and arousal (Delgado et al., Brain Res., 22, 1970). Using cats with chronically implanted bipolar electrodes located in the basolateral amygdala and medial forebrain bundle (MFB), each animal was reinforced for the occurrence of 40 Hz amygdaloid activity. Reinforcement consisted of MFB stimulation (60 Hz, 0.5 sec., 0.2-0.8 ma.) beginning with a CRF schedule and progressing to a FR 12 schedule. After 56 days of training, 30 min. per day, the cats showed a sixfold increase over initial 40 Hz levels. These animals were also capable of discriminating the differential contingencies under which they were trained. Following completion of this task the cats were extinguished until their preconditioning baselines were recovered. Correlates of increased 40 Hz amygdala activity included aggressiveness as manifested in difficulty in handling the animal by the experimenter, altered emotionality, and EEG time-period changes. Our results extend current biofeedback research by showing that high frequency activity in the basolateral amygdala is capable of being brought under operant control and further that alteration of amygdaloid complex activity is correlated with level of arousal.

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47.1 THE ABDOMINAL GANGLION OF APLYSIA WILLCOXI. J.E. Blankenship and R.E. Coggeshall. Marine Biomedical Institute and Departments of Physiology and Anatomy, University of Texas Medical Branch, Galveston, Texas 77550.

Comparative studies of the morphology and neurophysiological properties of identified neurons in the abdominal ganglion of 20 Aplysia willcoxi ranging in size from 15 to 350 grams have been done to determine if there are any differences between this species and A. californica. Ganglia were examined anatomically for cell and axon counts and individual neurons were studied with respect to their firing patterns, synaptic connections and responses to nerve stimulation and to acetylcholine. In general, there was a marked similarity between the ganglia of the two species. Of particular interest is the fact that interneuron I (cell L10) makes the same types of synaptic connections that characterize this cell in A. californica. Major differences include (1) the white cells, which are relatively large in A. willcoxi, do not send their processes into the connective tissue sheath of the ganglion, (2) the relative sizes of identified neurons in A. willcoxi are somewhat different from those in A. californica (the giant cell R2 for example is usually smaller, but the white cell R14 and several of the identified neurons on the left are relatively larger), (3) the five left upper quandrant cells L2-L6 in A. willcoxi are different from their counterparts in A. californica with two of these cells having different firing patterns and no obvious input from interneuron I. All these neurons can, however, be antidromically activated by stimulation of the pericardial nerve as in A. californica, and (4) an inhibitory follower cell of interneuron I has been found on the right side of the ganglion, a pattern as yet unreported in A. californica. (Supported by USPHS grants NS 09652 and NS 10161 and by a grant from the Moody Foundation of Galveston.)

47.2 **SYNAPTOLOGY OF AN INTERNEURON OF THE ABDOMINAL GANGLION OF APLYSIA STUDIED BY A NEW INTRACELLULAR STAINING TECHNIQUE.** **Rhanor Gillette* and Bruce Pomeranz (SPON: H. L. Atwood). Dept. Zool., Univ. Toronto, Toronto, Ont., Canada.**

A major interneuron (L10) and one of its follower cells (L12) in abdominal ganglia of the tectibranch gastropod Aplysia californica were studied by electron microscopy using a modified intracellular cobalt staining method to mark the cells. The method allows excellent fixation of nervous tissue and preserves the ultrastructure of the injected cell, while allowing identification of processes smaller than one micron in diameter. Details of the method are presented. The synaptology of L10 is discussed.

47.3 AUTORADIOGRAPHIC ANALYSIS WITH THE LIGHT AND ELECTRON MICROSCOPE OF APLYSIA IDENTIFIED NEURONS, THEIR PROCESSES, AND SYNAPSES AFTER INTRASOMATIC INJECTION OF ^{3}H-L-FUCOSE. E.B. Thompson, J.H. Schwartz*, and E.R. Kandel. Dept. of Neurobiol. and Behavior, Public Health Res. Inst. and NYU Medical School, N.Y., N.Y. 10016.

To study the fine structure of the cell body and processes of identified cells in the abdominal ganglion, we have injected ^{3}H-L-fucose intrasomatically into cholinergic neurons R2 and L10. Transport of label is restricted to the axonal tree of the injected neurons, making it possible to trace the three dimensional geometry of these neurons, to identify synapses and to examine synaptic morphology by using LM and EM autoradiography. Because silver grains appear over a larger area than the structures actually labeled, LM autoradiography can reveal fine processes below the resolution of light optics. Label is incorporated into glycoproteins, most of which enter newly synthesized membranes. We can thus study the distribution and fate of specific macromolecules and the organelles of which they are a part. After a 3 hr incubation label in the cell body of L10 is localized significantly over Golgi apparatus, smooth endoplasmic reticulum, mitochondria, and vesicles; by this time label is already present in intraganglionic processes and presumptive terminals. Within the main axon label appears over vesicles, smooth ER and mitochondria. In ganglia from young animals (20-70g) prefixed with glutaraldehyde, synaptic membrane densities appear to be rare. High concentrations of vesicles and mitochondria in one element of two apposed processes are criteria for presumed synapses. These cholinergic neurons possess 2 populations of vesicles: dense core (80-150nm) and moderately dense core (60-130nm). This technique offers the possibility of identifying the chemical and possibly the electrical synapses of identified cells with optimal preservation of fine structure. (Support: Sloan Foundation, NIH, and NSF.)

47.4 IDENTIFIED MOTOR NEURONS CONTROLLING THE CIRCULATION IN APLYSIA: SYNTHESIS OF TRANSMITTERS AND SYNAPTIC PHARMACOLOGY. G. Liebeswar*, J. Koester*, J.E. Goldman* (SPON: E.R. Kandel). Dept. Neurobiology and Behavior, Public Health Res. Inst. and NYU Med. Sch., 455 First Avenue, New York, N.Y. 10016.

The molluscan heart beat resembles that of vertebrates in being myogenic. The spontaneous heart beat is in turn modulated by neural activity. Specific nerve cells have been identified in the abdominal ganglion of Aplysia which control circulation. Two cells (RB_{HE}, L_{HE}) mediate excitation to the heart, two cells (LD_{HI} 1, LD_{HI} 2) mediate inhibition to the heart, and two cells (LB_{VC} 1, LB_{VC} 2) control vasomotor tone by exciting vascular muscle that constricts two of the three main arteries. The motor neurons control circulation by chemical transmission. We have examined the transmitter synthesis of 5 of the 6 motor cells by injecting radioactive precursors of putative transmitters into the motor neurons. We have found that RB_{HE} converts (^{3}H)-tryptophan into (^{3}H)-serotonin and that the LD_{HI} and LB_{VC} cells convert (^{3}H)-choline into (^{3}H)-acetylcholine. Control studies indicate that the ability to synthesize these transmitters is highly specific (Eisenstadt et al., in prep.). We have also applied serotonin and acetylcholine to the heart and to the main arteries and examined the effects of various blocking agents. The pharmacologic experiments support the notion that one of the heart excitors (RB_{HE}) is serotonergic and that the heart inhibitors and the vasoconstrictors are cholinergic. Thus, as in vertebrates, acetylcholine mediates inhibition to the heart. Unlike vertebrates, however, serotonin rather than noradrenaline mediates excitation to the heart, and acetylcholine mediates peripheral vasoconstriction.

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47.5 Stimulation-Induced Depletion of Synaptic Vesicles: Reversibility During Quiescent Recovery. J.J. Pysh, Ronald G. Wiley* and C.W. Spencer*. Depts. of Anatomy and Pharmacology, Northwestern University Medical School, Chicago, Illinois, 60611.

We have reported previously that repetitive preganglionic stimulation at 20-40 Hz produces a decrease in the number of synaptic vesicles and an increase in plasma membrane surface area of preganglionic nerve terminals of the in situ cat superior cervical ganglion. Stimulation at these frequencies also frequently resulted in swollen mitochondria. In addition, normal vesicle numbers and plasma membrane surface area failed to recover completely after rest periods up to 90 minutes after stimulation. Therefore, we have investigated the effects of lower stimulation frequencies lying within the physiological range followed by quiescent recovery. After stimulation at 10 Hz for 30 minutes, nerve terminals showed normal mitochondria, a 50% reduction in the number of synaptic vesicles and a concomitant significant increase in plasma membrane surface area. Allowing terminals to rest after stimulation (at 10 Hz for 30 minutes) resulted in incomplete recovery of vesicle numbers and plasma membrane during the first 15 minutes, whereas, complete recovery occurred after 60 minutes. These electron microscopic findings support the hypothesis that transmitter release occurs by exocytosis resulting in the net incorporation of vesicle membrane into plasma membrane during periods of sustained high transmitter release rates and that synaptic vesicles are reformed from plasma membrane during recovery.

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47.6 DEPLETION OF PRESYNAPTIC VESICLES AT A VERTEBRATE CENTRAL SYNAPSE FOLLOWING STIMULATION. P.G. Model* and M.V.L. Bennett. (SPON: G.D. Pappas). Dept. Anat., Albert Einstein Coll. Med., NYNY 10461.

Mauthner fiber-giant fiber synapses in the hatchetfish are chemically transmitting axo-axonic synapses in the medulla. Pre- and postsynaptic elements can be penetrated simultaneously with microelectrodes. These synapses can be easily identified in 4 μm Epon sections in the light microscope. Synapse-containing thick sections are mounted on Epon blocks and thin sections are cut from them for electron microscopy. The diameter of each synapse is 4-10 μm, but actual synaptic contact is made by projections from the postsynaptic giant fiber. These projections are separated from one another by large extracellular spaces. Presynaptic vesicles are clustered near the contact regions, and are generally round, clear, and 300-600 nm in diameter. Following stimulation of the Mauthner fiber at 10-20/sec for 10 min, there are profound changes in presynaptic structures. Synaptic vesicles are very few in number, mitochondria are swollen, the terminal cytoplasm shows increased density, and there is a marked accumulation of irregular membranous structures. These changes are at least partially reversible. Changes in postsynaptic potentials following stimulation (reported in another abstract) support the morphological evidence for depletion of vesicles. Our findings provide further evidence for the vesicular release of transmitter, in this case at a central synapse.

47.7 FATIGUE OF TRANSMISSION AT MAUTHNER FIBER -GIANT FIBER SYNAPSES OF THE HATCHET FISH. S.M. Highstein* and M.V.L. Bennett. Dept. Anat., Albert Einstein Col. Med., New York, N.Y. 10461 (SPON: M.B. Bender, Mt. Sinai Sch. Med., New York, N.Y. 10029)

These axo-axonic synapses lie in the medulla where both pre- and post-synaptic structures can be simultaneously penetrated by microelectrodes near the synaptic regions. Mauthner fibers (m.f.) can be stimulated intracellularly or by external electrodes on the caudal spinal cord. None of the effects reported below are due to changes in presynaptic (i.e., m.f.) spikes. Prolonged high frequency stimulation of both m.f. (h.f.s.) reduces EPSP amplitude recorded in giant fibers to a level comparable to that of spontaneous mineature (M) EPSPs without the occurrence of failures (J. Gen. Physiol. 53:183,1969). MEPSPs of normal size can occur during h.f.s. even though EPSP amplitude has become very small (Fed. Proc. 32: 443,Abs,1973). MEPSPs often cease as h.f.s. is continued and reappear when h.f.s. is terminated. Both MEPSPs and EPSPs are blocked by topically applied curare; presumably they arise at the same synapses. These results suggest that the reduced EPSP is composed of many quanta, each with a reduced size, and that high quantum number explains the lack of failures. Evidently the vesicular store of transmitter is depleted relatively quickly, and after depletion the contents of partially filled vesicles can be released by stimulation. Morphological evidence of depletion is discussed in another abstract. Failures of EPSPs could be seen by repeating h.f. trains at several per sec and are ascribable to depletion of an immediately available transmitter store. In agreement, amplitude distributions of the later EPSPs in the trains deviate from Poissonian towards binomial. Our findings at this vertebrate central synapse provide further evidence concerning the quantal nature of synaptic transmission.

47.8 PHYSIOLOGICAL AND PHARMACOLOGICAL PROPERTIES OF NEURONS IN THE SUBESOPHAGEAL GANGLION OF THE LEECH. Anna L. Kleinhaus* and James W. Prichard. Dept. Neurol., Yale Med. Sch., New Haven, Conn. 06510.

The subesophageal ganglion of the leech contains 4 pairs of large neurons (sub-Rs) which resemble the Retzius cells of segmental ganglia (seg-Rs). The electrophysiological properties of the sub-R cells have not been extensively studied. We have found them to have membrane potentials of 40-55 mV, action potentials of 60-70 mV, spontaneous and evoked EPSPs of 5-10 mV, and a variable zone of anomalous rectification 20 mV or more negative to the resting membrane potential. After equilibration to the electrode these cells either were silent or fired spontaneously in slow regular fashion every few seconds. During brief trains of hyperpolarizing current pulses of 4 nA or more the input resistance of sub-Rs rose rapidly for the first few pulses; this phenomonen was absent or minimal in seg-Rs. Drugs added to the fluid bathing the entire ganglion had the following effects on sub-Rs: Bemegride, sodium benzylpenicillin, and sodium phenobarbital, 1-10 mM, all caused large intermittant paroxysms of depolarization and rapid firing which were triggerable by synaptic input to the sub-Rs and were abolished by 20 mM Mg. In addition sodium phenobarbital caused a steady hyperpolarization which persisted in the presence of Mg and was probably secondary to increased potassium conductance. Pentylenetetrazol, 1-10 mM, and strychnine sulfate, 0.01-1 mM, both caused steady, Mg-resistant hyperpolarization secondary to increased chloride conductance. All of these sub-R drug responses closely resemble previously reported ones caused in seg-Rs by the same drugs. The data thus suggest that there is considerable physiological and pharmacological resemblance between the sub-R and seg-R cells, but they are not identical. The principal differences so far observed are the larger synaptic potentials of the sub-Rs and their behavior during repeated current pulses.

47.9 Two Components of Facilitation in Motor Neurons of Panulirus interruptus Cardiac Ganglion. W. Otto Friesen. Dept. Neurosciences, U.C.S.D., La Jolla, California 92037.

The time course of synaptic events in Panulirus interruptus cardiac ganglion large cells was studied with intracellular and extracellular electrodes. The normal rhythmic synaptic input to the large cells from small cells was eliminated either by cutting the ganglion just posterior to cell 5 or by applying procaine topically. The axon of the first small cell (cell 6) was selectively stimulated by passing current pulses through hook electrodes. Presynaptic nerve impulses were monitored and identified with multiple extracellular silver wire hook electrodes. Intracellular potentials in motor neurons were recorded with glass pipette microelectrodes. PSP's (postsynaptic potentials) evoked in large cells by presynaptic impulses from cell 6 exhibit both positive facilitation and negative facilitation (also termed "antifacilitation" or "defacilitation"). Facilitation is defined as $F = (V_t - V_o)/V_o$, where V_o is the size of the conditioning, unfacilitated PSP and V_t is the size of a PSP occuring some time after the conditioning PSP. During double-pulse experiments test PSP's were smaller than conditioning PSP's. The equation for this negative component of facilitation was $F = -1.0 \exp(-\Delta t/\tau)$, where Δt is the time in seconds between the conditioning and test PSP's and τ is 0.06 seconds. Experiments employing more than one conditioning PSP revealed a second facilitation component. Thus if the delay between the last of several closely spaced (20-50 msec apart) conditioning PSP's and the test PSP was greater than 150 msec, the size of the test PSP was greater than the first conditioning PSP. The equation for this positive component of facilitation was also an exponential with a time constant of about 1.5 seconds. This component depends in a complex way on both the number and the frequency of PSP's in the conditioning train. (Supported by NIH grant #NS-05628, and NIH #NS-0947 and NSF #GB-28620 to D. Hartline).

47.10 FUNCTION OF SYNAPTIC MODULATION OF ELECTROTONIC COUPLING BETWEEN NEURONS. M.E. Spira* and M.V.L. Bennett, Dept. of Anatomy, Albert Einstein Col. of Med., New York, N.Y. 10461, and Marine Biological Lab., Woods Hole, Massachusetts 02543.

The opisthobranch mollusc Navanax feeds by a rapid expansion of its pharynx that sucks in prey organisms. Neurons in the buccal ganglia control muscles causing pharyngeal expansion. These neurons are electrotonically coupled which presumably increases synchronization of firing and aids rapid expansion. Shortly after prey is ingested it is pushed on into the esophagous by peristalsis. Under these conditions expansion controlling neurons would be expected to fire asynchronously. We earlier observed in isolated ganglia that stimulation of pharyngeal nerves causes uncoupling of these neurons (Brain Research, 27: 169-175, 1971). The effect is explicable as resulting from decrease in input resistances by IPSPs generated in coupled cells without change in junctional resistances (although strategic localization of inhibitory and coupling synapses must be invoked). In spite of IPSPs the neurons were still observed to fire asynchronously in response to unidentified inputs. We now report that the physiological stimulus of pharyngeal inflation can trigger uncoupling followed by independent firing. We conclude that the uncoupling is not simply a by-product of widespread inhibition, but is a physiologically significant response that allows independent firing of normally coupled cells under appropriate conditions. The underlying mechanisms may be relevant to other systems in which neurons fire synchronously in some conditions and asynchronously in others. (Some readers may recognize this abstract as having been presented as the last Biophysical Society Meeting. We do expect to obtain many more data in the 6 months remaining before the Neuroscience Meeting.)

47.11 ELECTROTONIC DECREMENTS WITHIN *Aplysia* NEURONS. Katherine Graubard. Dept. Physiology & Biophysics, Univ. of Washington, Seattle, Wash. 98195.

The voltage attenuation between the soma and the synaptic regions of *Aplysia* abdominal ganglion neurons was computed for the steady-state case, based upon anatomical measurements. Intracellular injection of Procion Yellow dye revealed that most injected cells had a single large telodendron which branched in the neuropile. Large branches (>4μ) generally entered nerve trunks while small diameter processes (<2.5μ) were usually no more than 100μ in length and terminated within the neuropile. A survey of the neuropile with the electron microscope revealed that synapses occur between processes with diameters which correspond to the small processes seen in the light microscope. 40% of postsynaptic profiles contained vesicles which were identical to the synaptic vesicles seen in presynaptic profiles. Serial contacts were also seen. Axonal membrane infolding, measured in the right connective, increased linearly with diameter. Infolding was estimated to increase the somatic surface area of large cells at least 6X. The transient voltage response of cell L13 to a current step and the cell's input resistance were used with the cell's geometry to derive the membrane time constant (550 msec), unit membrane resistivity (440 to 690 Kohm·cm^2), specific axoplasmic resistivity (50 to 150 ohm·cm), and the unit membrane capacitance (0.8 to 1.3 μf/cm^2). The steady-state voltage attenuation between the soma and the neuropile regions was then computed. For simple cell geometries, voltages applied to the soma decrement by no more than 15% in transmission to any part of the cell within the neuropile (including fine branches). Voltages applied to the telodendron were calculated to decrement by no more than 10% in transmission to the soma. However, voltages applied to a 2μ diameter secondary process were predicted to undergo decrements of 80% in transmission to the telodendron or soma due to the impedance mismatch. (Supported by NIH grant).

47.12 EQUILIBRIUM POTENTIAL OF 5HT ACTION ON NEURONAL MEMBRANE IN MAMMALIAN BRAIN. Chuong C. Huang* and Amedeo S. Marrazzi. University of Missouri Institute of Psychiatry, St. Louis, Missouri 63139

We have previously reported that 5HT is the most powerful natural synaptic inhibitor in mammalian brain. Intracellular recording from the Betz cells in the pericruciate area of the cat has shown that the close-arterial injection of small doses of 5HT produces inhibition of spike discharge, hyperpolarization of membrane potential and increased transmembrane resistance (decreased conductance). An attempt was made in the present experiments to seek whether there is an equilibrium potential of the 5HT effect attributable to specific membrane ionic channels. Control resting membrane potential and its maximal hyperpolarization by 5HT was measured and determined. By using the same electrode for recording, current injection and membrane potential shift, the membrane potentials were artificially shifted to certain depolarizing or hyperpolarizing positions and 5HT was then injected. The maximal depolarizing or hyperpolarizing potentials of the 5HT effect were then plotted against the membrane potential before drug injection. The results show that the artificial hyperpolarizing potential shift increases the hyperpolarization of 5HT action and the depolarizing potential shift decreases the hyperpolarization of 5HT action. Connection of these points revealed that the equilibrium potential (zero shift) of 5HT action is about -30 mV (similar to that of HCO_3^- ion). We hope that further results with 5HT and other cerebral synaptic inhibitors will enable us to closely correlate cerebral cortical 5HT action with a specific ion channel and possibly with the intracellular metabolic changes, e.g. in cyclic AMP, controlling the ionic traffic involved. Supported by Psychiat. Res. Fndn. of Mo.

48.1 KINETIC PROPERTIES OF PURIFIED BRAIN L-GLUTAMATE DECARBOXYLASE. Jang-Yen Wu* and Eugene Roberts, City of Hope Medical Center, Duarte, California 91010

L-Glutamate decarboxylase (EC 4.1.1.15) (GAD), which catalyzes α-decarboxylation of L-glutamate to form γ-aminobutyric acid (GABA) and CO_2, now has been purified from mouse brain to apparent homogeneity. The activity of the purified enzyme was inhibited by several compounds. Carboxylic acids with a net negative charge are strong competitive inhibitors e.g. D-glutamate (K_i, 0.9 mM), α-ketoglutarate (αKG) (K_i, 1.2 mM), fumarate (K_i, 1.8 mM), DL-β-hydroxyglutamate (K_i, 2.8 mM), L-aspartate (K_i, 3.1 mM) and glutarate (K_i 3.5 mM). 2-Aminophosphonobutyric and 2-aminophosphonopropionic acids, phosphonic analogs of glutamate and aspartate, respectively, had no effect at 10 mM. Neutral substances such as GABA, L-glutamine, γ-methylene-L-glutamine, and α,γ-diaminoglutaric acid had no effect at 5 mM. Sulfhydryl reagents, 5,5'-dithiobis (2-nitrobenzoic acid) and p-chloromercuribenzoate were very potent competitive inhibitors (K_i, 10^{-8} M). The above inhibition was prevented in the presence of αKG, suggesting the involvement of an -SH group in or near the active site. Iodoacetamide and iodoacetic acid were less effective. Thio compounds of mono- or dicarboxylic acids e.g., 3-mercaptopropionic and mercaptosuccinic acids were more potent inhibitors than β-mercaptoethanol. 3-Mercaptopropionic, 2-mercaptopropionic and 2-mercaptoacetic acids were potent competitive inhibitors with K_i values of 1.8, 53 and 330 μM, respectively. Zn^{++} is the most potent inhibitor of the divalent cations tested (50% inhibition at 10 μM) followed by Cd^{++}, Hg^{++}, $Cu^{++} > Ni^{++} > Mn^{++} > Co^{++} > Ba^{++} > Ca^{++} > Mg^{++} > Sr^{++}$. Ethanol and dioxane inhibited to the extent of 20 and 50% at 10% (v/v), while slight activation was observed at low concentrations (0.1-1%) of both solvents. The above findings suggest minimally the presence of aldehyde, sulfhydryl and amino groups near the catalytic site of the enzyme.(NS-10622,NIH; MH-22438,NIMH)

48.2 IMMUNOCHEMICAL COMPARISON OF VERTEBRATE GLUTAMIC ACID DECARBOXYLASE. K. Saito*, J.-Y. Wu* and Eugene Roberts, Division of Neurosciences, City of Hope Medical Center, Duarte, California 91010. (Spon: A.R. Dravid)

The species specificity of glutamic acid decarboxylase (GAD) was studied employing antibodies produced in rabbits against the purified enzyme. Rabbits were immunized by subscapular injections of 1, 5, 10 and 150 μg of GAD. The serum obtained one week after the 6th injection of 10 or 150 μg of GAD gave a sharp precipitin band with purified GAD in diffusion tests. When the antiserum against the mouse enzyme was tested against GAD-containing water extracts of crude mitochondrial fractions from brain on agar plates, cross-reactivity was observed with GAD from rat, rabbit, guinea pig, human, calf, quail, pigeon and frog. Quail, pigeon and frog GAD showed spurs. Trout GAD did not show a precipitin band. GAD activities in the extracts of mouse and rat brains were inhibited to the extent of about 50% by anti-GAD IgG. GAD activity from the other species was not inhibited. In microcomplement fixation tests with anti-GAD IgG, the curves obtained with mouse, rat and human GAD were similar to each other. There was no complement fixation with quail, pigeon, frog and trout GAD. There was an intermediate degree of fixation with GAD from rabbit, calf and guinea pig. The immunological studies indicate the following order of relatedness to the mouse brain enzyme: rat > human > rabbit, calf, guinea pig >> pigeon, quail and trout. (Supported in part by Grant NS-01615, NIH, and MH-22438, NIMH)

48.3 STIMULUS-COUPLED SECRETION OF GABA FROM SYNAPTOSOMES. Dianna A. Redburn, William B. Levy*, and Carl W. Cotman. Dept. Psychobiol., Sch. Biol. Sci., UCI, Irvine, Cal. 92664

We have used synaptosomes to examine the control mechanisms of transmitter release in vitro. Synaptosomes were preloaded with radioactive GABA, entrapped on a filter, and rapidly perfused with different media. After a 1 min incubation period, 3-4% of the total bound GABA is released during a 2 sec perfusion "pulse" of 50 mM K; 1 mM Ca. The amount of GABA released is proportional to the {Ca} between 0 and 2-3 mM and is inhibited 50% in the presence of 16 mM Mg or 1 mM Mn. In this in vitro system, the important factors in the actual release process can be separated from the influence of related regulatory processes such as the effects of axoplasmic transport and re-uptake mechanisms. In synaptosomes where the role of axoplasmic transport should be minimal, the effects of the tubulin-binding drugs, colchicine and vinblastine, do not support any direct role for microtubules or tubulin in transmitter release. Neither drug has any effect at relatively low concentrations during short exposure times (10^{-4} - 10^{-5} M; 1-10 min). Although the release and re-uptake systems for GABA can function separately, there may be a physiologically important coupling of these two processes during synaptic transmission. Ca-dependent release is little affected by the blockage of re-uptake in Na-free media. However, conditions used to stimulate release (i.e., depolarizing levels of K) also inhibit the re-uptake of released GABA. Thus the increase in release and decrease in uptake may occur simultaneously in response to the same stimulus to increase the extracellular {GABA} during synaptic transmission. (Supported by NIH Grants NS 08597 and 1 F02 NS 55429-01.)

48.4 THE RELEASE OF AMINO ACIDS FROM SENSORY AND MOTOR ROOTS DURING STIMULATION. Daniel Weinreich* and Richard Hammerschlag* (SPON: J. E. Vaughn). City of Hope Medical Center, Division of Neurosciences, Duarte, Calif., 91010.

One of the many difficulties encountered in establishing acidic amino acids as neurotransmitters is their observed release from non-synaptic regions (Wheeler et al: J. Cell. Physiol. 67, 141, 1966; DeFeudis: Nature 227, 854, 1970). These reports were based on results from desheathed peripheral nerves. In the present study, intact isolated dorsal and ventral spinal roots from bullfrogs were incubated for varying time periods in a medium containing ^{14}C-glutamate (20 μM) and ^{3}H-mannitol at 4°C. At 24 hr, the release of radioactivity was measured under resting conditions and during electrical stimulation. Under resting conditions, release occurred in two phases: an initial rapid loss from extracellular compartments and a subsequent slower release presumably from intracellular stores. When a plateau was reached in the wash-out curve, a single 10-min period of stimulation was found to increase the rate of efflux of ^{14}C-material 6-10 fold above resting release. No significant release of ^{3}H was observed following stimulation. Analysis by paper electrophoresis and thin-layer chromatography revealed metabolites of glutamate in released material and in nerve extracts. In effluents from both types of roots, glutamate accounted for approximately 50% of total ^{14}C while greater than 90% of the remaining released counts were identified as glutamine and aspartate. The increased efflux was not reduced in calcium-free, magnesium supplemented (10 mM) medium. The nonspecific release of these amino acids from nerve fibers should be considered when evaluating the roles of glutamate and aspartate in synaptic transmission.

48.5 DIFFERENCES IN THE BINDING OF GABA AND GLYCINE TO SUBCELLULAR PARTICLES OF RAT CEREBRAL CORTEX AND SPINAL CORD. Francis V. DeFeudis. Dept. Anaesthesia Res., McGill Univ., Montreal, Canada

Synaptosome-enriched fractions of rat cerebral cortex and spinal cord were suspended in isosmotic sucrose solutions containing 40 mEq/l Na^+ + tracer amounts of ^{3}H-GABA and ^{14}C-glycine. Centrifugation of samples at 17,000 x g, 55 min, 0°C provided pellet and supernatant fractions which were analyzed for their contents of ^{3}H and ^{14}C using a double-isotope method. It was shown for all animals that more ^{3}H-GABA was bound to particles prepared from cerebral cortex than to particles prepared from spinal cord, and that more ^{14}C-glycine was bound to particles of spinal cord than to those of cerebral cortex. Although the retentions of both ^{3}H-GABA and ^{14}C-glycine were increased by allowing the particles to stand at 23°C for 15 min after their suspension, preferential binding of these amino acids still existed. By suspending the particles in equimolar (1.4×10^{-6} M) concentrations of the radioactive amino acids, it was shown on a molar basis, that the retention of ^{3}H-GABA was about 3 times as great as that for ^{14}C-glycine by particles of cerebral cortex and about 1.8 times as great as that for ^{14}C-glycine by particles of spinal cord. These data provide further support for the notion that GABA and glycine may be the respective inhibitory transmitter substances in the mammalian cerebral cortex and spinal cord. (Supported by the Medical Research Council of Canada)

48.6 N-METHYL BICUCULLINE AND THE γ-AMINOBUTYRIC ACID RECEPTOR. Ernest J. Peck, Jr.*, J. M. Schaeffer*, and J. H. Clark* (SPON: J. Altman). Baylor College of Medicine, Houston, Texas, 77025 and Purdue Univ., W. Lafayette, Indiana, 47907.

The phthalide isoquinoline alkaloid, bicuculline (BIC), is reported to be a specific antagonist of the inhibitory neurotransmitter, γ-aminobutyric acid (GABA) (Nature 226:1222, 1970). However, the value of bicuculline as a tool for the examination of post-synaptic events is limited by its insolubility at physiologic pH. Recently a quaternary ammonium derivative, N-methyl bicuculline (NMB), has been synthesized and examined for convulsant activity. NMB is much more soluble than BIC, relatively impermeable to the 'blood-brain barrier', and more potent than BIC on a molar basis as a convulsant (Nature 240:219, 1972; Brain Res. 42: 486, 1972). In the present investigation, we have examined the effect of NMB on the binding of ^{3}H-GABA to cerebellar cortical synaptosomes of the rat. Synaptosomes were pretreated with chlorpromazine to inhibit ^{3}H-GABA transport and subsequently incubated for 1 hour at 0-4°C with various concentrations of ^{3}H-GABA in the presence or absence of several concentrations of BIC or NMB. After incubation the synaptosomes were filtered and washed on Millipore filters (0.8 μ pore size). The filters were solubilized and bound ^{3}H-GABA was determined. Double reciprocal analyses of the binding data reveal that the K_d for the receptor-GABA complex is 18 μM and the values of K_I for BIC and NMB are 101 ± 25 μM and 34 ± 11 μM respectively. The similarity in K_I values for BIC and NMB suggests that the difference in convulsant activity of these compounds is due to their solubility properties and not to a difference in affinity for the GABA receptor (Supported by the Research Corp., Atlanta, Ga., and the National Institutes of Health, HD 04985).

48.7 AMINO ACID NEUROTRANSMITTERS: CEREBROSPINAL FLUID CHANGES IN AMMONIA INTOXICATION. Ralph G. Dacey*, William J. Logan. Dept. Neurology, Sch. Med., Univ. of Va., Charlottesville, Va., 22901

Hepatic encephalopathy has been considered to be a form of ammonia toxicity. However, the mechanism by which ammonia exerts its neural effects has not been elucidated. In order to study this phenomenon we have produced ammonia intoxication in rats by portocaval anastomosis and intraperitoneal (IP) ammonium acetate ($NH_4^+Ac^-$) injection. After injection rats initially became symptomatic with lethargy and ataxia, and with higher doses developed a hyperactive startle response. Cerebrospinal fluid (CSF) was obtained by cisternal puncture from control and experimental rats sedated with sodium pentobarbital. This was added to incubations containing rat cerebral cortex synaptosomes and isotopically-labeled glutamic acid (Glu) and gamma-aminobutyric acid (GABA) (Logan and Snyder, Brain Research 42:413-431, 1972.) CSF from ammonia-intoxicated rats inhibited the uptake of Glu but not that of GABA. Neither ammonium nor glutamine inhibited synaptosomal accumulation of these substances in concentrations up to 10^{-2}M. These findings demonstrate the release into CSF during $NH_4^+Ac^-$ intoxication of a neuronally active substance toxic to selective synaptosomal uptake mechanisms. $NH_4^+Ac^-$ intoxication also causes in vivo alteration of amino acid neurotransmitter production and release into CSF. Glucose C^{14}(U) was injected intra-cisternally into control and experimental rats and the appearance of isotope in various CSF metabolites including Glu and GABA was determined. In the experimental animals the ratio of labeled Glu to GABA (Glu/GABA) was increased compared to controls. These findings suggest that the putative neurotransmitters, Glu and GABA, play a role in mediating the central nervous system toxicity of ammonia.

48.8 MONOSODIUM GLUTAMATE (MSG) - A PRECURSOR OF ACETYLCHOLINE (ACh) SYNTHESIS IN RAT BRAIN - IN VIVO. Sudhir Kumar and Ramin Ghadimi*. Dept. of Pediatrics, Methodist Hospital, 506 Sixth Street, Brooklyn, N. Y. 11215

Adult rats were given a solution containing 15 mg of MSG/100 g body weight together with 25 μc of L-C^{14}-glutamic acid (uniformly labeled;sp.act. 150 mCi/nmole) and sacrificed by cervical dislocation at 0, 1, 2, 5, 10, 20 and 30 minutes after administration of the solution. ACh was isolated from the whole brain according to Nakamura et al. (Biochem. J. 118:443, 1970) and estimated by the method of Chang & Gaddum (J. Physiol., London 79:255, 1933). While the incorporation of radioactivity into the acetyl group of ACh increased and showed a steady rising slope up to 6 to 10-fold at 30 min., the sp. act. of ACh (μmoles of ACh/mg protein) decreased about 35% below the normal level in the first two min. after MSG ingestion following which an increase about 45% above the normal value was observed at 20 min. after ingestion. At 30 min. following ingestion, the sp. act. of ACh in brain was about 15% lower than the normal level. The results indicate that ingestion of MSG in rats in amounts comparable to those producing Chinese Restaurant Syndrome (Ghadimi, Kumar & Abaci. Biochem. Med. 5:447, 1971) causes an increased synthesis of ACh in rat brain. While earlier reports had suggested that Chinese Restaurant Syndrome is a peripheral phenomenon (Schaumberg et al. Science 163:826, 1969), our results indicate that at least in the rat, MSG ingestion has a central effect as well.

48.9 GLYCINE RECEPTOR BINDING IN THE CENTRAL NERVOUS SYSTEM. Anne B. Young and Solomon H. Snyder. Dept. of Pharmacol., Johns Hopkins Sch. of Med., Baltimore, Md. 21205.

There is much neurophysiologic and biochemical evidence suggesting glycine as a major inhibitory neurotransmitter in the mammalian CNS. Strychnine antagonizes selectively the inhibitory effects of glycine. We have demonstrated that [^{3}H]strychnine binds in a selective fashion indicating an interaction with post-synaptic glycine receptors. The displacement of strychnine binding by glycine and other amino acids parallels their glycine-like neurophysiological activity. The regional localization of strychnine binding in the central nervous system correlates closely with endogenous glycine levels, being highest in the spinal cord and medulla oblongata-pons, intermediate in the midbrain, hypothalamus, and thalamus and negligible in higher centers. Within the spinal cord, binding correlates with the distribution of interneurons. No binding is demonstrable in white matter. In subcellular fractionation experiments, strychnine binding is most enriched in synaptic membrane fractions. Strychnine binding is a saturable process with affinity constants for strychnine and glycine of 0.01 μM and 10 μM respectively. The rates of association and dissociation are 0.6×10^{7} $mole^{-1}sec^{-1}$ and $2.3 \times 10^{-2}sec^{-1}$, respectively. (Supported by USPHS grants MH 18501, NS 07275, a grant from the John A. Hartford Foundation and a fellowship to A.B.Y. from the Scottish Rite Foundation.)

48.10 HYPERPOLARIZING AND DEPOLARIZING RECEPTORS TO GLYCINE ON THE FROG MOTONEURONS. A. L. Padjen, R. A. Nicoll and J. L. Barker. Lab. of Neuropharmacology, NIMH, St. Elizabeths Hosp., Washington, D.C. 20032

The effect of glycine on the membrane potential of motoneurons in the isolated hemisected frog spinal cord was examined using sucrose gap recording from the ventral root. Varying the concentration of glycine applied to the spinal cord reveals hyperpolarizing and depolarizing components to the glycine response. These responses were unaffected by addition of 20 mM $MgSO_4$ (which blocked synaptic transmission) suggesting that both components are direct effects on motoneurons. The hyperpolarizations were associated with a decrease in motoneuron excitability, were blocked by strychnine, and were dependent on the presence of external chloride ions. The depolarizations were associated with an increase in excitability, were not blocked by strychnine, and were dependent on the presence of external sodium ions. There was a linear relationship between the size of the glycine (and glutamate) depolarization and the log of external sodium concentration. The isolated ventral root showed a small but consistent depolarization to glycine, but not glutamate, confirming the direct nature of the depolarizing component. Dual responses could also be shown with GABA and β-alanine, but the depolarizing components for these amino acids were small. The hyperpolarizing receptors are presumably involved in postsynaptic inhibition, while the depolarizing receptors for glycine, β-alanine and GABA may relate to a Na dependent uptake process.

49.1 INTERNEURONS IN MONKEY LATERAL GENICULATE NUCLEUS: PARTICIPATION IN "TRIADIC" AND "NON-TRIADIC" SYNAPSES. P. Pasik, T. Pasik, J. Hámori* and J. Szentágothai*. Dept. Neurol., Mount Sinai Sch. Med., CUNY, New York, 10029, and Dept. Anat., Semmelweis Univ. Med. Sch., Budapest, Hungary.

Electron microscopy of interneurons in lateral geniculate nucleus (LGN) of monkeys (Macaca mulatta) revealed that these cells have a scanty perikaryon which is poor in organelles. Occasionally, it shows ovoid vesicles close to a contact where the interneuron soma is presynaptic to a relay cell dendrite. The interneuron dendrites exhibit both postsynaptic and presynaptic sites, the latter having ovoid vesicles. The proximal portion of an axon could be seen emerging from a typical interneuron soma. Axonal endings may be represented by small profiles filled with ovoid vesicles which are seen infrequently within glomeruli in exclusively presynaptic locations. The most common synaptic arrangement with interneuron participation is a "triad" formed by a retinal terminal presynaptic to both relay cell dendrite and interneuron dendrite, the latter being in turn presynaptic to the same relay cell dendrite. This "triad" is seen in the glomerular complexes with the interneuron element bridging sometimes several adjacent glomeruli. "Triads" also appear in extraglomerular regions where either the relay cell or interneuron element is represented by the soma of the respective cell. Interneurons are also postsynaptic to axon terminals of cortical origin, dendrites of other interneurons, and axons of unknown origin. Findings suggest a mosaic composition of the interneuron membrane with both receptoric and effectoric sites as indicated by the ubiquitous presence of synaptic vesicles in the soma, dendrites and axon. The "triad" is the most typical arrangement within the LGN circuitry in both glomerular and extraglomerular regions. A functional model of LGN based on these findings will be presented. (Aided by U.S.P.H.S. Grants # MH-02261 and K3-EY-16,865).

49.2 RECEPTIVE FIELD PROPERTIES OF LATERAL GENICULATE NEURONS IN KITTENS. R. L. Glendenning and T. T. Norton. Depts. of Psychology and Physiology, Duke Univ., Durham, N. C. 27706.

Using standard extracellular single-unit recording procedures we have examined the receptive field organization of lateral geniculate nucleus (LGN) cells in paralyzed, anesthetized kittens 15-60 days of age. In many respects, cells in the LGN of even the youngest kittens resembled those found in adult cats. The topographic map of the retina in the LGN is at least grossly similar to the adult. Receptive fields were found for many cells, some ON-center, some OFF-center. The size of the field centers was as small as 0.5° in diameter, and some cells responded to even smaller spots of light. Most cells seemed to have an antagonistic surround. Responses to visual stimuli were usually brisk. Spontaneous activity often consisted of short bursts of spikes. Some cells in young kittens responded to selected stimuli moving at high velocity and probably are "Y" system neurons. In contrast to adult cats, we were unable to find receptive fields for some LGN cells in young kittens. Many of these neurons could be driven visually with a stroboscopic light. Cells with receptive fields occassionally showed fatigue (or habituation) upon repeated stimulation. In some cells in young kittens the antagonistic surround seemed quite weak since the cells gave equally strong responses to changes in diffuse illumination as they did to small spots centered in the receptive field. We conclude that although LGN neurons in kittens possess some aspects of adult receptive field organization, they are immature in several respects compared with LGN neurons in adult cats.
(Supported by National Eye Institute Grant EY-01085.)

49.3 BRIGHTNESS CONTRAST MECHANISMS OF THE PRIMATE LATERAL GENICULATE. D. Max Snodderly, Jr.[1], R. L. DeValois[2]*, E. William Yund[3]*, and Norva K. Hepler[2]*.

The spatial coding of brightness contrast was studied by recording the responses of macaque lateral geniculate neurons to white and black vertical bars centered on the receptive field. Most cells excited to either a light or a dark bar but usually not to both. This was true of both achromatic and chromatic cells and it argues for participation of the chromatic system in the coding of brightness contrast. Different cells responded best to different bar widths, as would be expected from receptive fields with a range of center sizes and from psychophysical evidence for channels tuned to particular stimulus sizes. Most cells peaked at bar widths of 1 degree or less and some gave maximal responses at our smallest stimulus width of 4 min. Spatial tuning appeared to be similar whether contrast was produced by changing the center or the flanks of the stimulus field. Neurons tuned to larger stimuli tended to give lower peak responses than those tuned to narrow bars. This may be related physiologically to an overlapping receptive field structure and psychophysically to the low-frequency attenuation of the modulation transfer function.

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49.4 DIFFERENTIAL MODIFICATION OF RESPONSES OF TONIC AND PHASIC LATERAL GENICULATE UNITS TO VISUAL FLASH STIMULI AFTER CLICK-FLASH PAIRING. Leo M. Chalupa*, Angelica W. Macadar* and Donald B. Lindsley. Depts. Psychol., Physiol., Psychiat. and Brain Res. Inst., UCLA, Los Angeles, 90024

Single unit, extracellular, responses were recorded in the dorsal lateral geniculate nucleus of semichronic cat preparations. For each unit the tonic or phasic response to steady light was determined and the locus and size of the receptive field plotted. Subsequently, responses to brief, diffuse flashes at the rate of 1 per 2 sec. were recorded for a 10 minute period, followed by a 5 minute period of binaural click-flash pairing at click-flash intervals of 0, 100 or 500 msec. After each period of pairing at different interstimulus intervals responses to flashes alone were recorded for a 10 minute period. Poststimulus time histograms were plotted for each stimulus condition. The following results were obtained. 1. All geniculate units tested were unresponsive to click stimuli alone. 2. Tonic units showed a decrease in responsivity to flashes during click-flash pairing and this decrement in response to flashes often persisted for 2 to 3 minutes during the subsequent flash alone period. 3. The responses of phasic units to flashes were not modified during, or after, click-flash pairing. These results provide further functional differentiation of tonically and phasically responding units. The modifiability of the response of tonic units to flash stimuli following pairing of click-flash stimuli suggests a plasticity for tonic units not found for phasic units. Supported by USPHS grant NS-8552 to D. B. Lindsley.

49.5 EXCITABILITY CHANGES OF LATERAL GENICULATE CELLS FOLLOWING SACCADIC EYE MOVEMENTS OF CHRONIC CATS. Hiroharu Noda and W. Ross Adey. Dept. Anat., Sch. Med., UCLA, Los Angeles,90024.

When optic chiasm was stimulated electrically, relay cells in lateral geniculate nucleus (LGN) responded with a single spike in 1-3 msec and it was followed by a prolonged silence of about 100-300 msec. A grouped firing appeared in many cells after the silent period. This silent period is generally attributed to an IPSP and the grouped firing is due to a postinhibitory rebound. The effects of saccadic eye movement on the LGN cells were studied by evaluating the firing probability of the initial evoked spike and the duration of the inhibitory period as a response to chiasmatic stimulation. By triggering a stimulator from potential shifts in electrooculogram and altering delays of the chiasmatic stimulation, the excitability of the LGN cells was studied from moment to moment during the course of saccades. When the eyes moved in the presence of stationary gratings, the firing probability of the initial evoked spike decreased greatly for a period of 150 msec after each eye movement. The effect was most prominent at about 70-100 msec after the saccades and the probability was less than half the control in many cells. At the same time,the duration of the inhibitory period became very short or almost completely disappeared in some cells. These effects, however, did not occur when the eyes moved in total darkness. They were probably caused by impulses from retinal ganglion cells which were excited whenever images of the stationary objects moved over the retina. (Supported by US Air Force Contract AFOSR F44620-70-C-0017 and NIH Grant GM-16058).

49.6 LATERAL GENICULATE POST-SYNAPTIC RESPONSES TO LIGHT STIMULI AND THEIR RELATION TO ENERGY SUMMATION AND VISUAL PERSISTENCE IN HUMAN VISUAL PSYCHOPHYSICS. David N. Young, Jr.* and Chester D. Hull. Dept. Psychiatry, Sch. Med., Mental Retardation Research Center, NPI, UCLA, Los Angeles.

Intracellular potentials from lateral geniculate cells, and spike potentials from optic tract fibers, were evoked by light stimuli of known intensity and duration presented in Maxwellian view to one eye of locally anesthetized, paralyzed cats. Both geniculate neurons (n=60) and optic nerve fibers (n=12) responded to long stimuli (>250 msec) with "on" (depolarizing or increased spike rate) or "off" (hyperpolarizing or decreased spike rate) responses. Optic nerve fibers gave similar responses to short stimuli, but geniculate neurons developed a complex response consisting of an initial depolarization followed by a long hyperpolarization. In some units at each location, the highest light intensities used (10^4 Trolands) evoked a complex oscillatory response, which was of much greater period in the case of the geniculate.

Some of these electrophysiological responses may be related to human perceptual responses reported in the psychophysical literature. The initial portion of the response of lateral geniculate and optic nerve "on" units shows energy summation as determined by the method of response equivalence. The logarithmic relationship observed between luminance and stimulus duration parallels that observed in human psychophysical experiments. Also the total duration of the complex response of lateral geniculate (but not optic nerve) "on" units parallels the changes in perceived visual persistence plus stimulus duration reported by Bowen, Pola and Matin (1972).

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49.7 AN ANALYSIS OF THE CONNECTIONS OF THE INFERIOR AND SUPERIOR DIVISIONS OF THE PULVINAR NUCLEUS OF THE BUSHBABY (GALAGO SENEGALENSIS). Karen K. Glendenning*, Vivien Casagrande, Janet A. Hall*, and William C. Hall. Depts. Anat. and Psychol., Duke University, Durham, N.C. 27706

The pulvinar nucleus of the bushbaby can be subdivided into an inferior and superior sector on the basis of cytoarchitecture and afferent connections. The inferior subdivision was found by means of anterograde degeneration techniques to receive visual input from the superficial layers of the superior colliculus. This subdivision of the pulvinar in turn projects to two distinct cytoarchitectonic regions in the middle of the temporal lobe. At least one of these regions contains a retinotopically organized representation of the contralateral visual field (Allman, Lane and Kaas, Brain Research '73). The superior division of the pulvinar nucleus does not receive major projections from the superior colliculus and its afferent connections are at present unknown. However, the superior pulvinar nucleus also appears to be related to the visual system since its cortical target includes extrastriate cortex. Together, the two subdivisions of the pulvinar nucleus project to an extensive cortical zone which extends from the lateral border of area 17 to the belt surrounding auditory cortex. Since the inferior pulvinar nucleus receives projections from the superior colliculus and since the superior pulvinar nucleus projects to the extrastriate cortex, the entire pulvinar complex of the bushbaby appears to be closely related to the visual system. (Supported by NINDS Grant NS-09623, awarded to W.C. Hall and NIMH Grant MH-4849, awarded to I. T. Diamond).

49.8 THE ROLE OF THE SUPERIOR COLLICULUS IN RELEARNING FOLLOWING UNILATERAL VISUAL CORTICAL LESIONS IN THE CAT. Bonnie S. Wood. Dept. Anat., Cornell Univ. Medical College, N.Y., N.Y. 10021

Following optic chiasm section and monocular learning of a two choice dark-light discrimination in a continuous-type Y-maze, cats were subjected to unilateral removal of the entire occipito-temporal neocortex. After this procedure, criterional performance was reestablished in fewer than 400 trials through the eye contralateral to the cortical lesion. After prolonged training (2,360 to 3,840 trials), criterional performance was also achieved through the eye ipsilateral to the cortical lesion. Following this relearning, the superior colliculus ipsilateral to the cortical lesion was removed. There was no evidence of relearning through the eye ipsilateral to the two lesions after 3,695 trials. This suggested that the superior colliculus ipsilateral to the cortical lesion had been involved in relearning following the cortical ablation. Facilitation of this relearning by the superior colliculus ipsilateral to the cortical ablation was accomplished by preceding unilateral cortical ablation by removal of the contralateral superior colliculus. The results support and extend the hypothesis of previous investigators that following unilateral removal of the posterior two-thirds of the neocortex, there was inhibition from the contralateral superior colliculus upon the ipsilateral superior colliculus.

49.9 EFFECTS OF ABLATION AND COOLING OF VISUAL CORTEX ON THE MONKEY SUPERIOR COLLICULUS. Michael P. Stryker. Dept. of Psychology, MIT, Cambridge, Mass. 02139.

The influence of corticotectal connections was investigated in the rhesus monkey by recording the activity of single cells in the superior colliculus following ablation of the occipital lobe or reversible inactivation of a region of area 17 by cooling. Both alert and paralyzed, anesthetized animals were studied. The receptive field properties of cells in the superficial grey and dorsal part of the optic layers of the colliculus were largely unaffected by visual cortex ablation and cooling. The foveal area of the visual field remained well represented on the colliculus, despite anatomical evidence for the virtual absence of a foveal retinotectal projection. In the deeper layers of the superior colliculus, visual responses could no longer be elicited after visual cortex ablation. In agreement with these findings, reversible cooling of area 17 suppressed the visually elicited responses of collicular units in this region. In alert monkeys, cells discharging in association with eye movement were still found in the deeper layers of the colliculus following visual cortex ablation, but they no longer had visual receptive fields. The results suggest that the occipital cortex plays an important role in the flow of visual information to the deeper layers of the rhesus monkey superior colliculus. (Supported by a Sloan Foundation grant to MIT and NIH EY00756 and EY00676.)

49.10 SEPARATION OF TECTAL AND THALAMIC VISUAL FUNCTIONS IN THE FROG D. Ingle, McLean Hospital, Belmont, Mass. 02178

Frogs appear "blind" to moving objects following ablation of the optic tectum, in that they neither pursue small moving stimuli as prey nor avoid large black objects that suddenly approach. Nevertheless, these frogs realistically avoid standing barriers and localize apertures during avoidance behavior. The high accuracy of barrier edge localization was measured by a method of cine analysis that avoid the subjectivity of on-line observations.

Those frogs that later show good regeneration of the cut optic tract to the ipsilateral tectum then recover the ability to strike at prey, but in the predicted mirror-symmetrical direction to their actual location. When avoidance of looming object also recovers, it is also directed in a maladaptive mirror-symmetrical fashion. Despite this wrong-way responding via the retinotectal pathway, the same frogs continue to avoid barriers realistically. Since pretectal damage often abolishes barrier avoidance without diminishing prey-catching activity, it seems likely that retinal input to pretectal structures plays a role in barrier detection quite independent of tectal function.

The duality of visual mechanisms in the frog is at least superficially similar to the edge-detecting vs. motion-detecting differences found within thalamo-cortical and tectal pathways respectively in mammals. These data, together with recent observations that sharks can discriminate stationary patterns after tectal ablation, suggest that the scope of thalamic visual function in lower vertebrates is greater than previously supposed.

49.11 ONTOGENIC DEVELOPMENT OF RETINOTOPIC ORGANIZATION OF THE SUPERIOR COLLICULUS OF RABBITS. C. Sitthi-amorn. Laboratory of Neurophysiology, U.W., 283 Med. Sc. Bldg., Madison, Wisconsin 53706

Postnatal development of retinotopic organization in the superior colliculus has been investigated in 30 rabbits using microelectrode recording of cluster responses and averaged evoked potentials. Cluster responses reveal that the retinotopic organization is present in the superior colliculus as early as the 8th postnatal day, when the eyes are still closed. Except for some unresponsive regions, the superior colliculus of an 8 day old rabbit has orderly retinotopic progression similar to that of the adult. However, in the 8 day old rabbit, only a very weak averaged evoked potential is produced by intense flash stimulation. Many receptive fields, particularly those located in more peripheral parts of the visual fields, have no clear boundary and respond only to very diffuse light. The diffuse receptive fields cannot be found after the 11th postnatal day, when the eyes open. At the 8th postnatal day, all receptive fields that have sharp boundaries are located more centrally within the part of the visual field corresponding to the specialized region of the retina, the visual streak. By the 9th-10th postnatal day, evoked potentials responding to intense short duration flashes are evident, having latencies of 80-110 msec. for the central fields and 120-200 msec. or more for the peripheral. Latencies of evoked responses shorten as maturation progresses. The rate of latency shortening is highest within the first two days after the eyes open (from the 11th-13th postnatal day), with gradual reduction thereafter, reaching the adult values of 22-32 msec at the age of 6-8 weeks. Latencies of evoked responses in the peripheral receptive fields shorten more rapidly than those in the central. It is concluded that central vision which is important for visual acuity develops before the peripheral but both reach maturation at approximately the same time.

49.12 THE MODE OF INNERVATION OF THE ANTERIOR AND POSTERIOR PRETECTAL NUCLEI OF THE RABBIT BY AXONS ARISING FROM THE VISUAL CORTEX. Roland A. Giolli and Lex C. Towns*. Depts. of Anatomy and Psychobiology, Univ. of Calif., Irvine, Calif. 92664.

In sections processed by the Cajal method, two distinct systems of fibers can be recognized within the anterior and posterior pretectal nuclei. One is a rostro-caudal system consisting of fiber bundles oriented in parallel with the superior quadrigeminal brachium; some fibers of this system mingle with the fibers of the brachium. The other is a latero-medial system composed of fibers directed perpendicularly to those of the rostro-caudal system. After lesions of the visual cortex, the study of sections prepared by the Nauta method shows fiber degeneration in both systems of the anterior and the posterior pretectal nucleus. The degenerating rostro-caudal fibers are corticotectal axons, and these send collateral branches into the latero-medial fiber system of each nucleus. Most, if not all, of the degenerating latero-medial fibers are the collateral branches of rostro-caudal fibers, and represent in addition the terminal portions of corticopretectal axons. These conclusions are supported by four of our findings. 1) The presence of degenerating rostro-caudal fibers that branch in, or closely adjacent to, the zones of degenerating latero-medial fibers but in no other parts of the pretectal nuclei. 2) The common orientation shared by these branches and the degenerating latero-medial fibers at any one location, suggesting that the two elements represent portions of the same fibers. 3) The morphology of the degenerating latero-medial fibers with their many short side branches indicating that these fibers are the terminal segments of the corticopretectal axons. 4) Our failure to demonstrate degenerating rostro-caudal fibers which pass into the latero-medial fiber system without branching. (Supported by USPHS grants RO1-EY00607 and MH11095-06.)

50.1 A MODEL FOR PASSIVE ELECTROCHEMICAL DYNAMICS IN EXCITABLE TISSUE. Jack Fromkin* (SPON: George P. Moore) Dept. of Biomedical Engrg. Univ. of So. Calif., Los Angeles, Calif. 90007.

A model for the passive electrochemical dynamics of excitable tissue was derived from consideration of inorganic ion movements, water movement and membrane potential under the assumptions that a negligible transmembrane pressure gradient exists and that changes in cell surface area may be ignored. The model was programmed in Fortran IV for use on a DEC PDP 11/20 computer. Provision was made for the inclusion of up to four substances in addition to the sodium potassium and chloride ions. Output was provided for recording and plotting up to 32 variables for each experiment simulated. The model exhibited the behavior observed in excitable tissue when the active processes are suppressed, i.e., depolarization and the diminution of concentration gradients. The model has no steady state at physiological levels but rather an intrinsic drift toward an ultimate (Gibbs-Donnan) equilibrium. Since, for long term processes, the variation of membrane permeability with other variables used is not well known, the model was further tested by simulation of an experiment in which the permeabilities may be assumed constant. This experiment consists of the application of a bathing solution made hypertonic by the addition of an uncharged, impermeant substance. Close agreement with various reported results was obtained when a simulation employing a 'prototype' tissue (mammalian muscle) was compared with results obtained on guinea pig smooth muscle and frog sartorius muscle. Still closer agreement was obtained when corrections were applied for the intrinsic drift rate of the model, suggesting that passive drift rates are a reasonable first approximation to the magnitude of the active processes. (This work was supported in part by National Institutes of Health grant GM 16437.

50.2 EFFECTS OF TEMPERATURE CHANGES ON THE SODIUM AND POTASSIUM CONDUCTANCES OF MYXICOLA GIANT AXONS. C. L. Schauf. Department of Neurological Sciences, Rush Medical College, Chicago, Illinois, 60612.

In the squid axon all rate constants vary with temperature with a Q_{10} of about 3. Similar data is available for frog myelinated fibers, but while in R. pipiens the temperature dependence is similar, in X. laevis, the rate constants for sodium activation (m) have significantly lower Q_{10}s than those for sodium inactivation (h) and potassium activation (n).

Myxicola giant axons were studied under voltage clamp conditions at temperatures ranging from 1°C to 18°C, and the resulting current records for step depolarizations of 20-150mv analysed by methods previously described (Goldman and Schauf, J. Gen. Physiol. 61:361, 1973). The Q_{10}'s for the maximum conductances were low (1.3-1.5) and not significantly different. The Q_{10}'s for the time constants were: 2.64 ± 0.2 for τ_m; 2.56 ±0.2 for τ_h; 3.02 ± 0.3 for τ_n. No voltage dependence could be detected. The steady-state values $m_\infty(V)$, $h_\infty(V)$, $n_\infty(V)$ were not temperature dependent. Action potential durations computed using the measured temperature dependence of the rate constants had a Q_{10} of 2.58, which agreed with the value of 2.46 ± 0.2 determined experimentally.

In addition to determination of the temperature dependence of τ_h from an analysis of the decline in sodium current during step depolarizations, a series of two pulse experiments (in which τ_h was determined from the effect of prepulse duration on the peak sodium current during a subsequent fixed test pulse) were also carried out at various temperatures. Goldman and Schauf (above ref.) demonstrated that inactivation time constants obtained by these two methods are different when compared at the same potential. Nevertheless, the Q_{10} for τ_h measured using prepulse experiments was 2.47 ± 0.2, the same as that obtained by the first method.

(Supported by the Morris Multiple Sclerosis Research Fund)

50.3 ANATOMICAL BASIS FOR APPARENT PARADOX CONCERNING CONDUCTION VELOCITIES OF TWO IDENTIFIED AXONS IN APLYSIA. H.M. Pinsker, R. Feinstein, R.E. Coggeshall. Marine Biomedical Institute, U.T.M.B., Galveston, Texas 77550.

Among the tenets of neurophysiology are that larger diameter axons have: 1) a lower threshold for electrical stimulation, 2) a faster conduction velocity, and 3) a larger amplitude extracellular spike than smaller diameter axons. However, in the right pleuro-visceral connective of the marine mollusc, Aplysia, the largest fiber, which is the axon of identified cell R2, has a higher threshold for electrical stimulation and a slower conduction velocity than does the smaller axon of R1, even though the amplitude of the R2 spike is larger than that of the R1 spike (Tauc, J. Physiol. [Paris] 49:973, 1957; Goldman, J.C.C.P. 57:185 1961; Frazier et al., J. Neurophysiol. 30:1288, 1967). To resolve this apparent paradox we measured cross-sectional area and perimeter of axons of R1 and R2 by light and electron microscopy in the same preparations in which we measured their conduction velocities. The surface membrane of the axon of R2 is much more infolded than that of R1. As a result of this difference in infolding, the surface area to volume ratio is greater for the axon of R2 than for that of R1. Using the axon perimeter as an index of capacitance and the cross-sectional area as an index of resistance, the anatomical data suggest that the increase in R2's capacitance is much greater than its decrease in internal resistance. This presumably explains why R2 has a higher threshold and a lower conduction velocity than R1. This is in agreement with the formulation of Hodgkin (J. Physiol. 125:221, 1954) that conduction velocity of unmyelinated fibers is proportional to the volume to surface area ratio. Our results also confirm Mirolli's suggestion that fiber diameter alone is a poor index of conduction velocity for invertebrate unmyelinated fibers (Mirolli and Talbott, J. Physiol. 227:19, 1972). (Supported by USPHS #NS10161 and a Moody Foundation grant.)

50.4 TETANIC AND POST-TETANIC CHANGES IN MEMBRANE POTENTIAL OF SINGLE MEDULLATED NERVE FIBERS. Gordon M. Schoepfle and Charles R. Katholi*, Departments of Psychiatry, Physiology and Biophysics and Biomathematics. Medical Center, University of Alabama in Birmingham, Alabama 35294

In the course of prolonged tetanization of a single medullated nerve fiber of Xenopus, the membrane potential at the end of an interspike interval may attain a value either slightly above or below that of the previous resting level. Peak value of post-tetanic hyperpolarization is attained within a time which varies between several tenths of a second and one or two seconds following termination of the last spike in the train of impulses. For reasons of establishing a true base line, it is suggested that the ordinates of a normal post-tetanic voltage-time curve be subtracted algebraically from those corresponding to the passive post-tetanic depolarization obtained after cyanide poisoning. This maneuver will then provide a voltage-time curve with a maximum at a time very near that for termination of the repetitive stimulation. Such a curve is to be expected from an electrogenic sodium pump mechanism whose rate should be maximal at termination of the tetanic interval. Consistent with this argument is the finding that there exists an inverse relation between rise time of the post-tetanic transient and extent of hyperpolarization at the end of the tetanic interspike interval. Isethionate substitution for chloride may lead to initial augmentation and eventual depression of post-tetanic hyperpolarization without change in the time parameters. Relatively brief post-tetanic hyperpolarization in Li_2SO_4 treated fibers is attributed to changes in potassium conductance. Supported by NIH Grant (5R01 NS09171) and NIH Grant (FR00-145).

50.5 SOLUTIONS OF THE HODGKIN-HUXLEY EQUATIONS MODIFIED FOR POTASSIUM ACCUMULATION IN PERIAXONAL SPACE. William J. Adelman, Jr., and Richard FitzHugh*. Laboratory of Biophysics, IR, NINDS, NIH, Bethesda, Md. 20014.

Hodgkin-Huxley equations were modified to include the properties of an external diffusion barrier separated from the axolemma by a thin periaxonal space in which K^+ accumulates as a function of membrane activity. Previous reports (Soc. Neurosci. Abs. 1972, p.79 and Biophysic. Soc. Abs. 1973, p.70a) described methods and gave values of potassium permeability of the outer diffusion barrier, P_K, and phenomenological space thickness, θ, for the Loligo pealei axons. As these reports showed that the potassium reversal potential, E_K, varies with I_K, a new dependent variable K_s, the [K] in the space, was introduced into the Hodgkin-Huxley equations through the driving force for I_K, $(E-E'_K)$, where $E'_K=(RT/F)\ln(K_s/K_i)$. K_s was described by: $dK_s/dt=[(I_K(1-t_K)/F)-P_K(K_s-K_o)]/\theta$, where t_K = the K transference number, F=Faraday, and K_o=[K] in the external solution. Equations were solved on a PDP-10 computer with NIH's modeling program MLAB, which uses the Nordsieck numerical method. The modified equations for membrane potentials gave: 1)increases in K_s of from 1 to 3 mM/impulse, 2)more accurate representation of the falling and undershoot phases of the action potential than the unmodified equations, 3)action potential trains similar to those recorded by Frankenhaeuser and Hodgkin (1956) with K accumulation during activity and wash-out of K following cessation of activity, 4)more accurate representation of thresholds and latencies, 5)somewhat more accurate representation of adaptation during repetitive firing. Solutions for voltage clamped membrane potassium currents had features found in experiments: 1) currents with "droop", 2)"tail" currents with correct time courses and signs, 3)instantaneous I/V relations with correct slopes and reversal potentials. Further modifications with new g_K and α_n and β_n values for L. pealei axons improved fitting of solutions to experimental data.

50.6 VOLTAGE CLAMP STABILITY WITH SERIES RESISTANCE COMPENSATION. Robert E Taylor and Francisco Bezanilla*. Laboratory of Biophysics, IR, NINDS, NIH, and Department of Physiology, University of Rochester Medical School.

Some results of measurements of current through cell membranes using voltage clamp techniques are seriously affected by the presence of unavoidable resistances (Rs) in series with the membrane capacity (Cm). In many cases later correction of results is difficult or impossible. Negative resistance (KRs), added by means of a subsidiary feedback loop, has been used by many investigators since this technique was introduced by Hodgkin, Huxley and Katz, but stability is a problem. We have shown that for a system using ideal operational amplifiers (6 db per octave fall-off, small signal unity gain fo (in Hz) and DC gain=A the fraction (K) of series resistance which can be compensated for without large oscillations is primarily determined by RsCmfo with A reasonably large (e.g., 10^5), is always greater than unity and is bounded by (Rs+Rm)/(Rs) for fo small. As K approaches the critical value for large oscillations, damped oscillations occur and with wide bandwidth systems full compensation of series resistance is not possible without distortions being introduced into the current records.

50.7 DIVALENT CATION REGULATION OF BURSTING PACEMAKER ACTIVITY IN MOLLUSCAN NEURONS. Jeffery L. Barker and Harold Gainer, Behav. Biol. Br., NICHD, NIH, Bethesda, Md. 20014.

The effects of external divalent cations (Ca, Mg, Sr) on bursting pacemaker potential (BPP) activity were studied in identified molluscan neurons by intracellular recording techniques. Removal of most of the Ca and Mg from the saline or their replacement with Sr induced BPPs and marked anomalous rectification (AR) in the normally silent giant neuron R_2. BPP activity and AR were inhibited most effectively by Ca, less so by Mg and not at all by Sr. BPP amplitude and AR were parabolically dependent on 1-5 mM Ca and 1-40 mM Mg and directly dependent on 1-60 mM Sr. These same membrane properties were directly dependent on Ca, Mg and Sr over the 1-60 mM range in the bursting pacemaker neuron R_{15}. Cobalt and ouabain abolished BPP activity and AR in these cells. The inhibitory effects of ouabain were divalent cation dependent. Similar experiments were performed in a bursting pacemaker neurosecretory cell in aestivated and activated land snails. Removal of Ca from the saline induced BPP and AR in the silent cell from the aestivated snail. BPP amplitude and AR were parabolically dependent on 1-5 mM Ca and 1-50 mM Mg and directly dependent on 1-60 mM Sr in cells from aestivated snails, while these properties were parabolically dependent on Ca and Mg over the 1-60 mM range and directly dependent on 1-60 mM Sr. The results demonstrate that divalent cations play important roles in the expression of BPP and AR, as well as in their seasonal modulation. It is probable that they are acting by regulating the monovalent cation conductances underlying BPP and AR.

50.8 POTASSIUM CONDUCTANCE CHANGE DURING NORMAL BURSTING IN THE APLYSIA R15 CELL. Douglas Junge and Cathy L. Stephens*. Sch. Dent. and Dept. Physiol., UCLA, Los Angeles, 90024

The hyperpolarization following a burst in the R15 cell was studied using separate stimulating and recording electrodes. The ganglion capsule was dissected open and experiments were usually done at room temperature. The post-burst hyperpolarization could be observed with ouabain, Li^+ or K-free solution if artificial inward current was applied. The hyperpolarization could be observed with dinitrophenol or cooling, with no applied current. Thus, the post-burst hyperpolarization was apparently not due to the cyclic activity of an electrogenic pump. A reversal potential for the hyperpolarization could be measured by passage of inward current between bursts. The reversal potential varied with external K^+, but not with Cl^- or Na^+. The waves observed in Ca-free solution containing tetrodotoxin (TTX) apparently gave rise to bursts during the onset of spike blockage. The post-wave hyperpolarization also showed a reversal potential. The waves in Ca-free + TTX medium were blocked by ouabain but could be reinstated by artificial inward current. The post-burst hyperpolarization and the post-wave hyperpolarization appeared to result from a cyclic increase in membrane conductance, primarily to potassium ions.

50.9 INTERACTION BETWEEN SYNAPTIC EVENTS IN A DENDRITIC CABLE. Richard Norman. Biological Sciences Group, Univ. of Connecticut, Storrs, Conn. 06268

When a dendritic cable is excited by more than one synaptic input, simple cable theory is inadequate to predict the resulting post-synaptic potential (psp) spread since each synapse acts as a time-varying impedance load on the cable. If two synapses are stimulated sequentially, the combined psp differs from the sum of the two individual psp's by an interaction term, which represents the influence of the conductance change at the second synapse on the spatial distribution of potential remaining from the first. This interaction can be measured experimentally as well as predicted theoretically. The experimental preparation consists of a vertebrate striated muscle fiber as a model cable, with the neuromuscular junction, partially blocked by curare, as one synapse. The second synapse is modeled with a voltage clamp using current-passing and potential-measuring microelectrodes placed the desired distance from the natural synapse. The time-varying synaptic conductance is produced by varying the loop gain of the voltage clamp apparatus. The synaptic reversal potential is determined by the clamp command potential. Cable theory computations are made by piecewise time-invariant approximations of the synaptic conductance changes. The spatial distribution of potential at the end of one epoch is used as initial conditions for the next. Results indicate how synaptic interaction can serve as an integrative mechanism. Inhibitory synapses located close to excitatory sources or distributed over a dendrite can cause permanent erasure of excitation, while inhibition near a spike generating locus only temporarily blocks the effect of distal excitation. The effective space constant for interaction is approximately one-half that for potential spread, as computed for frequencies corresponding to the time course of the conductance events.

Supported by the University of Connecticut Research Foundation.

50.10 SELECTIVE PERMANENT BLOCKADE OF EXCITATORY AND INHIBITORY POSTSYNAPTIC RECEPTORS BY p-NITROTHIOPHENOL AND PYRIDOXAL PHOSPHATE. Makoto Sato and Juro Maruhashi*, Neuroscience Lab., Division of Neurosurgery, University of Oregon Medical School, Portland, Oregon.

There are two types of cholinergic receptors in the Aplysia ganglion cells; one is excitatory or D-type and the other is inhibitory or H-type. Activation of D- receptors by acetylcholine (ACh) produces an increase in permeability of the receptor membrane toward Na^+ whereas that of H- receptors induces a permeability increase toward Cl^-. Using two microelectrodes inserted within a single cell, ACh-induced increase in membrane conductance (ΔG) was measured from both membranes. One mM solution of p-nitrothiophenol or pyridoxal phosphate was directly applied to each membrane by a constant perfusion. Neither the resting potential nor conductance was altered by these chemicals. p-Nitrothiophenol: A five min exposure to this solution irreversibly depressed ΔG of D- membrane to 60-70% of the control and an additional ten min exposure further decreased it to 30-40% of the control. On the other hand, one hour exposure to this solution did not alter the ΔG of the H- membranes. Pyridoxal phosphate: Five to ten min exposure to this solution irreversibly depressed the ΔG of the H- membrane to 50-70% of the control and additional 10-20 min exposure further decreased it to 20-30% of the control. In contrast, one hour exposure to the same solution did not alter the ΔG of D-type membranes.

Log [ACh] - ΔG curves showed a gradual decrease of the slope as the exposure time increased, suggesting that the blockade of either receptor by these chemicals was of a non-competitive nature. It was postulated that the Na^+-transfer across the D-type membrane is carried by either glutamate or asparate residue whereas the Cl^--transfer across the H-type membrane is mediated by lysine residue of the receptor protein. (Supported by USPHS Grant NSO-1687-14 and -15)

50.11 2,4 DINITROPHENOL: EFFECT ON MEMBRANE PERMEABILITY OF MOLLUSCAN NEURONS. H. Levitan and J. L. Barker, Dept. Zool., Univ. Md., College Park, Md., 20742 and NIH, Bethesda, Md. 20014.

We have applied 2,4 dinitrophenol (2,4 DNP) and several other phenol analogs to identified neurons in the isolated ganglion of the marine mollusc Navanax, while monitoring the membrane potential and conductance with double-barreled, intracellular microelectrodes. 2,4 DNP (0.3-10 mM) rapidly and reversibly increased the membrane potential and input conductance in a dose-dependent manner. These changes were associated with an increase in the potassium and decrease in the chloride conductance of the membrane. The phenols also altered the relative alkali-cation permeability of the membrane in a dose-dependent manner. The relative ability of the phenols to produce an increase in membrane potential was highly correlated with their octanol/water partition coefficient and dissociation constant, increasing with the hydrophobicity of the compound and the amount present in the dissociated form. The results suggest that 2,4 DNP acts in this system by adsorbing to the neuronal membrane thereby increasing its anionic field strength. The action is thus comparable to that previously described for salicylate derivatives (Science 1972, 176: 1423; 178: 63), suggesting that these uncouplers of oxidative phosphorylation probably have a direct effect on membrane permeability. Since the relative ability of these and other substances to uncouple mitochondrial oxidative phosphorylation is also highly correlated with hydrophobicity and pKa, the results support the hypothesis that a change in cation permeability of mitochondrial membranes underlies the uncoupling process (Mitchell, Nature 1961, 191: 144).

50.12 DIPHENYLHYDANTOIN AND CALCIUM MOVEMENT. J.H. Pincus, S.H. Lee* and Moshe Hasbani*. Dept. of Neurology, Yale Univ. School of Medicine., New Haven, Conn. 06510

Diphenylhydantoin (DPH) and calcium (Ca) have been shown to act antagonistically with respect to stimulus coupled norepinephrine (NEH^3) release from rat brain slices. DPH also reduces Ca^{45} uptake into brain tissue. Procaine has a similar effect on NEH^3 release and Ca^{45} uptake. HPPH, phenobarbital and tetrodotoxin (TTx) have no effect on either. DPH reduces Ca^{45} flow into and out of resting lobster axons and prevents the increase in Ca^{45} uptake which occurs in stimulated axons. Procaine has similar effects on resting and stimulated nerves. HPPH and TTx are without effect on Ca^{45} movement in lobster axons. These results are compatible with the hypothesis that DPH acts like a local anesthetic and primarily limits membrane permeability to Ca.

53.1 HISTOFLUORESCENCE STUDY OF CHROMAFFIN CELLS IN DISSOCIATED CELL CULTURES OF CHICK EMBRYO SYMPATHETIC GANGLIA. David M. Jacobowitz and Lloyd A. Greene*. Lab. of Clinical Science, NIMH and Lab. of Biochemical Genetics, Natl. Heart & Lung Inst., NIH, Bethesda, Maryland 20014.

Chromaffin cells of dissociated chick embryo sympathetic ganglia were studied by catecholamine fluorescence microscopy in long-term cell cultures. These cells were distinguishable in culture from the sympathetic ganglionic neurons by their small size, relative infrequency of occurrence, intense fluorescence and survival in the absence of nerve growth factor. By several weeks in culture, with or without nerve growth factor in the medium, the chromaffin cells produced extensive ramifications of fluorescent varicose processes. Chemical assay of these cells show that the amine present is norepinephrine/epinephrine rather than dopamine. It is suggested that at least part of the intraganglionic system of adrenergic varicose terminals arises from chromaffin cells. This capability with regard to fiber production lends credence to the suggestion that chromaffin cells may play an active role in ganglionic function.

53.2 FLUORESCENCE AND ELECTRON MICROSCOPIC STUDIES OF DEVELOPING SYMPATHETIC NEUROBLASTS IN THE FETAL RABBIT. Virginia M. Tennyson, Dept. Pathology, Division of Neuropathology and Neurology, Columbia University, College of Physicians and Surgeons, New York, New York, 10032.

Isolated intensely fluorescent yellow-green sympathetic neuroblasts with short processes are present dorsolateral to the aorta in the 11 to 13 day fetus. They form a continuous chain by day 14, and a segmented chain by day 18. Sympathetic neuroblasts begin to migrate through the adrenal cortex by day 15, and they form the adrenal medulla by day 18. Two kinds of sympathetic neuroblasts can be recognized by electron microscopy. One type, which has few dense core granules in its cytoplasm, appears to be the precursor of the principal cell of the sympathetic ganglion. A second type has moderately large dense core granules (600-1200 Å in diameter), which are characteristically aligned along the cell surface. There is frequent evidence suggesting exocytosis. Exocytosis of catecholamines from these fetal cells may be part of a mechanism which can direct their migration. The granule-containing cells are probably the precursors of the adrenal medullary cells and of other chromaffin tissue. With further maturation, the granules in the cells which enter the adrenal medulla increase in size and their content becomes heterogeneous. Some granule-containing cells may remain in the ganglion and give rise to interneurons.

Supported by NS-05184 and the Muscular Dystrophy Associations of America.

53.3 EXCESSIVE GLIAL CELL PROLIFERATION IN SYMPATHETIC RAT GANGLIA BY COMBINED NERVE GROWTH FACTOR (NGF) AND 6-HYDROXYDOPAMINE (6-OHDA) TREATMENT. Rita Levi-Montalcini. Lab. Biol. Cell. CNR, Rome, Italy and Dept. Biol., Washington Univ., St. Louis, Mo. 63130.

Subcutaneous daily injections of NGF in newborn rats call forth increase in size and number of adrenergic neurons in sympathetic ganglia. At the end of a 10-day period, the ganglia are 4-5 times larger than ganglia of control littermates. Daily injections of the ganglion-blocking agent, 6-OHDA, in newborn rats result instead in massive death of sympathetic neurons. The lethal action of this drug is due to destruction of the endoplasmic reticulum in the cell perikarya of immature neurons. At the end of a 10-day period, the ganglia are severely reduced in size and the sympathetic nerve cell population is about 20% of that of controls. The residual nerve cells are highly atrophic and undergo death in subsequent days. Thus the entire sympathetic nerve cell population is destroyed (chemical sympathectomy). Combined NGF and 6-OHDA treatment in newborn rats results in a striking size increase of the same ganglia which reach a volume about twice that of NGF-treated ganglia. Histological and E.M. studies performed on ganglia of animals treated with NGF and 6-OHDA show that the nerve cells are hypertrophic and manifest no impairment of the endoplasmic reticulum. A massive increase in glial cells is apparent both in the postganglionic nerve fibers and in the ganglia. More extensive treatment up to 19 days brings about an additional volume increase in the ganglia, which at the end of this period are about 3 times larger than ganglia treated only with the NGF. The working hypothesis that the dramatic glial cell increase might result from enhanced metabolic processes in the neuron perikarya by NGF and simultaneous 6-OHDA blocking action at the nerve end terminals is now being tested.

53.4 NON-NEURONAL AND NERVE GROWTH FACTOR INFLUENCES ON MOUSE GANGLIONIC NEURONS IN DISSOCIATED CULTURES. Silvio Varon, Patricia Burnham* and Charles Raiborn*. Dept. Biol., Sch. Med., UCSD, La Jolla, 92037

In cultures of dissociated newborn mouse dorsal root ganglia, neurons exhibit a Nerve Growth Factor (NGF) dependence not shown by testing intact ganglia; this NGF sensitivity disappears if the number of non-neurons is increased. Purified neuronal fractions can be made to exhibit similar time patterns for attachment and survival by: a) varying non-neuronal numbers without NGF, b) reducing non-neurons with high NGF, c) varying NGF with low non-neurons. Out of several types of non-neurons tested, only dorsal root ganglionic cells (mouse, and much less so rat and chick) supported the mouse neruons in the absence of NGF, and for each species the ganglionic non-neurons were most effective on their own homologous neuronal partners. With NGF all cells tested permitted the survival of mouse neurons but, where examined, required 1000x higher NGF levels. The model proposed by the dissociated cultures may be extrapolated to intact ganglia as follows: Neurons express their potential behavior to a degree that depends on their interaction with the partner non-neurons. When these are inadequate, NGF has room for substitute action. Non-neuronal inadequacy might be developmental, or imposed by artificial in vitro manipulations, or--possibly--the primary pathological condition underlying certain neuronal deficits.

53.5 SLOW SYNAPTIC INHIBITION AND ADRENERGIC ANTAGONISM IN SYMPATHETIC GANGLION. Forrest F. Weight. Lab. of Neuropharmacology, NIMH, St. Elizabeths Hosp., Washington, D.C. 20032.

The sympathetic ganglion of frog is particularly well suited for investigating slow synaptic potentials because the slow EPSP and the slow IPSP are generated in different cell types by separate inputs. The slow IPSP is generated in type C cells by stimulation of the VIIIth nerve, and has unique electrophysiological properties (Weight and Padjen, Brain Res., 55, 219, 1973). We previously reported that the iontophoretic administration of acetylcholine (ACh) hyperpolarizes C cells, and the electrophysiological properties of the ACh hyperpolarization mimic the properties of the slow IPSP, suggesting that the slow IPSP may be mediated by ACh (Weight and Padjen, Brain Res., 55, 225, 1973). On the other hand, Libet and coworkers (J. Neurophysiol., 31, 396, 1968) have proposed that the slow IPSP is mediated by an adrenergic mechanism. The question of the transmitter involved in slow synaptic inhibition was therefore tested further by using catecholamine antagonists. The Xth lumbar sympathetic ganglion of the bullfrog (Rana catesbeiana) was recorded by the sucrose gap method and drugs were added to the flowing oxygenated Ringer test solution containing nicotine ($3x10^{-5}M$) or d-tubocurarine ($7x10^{-4}M$). The alpha-adrenergic blocking agent, dihydroergotamine (DHE, $10^{-5}M$) effectively antagonized the hyperpolarization produced by $10^{-4}M$ epinephrine, norepinephrine and dopamine. During the DHE antagonism, the slow IPSP and the initial hyperpolarization produced by ACh ($10^{-4}M$) were not reduced in amplitude. On the other hand, atropine ($2x10^{-6}M$) antagonized both the slow IPSP and the ACh hyperpolarization. These data are consistent with the hypothesis that the slow IPSP is not mediated by an adrenergic mechanism, but by ACh in the frog sympathetic ganglion.

53.6 BLOCKADE BY POLYVALENT CATIONS OF TRANSMISSION THROUGH SYMPATHETIC GANGLIA OF BULLFROGS. G. P. Cooper, M. Houser*, and M. Lowenhaupt*. Depts. Environ. Health and Physiol., Coll. Med., Univ. Cincinnati, Cincinnati, Oh 45219.

The 9th or 10th sympathetic ganglion of the bullfrog (Rana catesbeiana), with associated preganglionic trunk and postganglionic nerve was mounted in a multi-compartment chamber. The ganglion was perfused with frog Ringer or Ringer modified by the addition of 0.001 to 0.1 mM chloride salts of Pb^{+2}, Hg^{+2}, Cd^{+2}, Zn^{+2}, La^{+3}, Ba^{+2}, Sr^{+2} and Mg^{+2}. All solutions were maintained at a pH of 6.9 and room temperature. The preganglionic trunk was stimulated once per second with single supramaximal pulses. Ag:AgCl:agar-Ringer electrodes were used for recording between the ganglionic Ringer pool and a postganglionic Ringer pool across an interposed sucrose gap. Responses were recorded first with the ganglion bathed in control Ringer, then after a 30-min exposure to one of the polyvalent cations, then again after a recovery period in control Ringer. The ganglionic response was depressed, in order of increasing potency, by Hg^{+2}, La^{+3}, Pb^{+2}, and Cd^{+2}. The magnitude of the depression was related approximately to the logarithm of the polyvalent cation concentration. Ba^{+2}, Sr^{+2}, Zn^{+2}, and Mg^{+2} had no detectable effects at the concentrations used. The effects of Cd^{+2}, Pb^{+2}, and La^{+3}, but not Hg^{+2}, were reversible by increasing the Ca^{+2} concentration. (Supported by USPHS grant ES 00159.)

54.1 CONVERGENCE OF ELECTRORECEPTOR, COMMON CUTANEOUS AND OPTIC INPUT TO THE TECTUM AND ELSEWHERE IN THE BRAIN OF TORPEDO AND OTHER ELASMOBRANCHS. T.H. Bullock, C.J. Platt*, G. Czéh*, H. Kovačević*, Dj. Konjević* and M. Gojković*. International Brain Research Laboratory, Kotor, Yugoslavia.

Contrary to expectation from Voronin et al. (Prog. Brain Res. 22:545, 1968) we find convergence of sensory inputs in the brains of lower vertebrates, by recording evoked potentials. Adequate stimulation of eye and electroreceptors has been used as well as direct shocks to optic, maxillary (chiefly electroreceptive, from ampullary organs) and supraorbital, supraoptic or spinal nerves (chiefly mechanoreceptive) in elasmobranchs. Each modality displays distinct forms of e.p. with a different dependence on recording locus and depth and a different sequence of recovery, facilitation and depression on stimulus repetition. Prominent, complex, long-lasting e.p.'s occur to each modality in contralateral tectum, but also ipsilaterally. Electro- and mechanoreceptor responses are prominent in anterolateral medulla bilaterally. All modalities tested evoke activity in cerebellum, telencephalon and structures deep to the tectum.

54.2 SOMATOSENSORY AFFERENTS TO THE EXTERNAL NUCLEUS OF THE INFERIOR COLLICULUS. D. M. Schroeder and J. A. Jane. Dept. Neurosurg., Univ. of Va. School of Med., Charlottesville,Va. 22901

The external nucleus of the inferior colliculus, often called the intercollicular nucleus, is situated lateral and rostral to the central nucleus. Whereas the central nucleus is solely involved with audition, the external nucleus appears to be involved also with somatosensory systems. The somatosensory pathways were studied anatomically in the hedgehog, tree shrew, slow loris (prosimian primate), marmoset and African green monkey. With silver impregnation techniques for staining degenerating axons, the spinotectal and medial lemniscal fibers were traced after hemisection of the cord and unilateral lesions in the dorsal column nuclei.

The spinotectal fibers and medial lemniscus project to the contralateral external nucleus and minimally to the ipsilateral side. This was the only area within the nervous system that received bilateral projections from the dorsal column nuclei. When the number of fibers that project to the thalamus were compared with those that project to the tectum, the number of thalamic afferents increased progressively, whereas the tectal afferents were more consistant among species.

These results, along with similar data available for a wide variety of other vertebrates, suggest that the external nucleus of the inferior colliculus is structurally similar in mammalian and some non-mammalian vertebrates. Functionally, this nucleus may represent a brainstem integration area for auditory and somatosensory systems. (Supported by: NIH 5 RO1 EY00154 and James Baur Research Fund).

54.3 SPLANCHNIC EVOKED POTENTIALS IN THE DORSAL MESENCEPHALON OF THE PENTOBARBITAL-ANESTHETIZED RAT. S. T. Huprich* and J. C. Liebeskind. Dept. Psychol., UCLA, Los Angeles, Ca., 90024.

Within a broader study of the functional organization of the dorsal mesencephalon (DM), the characteristics of input to this region from the greater splanchnic nerve, a major source of sympathetic visceral afferents, were examined, and compared with somatic input characteristics. A short latency (4-5 msec) complex waveform was evoked by splanchnic stimulation, with components similar in form to, but differing in latency and amplitude from those evoked by tail stimulation. In the dorsoventral dimension of the DM, a characteristic biphasic distribution of potential amplitude was observed for a prominent early component, C1, such that a negative maximum was recorded at the dorsal border of the central gray, with a positive maximum recorded within ventral central gray. The amplitude maxima of potentials evoked by tail stimulation for C1 always lay about .3 mm dorsal to the splanchnic maxima. Evidence indicated that for input from both sources the region of the negative response was the site of synaptic termination. Thus a feature of the dorsoventral organization of the DM was revealed: the region of synaptic termination for somatic input lies above the region of synaptic termination for visceral input, both above the sulcus limitans in the alar plate. This organization is consistent with that seen in the medulla and cord. In the rostrocaudal dimension of the DM the splanchnic representation was found to be integrated within the somatotopic organization seen there by our group (Brain Res. 27: 133, 1971): the C1 amplitude maximum occurred in the area of maximum trunk response. A similar organization is seen in cortical somatosensory areas. From these considerations it can be concluded: 1) there exists an important sympathetic visceral input to the DM, and 2) this visceral input is incorporated into a specific organization of the DM, consistent with organizational features observed at other levels of the neuraxis.(Supported by USPHS Grant NS07628)

54.4 CONTROL OF SENSORY TRANSMISSION IN SPINOTHALAMIC TRACT NEURONS. W.D. Willis, Jr., J.D. Coulter and R.A. Maunz*. Marine Biomedical Institute, University of Texas Medical Branch, Galveston, Texas 77550.

Cells of the spinothalamic tract in the lumbosacral spinal cord were identified by antidromic activation of their axons in the contralateral caudal diencephalon of anesthetized macaque monkeys (chloralose and pentobarbital). Natural mechanical and thermal stimuli were used to determine the location of the peripheral receptive fields on the ipsilateral hindlimb and to classify the responses of spinothalamic tract cells. Individual cells could be excited by deflection of single hairs, varying degrees of mechanical deformation of the skin or by noxious mechanical and thermal stimuli. Spontaneous and evoked discharges of spinothalamic tract cells could be depressed by natural stimulation of the hair and/or skin adjacent to the excitatory receptive field on the ipsilateral limb. Other cells showed a similar effect when the contralateral hindlimb was stimulated in the area corresponding to the excitatory field on the opposite hindlimb. Electrical stimulation in the hindlimb area of the contralateral sensorimotor cortex also depressed the activity of spinothalamic tract cells evoked by natural stimulation in the peripheral receptive field. The time course of this depression began as early as 20 msec following onset of the cortical stimulation, reached a maximum by 40-50 msec and persisted up to 200 msec. Stimulation of the ipsilateral dorsal columns was also effective in modifying evoked discharges of spinothalamic tract neurons. Spinothalamic tract cells responding to different types of sensory stimuli may be differentially sensitive to the effects of stimulating the cortex, dorsal columns or periphery. These findings are relevant to the role of the spinothalamic tract in mediating touch, pain and temperature sensibilities to higher centers. (Supported by USPHS grant NS 09743, Training Grant NS05743 and a grant from the Moody Foundation of Galveston.)

54.5 EFFECTS OF DORSAL COLUMN STIMULATION ON SOMATOSENSORY RESPONSES OF CELLS IN THE THALAMIC POSTERIOR GROUP OF NUCLEI. Willie K. Dong* and Irving H. Wagman. Dept. Animal Physiology, Univ. of Calif., Davis, Calif., 95616

Cells of the posterior group (PO) were extracellularly recorded in cats lightly anesthetized with sodium thiopental. Three groups of cells were studied. The receptive fields of all cells were variable in size but were often large, bilateral and discontinuous. 1) The most commonly found cells responded only to a brisk skin tap and also to electric stimulation of skin receptive fields and of contralateral dorsal column (DC) at the cervical level. The response consisted of 2-3 spikes with a latency ranging from 5-15 msec depending on locus stimulated. This brief excitatory response was followed by an inhibitory period of 80-100 msec duration. 2) The second group of cells responded only to noxious stimulation (e.g. pinching) Their receptive fields were generally smaller than those responding to tapping alone. 3) Cells comprising the third group, smaller in number than those of the other groups, responded to both tapping of the skin and strong pinch applied across skin and bone. Those PO cells of groups 2 and 3 when excited by noxious stimuli responded to single shock of contralateral DC or dorsal column nuclei (DCN) by a brief excitation of 2-3 spikes with a latency of 5-10 msec followed by a period of inhibition lasting from 50 msec to 1 sec. Spontaneous activity could also be inhibited for similar lengths of time. The reduction of PO activity was more marked when DC or DCN was stimulated at frequencies of 10-50/sec. This reduction outlasted such stimulation for 10-15 sec even during the application of noxious stimuli. These findings may be significant with respect to dorsal column stimulation for relief of pain. The inhibition of PO cell response to noxious stimulation may be mediated through ascending pathways from the dorsal horn as well as by a more direct lemniscal path to thalamic PO. (Supported in part by USPHS Grant No. NS07844.)

54.6 BLOCKAGE OF PAIN RESPONSES IN THALAMIC NEURONS BY MECHANICAL STIMULATION OF THE VAGINA IN RATS. B.R. Komisaruk and J. Wallman.* Institute of Animal Behavior, Rutgers University, Newark, New Jersey 07102

Mechanical stimulation of the vaginal cervix markedly attenuated or completely blocked the increase in firing rate of lateral thalamic neurons in response to pinching the skin. (Firm pressure was exerted against the vaginal cervix with a 1 cc syringe plunger for 30 sec; an alligator clip was used to pinch the skin; urethane-anesthetized, ovariectomized,estrogen treated rats were used. This is apparently a selective blockage of neuronal responsiveness to noxious stimulation, since in neurons which responded to both pinching the skin and gently stroking the fur, probing the vaginal cervix had no effect on the response to stroking the fur, while it attenuated the response to pinching. The responsiveness recovered within a few minutes after cessation of probing the vaginal cervix. Responses to scratching the cornea or stretching the stomach were also blocked by probing the vaginal cervix. This blockage can not be attributed to the induction of sleeplike activity resulting from probing the vaginal cervix (Ramirez, Komisaruk, Whitmoyer, and Sawyer, Am. J. Physiol., 212:1367, 1967), for even during EEG arousal induced by hypoxia, probing the vaginal cervix blocked the effect of noxious stimulation. Furthermore, the blockage was not due to "distraction," for pinch applied to a body region from which a neuronal response was not elicited, did not mimic the suppressive effect of probing the vaginal cervix. In parallel behavioral observations, vocalization in response to tail pinch was blocked by probing the vaginal cervix, but the rats were still capable of vocalizing in response to being lifted gently during the probing. These studies indicate that mechanical stimulation of the vaginal cervix has analgesic properties. Supported by NIMH grant MH13279 and Research Scientist Development Award 5K02-14711(BRK) and NINDS postdoctoral fellowship 1F10-NS02565(JW). The excellent assistance of J. Hassenbey and E. Azevedo is gratefully acknowledged.

54.7 PERSISTENCE OF PAIN AFTER SPINOTHALAMIC TRACTOTOMY AND ITS RELIEF BY DORSAL CORD STIMULATION. Howard L.Fields,M.D.,PhD., Depts. of Neurol. and Physiol., Univ.Calif., San Francisco 94122

Three patients with pain in lower back and leg were examined. In 2 patients pain had been temporarily relieved by laminectomy and discectomy but had recurred at least two years prior to spinothalamic tractotomy. Adequacy of tractotomy was confirmed by hypalgesia and thermal hypesthesia which included the painful area. Hypalgesia was complete for pinprick and pinch of skin but very firm deep pressure over bone and tendon elicited pain, though much reduced compared to the homologous, normally innervated areas. Regions which had been tender to touch prior to tractotomy remained tender in 2 patients. In these 2 patients light brushing of hairs in the hypalgesic region gave a distinctly unpleasant electric or rubbing feeling which was accurately localized.

Bipolar stimulating electrodes were placed above the dorsal columns in the subdural space. 0.5msec pulses were delivered at frequencies ranging from 15 to 150 Hz. Intensity was adjusted to give tingling or vibratory sensations symmetrically projected to levels below the implanted electrodes. With the stimulator properly adjusted, spontaneous pain was almost completely abolished, tender areas were much less tender and dysesthesiae were no longer produced by light stimuli. In the area of surgical hypalgesia much more intense stimuli were required to elicit pain during cord stimulation. In contrast, in the homologous normally innervated regions to which the tingling induced by cord stimulation was equally projected, there was no definite change in the quality or intensity of pinprick or pinch-induced sensation.

These results indicate that 'dorsal-column' stimulation may produce analgesia by mechanisms other than inhibition of spinothalamic tract neurons in their segment of origin.

54.8 SYNAPTIC ORGANIZATION OF SPINOTHALAMIC PROJECTIONS TO THE SQUIRREL MONKEY THALAMUS. Donna J. Forbes. Dept. Anat., Univ. Wis. Med. Sch., Madison, WI. 53706 and Dept. Biomedical Anat., Univ. Minn.-Duluth Med. Sch., Duluth, MI. 55812

Following unilateral section of the anterolateral spinal cord light and electron microscopic methods have been used to study the resultant thalamic degeneration. Survival times ranged from 3 to 12 days. With the Nauta method degeneration was found primarily ipsilateral to the lesion. It was distributed laterally throughout the ventral postero-lateral nucleus (VPL) and extended into the area of the posterior nuclear group (PO). A more medial projection appears to pass through n. parafascicularis (Pf) on its way to the n. centralis lateralis (CL). Smaller amounts of degeneration were seen in the contralateral VPL. With the electron microscope a variety of degenerative changes in the synaptic population of VPL were evident. These included swelling of vesicles, decrease in vesicle number, neurofilamentous hyperplasia, increase in electron density, and glial engulfment. Individual terminals appeared to exhibit various combinations of the alterations. There was no obvious time sequence since all of the changes were sometimes seen in the same animal. In most cases it appeared that the degenerating knobs were of the large type with round vesicles (RL) which I have previously shown to degenerate with lesions of the dorsal column nuclei. In other cases they were much smaller and probably were the small knobs with round vesicles (RS) seen in the normal population.

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54.9 SOMATOTOPIC ORGANIZATION AND SUBMODALITY DISTRIBUTION IN THE VENTROPOSTERIOR NUCLEUS OF THE THALAMUS OF THE MACAQUE. P. R. Loe, B. L. Whitsel, D. A. Dreyer, and C. B. Metz*. Dept. Physiol., Sch. Med., and Dental Res. Center, Univ. of N. C., Chapel Hill, N. C. 27514.

The ascending somatosensory afferent pathways undergo sorting processes which are independent: afferents are segregated according to submodality and, in addition, on the basis of receptive field location. As a consequence of these processes, mechanoreceptive information is represented at the level of the primary somatic sensory cortex (S-I) within the framework of a two-dimensional coordinate system in which one coordinate specifies location on the body and the other specifies submodality. We were interested in establishing the extent to which these same organizational principles determine the somatotopic organization and submodality distribution in those thalamic nuclei which project to S-I. Stereotaxic microelectrode penetrations of the thalamus were performed in unanesthetized macaques, and the receptive fields and submodality characteristics of neurons responsive to natural tactile stimuli were determined. The placements of all penetrations were verified histologically; electrolytic microlesions enabled us to determine precisely the locations of individual recording sites. With regard to the distribution of submodalities, our observations are in agreement with those of previous studies which reported that the deep submodalities are represented anteriorly and dorsally, whereas the cutaneous submodalities are represented posteriorly and ventrally. With respect to somatotopic organization, however, our observations tend to conflict with the widely held view that proximal body regions are represented dorsally and distal body regions are represented ventrally, and support the hypothesis that information about the submodality and place of occurrence of an impinging mechanical stimulus is arrayed independently in the somatosensory thalamus.

54.10 THE INTRINSIC CIRCUITRY OF THE VENTROBASAL THALAMUS OF THE CAT. Henry J. Ralston, III. Dept. Anat., University of California, San Francisco, 94122.

Details of thalamic circuitry have been explored by neuroanatomical methods and the results compared with electrophysiological studies upon the thalamus. The synaptic populations and the lemniscal afferent projections to the thalamus have been described previously. This present study identifies thalamocortical relay cells (TCR) by causing them to degenerate following lesions of the somatosensory cortex, or by labeling them with horseradish peroxidase transported to relay cells by retrograde axonal flow following microinjection of the peroxidase into sensory cortex. The results of these studies indicate that there is direct lemniscal input to TCR cells as well as to interneurons in VB. There are also direct lemniscal inputs to presynaptic dendrites, which then contact other thalamic neurons. It is likely that this circuitry subserves both lemniscal activation of TCR cells and feedforward excitatory or inhibitory mechanisms mediated by interneurons. (Supported by NS-09167 from USPHS).

54.11 ELECTROENCEPHALOGRAPHIC CORRELATES OF MUSCLE SPINDLE AFFERENTS. Micha Hohenberger*, Richard Herman and Michael Negin*. Dept. Rehab. Med., Temple Univ. Hlth. Scs. Ctr., Philadelphia, 19140.

The existence of direct projection of muscle spindle afferents to the somatosensory area of the cerebral cortex in man is the subject of investigation in this research. The method of investigation is based on the clonus phenomenon, often observed in patients with spasticity and increased stretch reflexes. Advantages of this approach lie in the periodic character of the clonus mechanism, and that it represents a single-modality afferent input to the central nervous system. The experiment is performed in an electrically and acoustically shielded room, where the subject is comfortably seated, and his affected foot placed in a Motor Joint Apparatus, with a built-in strain gage for measurement of torque about the ankle joint. Clonus of the extensor muscle is elicited, and recordings are taken from 3 surface EEG electrodes (above somatosensory area), 1 EMG channel (medial gastrocnemius muscle) and 1 torque channel. The data, recorded on analog tape, is then processed, using a PDP-12 digital computer. The data analysis method is based on the periodic character of the recorded signals. In an attempt to increase the signal-to-noise ratio in the averaged EEG, only those periods, which have inherently small background EEG perturbations are chosen for averaging. The results of the experiments suggest the existence of a clonus-related response in the EEG (latency of about 120 ms. from the peak of torque), which reflects the projection of the muscle-spindle afferents discharge in the somatosensory area of the cerebral cortex.

54.12 RESPONSES OF POSTCENTRAL CELLS DURING ACTIVE AND PASSIVE JOINT MOVEMENTS. M. Soso* and E.E. Fetz. Reg. Primat Res. Ctr and Depts. of Physiol. & Biophys., Psych. and Neurol. Surg., Univ. Wash., Seattle, Wash. 98195

In order to compare the responses of postcentral "sensory" cortex cells during active and passive movements, rhesus monkeys were trained (1) to actively flex and extend the elbow with the forearm held in a hinged cast, and (2) to passively allow similar movements to be imposed. Both active and passive movements consisted of a rapid change in joint angle followed by at least one second of maintained position. EMG activity of biceps and triceps was recorded during all movements. 234 cells in areas 3, 1, 2 and 5 (histologically confirmed) were classified as responding to stimulation of either skin, joint(s) or muscle. Activity of 48 cells was averaged over 70 cycles of active and passive movements; activity of an additional 10 was averaged for 70 cycles of active movements.

Cell responses were larger during phasic movement than tonically maintained position, and were often in the same direction for both active and passive movements. Only cells responding to stimulation of upper arm muscles (5 of 5) or the elbow joint (9 of 14) showed tonic activity related to elbow position during the active or passive conditions. The data are consistent with these cells mediating proprioception during both active and passive conditions.

For 1/3 of the active movements, the onset of unit activity preceded EMG activity by at least 100 msec. Occurrence of such early activity was independent of modality and receptive field location. Except for this early onset, our results are consistent with peripheral receptors supplying most of the input to postcentral cells during both active and passive movements.

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54.13 CHARACTERISTICS OF THE HEAD AND FACE REPRESENTATION IN THE POSTCENTRAL GYRUS OF MACAQUES. D.A. Dreyer, B.L. Whitsel, P.R. Loe, R.A. Elliott* and H.H. Smith*. Dept. Physiol., Sch. Med., and Dental Research Center, U. of N.C., Chapel Hill, N.C. 27514

The technique of single unit analysis was employed to determine the submodality composition and connectivity of the several representations of the extraoral tissues of the head and face which are found within widely separated regions of the postcentral gyrus (somatosensory area I). Experiments were performed in the absence of general anesthesia in 15 macaques (Macaca mulatta) under neuromuscular blockade with gallamine. Comparison of these data with others obtained during microelectrode penetrations of the areas which represent the forelimb, trunk, and the hindlimb reveal attributes common to all regions of the S-I map. Specifically, (1) in the face representation as well as in all the other topographic subdivisions of S-I a single body region is represented several times in widely separated regions; (2) the differential distribution of the submodalities in the face representation is similar to that found in all other topographic subdivisions of S-I; and (3) in the face representation as well as the other subdivisions of S-I only certain of the local neighborhood relations in the periphery are preserved. These results are interpreted as evidence that the map of the extraoral tissues of the head and face in S-I is generated by a mapping process which sorts afferents according to submodality and place.

54.14 "ON" AND "OFF" COMPONENTS IN THE SOMATOSENSORY EVOKED RESPONSE. Moshe Feinsod* Paul Bach-y-Rita and Edda Simoes* Smith-Kettlewell Institute of Visual Sciences, 2232 Webster Street, San Francisco, California 94115

The somatosensory evoked responses (SER) to vibro-tactile stimuli of low intensity was studied in 30 subjects.

The SER to stimuli of 1000 msec duration displays ON and OFF components. The latter consists of a surface negative deflection of about 120 msec peak latency, followed by a slower positive wave. The amplitude of the OFF response is more sensitive to changes in stimulus intensity than that of the ON response.

As in the averaged visual evoked response, an after activity of a frequency of 8-10 cycle/sec sometimes follows the ON component. This alpha-like activity may either mask the OFF component, be initiated by the termination of the stimulus or its rhythm can be interrupted by the stimulus end.

The similarity between the averaged evoked responses to visual and vibro-tactile stimuli may suggest that any modality of sensory information is processed by the brain according to a common pattern.

55.1 HUMAN SOMATOSENSORY BRAIN SIGNALS: SOME CRITERIA FOR CLINICAL USE. Hilton Stowell. Dept. Neurosurg., U. of Miss., Jackson, Miss. 39216

Stimulus-time-locked EEG summed during repetitive electrical and mechanical stimulation of the skin yields quantifiable data on the primary waveform (SER) derived from intact scalp and originating in representation areas of sensorimotor cortex. The SER to indentation of contralateral digits consists of a biphasic positive-negative (P_1 to N_H) having a mean half-period of 12 ms ($\pm$ 2) and a P_1 latency of 25-33 ms post-stimulus-onset, across normal adults. Amplitude and latency vary monotonically with stimulus intensity, and the time course is consistent with an origin in postsynaptic somadendritic activity of cortical layers 2-4. The SER is discriminable by latency criteria from (a) earlier components unlikely to represent cortical activity, and (b) later components probably common to other stimulus modalities. Its parameters are similar to those of the SER derived from the contralateral hand region of postcentral gyrus of ape and monkey during nembutal anesthesia. It is always discriminable from the acoustically driven response (AcER) recoverable from the same electrode, which has a first positive of 13-17 ms. Except for a few left-handed or ambidexterous cases, the ipsilateral SER is smaller and later, for digital stimuli. The SER for foot stimulation is later (predictable from pathway length and observed conduction velocities of primary mechanoreceptors), but lip and facial stimuli evoke a P_1 to N_H later than predicted. Local infiltration of Lidocaine around digital nerves reduces P_1 to N_H amplitude (without latency increase) by 15-72%, with extent and time course of attenuation very variable across subjects. At maximum attenuation, subjects report stimulus detection only at the wrist. These data may assist formulation of criteria for assessing central sensorimotor malfunctions without surgery.

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55.2 PRECISION IN LATENCY DETERMINATION OF EVOKED POTENTIAL. Bernard Saltzberg and Leonard S. Lustick*. Dept. Psych. & Neurol., Sch. Med., Tulane Univ., New Orleans, La. 70112.

One of the parameters of interest in EEG evoked potential studies is the latency of certain events such as peaks in the response. The problem addressed here is the inherent variability in latency determination due to noise. The analysis gives the precision limits, i.e., measurement error under conditions where one wishes to measure the latency to a particular peak in the evoked potential, or to compare the response latency of two realizations of the total evoked potential waveform. The variance in latency determination is shown to be proportional to the ratio of the noise power to the power in the derivative of the evoked potential. The frequency domain expression for the variance suggests the type of filtering that will decrease the variability (i.e., increase precision) in latency determination depending upon the particular portion of the evoked potential of interest in the experimental design. These results are important in experimental designs where one wishes to test the significance of a shift in average evoked potential latency due to an altered experimental state or the significance of the latency differences among subjects.

55.3 MOTOR AND COGNITIVE COMPONENTS OF RESPONSE-RELATED POTENTIALS: FORCEFULLY DISSECTED. Emanuel Donchin and Martin Kutas*. Dept. Psychol., Univ. of Ill., Champaign, Ill. 61820.

Subjects were required to squeeze a handle with either the right or the left hand. Squeeze force was measured, and the force level required of the subject was systematically varied. Electrocortical potentials, preceding and following the squeeze, were recorded over both hemispheres at a variety of scalp locations. We varied the degree to which the response was signalled, (subject responding to stimuli) and unsignalled (subject paces his own responses), and the extent to which the subject was, or was not informed of his response level. In analyzing the data we focus on two questions: The degree to which motor-related potentials show a cross-hemispheric asymmetry and the degree to which the force-level generated by the subject, and his knowledge of the level, determines the amplitude of these potentials. The data indicate that, especially for the slow, pre-response, negative potentials, both cognitive and motor factors determine the course and amplitude of the potentials and their distribution over the scalp. These data bear on the interpretation of the CNV and the motor potentials.

55.4 DIFFERENT SPATIAL DISTRIBUTION OF SCALP RECORDED SLOW POTENTIAL SHIFTS DEPENDENT ON DIFFERING TASK DEMANDS. Gail R. Marsh, Leonard Poon* and Larry W. Thompson*. Dept. Psychiatry and Ctr. for Study of Aging and Human Development, Duke Univ. Medical Ctr., Durham, N. C. 27710

The contingent negative variation (CNV), a slow potential shift occuring between a warning signal and a signal to respond, was recorded from three locations (frontal (F_z), vertex (C_z) and parietal (P_z)) along the midline of the scalp in sixteen normal human subjects. A parietal-dominant CNV was found during active problem-solving behavior. A central-dominant CNV was obtained when the subjects were merely performing a well-learned task. During a disjunctive reaction time task subjects produced an even more pronounced central-dominant CNV. The results were interpreted as supporting a model of cortical function which predicts shifts in cortical involvement as a function of type of information processing.

55.5 CONTEXTUAL MEANING EFFECTS ON SPEECH EVOKED POTENTIALS. Warren S. Brown*, James T. Marsh, and James C. Smith*. Dept. of Psychiatry and Brain Res. Inst., Sch. Med., UCLA, Los Angeles, 90024

Responses to spoken words embedded in speech context were recorded from scalp electrodes proximal to Wernicke's and Broca's areas and over homotopic points on the nondominant hemisphere. The waveform of averaged potentials evoked by the same word differed according to its contextual meaning. Thus, responses to the word "fire" differed when in the phrases "sit by the fire" and "ready, aim, fire". Waveform differences were significantly greater for left hemisphere, than for right hemisphere loci. When context was made ambiguous, as in the phrases "fire is hot" and "fire the gun" waveform differences disappeared. We interpret these results as a neural correlate of both cerebral dominance and the processing of contextual meaning in speech perception. Further experiments (a) compare speech evoked responses in this paradigm with the results of dichotic listening in both right and left handed groups; and (b) explore the role of lateralized EEG desynchrony as an additional, or alternative, source of evoked potential waveform differences.

55.6 CORRELATION OF EEG FREQUENCY WITH TEMPORAL RESOLUTION IN MAN. Stephen Coffin* and Leo Ganz* (Spon: L. Ungerleider). Dept. Psychol. Stanford Univ., Stanford, Calif., 94305.

Spectral analysis of human EEG recorded from the occiput was correlated with subjects' performance on two temporal tasks. Subjects were asked to estimate a five-second duration and to perform a two-flash discrimination with interstimulus interval set just at threshold. EEG data recorded during the estimation period showed higher frequency components when the subjects made shorter duration estimates than when they made longer estimates. Also, trials in which the subjects were able to resolve the flashes into two separate events showed higher EEG frequency components than when the flashes were subjectively fused into one event. Percent power multiplied by frequency at each point and then summed together yielded a numerical estimate of the frequency composition of the EEG. Comparison of this estimate for below-threshold vs. above-threshold trials on the two-flash discrimination and slow vs. fast response in the duration estimation experiment resulted in a significant Wilcoxon signed-rank test ($p<.05$). Primary differences occurred in the alpha frequency range (approximately 10 Hz.). It is suggested that components of the EEG may act as a temporal gating or pacing mechanism which controls information processing.

55.7 AVERAGE EVOKED POTENTIAL/INTELLIGENCE CORRELATIONS: LONG AUDITORY AEP LATENCIES WITH HIGH I.Q. Enoch Callaway, Hilary Naylor* and Sandra Van Beenan.* Langley Porter Neuropsychiatric Institute, San Francisco, CA 94122 and Naval Personnel and Training Research Laboratory, San Diego.

We report on four separate studies which gave evidence of an association between higher IQ's and longer auditory AEP latencies. One study was carried out on a group of 120 children, age 6-16. The other three studies were carried out on groups of Naval recruits comprising respectively 177, 60, and 50 subjects. Small (up to 0.3) but consistent and frequently significant positive correlations were found between IQ and latency to the first (around 70 msec) and second (around 180 msec) major positive waves.

Short visual AEP latencies have been reported to be associated with high IQ's. Others have considered this a reflection of some underlying superior "neural efficiency" in bright, short latency subjects. There are theoretical reasons to doubt such a simple explanation for negative visual AEP latency/IQ correlations, but the existence of the opposite (positive) relationship between auditory AEP latency and IQ provides an empirical basis for rejecting that hypothesis.

Any explanation for the auditory AEP latency/IQ correlations based on differences in attention between bright and dull subjects is suspect since the first of the components is slightly shorter with increased attention and the second is slightly longer. Shortening of auditory AEP latencies is associated with maturation of the auditory system and other evidence suggests that delayed auditory system maturation may be a factor underlying the concurrence of longer auditory AEP latency and higher IQ. Scatter plots indicate that short auditory AEP latencies may identify individuals of low intellectual potential more accurately than the low correlations would suggest.

55.8 DICHOTIC EAR-ORDER EFFECTS WITH NONVERBAL STIMULI. Marlene Oscar-Berman, Harold Goodglass* and Herman Donnenfeld*. Aphasia Research Center, Boston V.A. Hospital, and Dept. Neurol., B.U. Sch. Med., 150 So. Huntington Ave., Boston, Ma., 02130.

Normal right-handed subjects were required to identify four nonlinguistic sounds (pitch contours presented dichotically in pairs) under each of the following conditions: (1) identification of the 2 stimuli in any order; (2) identification of the two stimuli, first from one ear (e.g., always the left), and then from the other ear. Here, the report orders were known by the subject in advance of the onset of dichotic pairs; (3) identification in ear orders indicated only at the offset of each dichotic presentation; (4) identification (in any order) after verbal associates were taught to each stimulus.

All four conditions tested the efficiency of the right and left cerebral hemispheres in processing nonverbal information (as reflected in accuracy of identification from contralateral ears). Conditions (2) and (3) tested the efficiency of each ear as a report ear (first report) and as a storage ear (second report), and whether or not prior attentional set influences accuracy. The last condition assessed the effect of verbal labeling on left-hemispheric (right ear) accuracy in the perception of nonverbal material.

Perceptual lateralization was not obtained under conditions of free report, nor in first-ear reports. The use of verbal labels did not increase right-ear (left hemisphere) accuracy. When considering only those items reported second, i.e., the stored items, the left ear (right hemisphere) was more efficient than the right ear; this effect was enhanced in the preinstruction (attentional) condition. Results support the idea that the storage mechanism may be much more sensitive to laterality differences than the perceiving and reporting mechanism.

55.9 NORMAL MAN AND MONKEY SOMETIMES BEHAVE AS THOUGH "SPLIT-BRAINED". C. R. Butler and A. C. Francis*. Department of Neurosciences and MRC Group in Developmental Neurobiology, McMaster University, Hamilton, Ontario, Canada L8S 4J9.

A model based on the known anatomy of the corpus callosum of primates has been formulated. This model states that since the areas of the cortex which represent the hands do not have commissural connections subjects should behave as though "split-brained" on tasks learned only with the fingers of one hand when subsequently tested with the other hand. This model has been tested in man and in baboon using a size discrimination task. In monkey it was found that intermanual transfer did not occur but in man the result was mixed, some subjects showing almost complete transfer and others having to relearn the task with the second hand. Possible explanations for the findings are discussed in terms of the importance of handedness and which hand was trained first.

55.10 MEASUREMENT OF THE EEG AND EKG FROM NOVICE AND EXPERIENCED SPORT PARACHUTISTS DURING A PARACHUTE JUMP. James G. McElligott. Dept. of Pharmacology, Temple Medical School, Phila., Pa. 19140

The EEG and EKG of novice and experienced sport parachutists were continuously monitored before, during and after a parachute jump. The purpose of this study was to test the effect jumping had on these 2 physiological parameters and to compare them in novice (no previous jumps) and experienced (> 100 jumps) jumpers. After each of the 6 novice jumpers exited from the airplane at 3500 ft, their chutes automatically opened in about 3 sec. The 8 experienced parachutists made a total of 13 jumps. Each of these jumps consisted of a period of delayed opening or free fall that varied from 5 sec (exit altitude 3500 ft) to 60 sec (exit altitude 12,500 ft). With regard to EKG, the most notable feature was the tachycardia during the jump sequence. Maximum heart rates of 175-205 beats/min were obtained for both novice and experienced jumpers a few seconds after chute openings. For the experienced jumper this could be up to 60 seconds after exiting from the airplane. Auto-spectra histograms of EEG showed no consistent changes within or between each group that could be associated with the events of the jump sequence or with periods of accelerated heart rate.

(This work was performed at the Space Biology Lab (BRI) of UCLA and supported by USAF Grant # F44620-70-C-0017 and in part by NIH Grant # 1R01-NS-10488-01).

55.11 A SLEEP EEG ASSESSMENT OF THE ABSTINENCE SYNDROME FOLLOWING PROLONGED USE OF DIAZEPAM. Richard P. Allen* and Lino Covi. Department of Psychiatry and Behavioral Sciences, Johns Hopkins University. Baltimore, Maryland

All night sleep EEG's were obtained on 3 patients who had been taking diazepam for more than two years. Sleep was recorded for two nights on medication and for abstinence nights 1-2, 7-9, 29-30 (approximately) and 120-130 (approximately). The doses of diazepam were: 10 mg. daily (taken approximately 75% of the time, 10 mg. daily (taken very regularly) and 20 mg. daily (also taken very regularly). Daily clinical ratings were obtained during drug treatment and abstinence. Abstinence produced changes in R E M sleep, with a marked, lasting suppression for the patient on the highest dose and an elevation in the patient on the lowest doses. Slow wave sleep (stage 3 and 4) was suppressed on medication and slowly recovered during abstinence, requiring more than 18 weeks of abstinence for the patient on the highest dose. The highest dose patient showed a severe clinical abstinence syndrome involving nightmares and a psychotic episode, the other two patients showed less severe clinical symptoms in direct relation to their dosage frequency. These results are compared with the abstinence syndrome for alcohol and found to be remarkably similar.

55.12 STIMULUS AUGMENTING AND REDUCING IN MENTAL DISEASE. Victor Milstein*, Joyce G. Small*, Joseph E. Moore and Carole Corsaro. Larue D. Carter Memorial Hosp. & Indiana Univ. Med. Center, Indianapolis, Indiana 46260

Several studies have related the amplitude/intensity slope of visual evoked responses (VERs) to personality variables, and reported differences between psychiatric patients and normal controls. Recently, augmenting or reducing has been reported to differentiate bipolar and unipolar forms of manic depressive disease. These neurophysiological characteristics may also predict response to drug treatment. It may be that these observations indicate differential CNS processing of sensory inputs in various mental illnesses, but such can not be concluded until it is clarified whether they are mediated centrally and/or peripherally. The relative contributions to these scalp recorded events of variables such as pupillary size and response from the corneo-retinal field and orbital musculature need to be known to clarify the underlying mechanisms.

We examined the augmenting/reducing characteristics of VERs in 50 patients including bipolar and unipolar manic depressive types, schizophrenia and personality disorders. VERs were elicited at 4 different stimulus intensities, both before and after pupillary immobilization. Four channels of data were averaged simultaneously from mid-line occipital & central scalp and from periorbital areas. Preliminary analyses of the data support the observations of others in that patients with bipolar manic depressive disease tended to be augmenters more than other patient groups. However, augmenting or reducing was often dependent on which peak-to-peak amplitude was examined. It appeared that averaged activity from the orbital areas may have contributed to the scalp response. Additional data relating augmenting and reducing to diagnosis and variables of drug treatment will be reported and the possible mechanisms underlying these phenomena will be discussed.

55.13 THE AVERAGED VISUAL EVOKED POTENTIAL AS A TECHNIQUE FOR ASSESSING CEREBRAL DEATH. Edward C. Beck, Edward M. Behrens*, and Robert E. Dustman*. VA Hospital and University of Utah, Salt Lake City, Utah 84113

With advancing medical technology and with increasing demand for organ transplantation, a more reliable evaluation of cerebral death than is presently available becomes critical. The averaged evoked potential may be a more precise indicator of brain death than the conventional EEG. A computerized sum of a series of cerebral responses to many stimuli should indicate more clearly the presence or absence of electrophysiological activity than conventional recordings. With cats as subjects and three lethal conditions, cerebral anoxia, ischemia, and barbiturate intoxication, a comparison was made between EEG activity and the wave form configuration of the visual evoked response. Twelve cats, four for each condition, were permanently implanted stereotaxically with an array of cortical and subcortical electrodes under sodium pentobarbital anesthesia. This paper reports only results from cortical leads which were electrodes consisting of 5 mm stainless steel screws threaded through the calvarium to rest on dura overlying marginal and middle sylvian gyri. Measured resistance was 5 K ohms or less. Visual evoked responses were summed and averaged following 25 or more .01 msec flash presentations. Responses were analyzed with a PDP-9 computer at a sampling rate of 500/sec. EKG, ERG, arterial blood pressure, temperature and respiration were recorded concomitantly with EEG and evoked potentials. In all conditions evoked potentials continued during epochs of silent or "isoelectric" EEG. With barbiturate intoxication the evoked potential endured with little change in amplitude throughout all the experiments often after many hours of silent EEG. The results suggested that the evoked potential technique may prove valuable in the presence of ambiguous EEG activity, particularly with suspected deaths due to an overdose of barbiturate or other depressants.

55.14 ELECTROENCEPHALOGRAPHIC CORRELATES OF RENAL DISEASE, John R. Bourne and James W. Ward. Vanderbilt University, Nashville, Tennessee, 37235

Although it is well known that substantial slowing of the EEG occurs in uremic patients (Kiley, 1965), relatively little research has been conducted on quantification of this slowing. In the present study, EEG's were recorded from two groups of uremic patients and analyzed by autocorrelation and power spectral techniques. During a six-month period, ten out-patients (protocol A) on various dialysis schedules and nutritional protocols were studied. In addition, one malnourished in-patient (protocol B) was frequently examined.

Prior to computer analysis, all EEG's were visually scanned to eliminate artifacts and record sections which showed slowing due to sleep. Each EEG record was subjected to power spectral analysis and postanalyzed for percent power within selected frequency bandwidths. Plots of percent power below 7 Hz (PPB7H) versus time revealed dramatic pre- and post-dialysis differences. The protocol B patient showed clear increases in PPB7H before dialysis and a consistent return to a lower percent power after dialysis. For the protocol A patients, a distinct correlation was found between the PPB7H and the patient's dialysis protocol. In general, a higher average PPB7H was recorded from patients dialyzed twice weekly and a lower average PPB7H from patients dialyzed three times per week. In both protocol A and B patients observation of changes in the EEG PPB7H allowed a posteriori prediction of when dialysis had been given. This method of EEG quantification may be useful in aiding in the determination of when to optimally perform renal dialysis.

Kiley, J., and Hines, O. AMA Arch. Int. Med. 116:67, 1965.

56.1 **DISTRIBUTION AND PROPERTIES OF SEROTONIN-BINDING PROTEIN FROM RAT BRAIN.** Hadassah Tamir, Yung-yu L. Huang*, and Maurice M. Rapport. N. Y. State Psychiatric Inst. and Columbia Univ. Col. of Physicians and Surgeons, New York, N. Y. 10032.

In a previous communication we reported on the presence of a soluble protein in rat brain with high binding affinity for serotonin (apparent Km 1 x 10^{-8} M). Addition of Ca^{+2} or -SH blocking agents to the medium inhibited the binding. Administration of p-chlorophenylalanine or reserpine to the rats enhanced the binding capacity of the soluble protein fraction several fold. The binding protein comprised less than 10% of the total soluble protein as judged by gel electrophoresis. We now wish to report that the binding capacity of soluble proteins from subcellular fractions was highest in the synaptosomal (P_2B) and cytosol (S_3) fractions. In studies of the total soluble protein fraction from different regions (100,000 g supernatant), hypothalamus and the region of raphe nuclei were both found to have a higher binding capacity than either cortex, cerebellum, or white matter. Partial purification of the binding protein was achieved by ammonium sulfate fractionation (pH 7.5, 4°, 25 to 55% saturation) followed by DEAE column chromatography and batchwise adsorption and elution from hydroxylapatite. The partially purified protein was used to study the effects of dopamine, norepinephrine and indole derivatives on the binding of serotonin. Both dopamine and norepinephrine at 10^{-6} M inhibited the binding appreciably. Tryptamine, N-ω-methyl tryptamine and 5-HIAA had little or no effect on the binding.

(Supported in part by the Schizophrenia Research Program of the Supreme Council 33° A.A. Scottish Rite, Northern Masonic Jurisdiction)

56.2 EFFECT OF 5-HYDROXYTRYPTAMINE (5-HT) ON CEREBRAL PROTEIN SYNTHESIS: IN VIVO MEDIATION AND IN VITRO EFFECTS. Walter B. Essman and Eliahu Heldman*. Depts. of Psychology and Biochemistry, Queens College of the City Univ. of New York, Flushing, N.Y. 11367

A relationship between the behavioral effect of electroconvulsive shock (ECS), its effect upon cerebral 5-HT content and metabolism, and the contribution of both events to cerebral protein synthesis has been sought. Previous studies have shown that (1) post-training ECS cause a retrograde amnesia in rodents, (2) both treatments effect a significant inhibition of protein synthesis in vivo, and (3) 5-HT causes inhibition of protein synthesis in vitro in both microsomes and synaptosomes. The purpose of the present experiments was to describe the in vivo effects of increased brain 5-HT upon protein synthesis and further, the in vitro effects of 5-HT upon microsomal protein synthesis. A single ECS (10-20mA, 200 msc.) resulted in (1) increased free brain 5-HT concentration (12-17%), increased 5-HT turnover (~28%) and decreased C^{14} leucine incorporation into cerebral proteins (~50%). In vivo studies showed that intracranial 5-HT, but not analogs or metabolites thereof, could inhibit cerebral protein synthesis (15-32%), and such inhibition could be augmented by MAO inhibitors. In vitro approximation of similar status changes indicated C^{14} leucine incorporation into brain, but not liver, microsomes was decreased (25-35%) by 5-HT at concentrations (10^{-3}M-10^{-2}M) where this effect was augmented by MAO inhibitors to over 50%. 5-HT analogs or metabolites exerted no effect upon C^{14} amino acid incorporation. Soluble RNA, capable of binding free 5-HT blocked the inhibitory effect of the latter. Differences between the in vitro effects of 5-HT and the in vivo results probably depend upon the availability of sufficient free amine to sites regulating amino acid incorporation. (Supported in part by a Grant from the Council for Tobacco Research -- U.S.A.)

56.3 EFFECT OF 5,6- and 5,7-DIHYDROXYTRYPTAMINE ON REGIONAL BRAIN CHEMISTRY IN THE RAT. Peter J. Morgane*, William Forbes, Warren Stern and John Jalowiec* (Spon: Hudson Hoagland). Neurophysiol. Lab., Worcester Fndn. Exp. Biol., Shrewsbury, Mass. 01545.

In recent years much experimental use has been made of the chemical lesioning approach to dissecting neurotransmitter systems, e.g., with 6-hydroxydopamine. Two new serotonin analogues, 5,6- and 5,7-dihydroxytryptamine (DHT) have been reported to exert prolonged and specific destructive effects on serotonergic neurons. In order to study the specificity of chemical lesioning produced by these agents, they were injected intraventricularly in doses of 50 or 100 μg (25 μl volume). The regional effects on serotonin (5-HT) and norepinephrine (NE) levels were determined on post-injection days 2 and 10 (n=6 per group) in the telencephalon, diencephalon and lower brainstem. 5,6-DHT significantly lowered 5-HT levels to 50-65% of normals on days 2 and 10 in all brain regions while only transiently lowering NE on day 2. The degree of depression in 5-HT was as great or greater on 10 as day 2. On the other hand, the isomer of 5,6-DHT, 5,7-DHT, produces mixed results: both 5-HT and NE were lowered to 55-80% of normals on day 2 and these effects persisted on day 10. Vehicle injections produced minimal or no effects. These results indicate that while 5,6-DHT produces relatively specific depleting effects on 5-HT, 5,7-DHT produces less marked and essentially non-specific monoamine depletions in brain tissue in both the short and long-term. (Supported by NIMH grants 02211 and 10625.)

56.4 THE EFFECTS OF 5,7-DIHYDROXYTRYPTAMINE ON BRAIN SEROTONIN IN THE DEVELOPING RAT. Loy D. Lytle*, Jacob H. Jacoby*, and Richard J. Wurtman. Dept. Nutrition and Food Science, MIT, Cambridge, Mass., 02139

Littermate albino rats were injected intracisternally at birth with a single dose of 5,7-dihydroxytryptamine (5,7-DHT; 12.5, 25.0, or 50.0 μg) or an equivalent volume (15 μl) of the vehicle (1 mg/ml ascorbic acid in 0.9% saline). Animals were killed after 3, 12, 24, or 60 days, and brains and spinal cords analyzed for serotonin (5-HT) and 5-hydroxyindole acetic acid (5-HIAA). Brain concentrations of 5-HT in control animals were 40% of adult levels at birth; largest increases in the concentrations of this amine occurred during the third postnatal week. The administration of 5,7-DHT decreased the concentrations of 5-HT and 5-HIAA in brains and spinal cords at each age group (at 60 days of age, brain 5-HT was decreased to 65%, 40%, or 27% of control levels following injections of 12.5, 25, or 50 μg, respectively). In addition, small dose-related decreases in body weight were observed throughout the 60-day period following the injections.

The reductions in brain 5-HT following the neonatal injections are greater than those observed among adult rats injected with equivalent doses of the drug. Injection of this compound at birth may provide a useful preparation for assessing the functional significance of 5-HT-containing neurons.

56.5 TREATMENT BY DIMETHYL SULFOXIDE OF EXPERIMENTAL PARAPLEGIA SUBSEQUENT TO SPINAL CORD TRAUMA. J.C. de la Torre, Charles Johnson* and Sean Mullan*. Div. Neurosurgery, Univ. of Chicago Pritzker Sch. Med., Chicago, Ill. 60637

The effectiveness of dimethyl sulfoxide (DMSO) in the treatment of transient spinal cord injury has been reported. A 400 grams centimeter force (gcf) injury created at the thoraco-lumbar level of the dog spinal cord results in transient paraplegia, loss of bladder function and neuromorphological changes at the site of the lesion. In the present study, the effects of corticosterone and mannitol were evaluated in relation to DMSO to determine whether these drugs are able to reverse a 500 gcf which in non-treated animals results in irreversible loss of lower limb motor function and spasticity. Gross sensory-motor function and cortical evoked response following the 500 gcf spinal cord trauma were used to evaluate the performance of the corticosterone, mannitol, DMSO and control groups. Spinal cord tissue from injured and non-injured animals was also assayed biochemically 1 hour after injury to see whether monoamines levels were altered. The results show that DMSO when compared to the other groups, can significantly reverse the pathophysiological process that results in spastic paralysis subsequent to a 500 gcf spinal cord lesion. In addition, no changes in the noradrenaline, dopamine or serotonin levels were noted in spinal cord tissue following trauma.

56.6 PLATELETS AS MEDIATORS OF CNS DAMAGE IN COLD EDEMA. Jonathan L. Costa*, Umeo Ito*, Maria Spatz*, and Igor Klatzo. Lab. Neuropath. Neuroanat. Sci., NINDS, NIH, Bethesda, Md. 20014

Cold lesions as the experimental model for brain edema (Klatzo, et al., J. Neuropath. Exp. Neurol. 17: 548-564, 1958) have been produced in the cerebral cortex of the cat. In the area immediately below the exposed surface, there is a marked elevation in endogenous serotonin levels. Simultaneously, small arterioles in this region develop in their walls an intense yellow fluorescence, with an excitation-emission spectrum characteristic of serotonin. Serotonin accumulates within 30 minutes of the production of the lesion, and continues to increase up to 24 hours after the lesion. Labeling and drug studies suggest that the measured serotonin is released from platelets in the area of injury. The newly-released serotonin appears to be deposited in arteriolar walls, and may mediate some of the characteristic permeability changes seen in this lesion.

57.1 LOCALIZATION OF EXCITATORY AND INHIBITORY PATHWAYS FROM MEDULLARY NUCLEI TO SPINAL CARDIOACCELERATORY NEURONS IN THE CAT. James L. Henry and Franco R. Calaresu, Dept. Physiol., Univ. Western Ontario, London, Ontario.

It has recently been shown that discrete medullary nuclei give rise to excitatory and inhibitory fibers to spinal sympathetic neurons (Fed. Proc. 32:400,1973) but no information is available on the course of these fibers in the spinal cord. In 17 chloralosed cats medullary sites of autonomic neurons projecting to the spinal cord were identified by stimulation of fibers terminating at cardioacceleratory sites in the right intermediolateral nucleus (ILN) in T_2 and exploring the medulla for evoked antidromic responses. The cardiovascular function of positive sites of recording was determined by observing the effects on heart rate of electrical stimulation of these locations. The spinal pathways of descending fibers from these sites were then identified by observing the effects on the medullary evoked responses of restricted, histologically identified surgical and electrolytic lesions in spinal segments C_5-C_7. Ipsilateral inhibitory inputs to cardioacceleratory ILN neurons from 10 medullary sites were eliminated by selective lesion of either the ventral funiculus (VF; 8 sites) or the dorsolateral funiculus (DLF; 2 sites). Ipsilateral excitatory inputs from 3 medullary sites were eliminated by lesion of the DLF. Inputs from 4 left medullary sites at which electrical stimulation produced no change in heart rate were eliminated by lesion of the VF on the right side. It is concluded that a) inhibitory fibers from medullary nuclei to spinal cardioacceleratory neurons descend in the ipsilateral VF of the cervical spinal cord, b) excitatory and inhibitory ipsilateral fibers descend in the ipsilateral DLF, c) some fibers with no demonstrable cardiovascular function cross from the left side of the medulla to the right VF and terminate on sympathetic neurons on the right side. (Supported by the M.R.C. of Canada; J.L.H. is supported by the Ontario Heart Foundation.)

57.2 DORSOMEDIAL HYPOTHALAMIC INTERACTION WITH CAROTID SINUS BARORECEPTOR ACTIVITY. J. Randle Adair* and John W. Manning. Department of Physiology, Emory University, Atlanta, Georgia 30322

Previous studies have shown that dorsomedial hypothalamic (DMH) stimulation gives a strong, immediate systemic pressor response as well as sympathetic cholinergic vasodilatation (SCV) in skeletal muscle of the cat. SCV could be evoked by high carotid sinus (CS) pressure and was dependent on the integrity of the DMH, indicating a role of supramedullary structures in part of the CS baroreceptor reflex. Unit responses to CS nerve stimulation were recorded in the medulla with peak latencies (7 and 11 msec) consistent with the findings of other researchers for postsynaptic responses to primary CS baroreceptor afferents. Some longer latencies (30-50 msec) were noted, indicating possible 2nd or 3rd order neurons in the reflex arc. DMH stimulation prior to CS nerve stimulation produced inhibition of 60% of unit responses over a conditioning-testing interval of 30-120 msec, some units being inhibited as early as 7 msec, remaining inhibited as long as 790 msec. Units responsive to DMH stimulation could be noted in recording loci for baroreceptor units, differing in size, latency, frequencies of following and firing patterns. Two populations were noted, one with a peak latency 2-10 msec, another 10-30 msec. Both show a burst firing pattern to stimulation, followed by recurrent bursts in a poststimulus interval of 50-300 msec. These units can be found over a much wider range of recording loci than baroreceptor loci, notably near midline and inferior olivary structures. These units responsive to DMH stimulation may provide the neurophysiological substrate for the observed DMH modulation of afferent CS baroreceptor information, as well as the observations of others of modulation of cardiovascular activity with inferior olivary stimulation and primary afferent depolarization noted in the CS nerve with stimulation of the posterior hypothalamus. (Supported by USPHS, NIH Grant NS 02645 and -05669)

57.3 THE LIMBIC SYSTEM AS A SITE OF ACTION OF ANTIHYPERTENSIVE DRUGS.
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The role of the limbic system in the antihypertensive effects of both propranolol, a beta adrenergic blocking drug, and clonidine [2-(2,6, dichlorophenyl-1-amino)-2-imidazoline HCl], was investigated using chloralose-anesthetized cats and dogs. Recording concurrent changes in spontaneous efferent sympathetic and parasympathetic nerve activity, heart rate, blood pressure and dP/dT, it was observed that intra-arterial administration of both agents was associated with decreased blood pressure, heart rate, dP/dT and sympathetic nerve activity. Parasympathetic nerve activity was reflexly increased. Tissue assay for these drugs demonstrated highest uptake in areas of the limbic system. When clonidine was administered stereotaxically into septal areas, similar significant alterations in all parameters occurred. Stereotaxic administration of propranolol into the hippocampus and septum induced similar alterations in all cardiovascular and neural parameters. Significant antagonism occurred when both agents were simultaneously administered at these sites. It is concluded that the mechanism of the antihypertensive action of these drugs may involve alterations in the neural control of the cardiovascular system. (Supported by GRS Grant - NIH S-501-RR-05361-12).

57.4 DECREASED NOREPINEPHRINE TURNOVER IN THE BRAIN STEM OF HYPERTENSIVE RATS.
Jacques de Champlain and Marie-Reine van Ameringen*. Centre de Recherche en Sciences Neurologiques, Département de Physiologie, Université de Montréal, Montréal 101, Québec, Canada.

In rats made hypertensive with desoxycorticosterone and saline, an hyperactivity of both the peripheral sympathetic fibers and the adrenal medulla has been found to be the major substratum responsible for an elevation of blood pressure in this condition (de Champlain J. and van Ameringen M.R., Circulat. Res. 31: 617, 1972). Such a generalized activation suggested that the primary dysfunction responsible for this peripheral adrenergic hyperactivity could be localized elsewhere in the blood pressure regulatory mechanism. The norepinephrine (NE) turnover rate was studied after blockade of the biosynthesis with alpha methyl paratyrosine in various regions of the central nervous system. In contrast to the increased NE turnover found in most vascular peripheral organs, the turnover was significantly reduced (t 1/2 = 9.8 hrs) in the brain stem of hypertensive animals compared to that in control animals (t 1/2 = 4.5 hrs) whereas it was found normal in the spinal cord and in the telediencephalic portion of the brain. The spinal cord section (C6-C7) resulted in a rapid fall in blood pressure within normotensive levels in hypertensive animals while the NE turnover was restored to normal in peripheral organs. However, the NE turnover rate remained markedly reduced in the brain stem of these sectioned hypertensive rats despite the lowering in blood pressure thus indicating that the changes observed in the function of adrenergic fibers of the brain stem are not secondary to the elevation of blood pressure but could rather be a determinant factor responsible for the peripheral adrenergic hyperactivity. (Supported by MRC grants (Canada)).

57.5 BRAIN LESIONS, SERUM CHOLESTEROL LEVELS, AND "SPONTANEOUS" ARTERIOSCLEROSIS IN RABBITS, Cesar Somoza*. Veterans Administration Hospital and University of Cincinnati, Cincinnati, Ohio, 45220

One-hundred-sixty male albino rabbits weighing 2000 grams were used in these experiments. Lesions were produced with a stereotaxic apparatus in the anterior and posterior hypothalamus, infundibulum, and central gray substance of the tegmentum. All the operated upon animals and controls were allowed a 3-week resting period after the operations and then were fed 100 grams per day of a.4% cholesterol diet for 9 weeks. Food and water consumption were recorded daily. The rabbits of two groups were operated upon twice: first the lower portion of the infundibulum followed by the central gray substance and vice versa. At autopsy the aortas were examined for "spontaneous" arteriosclerotic lesions and section taken for microscopic examination. Sections were also taken of the other organs. Suitable blocks of brain were processed in a freeze-drying instrument for 7 days and then subjected to the fumes of paraformaldehyde for determination of fluorescent catecholamines. Determinations of serum cholesterol, triglycerides, phospholipids, cortisol, and growth hormones were performed at intervals during the experiment. Data available indicates that rabbits with lesions to the posterior hypothalamus exhibited significantly higher serum cholesterol values and a lower degree of arteriosclerosis than animals with damage to the infundibulum. There is an association between levels of growth hormone and serum cholesterol levels in rabbits with lesions to the posterior hypothalamus. Animals with lesions to the infundibulum followed by central gray damage have significantly higher incidence of arteriosclerosis than rabbits with the reverse procedure.

57.6 CONTINUOUS MONITORING OF INTERNAL CAROTID FLOW VELOCITY IN NEUROSURGICAL PATIENTS. C. P. McGraw and K. Iwata*. Univ. of Texas Med. Branch, Galveston, Texas, 77550

A method for obtaining continuous flow velocity was tested in dogs and measurements were obtained in five comatose patients. This was done by placing a 16 gauge Doppler probe on the internal carotid artery through a subcutaneous puncture. With an arteriogram the vessel diameter and the angle of the probe could be obtained for calculation of the vessel flow. This information was displayed on a polygraph with the vital signs, blood pressure, and intracranial pressure when possible. This has proven to be a reliable way of continuously monitoring internal carotid velocity and has been done for 36 hours. With this method it has been possible to observe dynamic changes in internal carotid velocity in response to norepinephrine and CO_2. Such recordings have also shown that there is an increase in internal carotid blood velocity that was correlated with the increase in heart rate at the termination of the plateau wave.

58.1 DARK NEURONS IN THE NORMAL AND DEAFFERENTATED LATERAL VESTIBULAR NUCLEUS: EXPERIMENTAL EFFECT OR ARTIFACT? John E. Johnson, Jr. Dept. Anat., Tulane Med. Sch., New Orleans, La. 70112

During an experiment designed to examine changes in the lateral vestibular nucleus of rats following destruction of one of its inputs, the anterior cerebellar vermis, it was observed that some lateral vestibular neurons stained more darkly than others. A subsequent experiment was performed to test the possibility that these dark cells were due to poor ventilation at perfusion, the anesthetic employed, or post-mortem trauma, rather than the deafferentation operation.

Five rats were used in the experiment. All were perfused with a mixture of paraformaldehyde and glutaraldehyde in phosphate buffer for 30 minutes. Except where noted, all were ventilated with 90% O_2-10% CO_2 and the brains carefully removed immediately following perfusion. Rat # 1 was ventilated, perfused and the brain removed immediately. This is essentially the same treatment given to the deafferentated animals described above. Rat # 2 was not ventilated at perfusion. Rat # 3 was given an extra sodium pentobarbital injection 3 days before perfusion. The brain of rat # 4 was removed and the brain stem torn from the cerebrum, placing maximum stress on the vestibular nuclei. The brain of rat # 5 was left undisturbed in the skull for 4 days before processing.

In none of the lateral vestibular nuclei of the 5 rats were there more than 1 or 2 dark neurons. This contrasts with the deafferentated rats in which numerous dark cells could be observed in one semi-thin section. The dark neurons, thus, do not appear to be caused by anoxia, the anesthetic, or post-mortem trauma.

58.2 PROJECTIONS OF THE PRIMARY AND SECONDARY AUDITORY FIBERS IN THE BULLFROG, (Rana catesbeiana). P. M. Fuller and S. O. E. Ebbesson. Depts. of Anatomy and Neurosurgery, University of Virginia Sch. Med., Charlottesville, Va. 22901.

Until recently, the precise pattern of interneuronal connections in amphibian brains were generally poorly understood because of the lack of adequate histological methods. The present study employs one of the new experimental techniques.

A lesion was made of the posterior branch of the VIIIth cranial nerve (auditory) in 10 adult bullfrogs. In addition, electrolytic lesions were made in the cochlear nucleus of 10 adult frogs. Following post-operative survival times of 5-25 days, the frogs were perfused with 10% formalin. The brains were processed according to various modifications of the Nauta and Fink-Heimer techniques, and the degenerating fibers traced to their termination.

The posterior branch of cranial nerve VIII contain the primary auditory fibers and primary vestibular fibers from the posterior semicircular canal. The vestibular fibers project to the vestibular nuclear complex, and the primary auditory fibers project to the cochlear nucleus. The cochlear nucleus, as defined by the extent of the terminal degenerating, is located at the dorsolateral edge of the medulla, and extends from the entrance of cranial nerve VIII, caudally to the level of cranial nerve IX. The fibers arising from the cochlear nucleus project to: 1)the contralateral cochlear nucleus, 2)the superior olivary nucleus bilaterally, with the major portion to the contralateral side, and 3)the central nucleus of torus semicircularis, bilaterally.

58.3 CORRELATION OF PERIODICITIES IN TWO PREGANGLIONIC SYMPATHETIC NERVES. P.M. Gootman and M.I. Cohen, Dept. of Physiology, Albert Einstein Col. Med., New York, N.Y. 10461.

The efferent discharges of the left greater splanchnic (Spl) and cervical sympathetic (CS) nerves were simultaneously recorded monophasically (bandpass 0.2 - 1250 Hz) in decerebrate or urethane-anesthetized, gallamine-paralyzed, thoracotomized cats. The recordings from the two nerves were analyzed both with averaging computation and with auto- and cross-correlation computation. The discharges in both nerves had oscillations in common: (a) periodicities in phase with the cardiac cycle, (b) periodicities in phase with the central respiratory cycle (indicated by efferent phrenic nerve discharge). Each nerve had a characteristic prominent periodicity (Spl, 10/sec; CS, 30-40/sec) which tended to be modulated by the cardiac and respiratory cycles. In some cats the CS discharge had a 10/sec periodicity which was locked to, but less prominent than, the 10/sec periodicity in Spl activity. The relations between the two discharges were also explored by electrical stimulation of sites within the medullary pressor and depressor regions (Gootman and Cohen, Exptl. Brain Res., 1971, 13: 1-14); stimulation of the former region produced evoked responses having different latencies in the two nerves (CS, 20 msec; Spl, 40 msec) as well as different time courses. The latency difference was comparable to the time lag of spontaneous activity between the two nerves as shown by cross-correlation. The existence of generalized activation is implied by the presence of similar oscillations of activity (usually cardiac and respiratory) in the two nerves, which indicates that both generating networks are driven from common sources, probably in the brainstem sympathetic centers. The presence of different oscillation frequencies in the Spl and CS nerves indicates specificity of organization within their respective generating networks. (Supported by NIH Grant NS-03970.)

58.4 SYNCHRONIZED BURST ACTIVITY IN THE INSPIRATORY NETWORK. Morton I. Cohen. Albert Einstein Col. Med., New York, N.Y. 10461.

In decerebrate, vagotomized, paralyzed cats, recordings were made of efferent phrenic discharge and of medullary inspiratory unit and wave activity. The occurrence in the population recordings of high-frequency oscillations (60-110/sec) during the inspiratory phase indicates that inspiratory neurons' discharges tend to be synchronized on a short time scale. Such oscillations, locked to phrenic oscillation, were found in the rostral medulla near the obex: a) in spike activity of inspiratory units of the dorsal and ventral respiratory nuclei; b) in wave activity (not associated with spikes) occurring during the inspiratory phase, recorded in the region medial to the nucleus ambiguus. The latter activity probably reflects synchronized synaptic potentials. Crosscorrelation analysis showed the relative timing of medullary and phrenic oscillations: peak spike activity and peak negativity of wave activity preceded peak phrenic discharge by 3-5 msec, for oscillation periods of 9-17 msec. These lags are comparable to latencies of phrenic responses evoked by stimuli in these regions, suggesting that the oscillatory activity occurs in neurons having fast projections to phrenic motoneurons. The short-term synchronization of inspiratory neurons' discharges probably arises from reexcitant connections, which cause oscillation by mutual excitation within a short time span, followed by synchronized time courses of recovery. Similar oscillations, locked to phrenic oscillation, were found in intracellular recordings of expiratory neurons, oscillatory synaptic potentials being superimposed on the hyperpolarization which occurs during the inspiratory phase (Mitchell & Herbert, Physiologist, 1971, 14: 196). This finding indicates the existence of strong, short-delay synaptic inputs from inspiratory to expiratory neurons. (Supported by NIH Grant NS-03970.)

58.5 CRANIAL MOTONEURONS: ASPECTS OF THEIR MOTOR CONTROL. Arthur J. Miller. Dept. Physiol., Sch. Med., Univ. Illinois Med. Center, Chicago, 60680

Synaptic influences on cranial motoneurons were studied by monitoring the discharge pattern of single motor units innervated by hypoglossal and motor trigeminal brain stem nuclei. Bipolar EMG electrodes designed to record 5-9 motor units were inserted in inframandibular musculature of urethane anesthesized cats and rhesus monkeys. Precentral motor cortex stimulation recruited inframandibular motor units in the preswallow preparatory activity and integrated motor responses involving several masticatory movements which culminated in a swallow. Motor units recruited by stimulation of a circumscribed region of the precentral cortex were also affected by peripheral sensory input from laryngeal mucosa and proprioceptive receptors innervated by the internal laryngeal nerve. 1st order latency analysis indicated a high correlation between the stimulus of the ILN and single motor unit responses suggesting a vagal-hypoglossal reflex involving laryngeal sensory input on tongue protruding musculature (i.e., genioglossus muscle). Laryngeal sensory input also affected hypoglossal motoneurons through excitation of an interceding medullary interneuronal pathway eliciting swallowing. Another synaptic input is the brain stem inspiratory pathway which affected cranial motoneurons such as those to the genioglossus muscle and recruited the smallest motor units in tonic activity and largest motor units only during maximum EMG intensity. 1st order interspike interval histograms and autocorrelation analysis of the discharge pattern of the genioglossus motor units demonstrated a significant difference in the majority of the units' (87%) activity in inspiration versus that of swallowing. This suggests two brain stem pathways are governing respiration and swallowing: one which rhythmically excites genioglossus motoneurons; the other a dominant synaptic input which irregularily activates these cranial motoneurons. (Supported by National Institute of Neurological Diseases and Stroke, NS10154.)

58.6 MIDBRAIN-FACIAL CONNECTIONS IN THE OPOSSUM, Didelphis marsupialis virginiana. George F. Martin, William Falls* and R. Dom. Dept. Anat., Sch. Med., The Ohio State Univ., Columbus, Ohio 43210

Although the available literature reveals no evidence for direct forebrain-facial projections in non-primates, stimulation of numerous areas (e.g. neocortex, amygdala and hypothalamus) can elicit facial responses. Our results offer evidence for several midbrain-facial projections which provide potential routes through which forebrain systems may affect facial muscles. The organization of the opossum facial nucleus was determined by noting the location of neurons showing decreased staining for acetylcholinesterase activity following transection of individual facial rami and the location of terminal degeneration plotted after specific midbrain lesions. Although brains with inferior collicular lesions demonstrate no discernible degeneration within the facial nucleus, those with destruction of the deep layers of the superior colliculus contain a few degenerating terminal fibers within the ipsilateral caudal auricular and contralateral zygomatic facial areas. Certain lesions of the red nucleus produce degeneration of terminal fibers within the zygomatic and buccolabial areas of the contralateral facial nucleus as well as within other facial areas which, for the most part, can be accounted for by unavoidable superior collicular and tegmental contamination. Although lesions of the deep tegmentum result in terminal debris within the facial nucleus (particularly the contralateral caudal auricular area), that present subsequent to destruction of the ventromedial tegmentum is particularly dense, bilateral, and localized within the cervical and caudal auricular areas. Because this tegmental area receives input from limbic and hypothalamic circuits, it provides one route through which these areas are able to influence facial musculature (e.g. ear flattening). Supported by USPHS grants NS-07410 and NS-08798.

58.7 AFFERENT CONNECTIONS OF CELLS IN THE SUPERIOR COLLICULUS OF THE CAT GIVING RISE TO THE TECTOSPINAL TRACT. V.C. Abrahams, P.K. Rose*. Dept. Physiology, Queen's University, Kingston, Ontario.

The tectospinal tract is one of two disynaptic pathways from the superior colliculus of the cat to motoneurones in the upper cervical cord supplying neck muscles. These pathways constitute the most direct route whereby the superior colliculus can control head movement. The neurones of origin of this pathway have been identified within the superior colliculus by antidromic activation. The cells were widely dispersed in the deep and intermediate layers of the superior colliculus. More than 40% of the neurones could be excited by both visual and neck muscle afferent stimuli and a further 30% could be activated by one or another stimulus. Since there is almost total convergence between extraocular and neck muscle afferents in the superior colliculus, it is likely that the tectospinal cells also receive a substantial extraocular muscle input. These experiments identify the tectospinal tract as one whose activity may be influenced by visual information as well as proprioceptive information from eye and neck muscles.

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58.8 VISUAL INPUT TO PONTINE NUCLEI IN MONKEY. Mitchell Glickstein, Mark Hollins, and Eileen LaBossiere*. Dept. Psychol., Brown Univ., Providence, R.I. 02912.

The pons is the major way station connecting the cerebral cortex with the cerebellum. We are interested in the way in which visual information is carried from the cerebral cortex to the cerebellum. Accordingly, we have been studying the anatomical input to the pontine nuclei from visual areas of the cerebral cortex of monkeys. We made lesions of striate and/or extrastriate visual areas in eight monkeys, and allowed them to survive from 4 to 8 days. Preterminal degenerating fibers were mapped among cells in the pontine nuclei using the Nauta stain and some of its recent modifications. We found only negligible degeneration in the pons after lesions were made which included the foveal region of striate cortex (area 17). Extrastriate visual areas send a dense system of fibers to a rostro-lateral region of the ipsilateral pontine nuclei. We are currently studying those brains in which the lesions were restricted to subdivisions of extrastriate visual cortex. These lesions were made on either bank of the lunate or the caudal bank of the superior temporal sulcus to see which of these regions give rise to a pontine input. Results to date are largely consistent with those seen earlier in the cat, with the exception that pontine fibers distribute somewhat more laterally in the rostral pons of monkeys than of cats.

58.9 EFFECT OF HARMALINE ON INFERIOR OLIVARY NEURONS. C. de Montigny* and Y. Lamarre (SPON: A.-M. Mouren-Mathieu). Dept. of Physiology, Univ. of Montreal, Montreal, Quebec.

Harmaline (5 mg/kg) injected intravenously in the decerebrate paralyzed cat induces rhythmic activation (8-12/sec) of the olivo-cerebello-bulbar pathways (Brain Res., 53: 81-95, 1973). Several experimental approaches were used to confirm the pacemaker-like behavior of the inferior olivary nuclei (I.O.) under harmaline in the decerebrate cat. Firstly, total cerebellectomy and spinal section at C2 level did not abolish harmaline-induced rhythmic bursting of I.O. neurons. Secondly, brain stem nuclei rostral to the I.O. were rendered ischemic by ligation of the common carotid arteries and of the basilar artery at its origin. Following harmaline administration, rhythmic discharges of I.O. neurons could still be recorded. Finally, twin-barrel micro-pipettes were used to inject harmaline (10 mg/ml) into the I.O. and to record extra-cellular neuronal activity. Micro-injections of 0.5 - 1.0 ngm of harmaline induced rhythmic activation of I.O. neurons, while control injections of NaCl and sucrose were ineffective. Harmaline injected in other brain stem nuclei did not provoke rhythmic activity. These findings suggest that the I.O. is the primary site of action of harmaline in the rhythmic activation of the olivo-cerebello-bulbar system.
(Supported by the M.R.C.).

58.10 INTRA-CELLULAR ANALYSIS OF THE NUCLEUS RETICULARIS TEGMENTI PONTIS (NRTP). T. Kiyohara*, S.T. Kitai, D.T. Kennedy and J.F. DeFrance. Morin Memorial Laboratory, Dept. of Anatomy, School of Medicine, Wayne State University, Detroit, Michigan 48201.

NRTP is one of the precerebellar nucleus in the pons. Recordings were made from NRTP neurons using KCl filled microelectrode with DC resistance of 10-20 meg ohms in cats anaesthetized with surital and chloralose. During recording cats were paralyzed with flaxedil. Electrical stimulation was applied through bipolar electrodes implanted in nucleus interpositus (IP) of cerebellum, brachium pontis (BP), brachium conjunctivum (BC), Deiters' nucleus (DN) and cerebral peduncle (CP). NRTP neurons were identified by antidromic activation following BP stimulation. Mono- and poly-synaptic EPSPs were recorded from NRTP cells following stimulation of IP, BP, BC, DN and CP. IPSPs were also observed following stimulation of some of the above structures. Some topographic organization exists in the NRTP with respect to the structures stimulated. Membrane characteristics of NRTP neurons were studied by intracellular current injection. NRTP neurons have relatively high membrane resistance, rectifying characteristics and is easily excitable with depolarizing current. Results indicate there is a two way connection between cerebellum and NRTP. Firing of NRTP neurons is influenced by supra-segmental and brain stem inputs. (Supported by NIH grants NS 00405, RR 5384 and NSF GB 35532)

58.11 THE DIFFERENTIAL CONNECTIVITY OF THREE DISTINCT POPULATIONS OF RUBRAL NEURONS. James S. King, R. Dom and George F. Martin. Dept. Anat., Coll. Med., Ohio State Univ., Columbus, Ohio 43210

The largest neurons of the opossum red nucleus (giant neurons, 45-70μ, King et al, '71) are restricted to its caudal-medial third. Orthograde and retrograde degeneration experiments reveal that giant neurons contribute to the crossed descending rubrospinal tract and give off relatively few brainstem collaterals. The entire red nucleus contains large-medium size neurons (25-40μ), many of which also project to the spinal cord and by way of collaterals to the contralateral brainstem. The smallest nerve cells of the opossum red nucleus (less than 20μ) are located throughout the nucleus, but are fewer in number. Several lines of evidence including Golgi impregnations indicate that the small rubral neuron is intrinsic to the red nucleus and may make synaptic contact with the somata of the larger (giant and large-medium) projection neurons. Previous experimental light and electron microscopic evidence (King et al, '72, '73) indicates that axons from the nucleus interpositus distribute throughout most of the red nucleus, but most extensively within its caudal-medial third. These degenerating axons terminate on the somata and proximal dendrites of giant and large-medium neurons. In contrast, cortical fibers are sparse in the caudal-medial third and terminate primarily on distal dendrites of large-medium neurons in the rostral 2/3 of the nucleus. Similar contacts with small neuron dendrites also are a distinct possibility. The dentate (lateral cerebellar nucleus) projects specifically to the rostral-dorsal red nucleus, and terminates primarily on the somata and proximal dendrites of the smaller large-medium neurons in that region. These latter neurons may be comparable to the parvocellular rubral neurons of the primate brain even though their cytoarchitecture is markedly different.

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58.12 PHARMACOLOGY OF RETICULAR SYSTEM PROJECTING TO THE SPINAL CORD IN CATS. Charles D. Barnes and F. P. White. Dept. of Life Sci., ISU, Terre Haute, Ind. 47809.

Sernylan$^{(R)}$ (1-(-phenylcyclohexyl) piperidine hydrochloride) is a dissociative anesthetic recommended for use on primates. We have investigated the effects of Sernylan on the reticular-spinal system in cats. Cats were decerebrated at the precollicular level and their spinal cord exposed at L_7. The amplitude of the monosynaptic reflex was used as the test with conditioning stimuli being applied to the ipsolateral gastrocnemius-soleus nerve at 10 times the test stimulus strength. Sernylan (2 mg/kg) injected IV decreased or wiped out both the facilitory and inhibitory phases of the spinal-bulbo-spinal (SBS) response pattern. Dicloroisoproterenol (4 mg/kg) a β adrenergic blocker and phenoxybenzamine (3 mg/kg), an α adrenergic blocker were used in an attempt to find an antagonist to Sernylan. Dicloroisoproterenol had no effect on the SBS pattern alone, nor did it antagonize Sernylan. Phenoxybenzamine, however, had an opposite effect to Sernylan on SBS (increasing both the facilitation and inhibition portions, but did not antagonize the effects of Sernylan at this dosage). We are now in the process of describing the dose response curves for both Sernylan and phenoxbenzamine and their possible interaction. We are also in the process of differentiating the possible spinal and reticular spinal effects of the above drugs and pentobarbital, a general anesthetic.

58.13 CENTRALLY EVOKED ELECTRODERMAL RESPONSES IN THE CAT: THE EFFECTS OF CHLORPROMAZINE AND RESERPINE. Meredith A. Davison* and Michael C. Koss. Dept. of Psychiatry and Behavioral Sciences and Dept. of Pharmacology, Univ. of Okla. Health Sciences Center, Oklahoma City, Oklahoma 73190

Electrodermal responses were evoked in a continuous pathway from the posterior hypothalamus through the ventrolateral brain stem to the cervical cord. Stimulation of this pathway yielded maximal, uniformly bilateral responses in the footpads of 20-30 millivolts. These responses were stable and could be maintained for periods of time up to six hours. Midline regions and classical cardiovascular regions of the dorsal medulla were unreactive. Loci were determined by direct stimulation with coaxial electrodes in cats anesthetized with chloralose (80 mg/kg) and paralyzed with gallamine triethiodide. Following definition of the excitatory regions, this system was used as a model with which to study drug effects of the central nervous system. Reserpine (2 mg/kg) was found to have no effect on either centrally or peripherally evoked electrodermal responses. In contrast, chlorpromazine (0.1-0.5 mg/kg) invariably reduced centrally evoked responses while having no effect on responses evoked peripherally. These data suggest that centrally evoked electrodermal responses provide a unique model system for the investigation of drugs affecting central sympathetic outflow. Since the neurotransmitter to the sweat glands is acetylcholine this system is particularly suitable for the study of those adrenergic drugs thought to have a central effect as well as their known peripheral effect. (Supported by NIMH grant MH 24083-01)

58.14 NEMBUTAL MODIFIES ACOUSTIC INPUT IN THE HYPOTHALAMUS: Nachum Dafny, Neurobiology, The University of Texas Medical School at Houston, Houston, Texas 77025.

Previous studies on evoked potentials and single unit activity have shown that acoustic stimuli have extensive input into the hypothalamus. Since most of the previous work was done in anesthetized animals; it is important to know how anesthetics influence hypothalamic activity. Since the rat has been the subject of extensive neuroendocrine studies, and since changes in endocrine function could be due to the stressful experience of anesthesia, acoustic evoked responses (AER) were simultaneously recorded in the anterior hypothalamus (AH) and ventromedial hypothalamus (VMH) from freely behaving rats previously implanted with permanent semimicroelectrodes.

If attention was distracted from the stimulus, the overall amplitude of the AER to that stimulus usually fell, mainly in AH; conversely, when attention was oriented towards the stimulus, the amplitude of the AER increased. The neural recovery function obtained by paired click stimuli separated by varying time intervals was studied and exhibited differences in recovery function between AH and VMH.

Low doses of nembutal increased the AER and improved the neural recovery in both AH and VMH. High doses of nembutal diminished the AER. Differences in sensitivity to nembutal was found between AH and VMH.

The data indicates that the afferent acoustic projection to the hypothalamus is polysynaptic and extends through the midbrain reticular formation (MRF). The MRF exerts tonic inhibition on this sensory pathway, and lower amounts of nembutal attenuated the inhibition. These data exhibits the acoustic projections to AH and VMH are modified differently suggesting that the acoustic projections to AH and VMH are not the same.

59.1 CENTRAL CONTROL OF *d*-AMPHETAMINE-INDUCED DISCRIMINATIVE STIMULI
Daniel W. Richards III*, Robert T. Harris*and Beng T. Ho (SPON: A. Moraczewski
Tex. Res. Inst. of Ment. Sci. and Baylor Col. Med., Houston, Texas 77025

Two studies investigated the general locus of drug action responsible for the stimulus state of *d*-amphetamine (A) by central and peripheral administration of A to rats implanted with intraventricular cannulae. The first experiment consisted of training 2 groups of S's to perform a 2-lever differential response task in chambers programmed for multiple schedule of reinforcement. Two intraperitoneal (ip) dosages (0.5 and 1.5 mg/kg) of A each paired with saline (S) during each training session. Following A-S differential response control, a randomly ordered series of 10 min generalization tests were administered every fifth session of retraining. Both groups responded on the S-lever to 2.0 mg/kg p-Hydroxyamphetamine (p-OHA) ip. Central administration of 50 µg or more of A produced A-lever responding in the 0.5 A-S group and 75-100 µg or greater doses produced similar A-lever choice in the 1.5 mg A-S group. The second experiment utilized intraventricular injections of 150 µg A-S (15 µl) as the two training stimulus conditions and ip injections of 0.5 and 1.5 mg/kg A, 2.0 mg/kg p-OHA, and S (1 ml/kg) in postdiscrimination generalization tests. The results of both studies demonstrate that central intraventricular dosages of *d*-A but not Ip injections of p-OHA produce dose-related discriminative stimuli which can control lever choice responses similar to that exhibited by rats given ip injections of 0.5 and 1.5 mg/kg A. These findings indicate that the discriminative stimulus properties of *d*-amphetamine are produced by the actions of the drug on central neurons rather than on the peripheral nervous systems.

59.2 THE ROLE OF MONOAMINES IN DISCRIMINATIVE RESPONSE CONTROL BY *d*-AMPHETAMINE.
Beng T. Ho and Jen-Tzaw Huang*. Texas Research Institute of Mental Sciences, Houston, Texas 77025.

We have studied the effects of various amphetamine derivatives on discriminative cue of *d*-amphetamine. In the present study the involvement of monoamines in producing this discriminative cue was investigated. Male Sprague-Dawley rats were trained in two-lever differential response tasks in chambers programmed for multiple schedule of reinforcement. Reward was contingent upon correct lever choices to the induced differential cue conditions of *d*-amphetamine (0.8 mg/kg) and saline throughout training. Pretreatment of rats with phentolamine, propranolol, methysergide, cinanserin or atropine did not block production of *d*-amphetamine cue. Nicotine, oxotremoline and STP could not produce the cue similar to that of *d*-amphetamine. These results indicate that noradrenergic, serotonergic or cholinergic neurons may not be involved in producing *d*-amphetamine cue. Chlorpromazine partially and pimozide completely blocked this cue, suggesting that dopaminergic neurons alone are responsible for the discriminative cue similar to amphetamine.

59.3 NORMALIZING EFFECTS OF d- AND l-AMPHETAMINE ON CEREBROVISCERAL PATHOLOGY.* E. O'Leary Corson, Samuel A. Corson, Vladimir Kirilcuk, and Jana Kirilcuk. Lab. of Cerebrovisceral Physiology, Dept. Psychiatry, College of Med., Ohio State Univ., Columbus, Ohio 43210.

Corson et al. (Intl. J. Psychobiol. 1:1-16, 1970) reported that some dogs, after repeated exposure to classical conditioning with electrocutaneous reinforcement, develop an almost inextinguishable persistent quintet of "fight or flight" responses to the entire conditioning room complex: marked tachycardia, polypnea, profuse salivation, a vasopressin type antidiuresis, and increased oxygen consumption. We referred to these animals as antidiuretic dogs (AD dogs). These reactions could be selectively inhibited by anxiolytic drugs (meprobamate, phenobarbital, diazepam) but not antipsychotic drugs, without affecting conditional Pavlovian motor defense or operant avoidance responses (Corson, 1968, In: Psychotropic Drugs in Internal Medicine, Excerpta Med. Intl. Congr. Series No. 182). d-Amphetamine (1 mg/kg per os) or l-amphetamine (4 mg/kg per os) produced a similar dramatic inhibition of the psychovisceral quintet of reactions. In a no-drug state, the AD dogs exhibited in the aversive conditioning room so much visceral turmoil that no distinct conditional cardiac responses were apparent. Amphetamines led to the appearance of clearly delineated discriminated conditional cardiac responses. The fact that four times as much l-amphetamine as the d-isomer was required for the attenuation of the visceral turmoil suggests that a noradrenergic (rather than a dopaminergic) system is involved in these effects (Taylor and Snyder, 1970, Science, 168:1487-1489). Supported in part by USPHS grants MH 12089 and MH 18098, Biomed. Sciences Support Grant RR-07074 to OSU, and State of Ohio Dept. of Mental Health and Mental Retardation, Div. of Mental Health.

59.4 AMPHETAMINE ANOREXIA: INTERACTION WITH STIMULUS-BOUND CONSUMMATORY BEHAVIOR. Thomas B. Wishart. Department of Psychology, University of Saskatchewan, Saskatoon, S7N 0W0, Canada.

Amphetamine has been reported to increase the threshold for stimulus-bound feeding behavior, but to be ineffective, even in high dosages, in reducing total food consumption in response to electrical stimulation of the lateral hypothalamus in food deprived rats. In the present study, the effects of various doses of d-amphetamine injected intraperitoneally in sated animals, on stimulus-bound consummatory behavior (drinking and feeding) were observed. Electrical stimulation was administered by two different methods; in one, the subject received programmed stimulation (a 30 second pulse train every 2.5 minutes), while in the second, the animal self-stimulated to obtain a 15 second train of pulses.

Electrical stimulation of the lateral hypothalamus elevated food intake significantly above control values in both the programmed and self-stimulation conditions. A d-amphetamine, dose-response anorexic effect was obtained under both conditions of stimulation. Higher doses than normal were however, required to reduce food consumption in response to brain stimulation. A 3 mg/kg injection of the drug was sufficient to completely inhibit stimulus-bound food consumption, although reflexive chewing and sniffing of the food continued to be elicited by the stimulation. In marked contrast, d-amphetamine had little or no effect on stimulus-bound drinking behavior or self-stimulation rates.

The results are indicative of a selective inhibitory action of d-amphetamine on a food-intake system located at the level of the lateral hypothalamus. This inhibitory action apparently does not extend to the water-intake or reward systems of the same area.

59.5 DOSE-RELATED SUPPRESSION BY AMPHETAMINE OF SPONTANEOUS LOCOMOTOR SHUTTLING ACTIVITY IN GOLDFISH. Frederick Petty, Rodney C. Bryant, and W. L. Byrne. Brain Research Institute and Department of Biochemistry, University of Tennessee Medical Units, Memphis, Tennessee, 38103.

Goldfish (Carassius auratus, 8-10 cm) exhibited a suppression in locomotor shuttling activity when treated with d-amphetamine sulfate (DEX), whether administered intracranially or by immersion. Activity was measured with an automated array of ten goldfish activity chambers (28.5 x 18 x 12.5 cm, lwd) with activity counts measured when the fish crossed the center of the box. Controls were run simultaneously with animals receiving DEX.

Intracranial injection (10 µl) with 1, 2, and 10 mg/kg DEX, after 13 minute baseline pretest, produced marked and significant suppression in spontaneous shuttling over a 3 hour experimental session. Similar dose-related effects were observed with DEX administered by immersing the fish in the drug solution (0.2, 2, 25, 50 and 100 mg/kg). The lowest dose (0.2 mg/l) did not significantly affect activity, while the higher doses suppressed shuttling in a dose-related manner. Pharmacologically active doses are 2-5% of lethal doses. Data are also presented on the uptake, distribution, and toxicity of d-amphetamine sulfate in the goldfish, administered by immersion and intracranial injection.

The observed effects of DEX on spontaneous locomotor activity in goldfish contrast with the effects reported with this sympathomimetic amine in other species. Possible reasons for this difference -- neuroanatomical, neurochemical, and procedural -- are discussed.

59.6 AMPHETAMINE INDUCED DYSKINESIAS IN CATS AND MONKEYS. A. Sudilovsky, E.H. Ellinwood*, and L. Nelson*. Duke Univ. Med. Ctr. Durham, N.C. 27710

The spectrum of dyskinetic manifestations elicited by chronic administration of Methamphetamine (M) was studied in 18 cats and 3 rhesus monkeys. Drug dosage was gradually increased from 15 to 35 mg/kg (via i.p.) over a period of 11 days for cats, and from 1 to 20 mg/kg (via i.m.) over a period of 4 months for the monkeys. Movies, video-tape recordings, and a detailed rating chart were used in the evaluation of postural and kinetic (stereotyped or transient) features. Results were analyzed by computer. Three independent symptomatological categories: hypokinesia, dystonia, and hyperkinesia with increased spontaneous reflex activity were discernible. In addition to stereotyped activity which was related to the acute effects of M, bizarre postures, akathisia, dyskinesias localized in the orofacial area and in the extremities, showed up increasingly over the intoxication cycle. These were comparable to side effects induced in human patients by prolonged treatment with L-Dopa or neuroleptic drugs, and to abnormal involuntary movements evoked from specific sites of the striatum in experimental animals after electrical stimulation, lesions, or injection of various drugs affecting receptors function. M induced imbalance of neurotransmitter's interactions with relative enhancement of dopaminergic activity in the striatum, adrenergic disinhibition, and secondary development of catecholamine receptors supersensitivity might contribute to the appearance of hyperkinetic symptomatology.

59.7 BEHAVIOR AND EEG ANALYSIS OF CHRONIC AMPHETAMINE EFFECT. Everett H. Ellinwood*, Abraham Sudilovsky, and Linda Nelson*. (Spon: B. Nashold) Duke Univ. Med Ctr. Durham, N. C. 27710

We are reporting on behavioral-electrophysiological correlations derived from analysis of simultaneous TV and analog EEG tape recordings in 46 cats. Using a 170 item behavior rating chart, we have been able to demonstrate that there are evolving behavioral changes over a period of amphetamine intoxication that not only are analogous to stages noted in amphetamine psychosis, but also reflect changes in the state of the catecholamine systems. The alterations reflect not only the stimulation of catecholamine mechanisms, but subsequently depletion supersensitivity as well as changes in the norepinephrine/dopamine ratio. The evolving behavioral states (including abnormal arousal, attitudes, and postural-motor aberrations) correlate with changes in the rhinencephalon "olfactory" spindle. Electrodes placed in catecholamine nuclei of the olfactory forebrain demonstrate changes (frequency, amplitude, and duration) in the olfactory spindle not seen with the normal behavioral states. Also, dramatic alteration in the rhinencephalon spindling precede and accompany stimulant induced seizures. Manipulation of the norepinephrine/dopamine ratio potentiates the seizure production as well as the abnormal behaviors preceding them.

59.8 THE ELECTROENCEPHALOGRAPHIC EFFECTS OF COCAINE AND D-AMPHETAMINE IN THE RHESUS MONKEY AS DESCRIBED BY PERIOD ANALYSIS. H. L. Altshuler and N. R. Burch* Texas Research Institute of Mental Sciences, Houston, Texas 77025

The electroencephalographic (EEG) descriptors of cocaine are poorly characterized and their mechanisms poorly understood. The effects of cocaine and d-amphetamine on the period analytic descriptors of the electroencephalogram of the monkey, Macaca mulatta, were evaluated when the animal was seated in a primate chair. Each animal served as his own control, and control studies were performed using intravenous (IV) saline injections. IV doses of cocaine (0.05-5.0 mg/kg) and d-amphetamine (0.05-5.0 mg/kg) were administered to each animal in accordance with a randomized experimental design and the EEG continuously recorded for 2 hrs after each dose. Periods of photic stimulation (3-30 Hz) were interspersed with periods of spontaneous EEG. A number of changes were observed in the period analytic descriptors. The major period (zero crossings) count was dramatically increased for 5 or more min post-dose. Intermediate period (first derivative) and minor period (second derivative) counts were more variable in their changes, although differences between the drugs were seen at all points of the dose-response curve, in most frequency bands and in responses to photic driving. Reserpine (0.5 mg/kg/day) and l-DOPA (100 mg/kg/day) were administered chronically to naive monkeys and those previously studied, and the acute effects of cocaine and d-amphetamine evaluated electrographically. Differences in the acute responses to the stimulants were seen in the pretreated animals when compared to the nonpretreated ones. These results implicate central biogenic amines in the actions of d-amphetamine and cocaine on the EEG.

59.9 d-AMPHETAMINE REDUCES THE SEVERITY OF SOUND-INDUCED SEIZURES IN DBA/2J AND C57BL/6J MICE. John M. Graham, Jr.*, Robert A. Schreiber and John W. Zemp. Dept. Biochem., Med. Univ. So. Car., Charleston, S.C. 29401

We have previously reported that d-amphetamine sulfate (DAMS) reduces the severity of audiogenic seizures (AGS) in DBA/2J mice, the amount of protection dependent on the age of the mouse. We present here dose-response data for DBA mice injected with various doses of DAMS and tested for AGS 15 min. later. Maximal reductions in the incidence of lethal seizures were seen with 0.5 to 2.0 mg/kg DAMS. C57BL/6J mice were also given acoustic priming at various ages. Mice primed at 16 days are maximally susceptible to AGS on day 21 (70% tonic seizures), with increases from 18 to 26 days. Mice primed at 28 days are maximally susceptible on day 36 (20% tonic seizures), with significant increases from day 34 to 40. DAMS is also effective in reducing the severity of seizures in C57 mice primed on day 16, and given 2 mg/kg DAMS 15 min. before testing on day 21. These data show that DAMS reduces the severity of AGS both in the normally susceptible DBA, and also in the audiogenically primable C57 strain of mouse. Since DAMS in doses yielding maximal protection from AGS is known to release catecholamines into the synaptic cleft, these data lend further support to the hypothesis that a defect in biogenic amine metabolism may be associated with sound-induced seizures. (Supported by NIH MH17455 to JWZ, by NIH GRS RR5420 to MUSC, and by 1972 So. Car. Appropriation for Research to MUSC, and NIH 1 FO2 MH53546-01 BLS to RAS)

59.10 BLOCKADE OF CENTRAL EFFECTS OF AMPHETAMINE BY OTHER STIMULANTS. William G. Clark and Lawrence K. Y. K. Yuen*. Psychopharmacology Research Laboratory, Veterans Administration Hospital, Sepulveda, California, 91343; and Dept. Biol. Chem., Sch. of Med., UCLA.

Our observations on the antiamphetamine effects of amantadine (Menon, Clark & Fleming, Europ. J. Pharmacol. 21:311, 1973) have been confirmed by others (J.E. Davies, Sympos. on Dopamine, Breda, The Netherlands, Sept. 8, 1972). In extending this to other stimulants, anorectics and analeptics, we have found that at the optimal doses and times, the following agents inhibit the central motor excitatory effects (measured on activity meters) of d-amphetamine in mice: amantadine (67% inhibition of amphetamine effect), picrotoxin (48%), pentylenetetrazol (43%), fenfluramine (38%), theobromine (34%), dimeflin (32%), SKF-139728A (28%), daptazol (26%), strychnine (24%), methylphenidate (12%). Compounds which did not inhibit the amphetamine effect, or were additive with it were: d-amphetamine itself, caffeine, phentermine, doxapran, diethylpropion, pyravalerone, pipradol, phenmetrazine, theophylline and diethadione. Others are being examined. The biochemical pharmacological mechanisms probably involve competitive occupation of receptors which are involved in the release of dopamine.

59.11 TISSUE DISTRIBUTION AND EXCRETION OF ^{3}H-TRIFLUOPERAZINE IN RATS. N.R. West and W.H. Vogel. Dept. Pharmacol., Thom. Jefferson Univ., Philadelphia, Pa. 19107

Adult male Spraque-Dawley rats were used to study the distribution and excretion of ^{3}H-trifluoperazine (^{3}H-TFP) after i.p. and oral injection. Total radioactivity was measured in various tissues, urine and feces and, using an extraction technique, trifluoperazine (TFP) and its sulfoxide (TFP-SO) were quantitated in plasma, brain, liver and lung. The time course and levels of drug and its sulfoxide in various tissues were different for i.p. and oral injections with 270 μg/kg ^{3}H-TFP though the differences were not consistent. In comparing these data with those of an earlier study using 5 mg/kg i.p., it was found that the tissue concentrations were not strictly dose dependent. Urinary excretion of TFP, TFP-SO and total ^{3}H during the first 24 hr was dose dependent and was 0.09%, 0.9% and 5.8% of the administered dose, respectively. Drugs such as chlorpromazine, haloperidol, imipramine and biperiden given in therapeutically comparable doses had no effect on urinary excretion of TFP and TFP-SO. Three weeks after daily i.p. administration of 270 μg/kg there was a slight but significant increase in the 24 hr urine excretion of TFP, TFP-SO, and total ^{3}H, probably due to an accumulation in the body. Considerable radioactivity was also found in the feces of rats receiving the drug.

59.12 AMPHETAMINE POTENTIATION OF PSYCHOSOCIAL THERAPY OF VIOLENT AND HYPOINHIBITORY (HYPERKINETIC) BEHAVIOR IN DOGS. S. A. Corson, E. O'L. Corson, V. Kirilcuk, J. Kirilcuk*, L. E. Arnold*, and W. Knopp. Lab. of Cerebrovisceral Physiol., Dept. Psychiat., Coll. Med., Ohio State Univ., Columbus, Ohio, 43210. (Illustr. with 16 mm B/W sound film, 20 min).

Studies were conducted on 10 normal and 7 naturally hypoinhibitory (hyperkinetic = hk) dogs who could not be conditioned and could not be trained to tolerate Pavlovian stand restraints even with the use of positive or negative reinforcement or anxiolytic or antipsychotic drugs. One of the dogs (Jackson) was also incorrigibly vicious to dogs and humans. Oral amphetamines disturbed the behavior of normal dogs, but controlled hk in 5 of the 7 hk dogs, as well as the violence in Jackson. The same dosages of d- and l-amphetamine (0.5-1.0 mg/kg) were effective in inhibiting viciousness, suggesting the involvement of a dopaminergic system. The control of hk required 4 times as much l- as d-, suggesting a noradrenergic system. Under amphetamine, the 5 hk dogs acquired discriminated classical and operant conditional responses which persisted in no-drug situations, thus contradicting the state-dependent learning theory. After several months of psychosocial therapy and conditioning under amphetamine, hk and viciousness did not reappear in Jackson upon drug withdrawal (13 months at this writing). We postulate that the primary defects in hk and violence are related to a deficiency in noradrenergic or dopaminergic transmitters in inhibitory brain areas. The beneficial amphetamine effects are thus not paradoxical, but normalizing by supplying the needed neurotransmitters in inhibitory brain systems. This hypothesis is susceptible to exptl. verification. Supported in part by USPHS grants MH 12089, MH 18098, Biomed. Sciences Support Grant RR-07074 to OSU, and State of Ohio Dept. of Mental Health and Mental Retardation, Div. of Mental Health.

59.13 A PRIMATE BEHAVORIAL PSYCHOSIS, A MODEL FOR STUDYING NEUROTRANSMITTERS AND NEUROLEPTICS. David L. Garver, Francis Schlemmer*, James W. Maas. Illinois State Psychiatric Institute, Chicago, 60612.

Previous work by several investigators has demonstrated a schizophrenic-like syndrome in human volunteers given large quantities of d-amphetamine. Aberrations in social and solitary behaviors in Macaca speciosa monkeys have similarly been induced by chronic administration of large quantities of d-amphetamine. Evidence is accumulating that such a behavorial model may be useful in evaluating the effect of potentially antipsychotic drugs and also may permit a functional dissection of catecholamine systems contributing to the process. Chronic d-amphetamine administration to selected members of a primate social colony induces striking changes in appearance and behavior. The treated aminals are hyperalert, agitated, isolated and display a variety of stereotypies with the disruption of many normal social interactions. Quantitative behavorial observations demonstrated significant changes in ten behavorial parameters: approaches, being approached, social grooming, initiated social interactions,distance, passivity, checking, indiscriminate self-grooming and stereotypies. Pretreatment with α-methyl-p-tyrosine, an inhibitor of catecholamine synthesis, and with haloperidol or pimozide, each an antipsychotic and dopamine receptor blocker, prevented the appearance of most of the elements of the syndrome, the most resistant element being checks which fell only at high dosage of haloperidol. In contrast, the non-neuroleptic phenothiazines promazine and promethazine, which fail to show dopamine receptor blocking properties, failed to alter the d-amphetamine induced syndrome. The d-amphetamine, non-human primate behavorial model gives promise of usefullness further in clarifying the roles of catecholamine systems (norepinephrine and dopamine) in severely disrupted behavior and potentially provides a non-human model for evaluating antipsychotic properties of new neuroleptics.

59.14 D OR L AMPHETAMINE AND SCHIZOPHRENIA. John M. Davis, M.D., David S. Janowsky*, M.D., M. Khalid El-Yousef*, M.D. Ill. State Psych. Inst., Uni. of Chicago, Chicago, Ill., TNI, Vanderbilt University, Nashville, Tenn., 37232, USA, Supported by MH 11468 and GM 15431.

D amphetamine is considerably more potent (5-10X) at releasing norepinephrine and is slightly more potent (2X) in releasing dopamine than L amphetamine. The psychomotor stimulants, methylphenidate and D and L amphetamine, offer pharmacologic tools for the investigation of the role of norepinephrine and dopamine in schizophrenia. In actively ill schizophrenic patients, it causes a dramatic intensification of pre-existing symptoms such as hallucinations and delusions. In this study, intravenous methylphenidate, D and L amphetamine in equimolecular doses were administered to schizophrenic patients. In each experiment, the rater and the patient were blind to when in a I.V. injection sequence active drug was substituted for placebo and which active drug was given. The results indicate that methylphenidate is a more potent behavioral activator than D amphetamine, which is approximately 2 times as potent as L amphetamine. If one assumes that the ratio of effectiveness of 2:1 for D and L amphetamine represents a dopaminergic phenomena, it would seem that the general activating effects of the above psychostimulants (D and L amphetamine) represent a dopaminergic phenomena, rather than an noradrenergic phenomena. However, it is important to note that the assumptions of differential effects of D and L amphetamine on human central catecholamines is based on data in rats, and is not based on direct evidence in man. L-Dopa (oral) also produced a worsening of schizophrenic symptoms. These findings suggest dopamine may play a role in the schozophrenic process.

60.1 DEVELOPMENTAL CHANGES IN SYNAPTOSOMAL AMINO ACID TRANSPORT. N. A. Peterson* and E. Raghupathy* (SPON: C. M. McKean). Brain-Behavior Research Center, Sonoma State Hospital, Eldridge, California 95431.

An earlier report from this laboratory (J. Neurochem., 19, 1423, 1972) described differences in accumulations of amino acids by synaptosomal fractions from immature (7-9 days) and adult rats. In this present investigation synaptosomal amino acid transport was studied in synaptosomal fractions obtained from brain cortices of rats over an age continuum. The fractions were prepared on ficoll gradients and incubated under varying conditions of ionic concentration, and under conditions which provided data for determination of Vmax and Km values. The accumulation rates of gly, ala, arg, leu, val, pro, asp, ser and thr all changed progressively with age, but the direction and pattern of the change varied from one amino acid to another. The uptakes of thr, ser and valine in Na^+-free medium, increased progressively with the age of the animal, whereas the uptakes of leu and arg in Na^+-free medium decreased. The rate of gly accumulation appeared to be a bimodel function of age, it being maximal between the 12-18th day. The greater uptake of gly during this period was characterized by a higher value for Vmax and a lower value for Km. The greatest net change during development was observed with thr; the accumulation of this amino acid increased nearly 8 fold during the first 15 postnatal days. The differences between newborn and adult animals in thr accumulation was characterized by a higher Vmax in the latter. The Km value for the transport was lower in the adult animal, but the magnitude of the difference was dependent on incubation temperatures. Plots of log Km vs the reciprocal of absolute temperature yielded values for ΔH° of 5600 cal for the newborn animal and 2520 cal for the adult animal.

60.2 THE EFFECT OF AMINO ACIDS AND OTHER PUTATIVE NEUROTRANSMITTERS ON THE CALCIUM BOUND TO SYNAPTIC MEMBRANES. A.T. Tan* (SPON: G. Mandl), Dept. of Research in Anaesthesia, McGill University, Montreal, Canada.

A fluorescent chelate probe, chlorotetracycline, or radioactive calcium-45 was used to study calcium bound to synaptic membranes isolated from guinea-pig brain. Amino acids with strong excitant properties displaced some of the membrane-bound calcium. The order of displacement potency - DL-homocysteic acid, N-methyl-DL-aspartic acid > L-aspartic acid, L-glutamic acid, N-methyl-DL-glutamic acid, L-cysteic acid > D-glutamic acid - corresponds approximately to that of their excitatory potency when tested on central neurons. Serotonin, dopamine, and d-tubocurarine chloride also mobilize the membrane-bound calcium, but to a lesser extent; whereas acetylcholine, noradrenaline, histamine, L-dopa and eighteen other amino acids, including glycine, glutamine and γ-aminobutyric acid are ineffective. Changes in pH in the range 7.4-3.0 do not alter the amount of membrane-bound calcium. These observations, which cannot be explained by chelation alone, suggest that the acidic amino acids have a specific ability to mobilize membrane-bound calcium; this is consistent with the proposed role of some of these compounds as excitatory transmitters in the central nervous system. (Supported by the Medical Research Council of Canada)

60.3 A UNIQUE DISTRIBUTION OF ASPARTATE IN FOUR GIANT AXONS OF THE CENTRAL NERVOUS SYSTEM OF THE LOBSTER. M.H. Aprison, A.R. Freeman, W.J. McBride, and L.T. Graham, Jr. Sections of Neurobiology and Neurophysiology, The Institute of Psychiatric Research and Departments of Biochemistry, Physiology and Psychiatry, Indiana University Medical Center, Indianapolis, Indiana 46202.

With the technique of gas-liquid chromatography, we have measured the distribution of alanine, proline, glycine, GABA, glutamate and aspartate in: (a) individual ganglia (the supraesophageal ganglion and the next 5 thoracic ganglia); (b) the associated nerve bundles between these ganglia; (c) the external cellular sheath between the supraesophageal ganglion and first thoracic ganglion and (d) 4 giant axons in the connective between these 2 ganglia after each tissue sample was isolated from 1.0 kg lobsters (Homarus americanus). GABA and aspartate content varied the most among the individual ganglia whereas the other amino acids varied little. Some variability in content of individual amino acids did occur in individual connectives. Glycine was the highest and GABA the lowest in both the ganglia and connectives. In the external cellular sheath, glycine was again highest (2.4, 3.7, 4.9 and 650 times higher than the levels of alanine, proline, glutamate and aspartate, respectively). In contrast, aspartate was present in highest amounts in the 4 giant axons. In the largest giant axon, the aspartate level was 3.8, 8.2, 9.8 and 35 times higher than the level of glycine, alanine, glutamate and proline, respectively. The pattern was the same for the other 3 axons. This asymmetric distribution of aspartate in neuronal elements as opposed to non-neuronal elements and its high content in the 4 giant axons may point to some specialized function for aspartate. This investigation was supported in part by funds from research grants GB-28715-X (NSF), MH 03225-13,14 (NIMH), the Scottish Rite Foundation.

60.4 CHANGES IN AMINO ACID COMPOSITION OF EXCISED TOAD BRAIN IN RESPONSE TO HYPEROSMOTIC MEDIUM. Joycelyn T. Whiten* and Claude F. Baxter. Neurochem. Labs, V.A. Hospital, Sepulveda 91343; Dept. Neuroscience, UCLA Sch. Med., Los Angeles 90024.

Excised whole brains of the toad, Bufo boreas, were incubated at 24°C for periods up to 6 hours in aerated isosmotic (AI), aerated hyperosmotic (AH) and non-aerated glucose-free hyperosmotic (NH) Ringer-like media. Changes in the concentration of 7 amino acids in the brain tissues were measured. In AI medium, the concentration of GLY, ALA and SER remained constant, ASP, GLU and GLN declined, and GABA levels were elevated. By comparison, in AH medium (400 mOs, pH 7.3: 10 mM urea, 180 mM NaCl, 25 mM $NaHCO_3$, 2 mM glucose, 2 mM KCl, 3 mM KH_2PO_4, 1 mM $MgCl_2$, 1 mM Na_2SO_4, 1 mM $CaCl_2$), levels of all amino acids, excepting ASP and GLN, increased. Although these changes in amino acid concentration differed from those observed in brains of toads adapted to an hyperosmotic environment in vivo (Baxter and Ortiz, Life Sci. 5, 2321, 1966), they could not be attributed to post-mortem changes. Levels of all amino acids in brains suspended in NH medium declined sharply. None of the changes reported here were the consequence of hydration or dehydration of the brain tissues. In isosmotic and hyperosmotic media, urea concentration in the isolated brain decreased by 50% within fifteen minutes of incubation. Substitution of mannitol for urea in the medium did not affect the decrease. The possibility that urea may serve as a source for nitrogen in the synthesis of amino acids in the isolated toad brain is under investigation. (Supported in part by NIH Grant NS 03743.)

60.5 DEPOLARIZING ACTION OF SUBSTANCE P IN THE CUNEATE NUCLEUS OF THE CAT. K. Krnjevic and Mary E. Morris, Dept. of Research in Anaesthesia, McGill University, Montreal, Canada.

The recent availability of pure synthetic Substance P has made it possible to re-examine more critically the hypothesis that Substance P is the main excitatory transmitter released by primary afferent fibres. Substance P (kindly given by Dr. S. Leeman, or purchased from Beckman Instruments Ltd.) was made up in solution of 10 mg/ml, acidified to pH 5-6; it was released electrically from compound micropipettes while recording spontaneous or evoked discharges. The presumed release of Substance P by outward currents (20-200nA) was frequently quite ineffective; but in certain cases, there was a delayed and slowly progressive increase in excitability, which persisted for several minutes after the end of the release, and was ultimately reversible; this was associated with a partial inactivation of responses evoked by L-glutamate. In other cases, the increase in excitability was transient or even absent, and the inactivation the predominant effect. These observations thus lend only partial support to reports that Substance P has a strong depolarizing action on central neurones innervated by dorsal root fibres. The great variability and slow time course of action do not seem consistent with the proposed transmitter function, though Substance P, if released naturally, evidently could strongly influence the responsiveness of certain neurones of the primary afferent relay.

Supported by the Canadian Medical Research Council.

60.6 VARIATION OF ENDOGENOUS AND EXOGENOUS PIPERIDINE IN THE BRAIN OF ACTIVE AND DORMANT SNAILS. Hana Dolezalova*, Matej Stepita-Klauco* and Ezio Giacobini*. (SPON: V. H. Denenberg). Dept. Biobehavioral Sciences, Univ. of Connecticut, Storrs, CT. 06268.

The distribution of endogenous piperidine and exogenous ^{3}H-piperidine in the brain and other tissues of the snail was studied by liquid scintillation and by a quantitative mass spectrometric method which can measure piperidine in amounts as small as 10^{-11}moles. Of the snail body, the brain contained the highest concentration of endogenous piperidine, 3,3 pmoles/mg, as compared to 2,0 pmoles/mg in intestine, 1,2 pmoles/mg in heart and muscle, and 0,6 pmoles/mg in liver, (Brain Res. 54, 1973). The concentration ratio between brain and blood was 50:1. When ^{3}H-piperidine was injected (1,8 x 10^{-9}mole), however, the brain contained the lowest amount of ^{3}H-piperidine, 0,125 pmoles/mg as compared to 27,1 pmoles/mg in kidney, 4,67 pmoles/mg in heart, and 3,12 pmoles/mg in liver. A blood/brain barrier for ^{3}H-piperidine maintained the concentration of ^{3}H-piperidine five times higher in the blood than in the brain. ^{3}H-piperidine was not metabolized in the brain or in body organs, and was excreted unchanged by the kidney. When active and dormant (in experimentally induced hibernation) snails were compared, the amount of endogenous piperidine was five times higher in the brain of dormant snails than in the brain of active snails and its concentration in the blood was about 3,75 times higher in dormant snails than in active snails. The higher rate of piperidine synthesis in the brain occuring during the hibernations suggests a possible involvement of piperidine in the sleep mechanism of the snail.

This investigation was supported by the University of Connecticut Research Foundation, grant no. 35-073.

61.1 CHARACTERISTICS OF THE BINDING OF ^{3}H-NALOXONE IN THE MOUSE BRAIN. Robert J. Hitzemann* and Horace H. Loh* (SPON: Harry Avis). Langley Porter Neuropsychiatric Institute and Dept. of Pharmacology, Univ. of Calif., San Francisco, Calif. 94122.

Pert and Snyder (Science 179:1011, 1973) have suggested that ^{3}H-naloxone may be used to measure the stereospecific binding of narcotic agonists in the rat brain. In the present study, we have examined the binding of ^{3}H-naloxone in the P_2 fraction of the whole mouse brain. Levorphanol (10^{-8} M) competitively inhibits the binding of ^{3}H-naloxone (10^{-7} to 5×10^{-9} M) in a 50 mM Tris buffer pH = 7.4. Kinetic data indicated levorphanol replaced ^{3}H-naloxone on a 1 for 1 basis. Dextrorphan was found to be 1/500 as potent as levorphanol. Concentrations of 10^{-7} M levorphanol and above were not able to block 30% of the ^{3}H-naloxone (2×10^{-8} M) binding suggesting that this binding is non-specific and non-narcotic related. P_2 pellets were rehomogenized in 20 mM Tris (pH = 7.4) and the effect of various cations on the binding of ^{3}H-naloxone and on the inhibition of binding by levorphanol was measured. 120 mM Na+ enhanced the binding of ^{3}H-naloxone 85% but abolished the inhibitory effect of levorphanol. 120 mM Li+ enhanced ^{3}H-naloxone binding but did not alter the effect of levorphanol. 120 mM K+ and NH_4+ had no effect on the binding of ^{3}H-naloxone or on the effect of levorphanol. Divalent cations blocked the binding of ^{3}H-naloxone with the order of potency being Ca++ > Mn++ > Mg++. The inhibitory effect of 4 mM Ca++ was reversed by prior digestion with neuramidase. Trypsin, phospholipase A and 0.1% triton but not phospholipase C, neuramidase or α-chymotrypsin blocked the binding of ^{3}H-naloxone.

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61.2 THE OPIATE RECEPTOR: INFLUENCE OF ENZYMES, IONS AND DETERGENTS. Gavril W. Pasternak* and Solomon H. Snyder (SPON: M. J. Kuhar). Dept. Pharm. and Exptl. Ther., Johns Hopkins Sch. of Med., Baltimore, Md. 21205.

The pharmacologically relevant opiate receptor can be assayed by the stereospecific binding of ^{3}H-opiates or their antagonists to rat brain homogenates (Pert and Snyder, SCIENCE 179: 1011, 1973). Analgesic effects of opiates are antagonized by calcium and enhanced by EDTA. Specific opiate receptor binding in rat brain homogenates is markedly enhanced by EDTA, EGTA and citrate. Calcium ion (5 mM) inhibits binding 50%. Trypsin and chymotrypsin reduce binding with respective ED_{50} values of 0.5 and 0.6 μg/ml. Dose-response relationships for both enzymes are non-linear, indicating more than one population of sensitive sites. Trypsin reduces the number of receptors, while chymotrypsin merely decreases their affinity. Receptor binding is drastically diminished by very low concentrations of commercial phospholipase A (ED_{50} - 0.05 μg/ml), is decreased by higher concentrations of phospholipase C and is insensitive to phospholipase D. Neuraminidase, in concentrations sufficient to liberate 98% of membrane bound sialic acid, has no effect. Detergents such as Triton X-100, Na dodecylsulfate, and deoxycholate, at concentrations too low to solubilize integral membrane proteins, completely abolish receptor binding. Affinity columns with opiate ligands have been synthesized and utilized for purification studies of the opiate-receptor complex. (Supported by NIMH Drug Abuse Research Center Grant DA-00246 and the Mutual of Omaha and the United Benefit Life Insurance Companies through the Insurance Medical Scientist Scholarship Fund to G.W.P.)

61.3 MORPHINE MODIFICATION OF BRAIN AMINO ACID LEVELS. L. Miller* and J. Harris. Dept. Neurobiol., Barrow Neur. Inst., Phoenix, 85013 & Dept. Chem., Ariz. St. Univ., Tempe 85281

Brain amine and pyridoxal phosphate (PyP) levels are changed by certain substances (1) which also modify the signs of precipitated morphine abstinence (2). In this series of experiments, high doses of PyP reduced the signs of precipitated abstinence in morphine dependent rats. We also found (3) that 30 minutes after acute morphinization there were increased levels of tyr, leu, i-leu, val and gly in brain while glu and taur decreased. After chronic morphinization his, asp, glu, gly, thr, taur, and ser + asn + gln decreased ($p<.05$).

Some of the amino acid changes could be mediated by the inhibition of norepinephrine (NE) reuptake into synaptosomes (4), resulting in free NE which competes for PyP of transaminases (5). Other changes could be mediated by morphine altered citric acid cycle activity (6). (Supported by PHS Grant MH 19382)

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61.4 EFFECTS OF MORPHINE ON CATECHOLAMINE TURNOVER, CYCLIC 3',5'-AMP CONCENTRATIONS AND TYROSINE HYDROXYLASE ACTIVITY IN RAT TISSUES. A. Carenzi* E. Costa, A. Guidotti* and A. Revuelta*. Lab. Preclinical Pharmacology, NIMH, Saint Elizabeths Hosp., Washington, D. C. 20032

The injection of morphine (from 13 to 52 μmoles/kg i.p.) fails to change the turnover rate of norepinephrine (NE) in spinal cord and cerebellum. An analgesic dose of morphine (52 μmoles/kg) increases significantly the turnover rate of striatal dopamine (DM). An increase of striatal DM turnover rate can be associated with either a stimulation of dopaminergic receptors (as described for amphetamine, Brit. J. Pharmacol. 44: 742, 1972) or a blockade of these receptors (as described for chlorpromazine, Handbook of Neurochemistry 4: 45, 1970). To decide the functional significance of the increase of striatal DM turnover rate we measured cyclic 3',5'-AMP (cAMP) concentrations in striatum of rats receiving either amphetamine (3.2 μmoles/kg i.p.) or morphine (26 to 260 μmoles/kg i.p.). We found that amphetamine and morphine (104 μmoles/kg i.p.) significantly increase the cAMP concentrations in striatum. Amphetamine failed to increase the cAMP concentrations in pituitary, adrenal cortex and medulla. In contrast, morphine increased the cAMP concentrations in adrenal medulla (52 μmoles/kg i.p.) and in higher doses (104 μmoles/kg i.p.) in pituitary and adrenal cortex. The significance of the second messenger increase is now being investigated. We have found that chronic morphine (1950 μmoles/kg in pellets) fails to increase the cAMP concentration in adrenals at the time in which the rats are tolerant to and dependent on morphine. Chronic morphine potentiates the increase of cAMP content of adrenal medulla elicited by cold. A single dose of morphine induces the tyrosine hydroxylase activity in adrenal medulla but not in striatum. Chronic morphine does not induce tyrosine hydroxylase activity in adrenal medulla.

61.5 EFFECTS OF MORPHINE ADMINISTRATION ON THE INCORPORATION OF URIDINE-^{3}H INTO BRAIN NUCLEOTIDES AND RIBONUCLEIC ACID. R. Adron Harris and Louis S. Harris. Depts. of Pharmacology, Univ. of North Carolina, Chapel Hill, N.C. 27514, and Medical College of Virginia, Richmond, VA 23219.

Swiss Webster mice were injected either intraperitoneally (i.p.) or intraventricularly (i.vent.) with uridine-5-^{3}H or orotic acid-5-^{3}H and after 30 min. or 24 hrs. the amount of radioactivity in total brain homogenate and in brain ribonucleic acid (RNA) was determined. The incorporation of radioactivity into RNA was calculated as (DPM in RNA)/ (DPM in total homogenate-DPM in RNA). The incorporation of i.p. injected uridine-^{3}H into brain RNA was decreased by acute administration of 30 or 100 mg/kg morphine sulfate and by chronic administration of morphine by the pellet implantation method. In contrast to the effects on brain RNA, the incorporation of uridine-^{3}H into liver RNA was not affected by chronic morphine administration. Neither acute nor chronic morphine treatment altered the incorporation of uridine-^{3}H or orotic acid-^{3}H into brain RNA when these precursors were injected i.vent. After short-term morphine pellet implantation (4 hrs), the conversion of i.p. injected uridine-^{3}H to uracil was increased while its conversion to uridine diphosphoglucose and uridine diphospho-N-acetylglucosamine was decreased. After long-term morphine pellet implantation (72 hrs.), the incorporation of uridine-^{3}H into uridine diphosphoglucose, uridine monophosphate, uridine diphosphate, and uridine triphosphate was decreased. These findings suggest that decreased incorporation of uridine into brain RNA may not be related to the development of tolerance or physical dependence, although alterations in the metabolism of uridine nucleotides and their derivatives may be related to the development of tolerance and physical dependence. (Supported in part by DA-300036-05).

61.6 NEUROPHYSIOLOGICAL CORRELATES OF HEROIN ADDICTION IN SQUIRREL MONKEYS. S. Jacobs*, Dept. of Bio Sci., UCSB, Santa Barbara, E.T. Angelakos*, Dept. of Physiol. and Bio Phys., Hahnemann Med. Col., Phila., and P. Lomax*, Dept. of Pharmacol., UCLA, Sch. Med., Los Angeles (SPON: T. Estrin, BRI, UCLA, Sch. Med., Los Angeles).

Chronically implanted squirrel monkeys were addicted to and withdrawn from heroin in an attempt to establish an electrophysiological end-point of both tolerance and withdrawal by recording single unit activity from the anterior cingulate cortex (area 24). This area, along with the cingulum bundle, have been implicated in the modification of the addictive process from studies of the effects of bilateral cingulotomy on humans for the relief of chronic disabling pain (Foltz, Ariz. Med. 6:1033, 1969). Nine-wire tungsten microelectrode arrays were stereotaxically inserted into the anterior cingulate cortex. Heroin HCl (5 mg/kg i.p.) was administered every 12 hours for 2 days, then 10 mg/kg every 12 hours for 2 days and finally 15 mg/kg every 12 hours for 2 days. Unit activity was recorded following each injection, and dependence was determined on the sixth day by challenging the animal with naloxone (3 mg/kg i.p.) which precipitated a withdrawal syndrome including hypothermia, salivation, agitation and escape-avoidance behavior. The bursting activity (60 impulses/sec. every 1.5 sec.) which is typical of area 24 (Jacobs and Lomax, Fifth Intern. Cong. Pharm., July, 1972), became periodic with a mean frequency of 32 impulses/sec. during the development of tolerance, but following withdrawal unit activity returned to the control level, except for the onset of an additional unit which characteristically appeared during the development of tolerance and remained following complete withdrawal. Supported by U.S. Navy Grant N00014-72-A-0317-001.

61.7 EFFECTS OF MORPHINE AND ANTAGONISTS ON HYPOTHALAMIC NEURONE ACTIVITY IN NAIVE AND ADDICTED RATS. Joseph N. Triplett*, George W. Beeler*, and Frederick W. L. Kerr. Sections of Neurologic Surgery and Biophysics, Mayo Medical School, Rochester, Minnesota, 55901.

The effects of morphine and of nalorphine and naloxone on the activity of populations of neurons in the brains of naive and addicted rats has been studied. Stereotaxically guided steel microelectrodes were used to record the activity of three (or more) single units simultaneously in two separate target areas; units were held for periods of 20 minutes and longer. The activity was stored on magnetic tape, units separated by window discriminators and computer generated firing frequency histograms obtained. Morphine administered intravenously consistently produced excitation of neurons in the Ventromedial hypothalamic nucleus (H.V.M.) and, with one exception, marked inhibition of neurons in the Lateral hypothalamic area (L.H.A.). These effects were consistently reversed by administration of antagonists. Nuclei having connections with the above nuclear groups showed the same pattern of response; thus, the amygdala responded in a similar manner to the H.V.M. and the ventral tegmental area responded as the L.H.A. Responses from the cerebral cortex were variable.

The effects obtained were similar in the naive and the addicted rats.

It is concluded that morphine and its antagonists have highly specific effects on individual nuclei, this being particularly prominent in the H.V.M. and L.H.A. where diametrically opposite responses occur. The relationship of these nuclei to appetitive drives and the hypothesis that craving for narcotics may be due to specific effects on these areas receives some further support.

61.8 CNS SITES OF MORPHINE ACTION: HYPO- OR HYPER-ALGESIA DEPENDING ON INJECTION SITE AND DOSE. Yasuko F. Jacquet* and Abel Lajtha. NY State Research Institute for Neurochemistry and Drug Addiction, Ward's Island, New York, N.Y., 10035.

Morphine is used therapeutically as an analgesic; yet very little is known about its CNS sites of action. Assays of different CNS regions following systemic administrations of morphine have failed to reveal any marked differential distribution of the drug. This may be due to the action of the "blood-brain" barrier, since it has been estimated that less than 0.1% of the administered dose reaches the CNS. By using fine-gauge cannula permanently implanted in various subcortical sites to inject morphine, we were able to deliver precise quantities of the drug to the intended sites. Morphine (10 μg) injected into the posterior hypothalamus (PH) and the 3rd ventricle resulted in signficant hypo-algesia, while the same dose injected into the caudate, the medial septal nucleus, and the periaqueductal gray matter (PGM) in the mesencephalon yielded hyper-algesia. Of the latter three, the last resulted in the most marked hyper-algesia, with rats unable to tolerate a low level of foot shock which normal rats tolerate without even flinching. This same area has been reported to give rise to profound analgesia when electrically stimulated. Morphine has been shown to block the release of acetylcholine in peripheral and central tissues; thus its action here may be the opposite of electrical stimulation and may block cholinergic neural transmission in what has been suggested to be pain-inhibitory pathways.

These results show that intracerebral injections of morphine differ in a significant manner from systemic injections of morphine, and result in either hypo- or hyper-algesia, depending on site and dose. These sites show specificity in that dextrorphan, the inactive isomer, had no effect at either the hypo- (PH) or hyper- (PGM) algesia sites.

61.9 LOCALIZATION IN THE PRIMATE BRAIN OF THE ANTINOCICEPTIVE ACTION OF MORPHINE. Tony L. Yaksh and Agu Pert. Medical Research Division, Biomedical Laboratory, Edgewood Arsenal, MD 21010 USA

Complete understanding of the antinociceptive action of morphine requires that the precise structures associated with this action be known. The definitive localization of this drug-function relationship in the primate brain has not been reported. To accomplish this aim, rhesus monkeys were implanted with arrays of 22 ga stainless steel guide cannulae into various CNS regions. Following recovery, microinjections of morphine sulfate (5-40 μg) were made using 28 ga injector cannulae extending 2 to 14 mm below the tip of the guide. Following completion of the mapping series, the cannula sites were located according to standard histological procedure. To measure the nociceptive threshold, the shock titration technique was employed (Weiss and Laties, Science, 128, 1575, 1958). In this paradigm electric shock, applied to the foot pads, was increased by 0.16 ma every 2 seconds. The animal, by responding on an available lever, was able to decrease the shock by an equal amount with each response. Analysis of the data collected at over 300 sites revealed that reliable analgesia could be elicited by injections at sites located within the periventricular, periaqueductal grey region of the brain stem. Specificity of this effect was verified both by the absence of effect following injections of the vehicle and by the immediate reversal of the analgesia by injection of naloxone either at the active site or intravenously (1-5 mg/kg). Injections in the same stereotaxic plane but more lateral or dorsal had no effect. Further, the application of morphine in doses as high as 80 μg had no effect when given into the septum, caudate nucleus, cortex, superior or inferior colliculi, thalamic nuclei (including the anterior and postero-lateral nuclear groups) or any fiber tracts including the corpus callosum, the fornix or the mammillo-thalamic tract.

61.10 EFFECT OF CINGULATE CORTEX LESIONS ON MORPHINE INTAKE IN PREMEDICATED AND NON-PREMEDICATED RATS. Clinton L. Trafton and Marcia Kahn*. Dept. Psych., Univ. of Arizona, Tucson 85721

Rats given anterior cingulate cortex lesions were randomly divided into two groups. One group was subjected to premedication with increasing doses of morphine over a twenty-day period. A second group was given an equal number of saline injections. Other rats given control operations were either premedicated with morphine or given saline injections to form two additional groups. All rats were then tested on ten, four-day cycles of no fluid (day 1), morphine solution only (day 2), water only (day 3), and morphine vs. water choice (day 4). Cingulate cortex lesions resulted in reduced morphine solution drinking on both day 2 and day 4 of the ten cycles. Non-premedicated rats with cingulate lesions in fact, completely rejected morphine solutions throughout the tests, although non-premedicated without cingulate lesions showed steadily increasing morphine intake throughout the tests. Thus, cingulate cortex lesions reduce morphine intake and the reduction is much greater in rats not previously premedicated with morphine injections.

61.11 EFFECTS OF DISCREET CNS LESIONS ON MORPHINE ADDICTION. Greg Little*, Kenneth Robinson,*, Pat D'Encarnacao* and Paul D'Encarnacao. (SPON. C.J. Long) Dept. of Psych., Memphis State Univ., Memphis, TN 38152.

Recent interest in the area of narcotic addiction has centered around the CNS site of action of the drug. Since several researchers have attempted to implicate different structures, this study was carried out to evaluate the significance of the various structures in narcotic addiction. Male albino rats had RF lesions placed stereotaxically in 1) the corpus striatum (CS) (Snyder & Pert, 1973), 2) the anterior thalamus (AT) (Buxbaum, 1971; Wei, Loh & Way, 1972; Masserano, Little, D'Encarnacao & D'Encarnacao, 1972); 3) ventral medial nucleus of the hypothalamus (VMN) (Kerr & Pozuelo, 1971). All animals were injected three times daily for 14 days with an increasing dosage of morphine sulfate. Injection schedule began with a 10 mg/kg dose and ended with 100 mg/kg. All animals were run for 30 minutes daily, in automated photoelectric activity cages after the final daily injection. At the end of the experimental period, the animals were challenged with naloxone and two observers graded their behavior under blind conditions using a withdrawal checklist. The results of the study indicated that there was little difference between the three experimentally lesioned groups, i.e., CS, AT and VMN. They did however differ quantitatively from the normal non-operated control. The conclusion reached was that a combination of CNS structures appears to be responsible for morphine addiction.

61.12 BLOCKADE OF DRINKING OF A MORPHINE SOLUTION BY HYPOTHALAMIC LESIONS AND 6-HYDROXYDOPAMINE (6-OHDA) INFUSIONS IN RATS. Z. Amit and Michael E. Corcoran† Dept. Psychol., Sir George Williams Univ., Montreal, and Dept. Psychiat., Univ. British Columbia, Vancouver.

Two stage bilateral electrolytic lesions of the ventral portions of the lateral hypothalamus were found to block completely the drinking of a morphine solution (0.5mg/ml) in male albino rats. The morphine solution was presented to the animals as their only available fluid with free access to standard lab chow. Animals with ventral hypothalamic lesions refused to drink morphine even after being in total deprivation for over seven days and a loss of more than 25% of their free feeding weight. Lesions of the more dorsal aspects of the lateral hypothalamus did not have any effect on morphine drinking and animals with these lesions began drinking morphine after a mean latency of 24 hours. Intraventricular infusions of 6-OHDA given twice on two consecutive days in a dose of 200 ug each day resulted in an effect similar to the one obtained with ventral lesions. These animals refused to drink morphine even after a loss of over 25% of their ad-lib weight. Both lesioned and infused animals drank readily a quinine solution (0.5mg/ml) after a mean latency of 48 hours. Six days of experience with drinking of morphine prior to the induction of lesions abolished the effects of the lesions.

61.13 THE CHOLINERGIC SYSTEM AND NOCICEPTION IN THE PRIMATE: INTERACTIONS WITH MORPHINE. Agu Pert. Experimental Medicine Branch, Biomedical Laboratory, Edgewood Arsenal, MD 21010 USA

The involvement of the cholinergic system in nociception and in morphine induced analgesia in the rhesus monkey was investigated employing the shock titration technique (Weiss and Laties Science, 128, 1575, 1958). Five classes of cholinergic compounds were examined for antinociceptive properties: muscarinic agonists, nicotinic agonists, antimuscarinics, antinicotinics, and anticholinesterases. Only antimuscarinic and anticholinesterase compounds were found to be effective antinociceptive agents. Scopolamine, at relatively low doses (.05 - 0.25 mg/kg IV), had a strong antinociceptive effect which lasted approximately 4-6 hrs. Physostigmine was effective only at high doses (0.25 mg/kg IV). The onset of action of this anticholinesterase compound was almost immediate but the antinociceptive effect lasted only 30-45 min. The peripherally acting analogs of these two compounds were ineffective at equipotent doses, indicating that the actions of scopolamine and physostigmine were mediated through the CNS. It appears that disruption of normal muscarinic-cholinergic CNS activity by either scopolamine or physostigmine may be sufficient to produce antinociception in the primate. Both physostigmine and scopolamine were found to potentiate the analgesic actions of morphine. Scopolamine appeared to exert an additive effect. In addition, it was found that tolerance to the analgesic actions of morphine, through repeated administrations, transferred to scopolamine (cross-tolerance), whereas production of tolerance to scopolamine was relatively ineffective in producing tolerance to morphine. The findings are discussed in light of the possibility that cholinergic compounds and morphine exert their antinociceptive properties through independent, although possibly convergent, substrates of the CNS.

61.14 MORPHINE WITHDRAWAL SYNDROME: SIMILARITY TO THERMOREGULATORY BEHAVIOR. E. Wei*, L.F. Tseng*, H.H. Loh* and E.L. Way* (SPON: N. Lee). School of Public Hlth., Univ. of Calif., Berkeley, Calif. 94720 and Dept. of Pharmacology, Univ. of Calif., San Francisco, Calif. 94122.

The brain areas where naloxone precipitates withdrawal in the morphine-dependent rat appear to be closely adjacent to brain pathways of heat dissipation and heat gain. During precipitated withdrawal at room temperature teeth chattering, wet shakes, vasoconstriction, ptosis and a huddled position may be observed. Such behavior may reflect activation of heat gain mechanisms. Other withdrawal signs are salivation, the active spreading of saliva on the body fur by licking and escape behavior. These latter signs are characteristic of heat loss mechanisms. To test this hypothesis, male Sprague-Dawley rats, rendered dependent on morphine by standardized procedures (Psychopharmacologia 28:35, 1973) were withdrawn by naloxone injection at low (10 C), medium (23 C) and high (33 C) ambient temperature. Withdrawal signs characteristic of heat gain behavior were increased at low ambient temperature. Similarly, withdrawal signs characteristic of heat loss behavior were increased at high ambient temperature. It is postulated that the abstinence syndrome, in part, reflects an imbalance in central thermoregulatory mechanisms, and that certain drugs which modify some abstinence signs may do so via indirect effects on thermoregulation.

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62.1 ELECTROPHYSIOLOGICAL MEASUREMENT OF THE NUMBER OF RHODOPSIN MOLECULES IN LIMULUS VENTRAL PHOTORECEPTOR CELLS. J.E. Lisman* and H. Bering* (SPON: G. Wald) Harvard Univ. Cambridge, Mass. 02138

Two methods were employed for measuring the number of rhodopsin molecules (R) in single photoreceptors. One method is based on measurements made with an intracellular microelectrode: specifically we determined the attenuation of 0.5 msec. flash required to just saturate the ERP, and the attenuation at which one quantum bump was evoked. From the ratio of these attenuations we computed $R = 5\text{-}10 \times 10^8$. In the second method, a calibrated photodiode was used to determine the absolute light energy required to evoke a quantum bump. $1.5 \pm 0.5 \times 10^3$ photons at 530 nm were incident per photon absorbed (assuming a quantum efficiency of excitation of 0.65). Assuming for the visual pigment a molar extinction of 40,000, $R = 10\text{-}20 \times 10^8$. The saturated R_2 of the ERP was 3 mv. Given a capacitance of 0.004-0.01 μf, the voltage could arise from the displacement of a single charge on rhodopsin of the order of 5Å.

62.2 CONTROL OF MEMBRANE PERMEABILITY IN A HYPERPOLARIZING PHOTORECEPTOR: SIMILAR EFFECTS OF LIGHT AND METABOLIC INHIBITORS. John S. McReynolds and A.L.F. Gorman*, NIH Bethesda, Md. 20014, and Boston University, Boston, Mass. 02118.

The distal photoreceptors of the mollusc Pecten irradians have a low resting potential (10-40mV) in darkness and respond to illumination with a large hyperpolarization of up to 70mV in amplitude. We have shown that this receptor potential is due to a selective increase in K^+ permeability. The low resting potential results from a relatively high P_{Na}/P_K ratio, which appears to be due to a low K^+ permeability, rather than a high Na^+ permeability as in vertebrate photoreceptors. Furthermore, the low K^+ permeability may be maintained by an active process requiring metabolic energy. Evidence for this comes from the observation that the metabolic inhibitors 2,4-dinitrophenol (DNP) and cyanide rapidly and reversibly increase P_K and hyperpolarize the cell, similar to the effect of light. These agents are known to raise intracellular Ca^{++} in cells by interfering with the energy production necessary for Ca^{++} pumping. Since an increase in intracellular Ca^{++} has been shown to increase P_K in other neurons, we suggest that the increase in P_K caused by DNP and cyanide, and possibly that caused by light, is mediated by an increase in intracellular Ca^{++} concentration.

62.3 STRUCTURAL CHANGES ASSOCIATED WITH ILLUMINATION IN THE APLYSIA GIANT NEURON. Maryanna Henkart, Nat. Inst. Hlth., NICHD, Bethesda, Md. 20014

The giant neuron (R_2) of Aplysia hyperpolarizes in response to light (Chalazonitis, Photochem. Photobiol. 3: 539, 1964). Brown and Brown (Science 178: 755, 1972) reported that this hyperpolarizing light response is due to an increase in K^+ conductance (g_K) of the membrane and suggested on the basis of other evidence that the action of light on g_K might be mediated by an increase in internal [Ca^{++}]. Chalazonitis suggested that "lipochondria" granules (LG) in R_2 contain the photopigment mediating the light response. This is a report of an EM study of R_2 LG in light and dark. LG in cells prepared in the dark (dim red light) appear uniformly granular and contain a fine electron-opaque precipitate. In cells incubated in physiological saline with Sr substituted for Ca many LG contain a more coarse and denser-appearing ppt. In cells prepared in white light some LG remain like those in the dark, but some are converted to concentric layers of membranes in which no ppt is visible. Intermediate forms including paracrystalline arrays of globular particles, areas of globular particles interspersed with small vesicular profiles, and membranous vesicles embedded in granular material adjacent to parallel membrane arrays are seen. In both light and dark LG are often found in close association with mitochondria and with cisternae of the endoplasmic reticulum, but although in light the configuration of many of the LG changes dramatically, the appearance of the mitochondria changes only slightly if at all. The appearance of a coarse dense precipitate in LG after Sr treatment suggests that they are capable of accumulating or binding divalent cations, and the striking change in configuration of the LG with a change only in illumination suggests that these structures should be considered a possible source of the intracellular Ca that may mediate the light-induced hyperpolarization.

62.4 SYNAPTIC ORGANIZATION OF THE INNER PLEXIFORM LAYER IN THE RETINA OF THE LARVAL TIGER SALAMANDER. M.T.T. Wong-Riley. Lab. Neurophysiology, NINDS, NIH, Bethesda, 20014

The synaptic morphology and organization of the inner plexiform layer of the larval salamander retina was examined in serial sections with the electron microscope. Amacrine processes always make conventional synapses, while bipolar processes make both ribbon and conventional synapses. For this reason, new and decisive criteria based on the differential morphology of synaptic vesicles and junctional membranes were sought to distinguish between the amacrine and bipolar processes in single sections. Amacrine processes contain a relatively uniform population of small round vesicles and they make symmetrical conventional synapses. Bipolar processes contain vesicles that are generally larger and more pleomorphic than those of the amacrine processes, and they make ribbon and conventional synapses of the asymmetrical type. Amacrine processes synapse upon other amacrine processes, bipolar axons, ganglion cell dendrites, and the perikarya of these three types of cells. Amacrine cells also give rise to somatodendritic synapses. Bipolar processes are presynaptic to amacrine processes, ganglion cell dendrites as well as other bipolar processes, but never on the somata of any cell. Both amacrine and bipolar processes are engaged in serial synapses, and these two groups often make reciprocal synapses with each other.

62.5 FOURIER ANALYSIS OF DYNAMICS OF EXCITATION AND INHIBITION IN THE EYE OF LIMULUS: AMPLITUDE, PHASE, AND DISTANCE. Floyd Ratliff, Bruce W.Knight, Jr., Frederick A.Dodge, Jr., and H.K.Hartline. Rockefeller University, New York, N.Y. 10021

Three basic processes -- excitation, self inhibition, and lateral inhibition -- govern the dynamics of the neural network in the lateral eye of Limulus (Knight et al, J.gen. Physiol., 56, 421, 1970). If I_m is amplitude of sinusoidal modulation of light intensity at frequency f on receptor unit m, the corresponding modulation of generator potential $E_m=G_m(f)I_m$, where $G_m(f)$ is the "transfer function" (amplitude gain and phase of E_m with respect to modulation I_m at the frequency f). To a good approximation, modulation of rate r of unit m is $r_m=E_m-T_S(f)K_m r_m-T_L(f)\Sigma k_{mn} r_n$. Self inhibition is represented by the transfer function $T_S(f)$ scaled by the self inhibitory coefficient K_m. Experiments show that all lateral inhibition may also be represented by a single transfer function $T_L(f)$ scaled by the summed lateral inhibitory coefficients (Σk_{mn}). Rates of discharge of three units were recorded simultaneously. Results: 1) Variation in amplitude of excitation produces proportional variation in amplitude of lateral inhibition on a neighboring unit at a fixed distance, but no phase shift. 2) The amplitude of lateral inhibition varies with distance to the units affected, but there is no phase shift. A partial test of this analysis was made by means of a synthesis (response to square wave computed from transfer functions) compared with results of experiment. There was excellent agreement. The similarity to dynamics of vertebrate eye is discussed.

62.6 CALCULATING THE FULL SPACE AND TIME DEPENDENCE OF NERVOUS ACTIVITY IN THE LIMULUS RETINAL NETWORK. Bruce W. Knight. Rockefeller University, New York, N.Y. 10021

The response of the Limulus retina to a stimulus which has arbitrary space and time dependence may be calculated in a simple way. This is possible because (1) the network is approximately invariant under spatial translations, and (2) its component neural processes may be expressed in terms of well specified linear dynamical relations (see abstract of Ratliff et al). In consequence the response of the entire interacting network, to a stimulus which is a spatial sine wave in uniform motion, will be a sine wave of moving neural activity, whose amplitude and phase-shift follow simply from the known dynamics of the component neural processes, and depend upon the velocity and spatial wavelength of the stimulus. To calculate the response to an arbitrary stimulus, we resolve that stimulus into moving sine waves, whose responses we superimpose. Calculations show strong responses to moving-edge stimuli: responses which become Mach bands in the limit of no motion, and become step-transients (see abstract of Ratliff et al) in the limit of no space-dependence. The method is applicable to other neural networks.

62.7 VISUAL ACUITY OF COMPOUND EYES. Robert B. Pinter* and John Palka (SPON: C.F. Stevens). University of Washington, Seattle, Washington 98195

Precise determination of visual acuity in organisms requires combining the mathematics of Fourier transforms with experimental neurophysiology. Erroneous conclusions have permeated the determination of acuity in the compound eye because of misapplications of Fourier and data processing methods. The earliest attempts to measure acuity involved rectangular gratings containing large artifacts due to edges. Later attempts using radial grating patterns were plagued by low frequency spatial artifacts, and some measurements were made using stimuli which did not have the intended spatial frequency composition. The thrust of these results has been a tenfold overestimation of acuity in the compound eye. An additional reason for use of spatially coherent stimuli is the possibility of measuring an entire Optical Transfer Function, which leads to the determination of the basic optics of the compound eye. We have used rotating precision radial grating intensity patterns as stimuli, and responses have been measured in the descending contralateral movement detector (DCMD), a much studied identified single unit in the ventral nerve cord of locusts. We have obtained responses exclusively from the range of pattern wavelength which our calculations show to be theoretically resolvable by the optical apparatus of a single ommatidium, obviating the need of the multiple aperture theory to explain acuity in the apposition compound eye as proposed by Burtt and Catton in 1965, on the basis of recordings from the locust DCMD. The Optical Transfer Function falls to zero at a pattern wavelength of 1.0° and our experimental determination of the same point falls between 1.2° and 1.5°, conclusively showing that there is even less acuity than that predicted by the single aperture theory. This difference can be ascribed to certain optical and neuronal factors. However, there is reasonable fit of the experimental to the theoretical Optical Transfer Function.

62.8 INTRACELLULAR RESPONSES FROM THE RETINA OF THE CAT. Ralph Nelson*, Astrid v. Lützow*, and Peter Gouras. Lab. of Vision Research, National Eye Institute, NIH, Bethesda, Md. 20014

Although much is known about the structure and connectivity of neurons in mammalian retinas, the physiological properties of most neurons in such retinas remains obscure. We have devised a perfused eyecup preparation of the cat in which it has been possible to record the responses of several kinds of neurons intracellularly and to stain them with the dye procion yellow. The staining has delineated fine cell processes, both axons and dendrites. Eyes enucleated from anesthetized cats were perfused through the ophthalmic artery with oxygenated medium. The cornea and lens were cut away and the vitreous body was removed after enzymatic softening. The resultant eyecup, drained to leave only a thin film of liquid covering the retinal surface, maintained a stable b-wave for up to 6 hours. Fine glass micropipettes filled with 5% procion yellow dye and having impedances of 100 to 300 megohms were advanced through the retina until responses that appeared to be intracellular were obtained. Cells were stained by injections of 5 to 10 nanoamperes of negative current for 1 to 2 minutes and often continued to be responsive after passage of current. The rod and cone inputs to a cell were determined by spectral studies. Several rod-cone horizontal cells and a horizontal cell axon terminal having rod input have been stained in this manner and observed by fluorescence microscopy. In addition we have identified the hyperpolarizing response of a rod bipolar and the depolarizing, rod dominated response of a Müller cell. Several ganglion cells have also been stained.

62.9 SYNAPSES IN THE RETINA OF THE CAT. Edward V. Famiglietti, Jr. and Helga Kolb*. National Eye Institute, N.I.H., Bethesda, Md., 20014.

Two-stage perfusion-fixation with aldehyde mixtures (Reese and Karnovsky, JCB34:207,1967; Famiglietti, BrRes20:181,1970b) has significantly improved the preservation of neuronal processes and synapses in the outer and inner plexiform layers (OPL,IPL) in the retina of the cat. Contacts in OPL between cone pedicles or rod spherules and the two classes of postsynaptic cell are of at least 5 varieties. The ribbon synapse on horizontal cell processes is slightly asymmetrical, and horizontal cells at the ribbon have a complex intercellular structure (cf.Dowling & Boycott, PRSocB166:80,1966; Lasansky, PTransB262:365,1971). Apically, in invaginated bipolar processes and laterally, where the distal junctions of Lasansky are found, there is little density postsynaptically. Basal contacts between cones and bipolars are symmetrical. Synaptic vesicles are associated prominently only with the ribbon synapse. In IPL dyads include asymmetric ribbon synapses at which the bipolar process is presynaptic (cf.Dowling & Boycott, 1966; Dubin, JCN 140:479,1970). Amacrine cell processes make typical, symmetrical "dendrodendritic" synapses on all types of neuronal process in IPL. "Tight" junctions have been reported in both plexiform layers of the rabbit's retina (Raviola & Raviola, AJAnat120:403,1967), and "gap" junctions in OPL of rabbit and monkey (Raviola, pc,1973). In the retina of the cat "gap" junctions are frequent in both plexiform layers. These junctions consist of long, parallel extents of two, closely apposed unit membranes, separated by a gap of about 20Å and accompanied by dense material disposed in varying amounts on the cytoplasmic faces of both membranes. In OPL such junctions, paired with puncta adhaerentia, occur between horizontal cell processes. In IPL often asymmetrical, extremely long, curved "gap" junctions, often associated with dyads, join descending bipolar processes and ganglion cell dendrites in all possible combinations. The likelihood of electrical transmission in the retina and its functional implications will be discussed.

62.10 ANATOMICAL EVIDENCE FOR TWO TYPES OF RECEPTORS IN GROUND SQUIRREL RETINA. Roger W. West. Harvard University, Dept. of Biology, Cambridge, Ma. 02138

Two types of retinal receptor cells can clearly be distinguished in ground squirrel (Citellus mexicanus) by using either light or electron microscopy. The most numerous type (Type I) is well known and has been thoroughly described elsewhere. However, about 10% of the receptors (Type II) have features that differ from Type I receptors in the following ways: 1) they have a more lucent cytoplasm in their pedicles and inner segments; 2) their pedicles are distally displaced from the line of Type I pedicles and are close to their nuclei which are usually confined to the proximal border of the outer nuclear layer; 3) their pedicles receive fewer invaginations than Type I pedicles and the only flat contacts they receive are from Type I receptors; 4) their ellipsoids are completely displaced proximally from the layer of Type I ellipsoids and their outer segments begin at an earlier level. Ground squirrels are green-blue dichromats and exhibit no Purkinje shift. Since Type II receptors maintain their relative numbers across the retina and have no pinching of the edges of the outer segment disks, it is possible that these Type II receptors are blue cones rather than rods.

62.11 MECHANISMS OF DIRECTIONAL SELECTIVITY IN RETINAL GANGLION CELLS OF THE RABBIT. Harry J. Wyatt* and Nigel W. Daw. Department of Physiology & Biophysics, Washington Univ. Med. Sch., St. Louis, Missouri 63110.

Directionally-selective ganglion cells in the rabbit retina have been studied by Barlow and Levick (J. Physiol. 178: 477, 1965). Their results suggest that an inhibitory influence, propagating laterally along the retina in one direction, is the principal cause of the selectivity. We have studied the receptive fields of directionally-selective ganglion cells in the unopened rabbit eye, using repeatable stimuli and accumulating post-stimulus-time-histograms. Experiments with two brief stimulus flashes, separated spatially and temporally, suggest that excitatory influences are an important factor in determining responses of directionally-selective cells.

Experiments with moving stimuli of different dimensions show that, for some cells, directional selectivity is much more precise for a wide stimulus than for a narrow one. For other cells, the most effective stimulus size is smaller than the excitatory area of the receptive field. Post-stimulus-time-histograms also show clear evidence of inhibition of background discharge for movement in the null direction in most cells, suggesting that this may not be a reliable criterion for distinguishing ganglion cells from geniculate cells.

Experiments have been performed to determine the susceptibility of directional selectivity to selective visual deprivation.

62.12 TWO-FLASH RECOVERY CYCLE IN RELATION TO THE SUPPRESSION-RECOVERY EFFECT: EVOKED POTENTIAL AND SINGLE UNIT ANALYSIS IN THE OPTIC TRACT OF THE CAT. Walter Salinger, Dept. Psych., UNC-Greensboro and Carol K. Peck, Pomona College.

The two-flash recovery cycle and the suppression-recovery effect both appear to represent initial responses of the visual system to a rapid increase in light input. In the two-flash recovery cycle, the first flash initiates the retinal response to light onset and the second flash produces an evoked potential which increases in amplitude with the progressive increase in the intervals between the two flashes. In the suppression-recovery effect, a train of flashes at 20 Hz is presented instead of two flashes separated by varying intervals. The response to the first flash in the train is large, the response to the next few flashes are markedly depressed, subsequently there is a progressive recovery in response amplitude which eventually stabilizes at a level somewhat less than that to the first flash. These two response patterns were studied with stainless steel macro- and microelectrodes in cats anesthetized with Nembutal.

The duration of the two-flash recovery cycle was comparable to that of the suppression-recovery effect with the recovery of amplitude of the evoked potential to the second flash in the two-flash paradigm paralleling the recovery phase of the suppression recovery effect. In contrast, single units were found whose activity changes either paralleled the evoked potential dynamics of the suppression-recovery effect (40%) or whose activity changes corresponded to the two-flash recovery cycle (20%). There was virtually no overlap between the two groups of units. This suggests that two different retinal processes may be represented in the activity evoked by the two stimulus patterns.

62.13 OBSERVATIONS ON THE B-WAVE OF THE MAMMALIAN ELECTRORETINOGRAM IN 20 mM POTASSIUM. Barry S. Winkler. Institute of Biological Sciences, Oakland University, Rochester, Michigan 48063.

The role of potassium in the generation of the b-wave of the electroretinogram (ERG) has received increasing attention since the recent suggestion of Miller and Dowling (J. Neurophysiol. 33:323, 1970) that the glial cell of the retina, the Muller cell, may be the site of origin of the b-wave in the mudpuppy retina. Miller (J. Neurophysiol. 36:28, 1973) showed that the b-wave of the ERG of the frog was reduced by increasing the concentration of potassium and correlated this finding with the properties of glial cells elsewhere in the nervous system, e.g., their specific sensitivity to extracellular potassium. The dependence of the b-wave of the ERG of the isolated rat retina upon changes in the concentration of potassium was investigated. The results to date show that the b-wave of the rat retina reacts differently to increases in the concentration of potassium (5-20 mM) than the b-wave of non-mammalian vertebrates. In the rat, raising the concentration of potassium from 5 (control) to 20 mM results in an increase in the amplitude of the b-wave. In 5 mM potassium, the b-wave is abolished by anoxia or by 2 mM cyanide. In striking contrast to these latter results, the b-wave in 20 mM potassium is insensitive to anoxia or to 2 mM cyanide. On the other hand, in 5 or 20 mM potassium the b-wave is abolished by 1 mM iodoacetic acid, a potent inhibitor of glycolysis. The differential effects of anoxia and cyanide in the presence of 5 or 20 mM potassium indicate that the dependence of the b-wave upon aerobic metabolism is markedly reduced in the high potassium medium, while the similarity of the effect of iodoacetic acid suggests that energy yielded by glycolytic mechanisms plays a fundamental role in the production of the b-wave. One possible site for this "regulatory" role of glycolysis is the visual cell synapse.

62.14 EFFECTS OF HYPOXIA ON RETINA, OPTIC NERVE, AND VISUAL CORTEX OF CAT Calvin K. Adams,* Jose M. Perez*, and William W. Dawson. Depts. Psychology, Physiol., and Ophthal., Univ. of Florida, Gainesville, Florida 32601

Cats with chronically implanted electrodes were maintained under neuromuscular block. Respiration values were adjusted to give an expired CO_2 value of 4.0% before hypoxia and maintained at those values throughout the experiment. Following baseline, inspired O_2 was reduced to 8, 10, 12 or 14% for 30-75 min then returned to normal. Xenon flashes were presented in triplets (at 0, 700, 800 ms) under dark adapted or light adapted conditions. Evoked responses from retina (ERG), optic nerve (ON) and visual cortex (CTX) were summed in an averaging computer and scorred for amplitude. Blood samples from femoral artery were analyzed for PO_2, PCO_2, and pH. The earliest and most pronounced hypoxic effects were on ERG b-wave amplitude; reductions at ON and CTX occurred later and were of smaller magnitude. Recovery from hypoxia was most rapid at CTX and ON; ERG b-wave recovery was much slower. At 8 and 10% inspired O_2, severe amplitude reductions were always produced. The b-wave amplitudes were reduced to 0-30% of pre-hypoxia value, the reductions beginning 5-20 min after hypoxia onset; ON and CTX amplitudes were reduced to 0-60% of pre-hypoxia value; the onset of reductions occurred considerably later (20-50 min). At 12% inspired O_2, only moderate (20-70%) reductions in b-wave amplitude were seen, with no significant reductions at ON or CTX. At 14% inspired O_2, no significant amplitude reductions were found at any recording site. Blood gas values showed immediate PO_2 changes proportional to % inspired O_2; small PCO_2 changes, and slow pH changes that were severe (pHs of 6.0-7.0) under 8 and 10% O_2 conditions. The time course of the pH changes and the changes in b-wave amplitude were roughly equivalent. These results extend previous findings on sensitivity of the visual system to hypoxic stress and begin to examine the underlying mechanisms.

65.1 THE DOSE RESPONSE RELATIONSHIP BETWEEN d, and l, TRANYLCYPROMINE AND SELF STIMULATION AT THREE LOCI. Zoltan Annau, Rickye Heffner* and Solomon H. Snyder. Department of Environmental Medicine and Pharmacology. Johns Hopkins University, School of Hygiene and Public Health, Baltimore, Maryland, 21205.

Seven male hooded rats were prepared with three chronic monopolar electrodes each aimed at the septal, anterior lateral and posterior lateral hypothalamic areas. The animals were trained to self stimulate on each electrode and then subsequently were placed in an experimental chamber equipped with three levers. Each lever activated a constant current device that stimulated a specific electrode. The animals lived in these chambers and could self stimulate at any time. Stable baselines were established on all three electrodes by adjusting current to produce approximately equivalent response rates on all three electrodes. Injections of 1,2,4 mg/kg of d, and 2,4,8 mg/kg of l, tranylcypromine were then started with each animal receiving a single dose a week. At the conclusion of the series, electrode preferences were altered by readjusting currents in order to increase response rates on electrodes less preferred in the first series. The animals were then injected with 2 mg/kg d tranylcypromine. The results of both series of injections indicate that regardless of normal preference patterns tranylcypromine potentiates posterior electrodes, followed by anterior electrodes. Septal electrodes are inhibited by the drugs. While the two isomers seem alike in their effect on the three electrodes the d isomer was at least twice as potent in enhancing self stimulation as the l isomer. It is concluded that the potent anti-depressant effects of tranylcypromine may be due to its excitatory effects on specific (posterior) limbic structures combined with its inhibitory effects on other (anterior) structures.

This work was supported by Drug Abuse Center Grant DA-00266 and RSDA Award MH 33128.

65.2 INHIBITORY EFFECTS OF ACETYLCHOLINE (ACh) IN THE LATERAL SEPTAL NUCLEUS (LSN) OF THE CAT. J.F. DeFrance, S.T. Kitai, R.A. McCrea* and H.Yoshihara* Department of Anatomy, School of Medicine, Wayne State University, Detroit, Michigan 48201.

The identities of the neurotransmitters mediating inhibition in the LSN were sought. Cats were anesthetized with either nembutal or surital-chloralose. Field, intra- and extracellular unitary potentials were recorded with microelectrodes following fimbria or hippocampal stimulation.

Hippocampal input to the LSN are monosynaptically excitatory, with the action currents of the target cells presented as the N_3 component of the field response. The typical duration of inhibition of N_3 in Zone I of the LSN is 400-600 msec. The inhibition is polysynaptic, probably mediated via septal interneurons. ACh increase the duration of this inhibition, while reducing the amplitude and elevating the threshold for the N_3 component. Physostigmine and edrophonium (anticholinesterases) also enhance the inhibition. On the other hand, atropine blocks a portion of the inhibition; the early phases being more effected. Moreover, the effects of atropine parallel those of strychnine. Intracellular recordings confirm that atropine and strychnine block some of the IPSP. Hence, it is suggested that ACh may be an inhibitory transmitter in the LSN.

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65.3 MODIFICATION OF INTRALIMBIC EVOKED POTENTIALS BY DIRECT APPLICATION OF CHOLINERGIC DRUGS AND HIGH FREQUENCY STIMULATION OF MIDBRAIN CENTRAL GRAY SUBSTANCE (MCGS). Ronald G. Wiley* and C.A. Berry. Pharmacology Dept., Northwestern Univ. Medical School, Chicago, 60611.

Systemic doses of eserine or central muscarinic agents, such as arecoline or pilocarpine, decrease the amplitude of ventral hippocampal (Hipp) and entorhinal cortex (EG) field potentials evoked by stimulation of the basolateral amygdala (Am). Systemic scopolamine reverses and blocks the effects of eserine and muscarinic agonists on the evoked responses and often enhances the responses. Responses evoked along Am to septum (Sep), Sep-Hipp (both ways), and Hipp-EC (both ways) pathways are not consistently altered by muscarinic drugs (Wiley & Berry, Fed. Proc., 31:250Abs, 1972, and 5th Int. Cong. Pharm., 1510Abs, 1972.) The present study reports that direct application of powdered neostigmine to Am or Hipp thru the center of a hollow macroelectrode causes a profound depression of Hipp responses to Am stimulation which is reversed by systemic scopolamine. Neostigmine applied directly to Am also depresses the EC response to Am stimulation whereas scopolamine methyl nitrate applied directly to Am enhances both Hipp and EC responses to Am stimulation while NaCl given in the same manner produces only a small, transient decrease in the responses. These findings suggest Am as one possible site of muscarinic drug action in the limbic system but do not rule out the possibility of muscarinic effects on Hipp also. In addition to the above drug effects, 100 Hz stimulation of the dorsolateral MCGS at the level of the superior colliculus also produces a profound and selective decrease in concurrent Hipp and EC responses to Am stimulation which is partially antagonized by i.v. scopolamine suggesting possibly important similarities between the effects of muscarinic drugs and MCGS stimulation. (Supported in part by Ill. Mental Health Dept. Grant 203-12-RD-16 and NIH Training Grant GM-00162-15.)

65.4 **PINEAL BODY AND HYPOTHALAMIC EVOKED RESPONSES FOLLOWING ACOUSTIC AND AMYGDALA STIMULATION IN FREELY BEHAVING RATS.** R. McClung*, N. Dafny, and S. J. Strada. The University of Texas Graduate School of Biomedical Sciences and The University of Texas Medical School at Houston, Houston, Texas 77025

The pineal body (PB) receives its primary input from nerves which originate in the superior cervical ganglia; however, the sites of action for pineal hormones may be in areas of the central nervous system such as the hypothalamus. To investigate the connections between the PB and central nervous system structures, we compared the average evoked responses (AER) in PB, anterior hypothalamus (AH) and ventromedial hypothalamus (VMH) following acoustic and amygdala stimulation in freely behaving rats permanently implanted with semimicroelectrodes (60μ). The AER following 16 repetitive acoustic stimuli evoked an initial positive wave (P_1) with latencies of 1.3 (PB), 34.9 (AH), and 32.0 (VMH) msec., followed by a negative deflection (N_1) with latencies of 2.2, 51.4 and 52.0 msec. The N_1 component was followed by a positive amplitude (P_2) with latencies of 2.9, 84.0 and 96.0 msec.; a second negative wave (N_2) with latencies of 4.0, 104.6 and 122.0 msec.; and a final positive amplitude (P_3) with latencies of 6.3, 128.9 and 151.0 msec. in PB, AH and VMH respectively. Amygdala stimulation initiated responses with only three components: P_1, N_1, and P_2 in all recorded areas. Latencies for P_1 were 6.0, 3.8, and 5.0 msec.; for N_1 12.6, 8.7 and 10.3 msec.; for P_2 21.6, 16.8, and 19.7 msec. in PB, AH, and VMH respectively. These data indicate that there are central connections between the PB and the pathways involved in acoustic and amygdala stimulation. Since the latencies of the PB to acoustic stimuli were shorter than those in AH and VMH, and the latencies to amygdala stimulation were longer in PB than in AH and VMH, they further indicate different pathways to the PB with acoustic and amygdala stimulation.

65.5 A COMPARISON OF UNILATERAL AND BILATERAL HIPPOCAMPAL LESIONS ON LIVER GLYCOGEN LEVELS AND BODY WEIGHT IN THE RAT. Helen M. Murphy, Cyrilla H. Wideman and Thomas S. Brown*. John Carroll Univ., Cleveland, Ohio 44118 and DePaul Univ., Chicago, Ill. 60614

This study attempts to correlate data on instrumental learning situations and biochemical mechanisms in rats with hippocampal lesions. Behavioral measurements, such as general activity, reversal learning, passive avoidance, active avoidance and extinction, have shown that rats with unilateral hippocampal damage are similar to normal animals and animals with neocortical damage, but that they are significantly different from animals with bilateral hippocampal damage. Some biochemical and endocrinological studies on ACTH and liver glycogen levels have shown differences between control animals and animals with bilateral hippocampal damage. In this study liver glycogen concentration and body weight were measured in rats with bilateral hippocampal lesions, unilateral hippocampal lesions, neocortical lesions and in normal control animals. Animals had ad-lib. access to food and water and were placed in alternating periods of light and darkness (12 hours each). Body weights were recorded weekly. Liver glycogen levels were obtained by a slight modification of the iodine method as explained by van der Vies. All liver glycogen tests were run between 9:30 and 11:00 a.m. At a point ten weeks postoperatively, rats with bilateral hippocampal lesions had a significantly higher concentration of liver glycogen and weighed significantly less than all other animals. The observed changes in liver glycogen and body weight may be explained in terms of known anatomical connections as well as biochemical and endocrinological mechanisms with particular emphasis on gluconeogenesis and the hypothalamic-pituitary-adrenal axis involved in ACTH release. The obtained biochemical results can be correlated with behavioral data.

65.6 THE EFFECT OF TIME AND THE LIGHT-DARK CYCLE ON LIVER GLYCOGEN LEVELS IN NORMAL, NEOCORTICAL LESIONED AND HIPPOCAMPAL LESIONED RATS. Cyrilla H. Wideman, Helen M. Murphy and Thomas S. Brown*. John Carroll Univ., Cleveland, Ohio 44118 and DePaul Univ., Chicago, Ill. 60614

This study attempts to analyze two aspects of the development of liver glycogen concentrations in normal as compared with hippocampal lesioned animals. The first aspect deals with the time interval (postoperatively) necessary for hippocampal lesioned animals to develop elevated liver glycogen levels. The second aspect is concerned with the importance of time of day when assessing liver glycogen levels. Two series of experiments were conducted. In the first set of experiments liver glycogen levels were determined 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10 weeks postoperatively and 8 and 17 months postoperatively. It was found that after one week, normal, neocortical control and hippocampal lesioned animals were not significantly different in liver glycogen content. By the end of the second week hippocampal lesioned animals were significantly higher than the control groups. By the end of the third week hippocampal lesioned animals had reached their peak, which remained unchanged throughout the rest of the series. No significant changes in liver glycogen levels were observed in the control groups. In the second series of experiments liver glycogen levels were compared in the a.m. and p.m. The animals were placed in alternating periods of light and darkness (12 hours each). Normal and neocortical control animals showed higher levels of liver glycogen in the a.m. than in the p.m. Hippocampal lesioned animals did not show a significant fluctuation, but remained relatively high throughout the day. The observed variations in the two series of experiments may be explained in terms of alterations in known homeostatic mechanisms controlling liver glycogen levels.

66.1 DEVELOPMENTAL AND REGIONAL DIFFERENCES IN MULTIPLE UNIT ACTIVITY OF YOUNG KITTEN. Thomas L. Davies*, Robert D. Lindsay*, Madge E. Scheibel, and Arnold B. Scheibel. Dept. Anat., Sch. Med., UCLA, Los Angeles, 90024

Unit activity using multiple electrodes was obtained from thalamus and midbrain tegmentum in more than 40 chronically implanted kittens. In the first 6-9 postnatal days unit activity is generally sparse and may be recorded from only one or two electrodes in a cluster. Exceptions to this are explained in terms of differences in gestation period before birth. Regional differences between lateral thalamus on the one hand and midline thalamus and midbrain tegmentum on the other are observed as early as 5 days of age. This is most apparent when unit discharges are condensed on a record for the purpose of viewing long epochs of time. Initially, the density of activity in the midline areas is much greater than the lateral thalamic region. Not infrequently, this high rate of activity is accompanied by amplitude modulation that may have a cycle time in the order of minutes. It is only with development (4-5 weeks) that the density of spike activity in the lateral thalamic nuclei approaches that of the midline thalamic and midbrain tegmental areas. We hope to demonstrate that there is a definite relationship between the morphological appearance of neurons found in these two regions of brain and the types of neuronal activity which they produce.

66.2 BRAIN STEM INFLUENCES ON EVOKED THALAMIC SYNCHRONIZING ACTIVITIES IN KITTENS. Richard W. Homan*, Robert J. Shofer and Dominick P. Purpura. Dept. Anat., Albert Einstein College of Medicine, Bronx, N.Y. 10461

Two events characterize the progressive development of evoked synchronization of thalamic neurons in kittens (a) postnatal increase in duration of IPSPs elicited by low frequency (3-5/sec) medial thalamic (MTh) stimulation and (b) increase in effectiveness of EPSPs which precede IPSPs (Thatcher and Purpura, Brain Res. 1972, 1973). In adult animals high frequency (60-100/sec) brain stem reticular (BSR) stimulation attenuates synchronizing IPSPs and increases excitatory drives on thalamic neurons (Shofer and Purpura, J. Neurophysiol. 1963). BSR stimulation in very young kittens (<1 week) produces minimal attenuation of MTh-evoked IPSPs in thalamic neurons but may suppress associated cortical EPs. However, BSR stimulation in older kittens (>12-14 days) elicits 30-50 msec lat. IPSP of .4-.6 sec duration in thalamic neurons which exhibit shorter latency IPSPs to MTh-stimulation. When BSR stimulation precedes MTh-stimulation attenuation of synchronizing IPSPs is prominent only during the initial 0.5 sec of BSR stimulation. IPSPs in thalamic neurons that follow 5/sec MTh-stimulation are sharply attenuated by subsequent BSR stimulation as are prior EPSPs and depolarizing responses that are frequently observed during late phases of IPSPs. Thus in contrast to the powerful excitatory action of high-frequency MTh-stimulation on thalamic neurons in 2-week-old kittens (Thatcher and Purpura, Brain Res. 1973) BSR stimulation elicits exclusively prolonged IPSPs at this developmental stage. Such an effect of BSR stimulation resembles that observed by high frequency MTh-stimulation in neonatal and 1-week-old kittens. Maturation of inhibitory inputs to thalamic neurons from MTh and BSR regions occurs early in postnatal development, whereas excitatory inputs from MTh are functionally demonstrable prior to BSR excitatory influences on thalamic neurons.

66.3 ELECTROPHYSIOLOGY AND PHARMACOLOGY OF PURKINJE CELLS IN RAT CEREBELLUM DEGRANULATED BY POSTNATAL X-IRRADIATION. Donald J. Woodward, Joseph Altman and Barry J. Hoffer. Dept. Physiol. U. Roch. Roch. N. Y. 14642, Dept. Biol. U. Purdue, Lafayette, Indiana, and Lab. Neuropharm., St. Elizabeth's Hosp. NIMH, Wash. D. C.

Unit recording and iontophoretic drug application studies were carried out on adult rat cerebellum subjected to a nearly complete destruction of the basket, stellate and granule cell populations by means of repeated doses of low level X-irradiation during the first two weeks of postnatal life. Purkinje cells in the irradiated cerebellum anesthetized with 0.5% Halothane fired spontaneously at sustained rates, 35-40 sec, similar to that in normal cerebellum. Bursts generated by climbing fiber excitatory input were not normal in that they often caused only full sized spikes rather than a spike followed by an inactivation response. Intracellular recording revealed bursts to be generated by climbing fiber EPSPs which appeared independently in time and at different discrete amplitudes. Stimulation of white matter indicated the existence of graded synaptic excitation and of a form of synaptic inhibition on Purkinje cells. Iontophoretic studies employing multibarrel pipettes demonstrated characteristic excitation by glutamate and inhibition by gamma amino butyric acid, serotonin, norepinephrine, and cyclic AMP, similar to corresponding effects in normal cerebellum. The results indicate a considerable autonomy in the development of Purkinje cells without the presence of normal interneuronal input. An abnormal synaptic relation appearing after irradiation is an excitation of single Purkinje cells by more than one climbing fiber. Supported in parts by NSF GB28873X, NIH NS09820, and T.I.S.T. Award 5 F11 NS 11,030-03 NSRB to D. J. Woodward.

66.4 DEVELOPMENT OF MOTOR COORDINATION IN 17- TO 21-DAY CHICK EMBRYOS. A.Bekoff* (SPON: V. Hamburger and P. S. G. Stein) Dept. Biol., Washington Univ., St.Louis, Mo. 63130.

Electromyographic records (EMGs) were recorded from identified agonist and antagonist muscles acting at knee and tarso-metatarsal joints in the hindlimb of chick embryos and were correlated with movement recorded simultaneously on videotapes. Between 17 and 21 days of incubation, two clearly different types of EMGs were observed as determined by differences in average burst length and amount of muscle activity per activity period. These corresponded with the two major types of motor activity (Type I and Type III) which have been described behaviorally by Hamburger and Oppenheim (JEZ 166:171 1967). Type III motor activity consists of relatively smooth "coordinated" movements which are used for the specific prehatching and hatching behaviors. Type I activity appears throughout incubation as jerky "uncoordinated" movements. It was of interest, therefore, to determine whether the two types of EMG records represent two different manifestations of the same patterned sequence of muscle activation or whether they represent two different patterns of muscle activation (e.g. one random and one patterned or two distinct patterns). In fact, neither type of muscle activity is random. In both cases antagonist muscles acting at the tarso-metatarsal joint are not co-active, but often alternate, indicating that this level of coordination, at least, is present in both Type I and Type III motor activity at the stages observed. However, while Type III movements during climax hatching behavior show several different stereotyped sequences of activation of muscles acting at knee and at tarso-metatarsal joints, Type I motility, although including elements of coordination, shows more variability in the sequence of muscle activation.

66.5 REFLEX SPECIFICITY FROM SUPERNUMERARY LIMBS OF XENOPUS LAEVIS, L. Mendell and M. Hollyday*. Duke Med. Ctr., Durham, N. C. 27710.

Moderate pressure to the foot of a spinal toad Xenopus laevis produces knee flexion as part of a withdrawal response. Pressure to the calf evokes knee extension. These responses have also been observed in immobilized (curare) spinal frogs by making simultaneous recordings from nerves to the knee flexors and extensors. Supernumerary hindlimb buds have been grafted to the back of tadpoles at stages 49-56 of Nieuwkoop and Faber. In the adult thoracically innervated limbs are ankylotic, atrophic and immobile, but limbs supplied by lumbar segments usually show some movement. In most animals, particularly those operated at younger stages, moderate pressure to the foot or calf of the supernumerary limb evokes appropriate reflexes in the normal ipsilateral hindlimb even when the former is supplied only by thoracic segments. In such animals stimulation of back skin supplied by the same thoracic segments evokes diffuse responses on the normal hindlimb. Appropriate reflexes are observed in motile supernumerary limbs. Stimulation of the supernumerary hindlimb in tadpoles evokes appropriate reflexes in the normal hindlimb although before stages 58-59 the response is characteristic of the young tadpole rather than the adult. Recordings from single identified supernumerary limb afferent fibers in the dorsal root reveal that none is a branch of an afferent fiber supplying the normal limb. Thus appropriate reflexes from the grafted limb do not result from outgrowth of branches of fibers from the normal limb to the homologous portion of the supernumerary limb; the central action of afferent fibers supplying the transplant limb may be specified by the extra limb itself. (Supported by NIH: NS 08411, NS 34680, GM 00929)

66.6 SPONTANEOUS ACTION POTENTIALS AND THE CELL CYCLE IN EMBRYONIC MOUSE HEART CELLS. Karen Arms. Section of Neurobiology and Behavior, Cornell Univ., Ithaca, N.Y. 14850.

Studies of the differentiation of mouse cardiac muscle cells in tissue culture and in vivo permit us to trace the embryonic development of the spontaneous electrical activity characteristic of adult heart cells. Electrophysiological recordings from these cells in solutions of different ionic composition reveal that the form, and probably the ionic basis, of the action potential of heart cells alters during the course of development. Autoradiography with tritiated thymidine correlated with electrophysiological studies has shown that spontaneous action potentials and contractions may be recorded from dividing as well as non-dividing cells.

67.1 MORPHOLOGICAL ORGANIZATION OF MONOAMINE-CONTAINING NEURONS IN THE TURTLE BRAIN. A. Parent. Lab. Neurobiol., Fac. Med., Laval Univ., Québec, Canada G1K 7P4

The study of the distribution of monoamine (MA)-containing neurons in the brain of the turtle (Chrysemys picta) by means of the Falck-Hillarp histofluorescence method has revealed the following facts. The largest group of catecholamine (CA) type perikarya was found in the rostral midbrain tegmentum whereas most serotonin type perikarya were disclosed within the raphae region of the turtle brain stem. The rostral portion of the basal striatum displayed the highest concentration of MA terminals. The large amount of CA terminals present in this area of the turtle brain appear to be part of a CA neuronal system, the cell bodies of which are lying in the rostral midbrain tegmentum. The ascending axons of this CA pathway are first coursing in the lateral hypothalamus and reach the basal striatum rostrally via the lateral forebrain bundle. Early after complete brain hemisection interrupting this ascending CA pathway at diencephalic level, a pronounced pile up of fluorescent material occured within the perikaryal portion of the CA neurons, caudal to the lesion. This hemisection caused also a marked decrease in the number of CA terminals of the ipsilateral basal striatum. A striking analogy can therefore be made between this midbrain-striatal CA pathway of the turtle brain and the well-documented nigro-striatal dopaminergic pathway of the mammalian brain. The fact that the morphological organization of MA neurons in this reptilian brain, as a whole, bears such a strong resemblance to the pattern of distribution of MA neurons in the rat brain, support the view that the brain MA-containing neuronal systems are phylogenetically ancient and thus constitute basic components of the vertebrate central nervous system (supported by the Medical Research Council of Canada).

67.2 EVOLUTION OF A PONTO-CEREBELLAR NORADRENERGIC NUCLEUS IN THE PRIMATE. Charles Demirjian,* Robert Grossman* and Robert Katzman. Depts. Neurol. and Neurosurg., Albert Einstein Coll. Med., New York, 10461.

In the classic studies of noradrenergic cell groups in the rat using the Falck-Hillarp histofluorescence technique, little attention has been paid to group A4, located on the roof and lateral recess of the fourth ventricle, because of the paucity of cells in this species. In the capuchin monkey, Cebus apella, this cell group is greatly enlarged in size. It is clearly distinct from the locus coeruleus, and, in fact, appears to be subdivided into two clusters of cells. We have established the noradrenergic nature of the cells by cytospectrofluorometry. Some of the cells are located close to the ependyma, and short axons can be seen forming axosomatic connections with non-fluorescent periependymal cells. The periventricular location of these cells raises the possibility of a chemoreceptor function. At the same time, this nuclear group is in an ideal location to send axons both into the cerebellum and into the brain stem to join the ascending noradrenergic projections.

This work is supported by NS 09649.

67.3 A PROJECTION OF THE NUCLEUS LOCUS COERULEUS TO THE HIPPOCAMPUS OF THE RAT. M. Segal and F. E. Bloom. Lab. of Neuropharmacology, NIMH, St. Elizabeths Hosp., Washington, D.C. 20032.

The hippocampus (HCP) is innervated by norepinephrine (NE) containing fibers which originate in the nucleus locus coeruleus (LC). The present experiments, performed on lightly anesthetized rats, were aimed at characterizing hippocampal responses to LC stimulation. Concentric stimulating electrodes were inserted into LC and stimulated with single shocks or trains of stimuli at 10/sec. Cellular activity was recorded from the dorsal HCP via glass pipettes. Single shocks produced long latency slowing (100 msec) of spontaneous firing of single cells. Multiple shocks produced long lasting inhibition of spontaneous firing (up to 2-3 min). Responses were blocked during iontophoretic application, at the recording site, of a beta adrenergic blocking agent (MJ-1999), as well as an adenyl cyclase inhibitor (prostaglandin E_1). They were augmented during application of a phosphodiesterase inhibitor (papaverine), and during the blockade of reuptake of NE with desmethylimipramine. Responses were not affected by a GABA blocking agent (bicuculline) and were absent in rats which were depleted of their central NE stores chronically (by means of 6-OHDA) or acutely (by means of Reserpine). It is concluded that there is a direct, but slowly conducting pathway between LC and the HCP, that the pathway utilizes NE as a transmitter and that the release of NE inhibits spontaneous firing of hippocampal pyramidal cells.

67.4 RESPONSES OF CORTICALLY MODULATED RAT STRIATAL CELLS TO IONTOPHORETICALLY APPLIED NEUROTRANSMITTER CANDIDATES. Hugh J.Spencer* and Vicktor Havlicek* (SPON: J.W.Phillis). Dept.Physiology, Fac.Medicine, U.of Manitoba,Winnipeg Manitoba R3E.0W3, Canada.

Carman et.al.(Brain 86, 525-562, 1963) and others have anatomically demonstrated the presence of a cortico-striate projection in mammals.A study was undertaken to determine the nature of this cortical drive. Lightly anaesthetised (0.1% Penthrane)hooded rats were used.Barbiturate anaesthesia was unsuitable as it suppressed the excitatory responses to acetylcholine (Ach.). An array of bipolar stimulating electrodes were inserted through burr holes on one side of the skull over the frontal, parietal and occipital cortices.Constant current stimuli (0.1mS,0.1-0.9mA) time-locked to a PSTH computer were delivered sequentially to these electrodes. A 7 barreled micropipette was used to record extra-cellularly from the ipsilateral striatum and to apply putative transmitter substances near the neurones. Glutamate (1-15 nA) was used to enhance the activity of slow but spontaneously firing neurones.

The dominant effect of the cortical modulation was inhibition (34%) or inhibition followed by excitation(20%), while in a few units direct excitation was observed (19%). Some of these units showed stimulus locked bursting Whether the cortical influence was mono- or poly-synaptically mediated is not yet clear. Of the cortically modulated cells, those that were inhibited were more likely to be depressed by Ach.and norepinephrine (NE), or excited by dopamine (Dop.). Cells having a biphasic or excitatory response showed a higher probability of being depressed by Dop.and NE.(injection currents 30-50nA for all drugs). Work to further elucidate these responses is in progress.

67.5 RESPONSES OF SQUIRREL MONKEY AUDITORY CORTEX NEURONS TO VOCALIZATIONS: CHANGES PRODUCED BY MICROIONTOPHORESIS OF PUTATIVE NEUROTRANSMITTERS. Stephen L. Foote, John Newman and Barry J. Hoffer*. Lab. of Neuropharmacology, NIMH, St. Elizabeths Hosp., Washington, D.C. 20032 and Behavioral Biology Branch, NICHD, Bethesda, Md. 20014.

Histochemical evidence of preterminal axons containing norepinephrine (NE) and 5-hydroxytryptamine (5-HT) has been obtained for various regions of squirrel monkey neocortex. The present investigation was undertaken to examine the roles these (and other) putative neurotransmitters may play in modulating responses of auditory cortex neurons to species-specific vocalizations. 5-Barrel microiontophoretic electrodes were used to record the activity of single neurons in the superior temporal gyrus of Halothane-anesthetized squirrel monkeys. The responses of each neuron to 1 to 9 different squirrel monkey vocalizations were quantified by presenting each vocalization 16 times and computing a post-stimulus-time histogram and raster display on-line. Typically, a neuron displayed a similar response on each successive presentation of a given stimulus, but a response of different strength, latency, and pattern was obtained upon the presentation of each different vocalization. This test procedure was then repeated during and after the iontophoretic ejection of glutamate (Glu), NE, gamma-aminobutyric acid (GABA), 5-HT, or acetylcholine. Appropriate current balancing was used during each ejection. In most of the cells studied, application of NE or GABA reduced both spontaneous and vocalization-evoked activity in an apparently non-selective fashion. Glu increased both types of activity. The effect of each chemical was dose-dependent. These results suggest that the discrete cortical activation produced by vocalizations can provide a convenient natural test system for evaluation of neurotransmitter actions.

67.6 EVIDENCE THAT 6-HYDROXYDOPAMINE (6-OHDA) IS A NON-SPECIFIC NEUROTOXIC AGENT WHEN ADMINISTERED INTRACEREBRALLY. Larry L. Butcher and Gordon K. Hodge*. Dept. of Psychology, UCLA, Los Angeles, CA, 90024, U.S.A.

Using monoamine histochemical, electron microscopic, and biochemical methods, several investigators have reported that 6-OHDA selectively destroys catecholamine neurons in the brain (Ungerstedt, Europ. J. Pharmac. 5: 107, 1968; Bloom, et al., Science 166: 1284, 1969; Breese and Traylor, J. Pharmac. exp. Ther. 174: 413, 1970). In these studies, however, only dopamine (DA), noradrenaline (NA), and 5-hydroxytryptamine were measured or extremely small areas of the brain were examined. Using more traditional histological procedures, we have been unable to confirm the hypothesis that 6-OHDA is a selective neurotoxic agent in rat brain: (I) Unilateral infusion (rate 1µl/min) into nuc. ruber of 8µg 6-OHDA in 4µl Ringer's-ascorbic acid solution produced within 48 hrs complete loss of neuron somata on the injected side accompanied by extensive gliosis (thionin stain). Although 8µg/4µl has been reported to produce selective degeneration of catecholamine neurons (Ungerstedt, 1968, above ref.), the cell bodies of nuc. ruber contain neither DA nor NA. They do contain acetylcholinesterase (AChE), and 6-OHDA produced extensive loss of AChE in nuc. ruber. (II) Unilateral injection of 4µg/2µl 6-OHDA into the zona compacta of the substantia nigra produced complete loss of neuron somata and AChE staining on the injected side. Bilateral intranigral administration of 6-OHDA produced hypokinesia and rigidity. This motor syndrome, as well as the histological findings detailed above for 6-OHDA, could be duplicated by bilateral intranigral injection of 2µg/2µl $CuSO_4$, a known non-specific cytotoxic agent. We conclude that "specificity" of neuron destruction can be achieved with 6-OHDA only to the extent that the drug is injected into brain regions which are neurochemically homogeneous. (Supported by University of California grant no. 2637 and NIMH grant no. 1 R03 MH 22284-01)

67.7 RECIPROCAL FIRING BY TWO NEURONAL GROUPS DURING THE SLEEP CYCLE. J.Allan Hobson, Robert W. McCarley, Peter W. Wyzinski, and R. Terry Pivik. Dept. of Psychiatry, Harvard Medical School, Boston, Mass. 02115

The active central control theory of desynchronized sleep (D) postulates driving of diffuse neural elements by neurons localized in the pontine brain stem. The giant cells of the tegmental fields (FTG) fulfill several a priori criteria for such a function. Massive shifts in excitability of FTG neurons during the sleep cycle are suggested by several findings and self-reexcitation is a possible mechanism for producing the bursts of discharge seen once the FTG neurons are tonically brought to threshold. This tonic change could occur by an increase in excitatory input from another source or by withdrawal of tonic inhibition from another source. If the latter mechanism exists, one would expect to see a reciprocal relation of tonic firing by FTG and other neurons.

In our first 75 microelectrode explorations of the brain stem of 10 cats we found only 10 of 100 neurons to have rates of discharge that were lower in D sleep than in waking or synchronized sleep (S). We were thus interested to note that 8 of the 10 cells came from 3 descents that passed through the anterior pontine tegmentum and could be localized to the posterior pole of the nucleus locus coeruleus (LC) and the nucleus subcoeruleus. Mean rates of these LC neurons yielded selectivity ratios of D/W = 0.2 and D/S = 0.3, values which are 500 times less than those of the FTG (D/W 100, D/S 50). In addition, the time course of the rate deceleration for LC neurons in transition from S to D was found to be the mirror image of the acceleration characteristic of FTG neurons. It thus appears likely that some neurons having reciprocal rate relations with the FTG may be localized in or near the LC. This finding suggest the possibility of a functional interaction between the two cell groups. If verified, this interaction could provide a basis for sleep stage oscillation.

68.1 EFFECTS OF HYPOXIA AND HYPERCAPNIA ON GLUCOSE TRANSFER ACROSS THE BLOOD-BRAIN BARRIER IN RABBITS. Frank Berson*, Maria Spatz* and Igor Klatzo. Lab. Neuropath. Neuroanat. Sci., NINDS, NIH, Bethesda, Md. 20014

Hypoxia and hypercapnia were produced separately in rabbits in order to investigate the effect of each on the uptake of glucose by the brain. All rabbits underwent a tracheotomy under general anesthesia and their respiration controlled with a small animal ventilator. A catheter was also placed in the femoral artery to monitor blood pressure and withdraw samples for blood gas analysis. Using a modified Oldendorf double isotope technique, the labeled glucose was introduced into the cerebral circulation via a cannula in the common carotid artery. Preliminary data showed that in severe hypoxia the Brain Uptake Index (BUI) for 2-deoxy-D-glucose was 38.0 (pO_2=10-15, mean systolic blood pressure=80-100) compared with a normal BUI of 65.0. Similarly, the BUI in moderate hypercapnia (pCO_2= 75-82, pH=7.20-7.27, mean systolic blood pressure=80-100) was 38.5. The results suggest that both hypoxia, without hypercapnia or hypotension, and hypercapnia, without hypoxia or hypotension, decrease the transfer of 2-deoxy-D-glucose from blood to brain.

68.2 ACCUMULATION OF A RADIOLABELLED NEUTRAL AMINO ACID BY CANINE DURA-ARACHNOID. L.A. O'Tuama, M. P. Remler and H. N. Nichols* Biol. Sci. Res. Ctr., Depts. Med. (Neurology) and Peds., Univ. N. Carolina Sch. Med., Chapel Hill, N.C. 27514

Lorenzo and Snodgrass (J. Neurochem. 19: 1287, 1972) demonstrated a concentration-dependent clearance of [^{14}C-] leucine from the cranial subarachnoid space in the cat. These findings suggested an investigation of the dura-arachnoid membrane (DA) as a possible site of this transport. Parasagittal DA excised from adult dogs and incubated for 4 h. in artificial CSF under aerobic conditions concentrated α-amino [1-^{14}C] isobutyric acid ([^{14}C-]AIB) against a concentration gradient, the average tissue-to-medium ratio being 1.90. Anoxia, and the addition of ouabain (6.7×10^{-5}M) or unlabelled AIB (10mM) each inhibited the uptake significantly, by 53% - 61% of control values. The average net transport of [^{14}C-] AIB was 24nM/ml/h. and this amounted to 40% of the transport of [^{14}C-]AIB by choroid plexus incubated simultaneously. Calculations based on the respective surface areas suggest that accumulation of [^{14}C-]AIB by the total DA exceeds considerably that attributable to the total choroid plexus. These results, together with the in vivo study cited, suggest that mammalian DA regulates the concentration of neutral amino acids in extraventricular CSF.

68.3 BLOOD FLOW AND TISSUE OXYGEN IN EXPERIMENTAL PARAPLEGIA. Thomas B. Ducker and Phanor L. Perot, Jr. Div. of Neuro., Medical University of South Carolina, Charleston, S.C. 29401

Our laboratory and others have shown that spinal cord blood flow in the normal monkey is around 15 $\pm$ 5 ml/min/100 grams of tissue. Also, composite tissue oxygen in the central nervous system is approximately 35-40 mm Hg. After cord injury sufficient to produce paraplegia, there is progressive ischemia and hypoxia causing spinal cord blood flow and tissue oxygen to diminish markedly over 1-2 hours. This report deals with cord injuries where there is recovery. We are attempting to determine what happens to blood flow in animals whose cords are able to mend. Twenty rhesus monkeys were studied. Trauma was inflicted by means of a 50 gram weight dropped from a height of 10cm above the cord. The monkeys were treated with large doses of glucocorticoid steroids with varying degrees of recovery. Approximately 1/3 of the animals remained paraplegic, 1/3 could use their extremities and 1/3 could walk or run. The ones that were paraplegic showed ischemia and hypoxic responses. The monkeys with reversed cord lesions, on the other hand, showed hyperemia and elevated tissue oxygen. Their spinal cord blood flow was over 25ml/min/100 grams within one or two hours and remained elevated over one week. Tissue oxygen in these animals was approximately 55 mm Hg. Functional recovery correlated with the degree of hyperemia and hyperperfusion.

68.4 THE RELATIONSHIP OF EDEMA TO THE DEVELOPMENT OF MICROVASCULAR OBSTRUCTION IN CEREBRAL ISCHEMIA. Gary Wise, Mary Stevens*, E. C. Shuttleworth, and Norman Allen. Div. of Neurology, Ohio State University, Columbus, 43210.

The gerbil is an ideal animal for the study of the pathophysiology of brain ischemia since there is no significant blood flow to the cerebral hemispheres during bilateral carotid occlusion. Normal filling of the microvasculature of the brain stem, cerebellum, and hypothalamic region occurs when colloidal carbon is injected into the left ventricle of the heart during bilateral carotid obstruction, but the microvasculature in the cerebral hemispheres usually does not fill. This is the only animal model described where complete cerebral ischemia can be produced without insulting the systemic vessels, heart, or brain vasomotor centers.

Bilateral carotid obstruction of less than 30 minutes duration is associated with brain infarction in less than 20 percent of gerbils. Thirty minutes of carotid obstruction produced death in 20 of 24 animals in 24 hours due to brain infarction; this was associated with microvascular obstruction but the carotid and major cerebral arteries were patent. Cerebral edema was significant with 10 minutes of carotid obstruction. The amount of cerebral water (wet weight - dry weight/wet weight) increased progressively with 15, 20, and 30 minutes of carotid obstruction while microvascular obstruction was seldom seen with less than 30 minutes of ischemia. Recovery of cerebral edema occurred over the next 3 hours with 15 minutes of temporary carotid obstruction while there was no recovery in the 30 minute group. Neuronal damage appears to be preceded by microvascular obstruction in cerebral ischemia, and microvascular obstruction is preceded by edema. The effect of therapy upon the amount of edema present at 3 hours would be appropriate in the evaluation of therapeutic agents in cerebral ischemia in this model.

68.5 OBSERVATION ON NO-REFLOW PHENOMENON IN THE BRAIN OF MONGOLIAN GERBILS. Umeo Ito*, Igor Klatzo, and Maria Spatz*. Lab. Neuropath. and Neuroanat. Sci., NINDS, NIH, Bethesda, Maryland 20014

Studies on no-reflow phenomenon were carried out in Mongolian gerbils (Meriones unguiculatus) characterized by frequent absence or deficiency of connecting arteries between the basilar and carotid systems. In these animals, occlusions of the common carotid artery results in the infarction of the ipsilateral hemisphere in about 30% of gerbils. The status of cerebral vasculature and circulation was assessed by cerebral blood flow, by terminal intravascular carbon black perfusions, and by benzidine stain demonstrating the presence of the red blood cells. The behavior of the blood-brain barrier was studied with Evans Blue tracer. The experiments revealed a markedly reduced cerebral blood flow in the infarcted areas, whereas the adjacent zones frequently showed a "luxury perfusion syndrome." The changes in the blood-brain barrier were demonstrable only 18 hours after ligation. Evaluation of carbon black perfusions carried out at various time intervals after unilateral or bilateral carotid occlusion showed a "no reflow phenomenon" conspicuous by the filling defects of blood vessels in certain areas of the brain. The no-reflow phenomenon was demonstrable for about 30 minutes only. It could be reduced or abolished either by epinephrine or by 100% oxygen treatment.

68.6 TRANSIENT GLOBAL AMNESIA DUE TO ARTERIAL EMBOLISM. Edwin Shuttleworth, Gary Wise. Div. of Neurology, Ohio State University, Columbus, 43210.

While the clinical features of transient global amnesia are well-known, considerable controversy exists concerning its pathophysiology. Most observers have favored a vascular etiology but others have thought that it is a seizure phenomenon. We have observed 2 cases of transient global amnesia due to arterial embolism associated with cardiac catheterization and arteriography. The immediate recall (less than one minute) was normal, and the remote memory was reasonably intact within the limits of a shrinking retrograde amnesia of a few years duration at onset. On the other hand, these patients could not retain any new memory of where they were or what they observed in their environment for longer than one minute. The recent memory defect was demonstrated to be truly global since tests were performed with visual, olfactory, tactile, proprioceptive, and auditory memoranda presentations. Cerebral and brain stem function were otherwise completely normal during the amnestic episode which lasted a few hours. Recovery was complete except for a persisting amnesia for the duration of the attack.

Permanent amnesia can occur if there is extensive bilateral infarction of the hippocampus. It appears that these 2 patients had the sudden onset of hippocampal dysfunction due to temporary ischemia induced by arterial embolization since there was a damped arterial pulse pressure measurement through the catheter which became normal after the embolic episode, suggesting dislodgement of a thrombus. This is the most clear demonstration of a vascular etiology for the transient global amnestic episode yet reported. It was also demonstrated for the first time in this disorder that the amnesia is present for all modalities of sensory presentation.

70 SYMPOSIUM

UNDERWATER PHYSIOLOGY: CHANGES IN BRAIN FUNCTIONS AT HIGH PRESSURE

Co-Chairmen: A. J. Bachrach and P. B. Bennett

Neurophysiological problems at high pressure.
A. J. Bachrach, Naval Medical Research Institute, Bethesda, MD

The aetiology and prevention of the high pressure nervous syndrome in man during oxygen/helium diving.
P. B. Bennett, Duke University School of Medicine, Durham, NC

Electrophysiological approach to the high pressure nervous syndrome: Variations due to the mode of compression.
R. Naquet and J. C. Rostain, C.N.R.S., Institut de Neurophysiologie et de psychophysiologie, Marseilles, France

The critical volume hypothesis and the high pressure nervous syndrome.
K. Miller, Harvard Medical School, Boston, Mass.

Genesis of the high pressure neurological syndrome.
R. Brauer, Wrightsville Marine Bio-Medical Lab., Wilmington, NC

In the past few years research on animal and human subjects in hyperbaric chambers and open sea dives has delineated a group of neurological symptoms collectively referred to as the "High Pressure Nervous Syndrome" or the "High Pressure Neurological Syndrome: (HPNS). At depths below 1000 ft of sea water the symptoms are frequently observed and pronounced: lowered vigilance, microsleep, tremor and EEG anomalies (increased theta activity and general depression of EEG) are the major ones reported in various dives. The symposium speakers will consider effects of compression rate, breathing mixtures (such as helium/oxygen and neon/oxygen) used in deep dives and the effects of hydrostatic pressure on the HPNS, concentrating on mechanisms such as biophysical and neurological events underlying HPNS in the light of pharmacological and neurophysiological data, theoretical bases of pressure effects and measurement techniques.

71.1 AROUSAL STATES AND HABITUATION PROCEDURE IN THE MUDPUPPY, NECTURUS MACULOSUS. David A. Goodman and Charles J. Swigert*. Newport Neuroscience Center, Culver City, Calif. 90230

Systematic input-output studies on behavior in the neotenic salamander Necturus maculosus using habituation procedure suggest that there are multiple determinants to the form and magnitude of any response in a response series. In general terms, these determinants include stimulus, experience and state. Although the first two have been studied in detail, state (of arousal) has been described infrequently and unsystematically. In order to identify the effects of arousal state on response, a testing technique was developed to keep incidental and extraneous stimulation to a minimum. From these studies using remote sensing to monitor somatic and autonomic systems indirectly, an abundance of data were collected on the effects of state on response. The data indicate that state influences whether the salamander responds to the stimulus, what form the response will take and the response magnitude. The influence of state on input-output sequences can be described using the formalism of automata theory. For stimuli presented infrequently, the behavioral data can be modeled by a finite state sequential machine in which output and subsequent state are determined by input and existing state. A state table and an output table will be presented to illustrate the salamander's multiple arousal states and the fine structure of its responses to a repetitive stimulus. (Behavioral research supported by grant MH 11250 to N.M. Weinberger).

71.2 A LEECH WITH ABNORMAL GANGLIA CONTAINING SUPERNUMERARY SENSORY AND MOTOR NEURONS. D. Kuffler* and K.J. Muller* (SPON. J.G. Nicholls). Dept. of Zool., Univ. of Calif., Los Angeles, Calif. 90024, and Dept. of Neurobiol., Harvard Med. Sch., Boston 02115.

A leech was found which, through developmental or genetic error, had an extra number of neurons in each ganglion. For example in the ganglia of this leech there were sometimes 3 large Retzius cells instead of 2. Similarly the ganglia contained extra sensory cells, each with the characteristic membrane properties, shapes and positions of touch, pressure or nociceptive cells. These neurons innervated the skin and responded to the appropriate type of mechanical stimulus. In ganglia with one extra cell of a particular type, both cells had normally shaped receptive fields which overlapped extensively in the usual region of the body wall. However, when there were two supernumerary cells, the receptive fields were often shifted in position or reduced. Extra motoneurons were also found and they innervated normal regions of body wall musculature. Connections within the C.N.S. were convergent, so that a sensory neuron and its duplicate made effective synapses with the appropriate motoneuron. Although the life cycle of the leech is too slow for genetic studies, other abnormal animals may provide additional information about factors influencing the specificity of neuronal connections.

71.3 STIMULUS SPECIFICITY OF HABITUATION TO VIBRATORY STIMULUS IN SPIROSTOMUM. William B. Rucker and Joseph C. Huber. Dept. Psychol., Mankato State College, Mankato, Minn. 56001; and Dept. Psychol., Faribault State Hospital, Faribault, Minn. 55021.

The ciliated protozoan Spirostomum ambiguum contracts when touched or stimulated by mechanical shock, electrical shock, or ultraviolet radiation. Upon repeated mechanical stimulation provided by dropping a solenoid on a depression slide containing the subjects, Spriostomum respond less frequently. Applewhite, Gardner, and Lapan (Trans. N. Y. Acad. Sci. 31: 842-849, 1969) argue that this waning of the response must be habituation, since stimulated animals are still responsive to more intense stimulation in the same mode or to electrical shock. While this may rule out fatigue as an explanation, it does not rule out sensory adaptation since Eisenstein (Brain Research Institute 10th Annual Symposia, BIS, UCLA, 1972) was unable to produce response waning with electrical shock. To test the hypothesis that the waning of contraction was specific to the stimulus of training, a depression slide was glued to a speaker nested in the base of a microscope. Single Spirostomum were presented with 1 sec. tones of constant intensity (1.6 V.) at 5 sec. intervals for 90 trials. The frequency of the tones (either 300 or 500 Hz.) was the same over all trials for half the subjects, but changed to the alternate stimulus in the last 30 trials for the others. Over blocks of 10 trials, the response of the changeover group waned less than the constant stimulus group ($F = 2.33$, $df = 8/256$, $p < .05$), indicating stimulus-specific habituation of the response. Supported by Mankato State College Research Council.

71.4 MEDIUM RECEPTOR MEDIATION OF THE ECHO RESPONSE, AN ELECTRICAL INTERACTION BETWEEN MORMYRID FISH. C. J. Russell and C. C. Bell. Neurophysiology Laboratory, Good Samaritan Hospital & Medical Center, Portland, Oregon 97210.

When two Gnathonemus petersii are in close proximity, each tends to discharge its electric organ between 11 and 15 msec after the electric organ discharge (EOD) of the other. This phenomenon has been termed the "echo response". Artificial electrical stimuli were presented to intact fish to study this response in detail. Voltage threshold of response and intensity-related latency variation were what would be expected if medium receptors were involved (Bennett, Cold Spring Harbor Symp., 30: 245, 1965; Szabo & Hagiwara, Physiol. Behav., 2: 331, 1967). With stimuli of short duration, the response threshold was lower to head-negative than to head-positive pulses. With longer durations however, response occurred on "make" of head-positive and on "break" of head-negative stimuli. These polarity characteristics indicate that the medium receptors involved are located in the head region of the animal.

Spontaneous EOD's were followed by a refractory period in which no response could be evoked. Beyond this period, response probability increased with increasing stimulus delay, approaching unity. Stimuli delivered after short delays were more likely to evoke a response if the fish increased its EOD rate. The response in turn affected the EOD rhythm by resetting it. These findings indicate two properties of the echo response: 1) a probability of occurrence which is dependent on instantaneous EOD frequency, and 2) resetting of the EOD rhythm. These two properties and what is known of the physiology (Bennett et al, J. Neurophysiol., 30: 180, 1967) suggest that the echo pathway from the medium receptors directly excites the command nucleus. (USPHS NIH NS06728 and Gertrude Cammack Foundation)

71.5 ELECTRICAL SENSITIVITY IN TWO SYMPATRIC SPECIES OF GYMNOTID FISH. Eric I. Knudsen* (SPON: T.H.Bullock). Dept. Neurosciences, Sch. Med., UCSD, San Diego 92037.

Behavioral sensitivity spectra to imposed sine wave fields were measured through operant conditioning techniques using a modified T-maze with food reward for a correct choice and aversive mechanical stimulation for an incorrect choice. Seventy percent correct response designated threshold field strength at a given frequency. Threshold versus stimulus frequency plots indicate pronounced species-specific sensitivity for both Eigenmannia virescens (1.15 μV/cm at 250-600 Hz) and Apteronotus albifrons (0.22 μV/cm at 750-1200 Hz). The sensitivity spectrum for Eigenmannia is unimodal and asymmetrically skewed toward low frequencies, with a marked increase in sensitivity (0.40 μV/cm) at its own electric organ frequency. In contrast, Aperonotus exhibits a bimodal sensitivity spectrum with discrete low (1-20 Hz) and high (750-1200) frequency maxima. Species-specific tuning provides a mechanism for increasing the signal to noise ratio for intraspecific communication.

The guidance of Drs. Theodore H. Bullock and Carl D. Hopkins is gratefully acknowledged.

71.6 CONNECTIONS AMONG LEECH MOTOR NEURONS. Carol A. Ort*, William B. Kristan, and Gunther S. Stent*. Dept. MOL. BIOL., U. of Calif., Berkeley, 94720.

Leeches swim by producing a metachronal rhythm of alternate contractions of the dorsal and ventral longitudinal muscles in the body wall of successive segments. Both excitatory(EX) and inhibitory(INH) motor neurons to these muscles are located in the ganglion of the ventral nerve cord that innervates each segment. We have recorded intracellularly from these motor neurons in a semi-intact swimming leech preparation. During swimming the motor neurons undergo membrane potential oscillations(MPO) of the same period as the swim, with spike bursts occurring during the depolarized phase of each MPO. As is to be expected, the MPO of EX motor neurons innervating the dorsal and ventral muscles are antiphasic, as are the MPO of the INH and EX motor neurons innervating either set of muscles. Examination of the central connections between these motor neurons has shown that INH motor neurons to either dorsal or ventral muscles also have central inhibitory connections to the corresponding dorsal or ventral EX motor neurons. The hyperpolarizing phase of the MPO of the EX motor neurons is partially produced by the antiphasic activity of the corresponding INH motor neurons via these connections. A motor neuron, L, whose field of innervation includes both dorsal and ventral longitudinal muscles and whose activity causes simultaneous contraction of the entire longitudinal musculature, is continuously hyperpolarized during swimming. The L motor neuron is connected to both the dorsal and ventral EX motor neurons by rectifying electrical junctions which allow the hyperpolarizing, but not the depolarizing, phase of the MPO to pass from an EX motor neuron to the L motor neuron. Via these connections the antiphasic hyperpolarizations of the dorsal and ventral EX motor neurons produce a continuous hyperpolarization of the L motor neuron during swimming.

71.7 INNERVATION AND REFLEX ACTIVITY OF THE DORSAL SUPERFICIAL MUSCLES OF THE ABDOMEN OF THE HERMIT CRAB, PAGURUS POLLICARUS. William D. Chapple, Biological Sciences Group, University of Connecticut, Storrs, Conn. 06268

The innervation and reflex activation of the superficial dorsal muscles of the hermit crab abdomen were studied with intracellular and chronic extracellular techniques. Five excitors and one inhibitor innervate the segmental muscles on each side (which consists of a single layer of longitudinally oriented muscle fibers). Two of the excitors which produce non-spiking EJPs innervate adjacent longitudinal strips of muscle fibers; the same muscle fibers are also innervated by higher threshold (to mechanical stimulation of the epidermis) excitors that produce an active response. Uropod abduction is the most potent form of reflex activation; the dorsal muscles are coupled synergistically (rather than antagonistically as in the crayfish) with the ventral superficial muscles. No muscle receptor organs were found in the first, second, or third segments; this may be related to the inability of the hermit crab to maintain its shell at a constant position above the substrate.

71.8 ANATOMY OF THE HERMIT CRAB, PAGURUS POLLICARUS, DEEP ABDOMINAL MUSCLE AND NERVOUS SYSTEM. Jack D. Marrelli* (SPON: T. Schwartz). Univ. of Conn., Storrs, Ct. 06268

The anatomy of the deep abdominal muscle system of the hermit crab, Pagurus pollicarus, was studied. This muscle system is shown to be homologous with previously described deep abdominal flexor muscle systems in decapod crustaceans (Daniel, Report for 1930 on the Lancs. Sea-Fisheries Lab., 1931). There has been complete loss of the posterior oblique muscles and most of the central muscles relative to the lobster, crayfish and shrimp. The anterior oblique muscles comprise the bulk of the existing muscles. The reduction in muscles is reflected in the CNS by a reduced number of motoneurons compared with the crayfish deep abdominal system. The bilateral asymmetry of the deep muscles is also reflected in the CNS as a reduction in the number of motoneurons innervating the reduced, left side of the abdomen. The cellular morphology of the motoneurons innervating the right side of the deep abdominal muscles of the third abdominal segment was examined with intracellularly introduced cobalt chloride and procion yellow dyes. Dendritic structure and soma position are related to specific ganglionic landmarks such as fiber tracts, other somas and the medial giant fibers.

72.1 ADENOSINE MEDIATED ELEVATION OF cAMP LEVELS IN CULTURED MOUSE NEUROBLASTOMA CELLS. A.J. Blume*, C. Dalton* and H. Sheppard* (SPON: F.L. Margolis). Dept. of Physiol. Chem., Roche Inst. Mol. Biol. and Dept. of Cell Biol., Hoffmann-La Roche, Nutley, N.J. 07110.

In various heterogeneous nerve tissue preparations which contain neural as well as glial elements, the formation of cAMP has been shown to be stimulated by catecholamines, histamine, adenosine, prostaglandin E_1 and depolarizing agents. Of the above effectors, only PGE_1 has been shown to increase cAMP levels in homogeneous preparations of mouse neuroblastoma cells. We are now able to demonstrate an adenosine mediated accumulation of cAMP in neuroblastoma. This response was only manifested in cells exposed to the cAMP phosphodiesterase inhibitor, Ro 20-1724; in its absence no significant adenosine stimulation was observable. Incubation of two cell lines, N1E and NS 20, in 0.2 mM adenosine and 0.7 mM Ro 20-1724, after 45 minutes at 22°C caused a 10 and 27 fold increase in cAMP respectively. The half maximal effect of adenosine was found to occur at 1.6 μM. Although Ro 20-1724 alone had no effect on basal cAMP levels in line NS 20, it caused a 3-fold increase in cAMP and N1E cells. With Ro-20-1724 treated cells, it was shown that neither adenine, guanine, guanosine or GTP could substitute for adenosine as a cAMP stimulator. To further characterize the adenosine response we are investigating the effects of other adenosine analogues and phosphodiesterase inhibitors. Since we have also found that in the presence of Ro 20-1724, histamine, isoproterenol or acetylcholine do not effect cAMP levels, it appears that Ro 20-1724 specifically unmasks the adenosine regulatory mechanism involved in controlling cAMP levels in these cells. Therefore, neuroblastoma can be used to study the role of adenosine mediated changes in cAMP and nerve cell functions.

72.2 CYCLIC AMP AND CYCLIC GMP IN NORMAL AND DEGENERATIVE RETINAE OF MICE. D. B. Farber* and R. N. Lolley. V.A. Hospital, Sepulveda 91343, and UCLA Sch. Med., Los Angeles, CA 90024.

Due to an inherited mutation (rd), the photoreceptor cells of the retina of C3H mice begin to degenerate in the second postnatal week; the cells of the inner layers survive the disease. A deficiency in phosphodiesterase (PDE) activity of the C3H retina has been shown to occur before ultrastructural degeneration. In developing normal retina of DBA/1J mice, two kinetic classes of PDE can be demonstrated using cAMP as substrate: a low K_m-PDE concentrated in the inner layers and a high K_m-PDE restricted to the photoreceptor layer. In developing C3H retina, the activity of low Km-PDE is normal and the activity of high Km-PDE is missing throughout postnatal life. With cGMP as substrate, a single Km value, intermediate to those of the high and low K_m-PDE values with cAMP, is observed in both DBA and C3H retinae. During development, the contents of cAMP in normal and C3H retinae increase comparably until the 9th day of life when cAMP accumulates in the C3H retina. Peak levels occur at 15 days, which are 2.2-fold greater than normal. The contents of cGMP in normal and C3H retinae increase comparably for the first 7 days of life, when the developmental increase is arrested in the C3H retina. By adulthood, the cGMP content of the C3H retina is 1.8-fold below normal. The relationship between high Km-PDE activity and photoreceptor cell degeneration will be discussed in terms of the distribution of the cyclic nucleotides within the retina and of the inferred role of the PDE in the etiology of the inherited disease. (Supported in part by NIH Grant EY00395.)

72.3 REGULATION OF CYCLIC NUCLEOTIDES IN ADRENAL MEDULLA OF RAT: POSSIBLE INVOLVEMENT OF NICOTINIC RECEPTORS. A. Guidotti*, H. Gerhards*, C. Mao* and E. Costa. Lab. Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, D. C. 20032

Occupancy of cholinergic and adrenergic receptors by an agonist may change the ratio of tissue concentrations of guanosine 3',5'-monophosphate (cGMP) and adenosine 3',5'-monophosphate (cAMP). Agonists of muscarinic receptors lower the cGMP concentrations (Proc. Natl. Acad. Sci. 69: 3287, 1972). We are now presenting evidence that in adrenal medulla of rat the release of the endogenous agonist on the nicotinic receptors increases cAMP and decreases cGMP concentrations. The injection of synthetic analogues of this agonist also enhance cAMP/cGMP ratios. In adrenal medulla of rats exposed to cold (4°C) there is a sudden increase of cAMP concentration. This increase reaches its maximum (about 10 times) after 30 minutes at 4°C, and it is prevented monolaterally by ipsilateral splanchnicotomy. Carbamylcholine (5.4 μmoles/kg i.p.) elicited a 15-fold increase of cAMP concentration in adrenal medulla and this increase is not prevented by denervation. Intraperitoneal injections of nicotinic receptor antagonists, mecamylamine (15 μmole/kg i.p.) and hexamethonium (45 μmoles/kg i.p.) antagonize the activation of chromaffin cells adenylcyclase elicited by cold exposure and carbamylcholine injections. As release of endogenous catecholamines or the injection of adrenergic receptor agonists does not produce any significant changes of medullary cAMP in chromaffin cells, the specificity of the relationship between nicotinic receptor activation and increase in the cAMP/cGMP ratios is emphasized. The relationship between activation of nicotinic receptors and second messenger responses cannot be generalized using chromaffin cells as a model. In preliminary experiments, we observed that exposure to 4°C increases by about 50% the cGMP concentration of superior cervical ganglia without significantly affecting the cAMP concentration.

72.4 ADENYLATE ENERGY LEVELS DURING BRAIN ISCHEMIA AND RECOVERY. C.-L. Liao* and F. M. Yatsu* (SPON: F. J. Seil). Dept. of Neurology, University of California, School of Medicine, San Francisco, CA 94122

A rapid depression of brain adenylate energy levels occurs during ischemia (Lowry et al, J Biol Chem 239:18, 1964). The exact relationship between adenylate energy to ischemic brain damage is uncertain. Our experiments were designed to clarify this by assessing adenylate levels during varying periods of ischemia and circulatory restoration. The rabbit model for brain ischemia is created by the double insults of hypotension (i.v. Arfonad) and hypoxia (4% oxygen) and monitored by the duration of an isoelectric EEG (Yatsu et al, Stroke 3:726, 1971). With 3 min of an isoelectric EEG, rabbits recover after circulatory restoration, while after 5 min the rabbits show neurologic impairment. ATP, ADP and AMP were quantitated enzymatically (Lowry et al, J Biol Chem 239:18, 1964) on a cerebral cortex obtained through a craniectomy and quickly frozen in liquid nitrogen. ATP decreased to 55% and 25% of control levels (1.7-2.0 nmoles/mg wet weight) after 3 and 5 min of ischemia, respectively. Following circulatory restoration, ATP returned to 80% and 40%, respectively, of control levels in 8 min. Calculation of energy charge (EC = [ATP + 0.5 x ADP]/[ATP + ADP + AMP]), a major regulator of bioenergetic functions as proposed by Atkinson (Biochemistry 7:4030, 1968), shows that during these same periods EC is 0.86 and 0.82, respectively; preischemia is 0.9. Our results showing EC recovery following ischemia suggest that it is not implicated in ischemic brain damage, although the total adenylate pool may play a role. (NIH grants NS-07769 and NS-09128).

72.5 THE POTASSIUM DEPENDENCE OF THE CYTOCHROME REDOX POTENTIAL OF BRAIN SLICES. R. J. Bull* and J. T. Cummins (SPON: J. J. O'Neill) Environmental Protection Agency, Cincinnati, Ohio 45268, and VA Hospital, Sepulveda, Calif.

The oxidation-reduction states of cytochromes b and c were monitored in brain slices using dual-wavelength, dual-beam spectroscopy to measure α-band absorbance in the 540-575 nm region. It was found that 3 mM K^+ in the incubation media maintained absorbance at approximately 70% of the initial value over a 2 hour test period. In contrast, absence of K^+ resulted in only 30% retention of the initial value. Loss of absorbance in the absence of K^+ could be attenuated over a short time interval by including 1 mM Ca++ in the media. Both in the presence or absence of Ca++, the absorbance decay can be accelerated by 50 μM ouabain. The effects of K^+ removal could be reversed by addition of K^+ to the media. However, an increase in the concentration required was observed in the presence of ouabain. The effects of K^+ and Ca^{++} appear to be antagonistic at low concentrations of K^+ (3 mM) and synergistic at higher concentrations (30 mM). Although addition of K^+ does substantially increase O_2 uptake of brain slices for a brief period (4-5 min.), these changes in absorbance do not appear to be directly related to changes in steady-state respiration. These data suggest that K^+ plays an important role in maintaining an adequate flow of reducing equivalents through a site(s) preceding the cytochrome chain of brain slices. It was clear that Ca^{++} was capable of modifying this effect of K^+; either directly or perhaps indirectly as a result of its ability to stabilize excitable membranes.

72.6 MEASUREMENT OF FAST BRAIN RESPONSES TO K^+ IN VITRO. **J.T. Cummins and R. Bull*. V.A. Hospital, Sepulveda, California 91343, Dept. Med. Pharmacol. & Therap., U.C. Irvine and Environmental Protection Agency, Cincinnati, Ohio.**

Techniques have been developed for the measurement of rapid respiratory responses in isolated brain tissue. Brain slices are maintained in Krebs-Ringer and are held in a specially constructed cuvette. Respiratory intermediates are measured by dual wavelength spectrophotometry and light scattering changes are followed by a tissue photometer. Changing the concentration of K^+ from 5 to 30 mM in the media bathing the slice causes simultaneous changes in pyridine nucleotides (340-376 nm), cytochrome b (562-575 nm) and light scattering. The kinetics of these changes are similar in that they occur within a second of the K^+ addition and go through a single oscillation over a period of minutes. However, each metabolic parameter gives a somewhat different long-term kinetic response, relative to the original baseline. The response of the three parameters to 30 mM K^+ is eliminated by metabolic inhibitors but tetradotoxin (10^{-5}M) did not affect the K^+-stimulated light scattering response. The absence of Ca^{++} greatly affected the light scattering response to K^+ and caused complex changes in the respiratory compounds. It seems probable that these changes are bioenergetic responses associated with K^+ depolarization.

72.7 Measurement of glucose utilization in rat brain in vivo.
Richard A. Hawkins, Alexander L. Miller*, Jill E. Cremer* and Richard L. Veech*. Section on Neurochemistry, NIMH, Saint Elizabeths Hospital, Washington, D.C. 20032

The rate of glucose utilization by brain has been estimated in larger species by measuring the arterio-venous difference of glucose and brain blood flow. However, present methods for the measurement of whole brain blood flow are technically difficult to apply to rats. An alternative method has been developed which conveniently measures the rate of glucose utilization by the whole brain of rats. The basis of the method is the uptake of [2-^{14}C]glucose. Catheters are placed in the femoral artery and vein under light ether anesthesia. After full recovery of consciousness a single injection of [2-^{14}C]glucose is given and arterial blood samples taken at intervals. Immediately after the last sample is taken the brain is removed and frozen within 1 s and the accumulation of ^{14}C into the total intermediary metabolite pool is measured. The rate of glucose utilization is calculated according to the equation:

$$\text{rate of glucose utilization (umol/min/g)} = \frac{^{14}\text{C accumulated by brain}}{\int_0^t \text{glucose specific activity (DPM x min/umol)}}$$

Assuming that brain cell and plasma glucose rapidly equilibrate the integral is evaluated from the plasma glucose specific activity curve. The rate of glucose utilization measured by this method in whole brain of conscious fed rats was 0.6 umol/min/g while a value of 0.3 umol/min/g was measured in pentobarbital sodium anesthetized rats (40 mg/kg body wt).

72.8 OXIDATION OF NICOTINAMIDE ADENINE DINULEOTIDE DURING INTERMITTENT STIMULATION IN DORSAL ROOT GANGLION NEURONS.
Carlos Rodríguez-Estrada. Cátedra de Fisiología, I.M.E., Facultad de Medicina, Universidad Central de Venezuela, Caracas, Venezuela.

Previous reports had shown that repeated short term nerve stimulation of dorsal root ganglia produced a change in the level of reduced Nicotinamide Adenine Dinucleotide (NADH) on the surface of this tissue. The first stimulation period produce a decrease of NADH (oxidation) followed by an increase of NADH content (reduction). The second and subsequent periods of stimulation always produced an oxidation, but the increase of NADH level progressively diminished until further stimulation had no effect. In this study fluorometric determination were made of the level of NADH following several short periods of peripheral nerve stimulation of dorsal root ganglion and related to intracellular action potentials. Isolated dorsal root ganglia of frogs (Rana palmipes spix) were used. The preparation was kept in a moist chamber (15°C). Electrical stimulation periods of 5 sec, repeated at varied intervals were used (square pulses, 0.1 msec duration, 20/sec, twice threshold). The first stimulation produced an oxidation followed by reduction of the NADH level, the second and subsequent periods of stimulation produced an oxidation, but the increase of NADH level progressively diminished until further stimulation had no effect, furthermore, a stimulation no longer produced oxidation. A new stimulation after a short resting period produced again oxidation and after a longer period oxidation and reduction. The results suggest that the oxidation and reduction od NADH is blocked by intermediary. metabolite (s) that controls the metabolic activity of this hydrogen carrier.

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72.9 REGIONAL DISTRIBUTION OF PYRUVATE DEHYDROGENASE IN CAT BRAIN AND ITS RELATION TO DISORDERS OF PYRUVATE METABOLISM. Susan F. Reynolds*, John P. Blass and Richard Jope*. Dept. of Biological Chemistry and Mental Retardation Center, UCLA Medical School, Los Angeles, CA 90024.

Regional differences in the distribution of pyruvate dehydrogenase (PDH) have been found in cat brain. Activity was measured free of mitochondrial controls with a radiochemical assay. PDH activity was highest in caudate nucleus (2.20 ± 0.29 nmoles/min per mg wet wt, ± SEM), intermediate in thalamus (1.64 ± 0.28), precruciate cortex (1.58 ± 0.21), postcruciate cortex (1.36 ± 0.16), and medulla (1.00 ± 0.16), and lowest in cerebellar cortex (0.76 ± 0.19). The distribution of PDH was similar when calculated per mg protein or per mg DNA, and resembled that of choline acetyltransferase but not that of the mitochondrial markers succinic dehydrogenase and cytochrome oxidase. This observation suggests that cholinergic mitochondria may be particularly rich in PDH. When PDH activity is compared to reported values for oxygen consumption, only the cerebellar cortex shows a relatively low excess of PDH available for non-energy producing pathways such as acetyl choline biosynthesis. Certain disorders of pyruvate metabolism such as thiamine deficiency are associated with cerebellar ataxia. Since the cerebellar cortex has low PDH activity but high oxygen utilization, it may be particularly susceptible to partial defects in the PDH complex.
(Supported in part by grants HD 05061, 00345, and 04612, GM 364, and by the California State Department of Mental Hygiene.)

72.10 CHANGES IN ENERGY METABOLISM IN ANOXIC NEONATAL RATS. Cyril L. Moore*and Jerry L. Myers*(SPON: James H. Pirch). Dept. Pedi. UTMB, Galveston, Texas 77550

Maintaining neonatal rats in nitrogen atmospheres for periods of 30 to 60 minutes results in changes in both anaerobic glycolysis and oxidative phosphorylation. Initial studies on brain tissue indicated that while the glycolytic flux continued at a maximum rate the soluble form of hexokinase was the only key enzyme in glycolysis to exhibit an increase in activity. This increase in soluble hexokinase is the result of a release of the bound particulate form. Mitochondria from brain tissue of anoxic animals are capable of utilizing both glutamate-malate and succinate as substrates in respiration, however, the rates are somewhat slower than control values. Coupling of respiration with phosphorylation is slightly slower but the maximum rate with TMPD(tetramethylephenylenediamine) is higher in mitochondria from anoxic animals. Spectral analysis of the cytochromes from anoxic mitochondria shows an increase in the cytochrome $a + a_3$ peak in the soret region at 447 mu. Indications are that the immature rat is compensating for a lack of energy production by increased glycolysis and increased synthesis of cytochrome oxidase.

72.11 The Effect of Brain Injury on Cerebral Glycogen Metabolism and Related Metabolites and Enzymes. J. V. Passonneau and H. Watanabe, NIH, Bethesda, 20014.

Glycogen has been demonstrated to accumulate in the brain following trauma. In the present study the effects of stab wound in the cerebral cortex have been investigated using quantitative chemical methods and ^{14}C-glucose incorporation into glycogen. Glycogen concentration in the area of the stab wound decreased in the first 10 min after injury, and subsequently increased at 2.5 hours and remained elevated for 24 hours. The amount of glucose in the brain decreased at 1 min after injury, then increased 3-fold at 10 min and remained elevated for 24 hours. No significant changes were observed in the concentration of uridine diphosphoglucose. The metabolic rate decreased to 50% of control values immediately following injury (1 min) and increased almost 2-fold at 10 min after injury. Cyclic AMP concentrations increased 7-fold 1 min after injury and subsequently decreased to control values (30 min). The turnover of cerebral glycogen was accelerated 30 min after injury, and was decreased 24 hours later. The percent of phosphorylase a was increased 1 min and 10 min after injury and subsequently decreased. The percent of glycogen synthetase in the I form was increased over control values 10 min after injury. The slower rate of loss of ^{14}C from cerebral glycogen and the decrease in the active form of phosphorylase in the injured brains indicate that the accumulation of glycogen can be attributed to decreased glycogenolysis. The data are consistent with an early phase of ischemia-anoxia, followed by a slow recovery to the condition existing before trauma, with the exception of the increases in glycogen.

72.12 EFFECT OF OUABAIN AND AMOBARBITAL ON CORTICAL METABOLISM ASSOCIATED WITH EVOKED POTENTIALS AND SPREADING DEPRESSION IN SITU. JOSEPH C. LAMANNA*, FRANS F. JOBSIS*, AND MYRON ROSENTHAL, Dept. of Physiology, Duke University, Durham, N.C. 27710

Evoked potentials, shifts of the steady potential and spreading depression (SD) have been shown to be associated with transient changes in the oxidative metabolic activity of the cerebral cortex of cats. The metabolic activity is measured at the intact surface by the intensity of the fluorescence emitted at 460 nm when the tissue is illuminated at 366 nm. The intensity of the fluorescence signal is related to the oxidation-reduction level of intramitochondrial NADH which is, itself, related to the ATP/ADP ratio and the rate of oxygen consumption.

In this study, the transient changes in metabolic activity with evoked potentials and SD are broken down into component parts by means of kinetic analysis. The Na-K ATPase inhibitor, ouabain (0.1mM) introduced directly under the cortical surface, markedly slows the on-kinetics with no change in recovery metabolism during SD. Amytal, a mitochondrial respiratory chain inhibitor in vitro, delays the reduction of NAD^+ (off-kinetics) during the response to SD and also during the small transient shift associated with electrically evoked potentials.

Thus, the transient fluorometric response to evoked potentials or SD is confirmed as a measure of ATP breakdown and oxidative rephosphorylation. The rate of NADH oxidation is a measure of the rising ADP concentration due to the action of the Na-K ATPase. The rate of return of the fluorescence to baseline levels (reduction of NADH) is a function of the respiratory chain. (Supported by NIH grants NS 10384 and NS 06233).

73.1 UNMYELINATED FIBERS IN THE VENTRAL ROOT. R.E. Coggeshall, J.D. Coulter and W.D. Willis, Jr. Marine Biomedical Insitute and Departments of Anatomy and Physiology, University of Texas Medical Branch, Galveston, Texas 77550.

Electron microscopy of the L_7 or S_1 ventral root in cats reveals that approximately 30% of the axons are unmyelinated. These axons are numerous enough to give a "C" fiber volley in excised, stimulated roots. Almost all the unmyelinated axons disappear proximal to a section of the root performed 7-11 days earlier, whereas the myelinated fibers degenerate distally. Thus, the cell bodies of the unmyelinated fibers are distal to the ventral root section. Four surgical excisions were used to locate the cell bodies that give rise to the ventral root unmyelinated fibers. In 3 cats sympathectomy did not change the ratio of myelinated to unmyelinated fibers. In one cat dorsal root section had no effect. In one cat peripheral nerve section had no effect. In 2 cats, removal of most of the dorsal root ganglion caused most of the unmyelinated fibers to disappear and greatly increased the ratio of myelinated to unmyelinated fibers. Thus, we tentatively conclude that the unmyelinated fibers in the ventral root arise from dorsal root ganglion cells. If this is the case, then preseumably the ventral root unmyelinated fibers carry information relating to sensation and 30% of the ventral root would be sensory. Physiological experiments designed to elucidate the function of the unmyelinated fibers are under way. Ventral root unmyelinated fibers have also been found in large numbers in frog and monkey. In the L_5 human ventral root approximately 35% of the axons are unmyelinated. (Supported by USPHS grants NS 10161 and NS 09743, USPHS Training Grant NS 05743, and a grant from the Moody Foundation of Galveston).

73.2 PROJECTION OF SUPRASPINAL FIBERS TO THE SPINAL CORD OF THE TEGU LIZARD, TUPINAMBIS NIGROPUNCTATUS. William L.R. Cruce. Anatomy Dept., Univ. of Wisconsin, Madison, WI. 53706.

Descending fiber projections to the lizard spinal cord were studied using anterograde axonal degeneration. Following hemisection of the cord at the 1st spinal segment and survival for 2-6 weeks, degeneration was found in the white and gray matter of transverse and horizontal sections at brachial and lumbar levels. Degeneration in the white matter was confined to the ipsilateral side and was found in the medial longitudinal fasiculus and the outer half of the lateral and ventral funiculi. Degeneration was more intense in the dorsolateral and ventromedial funiculi than in the ventrolateral funiculus.

Degeneration was seen in the medial half of the intermediate gray and ventral horn on ipsilateral and contralateral sides but was more intense on the ipsilateral side. Degeneration on the two sides of the cord was in apparent continuity with degeneration in the dorsal gray commissure and in the ventral accessory white commissure. In addition, sparse degeneration was seen in the lateral intermediate gray and in the dorsolateral ventral horn on the ipsilateral side. Thus degenerating elements were seen bilaterally near medial motoneurons and ipsilaterally (though sparsely) near the more dorsal of the lateral motoneurons.

Degeneration in both white and gray matter was only slightly less intense at lumbar than at brachial levels.

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73.3 CAT MEDIAL SUPERIOR OLIVARY NUCLEUS(MSO): FINE STRUCTURE AND DENDRITIC SPECIFICITY OF COCHLEAR NUCLEUS(CN) AFFERENTS. Bruce G. Lindsey*(SPON:J.C.Liu) Dept. Anat., Sch. Med., U. of Pennsylvania, Philadelphia, Pa. 19104.

The morphology of normal and degenerating synapses and their distribution upon the surface of cat MSO neurons have been analyzed by electron microscopy. Individual neurons or groups of cells oriented such that substantial lengths of their dendrites were within a 5-7μ thick section were selected for detailed study. Serial thin sections were cut from remounted thick sections. Terminals with round vesicles and boutons with flat and occasionally dense core vesicles were found upon normal neurons. Following unilateral CN lesions degenerating round vesicle terminals (enlarged vesicles, exaggerated filaments, "dark" and shrunken appearance) were observed on the lateral dendrites and somata of ipsilateral bipolar central column cells and the medial dendrites and somata of contralateral cells. Degenerating terminals were rarely seen on the opposite dendrite (1 of 39 cells). In 6 of 7 instances where medial and lateral dendrites of two cells overlapped degeneration was limited to the one oriented toward the lesion. Marginal cells examined received afferents predominantly from one CN. Flat vesicle terminals persisted on the somata and dendrites of all neurons examined, including cells from one cat with bilateral lesions. These data support the suggestion that the MSO is a model system in which to study: 1) the role of afferents in maintaining dendrite morphology (Liu& Liu,Anat. Rec.109: 369, 1971) and 2) neural plasticity. Supported by USPHS Grant #NB08768.

73.4 INVESTIGATIONS OF "NONSPECIFIC" THALAMIC PROJECTIONS TO PARIETAL REGIONS OF CEREBRAL CORTEX. Richard T. Robertson. Section of Behavioral Physiology, The Fels Research Institute, Yellow Springs, Ohio, 45387

Unilateral ablations of parietal cortex (middle suprasylvian and/or anterior lateral gyri) were performed in 8-17 day-old kittens and adult cats. Following survival periods of 6 days to 3 months, Nissl stained material from thalamus and cortex was examined with conventional light microscopical techniques. Retrograde degeneration, indicated by chromatolytic cell bodies associated with a significant cell loss, was observed in the rostral parts of lateralis posterior (LP) and pulvinar (Pul) and the ventral part of lateralis dorsalis (LD) as expected from anterograde degeneration thalamocortical studies (Graybiel, Brain Res., 1972, 44, 99). In addition, when lesions were performed in kittens, clear chromatolytic changes and cell loss were consistently observed in ventralis anterior (VA), particularly its dorsolateral extent. Other thalamic nuclei which have been suggested to project to parietal "association" areas (nucleus reticularis (R) and centralis lateralis (CL)) do not exhibit the chromatolytic changes characteristic of retrograde degeneration, but do often show a shrinkage and pyknosis of cell bodies, which is interpreted as anterograde transneuronal degeneration due to the loss of cortical afferents. It is suggested that this projection from VA to parietal cortex may mediate the EEG spindles and polysensory evoked potentials which can be recorded in parietal cortex (Phillips, et al., Physiol. Behav., 1972, 8, 269).

73.5 CENTRAL CONNECTIONS OF THE FROG'S RETINA AS DEMONSTRATED WITH COBALT IMPREGNATION. Kalman Rubinson. Dept. Cell Biol., Sch. Med., NYU and Dept. Neurobiol. and Behavior, Pub. Health Res. Inst., New York 10016

Infusion of cobalt chloride into optic nerve fibres and precipitation of the cobalt as cobalt sulfide marked the fibres in the brain. The intracellular injection technique of Pitman et al. (Science, 176: 412, 1972) was adapted by packing the eye with cobalt impregnated gelatin foam after a retinal lesion and brief wash in distilled water. Survival interval (20-72 hours at 7°C or room temperature) was followed by intracardiac perfusion of chilled 2.5% glutaraldehyde and then 1% ammonium sulfide. The brains were removed, soaked in 1% ammonium sulfide (20-60 min) and fixed again in glutaraldehyde for 2 hours. Alcohol dehydration with clearing in methyl salicylate resulted in transparent specimens bearing black optic pathways. Paraffin embedding enabled counterstaining of the sections with little loss of precipitate.

The pathways revealed are identical to those shown with degeneration in the contralateral thalamus and midbrain. Ipsilateral impregnation was poor. In addition, some neuronal perikarya contralateral to the injection site were impregnated. These neurons are possible candidates for the source of the efferent fibres of the optic nerve.

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73.6 **INTRINSIC CONNECTIONS IN THE FROG OPTIC TECTUM.** Michael C. Trachtenberg. McLean Hosp., Belmont, MA 02178.

Golgi and EM studies indicate that: a) the overwhelming majority of axons of tectal neurons remain within the tectum; b) the axons are predominantly vertically organized; c) dendrites, which are also vertically organized, may, in lamina (l.) 9, be presynaptic elements. Golgi and EM data provide no information on the lateral extent of these connections, their laminar density nor the specific laminar contribution to this intratectal projection system. Discrete electrolytic lesions of 75-150 μm diameter were placed in the tectum, under physiological guidance, of normal, monocularly enucleate, unitectal, and enucleate and unitectal frogs. Modified Fink-Heimer staining was performed following a 4-5 day survival at 27°C. A lesion of all 9 laminae results in a symmetrical cylinder of degeneration highlighted by a central, dorsally expanding cone of coarse particles with a major protuberance in l.8 and the immediately adjacent regions. Degenerating fibers are seen only in l.5-7. A 100 μm diameter lesion results in degeneration extending up to 1000 μm in diameter. The major contributors to this pattern are l.8, 6, and 9 respectively, while all laminae contribute to the central 300 μm of degeneration. The degeneration following l.8 lesion is confined to the superficial tectum whereas that from l.6 extends into l.5 and 6 though it is not as prominent in l.8 and 9 as is the case after l.8 lesion. The horizontal extent of coarse degeneration corresponds to no more than 40° of visual angle. Thus lateral modulation in the tectum is more extensive than in the retina but not extensive enough to account for observed inhibition at up to 90° lateral to the excitatory receptive field. The data indicate that extensive modulation occurs not only in l.9, the optic input layer, but in and around l.8 where most of the axons, intrinsic and extrinsic, arise from their parent cells.

73.7 AXON DIAMETERS IN THE LATERAL HYPOTHALAMUS OF THE RAT. R. H. Thalmann*and L. A. Forsyth*(SPON: R. Bruce Szamier) Dept. Cell Biol., Baylor Col. Med., Houston, TX. 77025.

Recent behavioral and neurophysiological experiments have suggested that it may be possible to link different behavioral effects due to electrical stimulation of lateral hypothalamus(LH) to medial forebrain bundle(MFB)axons with different refractory periods, and thus to axons with different average diameters(e.g., Rolls, Br. Res. 45:365, 1972). Since inferences of this sort invite more direct information about the axons which are available to serve as substrates for these effects we have estimated axon diameters in .3 micron(μ) thick sections of LH which had been prepared for light microscopy. After LH tissue had been fixed with paraformaldehyde-gluteraldehyde, postfixed in osmic acid, and embedded in araldite, coronal sections through this tissue at the anterior-posterior level of the ventromedial nucleus were stained with tolouidine blue. The inside diameters of myelin profiles were taken as the estimate of axon diameters. Profiles which suggested axons travelling parallel to the plane of section were not included in this analysis. Although, as expected, numerous myelin profiles with inside diameters ranging from less than 1 μ up to 3μ were found throughout the MFB region, much larger profiles were also observed. A cluster of profiles up to 7.5μ in diameter occurred in the ventrolateral portion of the MFB, and scattered profiles which approached this size occurred in other areas of MFB. For example, profiles up to 6μ in diameter have been measured within the perifornical area of LH. In view of the density of stain which occurs in the fornix itself with routine myelin staining of thick(25μ) sections by the method of Weil, it was notable that the fornix at this level did not contain such large diameter axons, but was rather comprised of densely packed myelin profiles whose inside diameters varied from less than 1μ to about 2.5μ.

73.8 THE FINE STRUCTURE OF THE THORACIC SPINAL CORD FOLLOWING EXPERIMENTAL COMPRESSION. C. Wakefield and E. Eidelberg. Barrow Neurological Institute of St. Joseph's Hospital and Medical Center, Phoenix, Arizona 85013.

Injury to the spinal cord results in pathological alterations of the tissue and limited regeneration of interrupted axons. In order to evaluate the effectiveness of therapeutic agents to promote axon growth, the inflammatory process was studied using light and electron microscopic techniques. Experimental compression of the cord was performed according to the method described by Eidelberg (J. Neurosurg., 38: 326-331, 1973). The cats were allowed to survive for intervals of 2,3,7,14 and 60 days. Two days after the compression there were areas of necrosis in the gray matter and swelling of some axons in the dorsal columns. Agranular leukocytes and plasma cells had infiltrated both gray and white matter. There was a marked increase in the extracellular space. By 3 days mononuclear cells containing myelin fragments and large vacuoles were seen frequently. An increase in the electron density of the axoplasm was evident. Many degenerated axon fragments were being ingested by macrophages and the processes of astrocytes began to fill the extracellular spaces between 3 and 14 days. By 60 days macrophages, glial cells and a few normal axons remained. This data indicates that degeneration and phagocytosis in the injured spinal cord progresses over a period of months.

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73.9 EVALUATION OF NORMOTHERMIC SPINAL CORD PERFUSION AFTER IMPACT INJURY. Maurice S. Albin and Robert J. White. Depts. Anes. & Neurosurg., Univ. Pittsburgh Sch. Med., Pittsburgh, Pa. 15213 and Case Western Reserve Univ. Sch. Med., Cleveland, Ohio 44109

In previous reports we noted that significant functional recovery occurred in both subhuman primates and canines after impact injury to the spinal cord when prolonged selective hypothermic perfusion was employed. For controls, we used comparable animal groups that were subjected to the same impact injury forces but received no perfusion cooling. Employing acute spinal cord compression to produce a standard injury, Tator and Deecke (1972) reported that normothermic perfusion was apparently more effective than hypothermic perfusion in obtaining functional recovery. In order to evaluate the effect of normothermic perfusion, six dogs and six monkeys were subjected to impact injury forces (prior laminectomy at T_{10} vertebrae level, injury unit consisting of a mass dropping a known distance on the exposed cord) that rendered the non-perfusion controls paraplegic (400 gram-centimeters and 300 gram-centimeters of force respectively). After a four hour delay, the investing membranes were incised and perfusion carried out (using a pump, heat exchanger and sterile isotonic saline) with the inflow perfusate entering and maintained at the preperfusion spinal cord temperature (36.5^{o} C $\pm$ 1.0^{o}) for three hours at a flow of 150 ml/min. The animals were observed for three months and then sacrificed for histological study. All animals developed paraplegia after impact injury and normothermic perfusion and remained paraplegic till sacrifice three months later. It is clear that normothermic perfusion affords no protection from linear impact injury forces employed at or above paraplegic threshold levels. The neurological, behavioral and histological results will be discussed and the question of spinal cord injury models detailed.

73.10 MICROSCOPIC STUDIES OF DEGENERATION IN THE CRAYFISH BRAIN FOLLOWING ANTENNULE REMOVAL. Edith A. Maynard. Biol. Dept., Univ. of Oregon, Eugene, 97403 (supported by USPHS NS 09614)

The proximal stump of the antennular nerve and various tracts and synaptic neuropil areas of the crayfish brain were examined from 24 hrs to 5 mo after unilateral antennule removal between the basal and second segments. At 22-27°C, 3 days to 1 wk post-operative (PO), osmiophilic debris is seen in homolateral antennular synaptic regions of the brain, and the persisting stump of the cut nerve shows degenerative changes (disorganization, phagocytes) in many nerve fiber bundles (4μ sections of glutaraldehyde pre-fixed, osmium tetroxide post-fixed, plastic embedded tissues were used). At 1 wk PO, silver impregnation studies of paraffin-embedded brains reveal loss of elements from the inner, glomerular synaptic region of the olfactory lobe. Progressive degenerative changes over the next 5-6 weeks culminate in a severely altered brain morphology homolaterally. At 6-13 wks, in animals staying in intermolt throughout the PO interval, or in early premolt at the time of killing, these changes include (in silver stains): loss of 90-95% of the outer (afferent fiber) layer of the olfactory lobe with local increase in glial cells; altered staining and decreased thickness of the second, synaptic layer of this lobe in addition to the earlier loss of glomerular elements from the deeper synaptic zone; selective loss of certain fiber tracts originating in the antennular nerve. The changes are reversed upon regeneration of a new antennule. The results establish a time course for degenerative phenomena in crustacean sensory axons entering the CNS.

73.11 DEATH OF THE INTRINSIC NEURON: AN ELECTRON MICROSCOPIC STUDY OF THALAMIC RETROGRADE DEGENERATION FOLLOWING CORTICAL ABLATION. Murray A. Matthews
Dept. Anat., L.S.U. Med. Center, New Orleans, Louisiana 70119

A series of twenty-seven rabbits were subjected to extensive aspiration lesions of limbic, striate and somato-sensory cortex, followed by electron microscopic examination of the antero-ventral, dorsal lateral geniculate and ventro-basal thalamic nuclei at various post-operative periods ranging from one to 238 days. Terminal degeneration occurs after twenty-four hours and is seen in abundance during the second and third day. Neuronal perikaryal alterations become evident by day 2 and include the deterioration of endoplasmic reticulum with an apparent significant ribosomal loss, in addition to the incremental appearance of vacuoles and large homogeneous dense bodies. During the second and third post-operative weeks, a period in which the rate of neuronal depletion is maximal, many degenerating cells are characterized both by disruption of nuclear and cytoplasmic components, and the appearance of complex pleomorphic electron-dense bodies thought to constitute cites of perikaryal autolysis. From the fourth through thirty-fourth post-operative week, virtually all remaining neurons gradually disappear from the zones of degeneration.

Neuronal degeneration is accompanied by astrocytic hypertrophy and infiltration of the degenerating neuropil by mesodermal elements, tentatively designated as "M" cells, (Matthews and Kruger, 1973). However, despite this extensive non-neuronal reaction, little evidence for significant neuronophagia could be found. Loss of axoplasm, destruction of thalamo-cortical synaptic connections and massive deafferentation of thalamic neurons, partially due to anterograde degeneration of cortico-fugal axons, are discussed as possible factors which influence the rate and severity of retrograde atrophy.

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73.12 HISTOLOGICAL PATTERNS OF FIBRILLARY NEURONAL DEGENERATION IN ALZHEIMER'S DISEASE AND ATYPICAL FORMS OF DEMENTIA. Leopold Liss, M.D., Div. of Neuropathology, Dept. of Pathology, Ohio State University College of Medicine.

The senile plaques and the neuronal fibrillary degeneration which are the recognized histological substrate of senile dementia and Alzheimer's Disease represent a specific result of neuronal degeneration, affecting significantly the atrophic frontal and temporal lobes, and especially, the hippocampus. The co-existence or lack of concomittant occurrence of the plaques and this fibrillary neuronal degeneration does not appear to have significant correlation with patient behavior. Fibrillary degeneration of the large neurons in the periaqueductal gray has been in the past either neglected or unknown. In patients who have these lesions, the pattern of violent behavior, either with or without dementia, represents significant aspect of their psychiatric symptomatology. The correlation between the clinical symptomatology and histopathological findings will be presented and illustrated with histological variants of neurofibrillary degeneration patterns.

74.1 SURFACE ELECTROSPINOGRAM (ESG) RECORDINGS IN MAN FOLLOWING SYNCHRONOUS ACTIVATION OF AFFERENT FIBERS. A.Willem Monster. Dept. Rehab. Med., Temple Univ. Hlth. Scs. Ctr., Philadelphia

Electrical stimuli (pulse width 0.2-2 msec) were applied to the tibial nerve in the popliteal fossa (8 subjects). The evoked afferent volleys were followed along the spine from the lower lumbar up to the cervical cord. The shape and size of the evoked wave varies along the cord. The cauda equina response (L1-L4) is triphasic with both the presynaptic (ascending) and the postsynaptic (descending) wave being visible, partly superimposed and dependent on stimulus size. The waves are usually several milliseconds wide, first positive going, and the latency varying between 8-10 msec, depending on the individual's size. The size of the response increases over the lower thoracic cord (T12-T8). This may be due to the increased volume of active tissue and/or slowing down of the conduction at the branching points and formation of the long ascending tracts. The wave decreases in size more rostrally, is mostly biphasic and there is a widening of the wave shape. This may be the result of temporal dispersion. ESG waves evoked by phasic muscle stretch (taps to Achilles tendon) have also been measured. The ratio of afferent-to-efferent activity is much reduced in comparison to the electrical stimulus, unless the latter is substantially below threshold for a minimal motor response. This technique has so far been used to study chronic (patients with spasticity) and transient (normals during initiation of a voluntary contraction) changes in the peripheral and central components of the monosynaptic reflex of the triceps surae muscle.

74.2 TIME SERIES ANALYSIS OF PARKINSONIAN HAND TREMORS. Robert S. Pozos and Robert N. Stiles. Univ. Tennessee Medical Units, Memphis, Tenn. 38103

Acceleration records of hand tremor from Parkinsonian subjects were analysed in both the frequency and time domains to derive amplitude, frequency, and waveform information. Amplitude and frequency values in the frequency domain were obtained by power spectral analysis. Digital filtering provided separation without phase shift of different frequency components in the time domain. For the tremor records of some subjects, spectral analysis revealed two frequency components whose frequency values were harmonicly related. Separation of these two frequencies in the time domain indicated that one frequency component was amplitude-modulated at the frequency of the second component. For certain of these records with harmonic frequencies which had small displacement amplitudes (less than 1 mm), frequency and waveform patterns were similar to those found in records with large displacement amplitudes. However, in some records of both large and small displacement tremors obtained from the same Parkinsonian subject, spectral analysis revealed two harmonics during large displacement oscillations and a single, intermediate-valued frequency which occurred during small displacement oscillations. The results of these combined methods of analysis indicate that two (or perhaps three) separate mechanisms may be involved for certain Parkinsonian tremors.

This work was supported by Research Grant NS-08692 from the National Institutes of Health.

74.3 PATTERNS OF CORTICAL PROJECTION TO HINDLIMB MOTONEURONE POOLS. Floyd J. Thompson, Julio J. Fernandez* The Rockefeller University, New York, New York 10021

It has been shown that there are discrete cortical neuron colonies which project to individual forelimb muscles. On the other hand indirect evidence has suggested that cortical control of hindlimb muscles is topographically less specific. The present study was undertaken to determine if there also exist discrete colonies of neurones in the cortex which control individual hindlimb muscles. Nembutalized and curarized cats were used. Sequential penetrations with a stimulating microelectrode were made in the hindlimb area of the motor cortex. The effects of weak stimulating current pulses of less than 10 ua were examined on monosynaptic reflexes in individual muscle nerves. It was found that facilitation or inhibition of a given monosynaptic reflex was produced from a circumscribed area of the cortex having a diameter of somewhere between 1.0 to 1.5 mm. The fringes of a given effective zone frequently overlapped with the fringes of another effective zone. Stimulation within an effective zone produced facilitation or inhibition of a given reflex and was not combined with reciprocal effects on the reflex of the antagonist. Stimulation at the overlapping area produced simultaneous facilitation sometimes in the synergists and other times in the antagonists. It is concluded that the cortical neurones which control the contraction of hindlimb muscles are organized into discrete efferent zones. Our findings suggest that these efferent zones can control contraction of individual muscles independently of spinal reciprocal mechanisms.

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74.4 CORTICAL LOAD COMPENSATION DURING VOLUNTARY ELBOW MOVEMENTS. B. Conrad*, K. Matsunami*, M. Wiesendanger* and V. B. Brooks. Dept. Physiol., Univ. of Western Ontario, London N6A 3K7, Canada.

Records were made of precentral neuron activity that was related to alternate elbow flexions and extensions made by a Cebus monkey into target zones (Brooks et al, Brain Res., 1972, 40, 85). Unexpected transient load changes were applied to the handle that the monkey was guiding during randomly selected movements (torque pulses of 100 g for 10 msec triggered at 75 deg/sec.). Load increases caused spinal stretch reflexes of the agonist 10-15 msec after torque onset, while equivalent unloading caused agonist inhibition 15 msec after torque onset. Firing patterns of 30 out of 36 movement-related precentral neurons were modulated by transient load changes applied during contraction. Discharges were increased for 9 triceps- and 4 biceps-related cells after loading of their agonist muscles, and were decreased by unloading, with latencies from torque onset of 30-60 and 20-40 msec. These consistent responses of movement-linked precentral neurons to peripheral load changes could contribute to cortical load compensation (Phillips, Proc. Roy.Soc.B, 1969, 173, 141); which finds its expression in later EMG changes, that could start 80 msec after torque-onset. Thus these cortical neurons received input and provided output appropriate for adjustments of unexpected load changes (Evarts, Science, 1973, 179, 501), so that trained voluntary movements could continue successfully.
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74.5 MOTOR REFLEXES DURING OPERANTLY CONDITIONED ACTIVITY (12 - 14 cps) OF THE SENSORIMOTOR CORTEX. Michael H. Chase and Margaret Babb. Depts. Anat. and Physiol., Sch. Med., UCLA, Los Angeles, 90024.

A specific EEG rhythm is generated by the sensorimotor cortex during states of behavioral immobility or internal inhibition (SMR – 12-14 cps). By studying somatic reflex activity during operantly conditioned SMR we sought to examine the bases for the accompanying lack of movement. Eight adult cats were implanted in a manner to enable chronic stimulation and recording in the freely moving animal. The masseteric monosynaptic (jaw-closing) reflex was induced by stimulation of the mesencephalic nucleus of the trigeminal nerve, and the digastric polysynaptic (jaw-opening) reflex by excitation of the inferior dental nerve. The reflex responses were recorded from wire loops in the masseter and digastric muscles, respectively. Other electrodes were placed to monitor the EEG, eye EOG and neck EMG. As previously reported, SMR episodes were accompanied by a cessation of limb, trunk, and ocular movements. During conditioned SMR there was a reduction in amplitude of the masseteric reflex but no variation was apparent in digastric reflex amplitude. Thus, the decrease in masseteric reflex amplitude was consistent with the other motor variations which are correlated with SMR production. The lack of variation for the digastric reflex may be due to the polysynaptic nature of this reflex or its lack of gamma motoneurons and muscle spindles, which are present in the neck and masseter musculature. It is therefore possible that the mechanisms which promote the tonic aspects of motor inhibition during SMR act by reducing gamma motoneuron discharge.

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74.6 A QUANTITATIVE DESCRIPTION OF POSTURAL CONTROL IN THE DOG DURING SINUSOIDAL PERTURBATION. Richard E. Talbott. Dept. Physiol., Univ. Oregon Med. Sch., Portland, 97201.

A linear model of the torques developed at the various fore and hind limb joints of the dog was formulated from quantitative measures of postural response during static (quiet standing) and dynamic (step displacement) conditions. In order to extend the model to the case in which the dog was required to make continuous postural adjustments to a sinusoidal displacement of the supporting platform, a Fourier analysis was made of several external measures of the response: vertical force, horizontal force, joint angle changes of the hind leg, pelvis displacement in the horizontal plane, and platform position. In particular, the response to a 1 Hz x 8 cm (peak to peak) sinusoidal displacement of the platform revealed that the harmonic distortion of the joint angle measures ranged from 68% to 87%, that of the pelvis displacement was 74%, and that of the driving force was only 8% when the first 64 Fourier coefficients were computed from data records comprising 8 cycles of the forcing frequency. When only those harmonic coefficients were retained which were integral multiples of the input frequency, the harmonic distortion of the joint motion still ranged from 13% to 38% while that of the pelvis motion was reduced to 8% and that of the table motion was reduced to 4%. Hence, the postural control system of the dog appears to behave like a non-linear system for the control of joint angle and, by extension, torque at a joint, but to approximate a linear system for the control of body position during the response to continuous sinusoidal displacement.
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74.7 ACTIVITY OF NEURONS IN THE LOWER PRECENTRAL CORTEX OF MACACA MULATTA DURING JAW MOVEMENTS. J.P. Lund* and Y. Lamarre. Centre de Recherches en Sciences Neurologiques, Université de Montréal, Montréal 101, Qué., Canada.

Repetitive electrical stimulation of the lower precentral gyrus evokes rhythmical masticatory movements, but since simple repetitive jaw movements occur in decerebrate animals, cortical control of jaw movements has been disputed. Recordings were made from neurons in this region while monkeys opened their mouths to receive a cola reward, made rhythmical post-ingestive tasting movements, or chewed apple. Fifteen neurons discharged phasically with opening and in 9 cases the frequency was increased before movement began. They received a proprioceptive input and fired during passive opening of the jaw. Their maximum discharge frequency during opening was proportional to the maximum displacement, and loads aiding opening increased their discharge rate. It is suggested that these neurons encode the degree of jaw opening. Thirty-six neurons fired with a weaker phase relationship to jaw opening, 25 when the jaw was open and 5 with tongue protrusion. These neurons may control the jaw, tongue and face muscles which are not principally responsible for opening or closing the jaw. Thirteen neurons discharged when the teeth were in contact, or when food was crushed between the teeth, and probably receive input from periodontal pressoreceptors. These neurons could control the tension developed in jaw closing muscles when there is food between the teeth. However unopposed closing movements, such as occur during rhythmical tasting, are probably controlled by the brain stem, since no cortical neurons were found whose discharge frequency could be correlated with the parameters of such movements.

74.8 SYNAPTIC ORGANIZATION AND FUNCTIONAL IDENTIFICATION OF INHIBITORY NEURONS IN THE SENSORIMOTOR CORTEX. Leo P. Renaud and John S. Kelly*. Dept. Res. in Anaesthesia, McGill Univ., Montreal 101, Canada

Direct neuronal interconnections can be inferred on the basis of evidence of significant short latency interactions between spike trains recorded simultaneously from two or more neurons. Asymmetrical negative cross-correlations, suggesting monosynaptic inhibition have been found useful in the study of cortical inhibitory pathways, particularly as an aid in the identification of possible inhibitory neurons. A LINC-8 computer was used to analyze spontaneous or glutamate-evoked spike discharges from 110 pairs of identified pyramidal tract (PT) and other (non-PT) neurons, recorded with two independent microelectrodes positioned less than 700 microns apart in the pericruciate cortex of the pentobarbital anaesthetized cat. With 10 pairs of neurons (9.1%) a low density of points along the 45° line of joint scatter diagrams (Gerstein and Perkel, Sci. 164: 828, 1969) and a very short latency (less than 2 msec) asymmetrical negative cross-correlogram suggested a direct inhibitory connection between the two cells. Inhibited cells were either PT or non-PT neurons. "Inhibitory" neurons were always non-PT cells, located at various cortical depths and generally insensitive to iontophoretically applied acetylcholine. Antidromic stimulation of the pyramidal tract evoked an orthodromic burst of spikes from some of these non-PT inhibitory cells, the first spike always occurring at least 0.7 msec later than the PT antidromic spike, suggesting that these may be inhibitory interneurons situated in the PT recurrent inhibitory pathway.

(Supported by the Canadian Medical Research Council)

74.9 INITIATION OF HUMAN GAIT CYCLE: ROLE OF CENTRAL AND PERIPHERAL MECHANISMS. Richard Herman, Thomas Cook* and Barbara Cozzens*. Dept. Rehab. Med., Temple Univ. Hlth. Scs. Ctr., Philadelphia, 19140.

The initiation of the gait cycle was evaluated during two phases: a pre-locomotion (auditory signal to toe off of the swing limb) and a locomotion (initial step swing and stance cycle) phase. The following factors were examined during both phases: amplitude and position of vertical forces under each limb, resolution of these forces, position (including velocity and acceleration) of ankle, knee and hip joints, moments about each ankle joint and the electromyogram of flexor and extensor muscles controlling the three joints. All normal subjects demonstrated tight spatio-temporal coupling of myoelectric potentials during each phase. These patterns appear to be generated by a central program as immobilization of the ankle joint, complete narcotization of the ankle joint, differential suppression of the tibial nerve and depression of active torque following Dantrolene administration do not appear to interfere with synergistic relationships and with timing of the myoelectric discharges related to joint position and force development.

74.10 GATING OF MOTOR CORTEX REFLEXES BY PRIOR INSTRUCTION. Jun Tanji* and E.V. Evarts. Lab. Neurophysiology, NIMH, Bethesda, Md. 20014.

A previous study (Science 179: 501-503, 1973) showed that sensory input can generate reflex motor cortex output in association with learned movement when the sensory input has a strong connection to the motor cortex--e.g., when a stimulus calling for repositioning of the hand consists of a perturbation of hand position. The present study has shown that motor cortex reflexes can be "gated" on or off by the voluntary "set" of the monkey. Monkeys were trained to grasp a handle and maintain it in a certain position for 2 to 4 sec; they were then given an "instruction" as to how they should respond to a forthcoming perturbation of the handle. The "instruction" was a red or green light which appeared between 0.6 and 1.2 sec prior to the handle perturbation. The red light signalled that the monkey should pull toward himself when the perturbation occurred, and the green light meant that he should push away when the perturbation occurred. Two different sorts of perturbation were used, one being a movement of the handle toward the monkey and the other away from the monkey. A given instruction called for a movement synergistic with segmental stretch reflexes for one of the perturbations and antagonistic to these reflexes for the other. Following training, activity of motor cortex neurons was recorded during task performance. Neurons in precentral motor cortex showed changes of activity according to the "instruction" as early as 200 msec following the onset of red or green light. In addition, the short (20 msec) latency motor cortex responses evoked by the subsequent perturbing stimuli differed markedly depending upon the prior instruction. The finding that the set and expectancy of the monkey could profoundly modify this "reflex" response indicates that the transcortical servo-loop proposed by Phillips is subject to powerful modulation as a function of learning and volition.

75.1 BIOCHEMICAL CORRELATES OF NEUROBLASTOMA DIFFERENTIATION. Vincent J. Aloyo, * Jerome B. Witherington, III,* Samuel V. Molinary,* and William L. Byrne (SPON: Larry A. Kepner). Brain Research Institute, Department of Biochemistry, and Child Development Center, University of Tennessee Medical Units, Memphis, Tennessee 38103.

It has been well established that the differentiation of logarithmically growing mouse neuroblastoma C 1300 is accompanied by a variety of biochemical changes as well as axon formation. We have shown that in clone N18, increased $^{35}SO_4^{-2}$ incorporation and increased colchicine binding correlate with axon formation. Bromodeoxyuridine (Brdu)-induced neuroblastoma incorporate 50 to 60% more $^{35}SO_4^{-2}$ than logarithmically growing controls at concentrations of Brdu which have been reported to result in numerous changes in the protein composition. The neuroblastoma were treated for six days with 10^{-6}M Brdu in Eagle's medium. During the last 48 hours of the Brdu treatment the cells were incubated with $^{35}SO_4^{-2}$. The cells were then harvested and extracted by a procedure designed for the extraction of mucopolysaccharides. Similar elevated $^{35}SO_4^{-2}$ incorporation by axonated cells was obtained when axonation was induced by lowering the concentration of fetal bovine serum (FBS) from 10% to 1% for six days. In separate experiments, neuroblastoma induced to axonate by complete removal of the FBS for four days showed a significant increase in ^{3}H-colchicine bound per milligram protein. This is in contrast to previously reported work where no increase in colchicine-binding protein was obtained by analysis of the high speed supernatant fraction. In our experiments colchicine binding was carried out by adding ^{3}H-colchicine to the intact cells, excess ^{3}H-colchicine was removed by washing the bound colchicine was extracted with 0.1N NaOH.

75.2 UPTAKE OF 3H-γ-AMINOBUTYRIC ACID BY NEURONS IN CULTURES OF DISSOCIATED DEVELOPING RAT CNS. Robert S. Lasher. Dept. Anat., Univ. Col. Med. Sch. Denver, Co. 80220.

Previous studies of 3H-γ-aminobutyric acid (GABA) uptake in cultures of postnatal (pn) rat cerebellum (R.S. Lasher and I.S Zagon, Brain Res.41:482, 1972) demonstrated localization of label in those types of neurons known to be inhibitory. The aim of this study was to examine 3H-GABA uptake in other regions of the developing rat CNS to determine the distribution and morphology of possible GABA neurons. Dissociated cultures of 16 day (d) embryo rat cerebral hemispheres (CH), hindbrain, and spinal cord (all 18 ds in vitro-DIV), 1 d pn rat hippocampus+dentate gyrus(6-19 DIV), and 2 d pn rat pons (21 DIV) were incubated in Hanks saline G with 0.3-0.5μM 3H-GABA at room temp for 15 min, rinsed 2X in cold saline, fixed in glutaraldehyde, and processed for autoradiography. The ratio of labeled to unlabeled neurons in cultures of CH was found to be quite low, but was very high in cultures of all other areas. In all cultures, the labeled neurons were predominately isodendritic, with either a spherical soma (ca. 10-13μ dia) or oval soma (ca. 13 x 20μ or 20 x 30μ dia). The smaller cells generally had 3-5 dendrites 60-200μ long, and a axon up to 700μ long. The larger cells generally had 2 large dendrites at opposite poles 150-300μ long (some had 3-5 large dendrites), and an axon up to 1 mm long. Also, in cultures of pons there were groups of allodendritic neurons with 3-4 short dendrites, and isodendritic neurons with 6-10 dendrites radiating from the cell body. There appears, therefore, to be a close morphological resemblance between neurons taking-up GABA in the cultures and inhibitory neurons in the CNS. Supported by NIH grant NS-09641.

75.3 UPTAKE OF CHOLINE BY CLONAL LINES OF ASTROCYTOMA AND NEUROBLASTOMA IN CULTURE. B. Haber, T. Colmore*, K. Werrbach* and H.T. Hutchison* (SPON: S.G. Wolf). Division of Comparative Neurobiology, Marine Biomedical Institute, and Department of Human Biological Chemistry and Genetics, University of Texas Medical Branch, Galveston, Texas 77550.

The reuptake of choline produced by hydrolysis of acetylcholine (Ach) is necessary for cholinergic function and is thought to be associated specifically with cholinergic terminals and the synthesis of Ach. Glial cells may modulate synaptic function by participating in the reuptake of choline. The C6 rat astrocytoma and mouse NB41 neuroblastoma cell lines have been used in our laboratories as glial and neuronal model systems. Kinetic analysis indicates that choline uptake in NB41 and C6 cells is mediated by a high-affinity, carrier-mediated transport system (K_m = 9 μM and 11 μM, respectively) and a second mechanism which is not saturated at 100 μM choline. These values of the Michaelis constants for high-affinity choline transport in neuroblastoma and astrocytoma cells are somewhat higher than the values reported by Richelson and Thompson (1973). Marchbanks (1969) has reported that eserine, a cholinesterase inhibitor, inhibits the uptake of both choline and Ach in synaptosomes. We found that 10^{-4} M neostigmine reduces choline transport in these cells by about twofold. The C6 and NB41 cell lines have low, but detectable, choline acetyl transferase (CAT) activities. The CAT specific activites, as determined in our laboratory, are 6.4% for NB41 and 3.3% for C6, as compared to whole mouse brain homogenate values. These results suggest that both cell lines have some capability for Ach synthesis. The suggestion that high affinity uptake systems for choline are linked to Ach synthesis (Yamamura and Snyder, 1972) are being tested in several clonal lines of neuroblastoma. (Supported by USPHS grant MH 19502, a grant from the Robert A. Welch Foundation (H-504) and a grant from the Moody Foundation of Galveston.)

75.4 QUINAZOLINE ANTIFOLATES AS INHIBITORS OF THE GROWTH, DIHYDROFOLATE REDUCTASE AND THYMIDYLATE SYNTHETASE OF MOUSE NEUROBLASTOMA CELLS IN CULTURE. Steven C. Carlin*, Roger N. Rosenberg, Larry VandeVenter* and Morris Friedkin*. Depts. Neurosci., Peds., Biol., Sch. Med., UCSD, La Jolla, 92037

Correlations of growth inhibition and enzyme inhibition by several quinazoline analogs of folic acid have been made with two lines of C1300 mouse neuroblastoma cells, one sensitive and one resistant to quinazoline analogs. The quinazoline analogs studied fell into two classes: the 2, 4-diaminoquinazoline analogs DAQ (N-[p-[[(2,4-diamino-6-quinazolinyl) methyl]methylamino]-benzoyl]-L-glutamic acid) and Methasquin (N-[p-[[(2, 4-diamino-5-methylquinazolinyl)methylamino]benzoyl]-L-aspartate) were potent inhibitors of growth and of dihydrofolate reductase but only weak inhibitors of thymidylate synthetase, whereas the 2-amino-4-hydroxyquinazoline analog AHQ (N-[p-[[(2-amino-4-hydroxy-6-quinazolinyl)methyl] methylamino]-benzoyl]-L-glutamic acid) was less potent as an inhibitor of growth and of dihydrofolate reductase but more potent towards thymidylate synthetase. With the 2,4-diaminoquinazoline analogs there was a good correlation between growth inhibition and dihydrofolate reductase inhibition. With AHQ, however, growth inhibition seemed to depend upon the inhibition of both dihydrofolate reductase and thymidylate synthetase. Although it is less effective than the diaminoquinazolines as an inhibitor of neuroblastoma growth in culture, AHQ may be useful in the chemotherapy of neuroblastoma because of its unique potency towards thymidylate synthetase.

75.5 PROTEIN-INDUCED ALTERATION OF CELL MORPHOLOGY. Ramon Lim and Katsusuke Mitsunobu* Division of Neurosurgery and Department of Biochemistry, University of Chicago, Chicago, Illinois 60637

Brain cells from rat embryos were dissociated and grown in a monolayer culture. After one or two subcultures, a primitive cell type, having thin, spread-out cell bodies and devoid of processes, outgrew all other cell types. We reported in this meeting a year ago that a macromolecular factor from adult brain is capable of transforming these cells to multipolar cells resembling mature astrocytes. Our laboratory has now attained a 20-fold purification of this factor using ethanol precipitation and gel filtration. The factor is a high molecular weight protein as evidenced by its exclusion by Sephadex G-100 and susceptibility to Pronase digestion. The activity is resistant to trypsin, DNase, RNase, and periodate oxidation. All the commercially available proteins and non-protein macromolecules tested so far fail to reproduce the effect of this brain protein. The activity is antagonized by fetal calf serum but potentiated by theophylline. Dibutyryl cyclic AMP but not cyclic AMP at 1 mM concentration causes similar transformation. On the other hand, pre-incubation of the brain protein with cyclic AMP phosphodiesterase did not abolish the transforming activity. Prostaglandin E_1 at 10 μg/ml did not affect the morphology of these cells. Nor was any effect observed with material extracted from the brain sample according to the established procedures for the isolation of prostaglandins. A starvation response secondary to the absence of serum has been ruled out since all the experiments were conducted under conditions where serum withdrawal per se did not induce morphological differentiation. We believe that the observed phenomenon results from a partial restoration of the cerebral chemical environment to the cultured cells. (Supported by U.S. Public Health Service grants no. NS-09228 and NB-07376.)

75.6 SURVIVAL AND TROPHIC FUNCTION OF HOMOGRAFTED NEURONS BY IMMUNOSUPPRESSION. A. A. Zalewski and W. K. Silvers*. NIH, Bethesda, Md. 20014; Dept. Med. Genetics, Univ. of Pa., Phila., Pa. 19104.

A major histoincompatibility exists between Brown Norway (BN) and Lewis (LE) rats so that organs homografted between them are rejected by an immune reaction. This reaction can be suppressed by injecting the rats at birth with bone marrow or lymph node cells from hybrid (LEXBN) adult rats. The present study was performed to determine whether homografted neurons would survive in such pretreated rats. In untreated animals, all neurons in sensory ganglia (vagal nodose) homografted from LE donors to the anterior chamber of the eye of BN hosts were rejected at 35 days. However, when neonatal BN rats were injected with adult (LEXBN) F_1 hybrid bone marrow or lymph node cells and challenged as adults with LE ganglion grafts neurons survived beyond 100 days. Furthermore, when LE ganglia and BN vallate papillae were combined in the eye of BN hosts, nerve fibers from the surviving neurons grew into the papilla and caused the formation of taste buds. Papillae isografted without ganglia lacked buds. These results demonstrate that the rejection of neurons between rats exhibiting major histoincompatibility can be prevented and that these neurons can regenerate their nerve fibers and function trophically (i.e. induce and maintain taste bud formation) during immunosuppression.

75.7 THE EFFECTS OF GANGLIONIC NON-NEURONAL CELLS AND NERVE GROWTH FACTOR ON BIOELECTRIC ACTIVITY IN DORSAL ROOT GANGLION NEURONS GROWN IN CELL CULTURES. Edward Tyszka. Dept. Biol., UCSD, La Jolla, 92037

Sufficient numbers of additional non-neuronal cells have been shown to mimic the ability of the Nerve Growth Factor (NGF) to enhance the attachment, fiber generation and survival of neurons in cell cultures of dissociated dorsal root ganglia (DRG's) of the newborn mouse. The possibility that non-neuronal cells could also influence bioelectric phenomena was explored by examining the intracellularly-evoked action potentials (AP's) of neurons grown under various conditions of non-neuronal and NGF support. Of the parameters studied, the amplitude of the AP was the most markedly affected. Under conditions of optimal non-neuronal supplementation (with or without NGF) about 40% of the neurons had AP amplitudes of 85 mV or more, whereas only 4% of the neurons of cultures containing only NGF had AP's in this range. In addition, the numbers of cells having low AP amplitudes decreased as the number of added non-neuronal cells was increased--even in the presence of NGF. None of the above differences were observed in young cultures (3-12 hrs old). The results suggest that non-neuronal cells may influence neuron function in a way not related to the mere promotion of neuronal attachment to a culture substrate.

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75.8 INTERACTION BETWEEN THE NERVE FIBER AND THE GLIAL CELL DURING GROWTH IN CULTURES OF THE CENTRAL NERVOUS TISSUE. Hanna M. Sobkowicz, David Golueke* and Burt L. Lowry*. Dept. Neur. and Lab. Neurophysiol., Sch. Med., UW, Madison, Wisconsin, 53706.

There is ample evidence that during growth a nerve fiber tip may attach to a solid substrate and may follow the structural arrangement of the latter. Studies of the nerve fibers in CNS cultures indicate the existence of an intimate relationship between a growing nerve tip and a glial cell during the early growth period. Time-lapse cinematography shows that, in fact, it is the glial cell which adhears onto and glides over the substrate carrying the growing nerve tips within the territory of its cytoplasm. Thus the nerve endings advance into the outgrowth zone encased in the glial cytoplasm. The glial cells show EM features of young undifferentiated or astrocytic cells (J.Comp.Neur. 140:1, 1970). In the pursuit of a leading glial cell, nerve fibers gather into bundles and the direction of their growth follows that of the cell. It is also the glial cell which may bring together different nerve bundles, although it is not known how permanent such formations are. It is suggested that in cultures, which show specific patterns of neuronal growth, there is a continuous interaction between a growing nerve fiber and its guiding glial cell. This relationship seems essential for the survival, bundle formation and importantly for the directional growth of nerve fibers.

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75.9 EFFECTS OF GOLD THIOGLUCOSE ON THE MOUSE VENTROMEDIAL HYPOTHALAMUS IN VITRO. Mary M. Herman and Murray B. Bornstein. Dept. Pathology (Neuropathology), Sch. Med., Stanford Univ., Stanford, 94305, and Dept. Neurology, Albert Einstein College Med., Bronx, 10461.

Gold thioglucose (GTG), an obesifying agent in mice, causes destruction of the ventromedial nucleus of the hypothalamus. The present study was undertaken to determine the intracellular site of action of GTG on hypothalamus explants under controlled in vitro conditions. The ventromedial hypothalamus was dissected from newborn Charles River albino mice. Explants were trimmed with the ventricular surface on one margin. Established explants (30 days or longer in vitro) were exposed for up to one month to GTG (0.001 to 2 mg/ml) added biweekly to the nutrient medium. At concentrations of 0.01 mg/ml and greater, the earliest changes were marked activation of macrophages. At concentrations of 1-2 mg/ml, there was partial destruction of glia and fibroblasts in the outgrowth zone within a few days and total explant necrosis occurred after a single feeding of 2 mg/ml. Nerve cell loss was striking after several applications of 0.5 and 1 mg/ml. With electron microscopy, increased numbers of lysosomes were found in macrophages, glia and some of the surviving neurons. Focal electron opacities, probably representing gold, were seen in unosmicated unstained sections. β -D-thioglucose (TG) and gold sodium thiosulfate (GTS) at comparable concentrations produced different effects. At highest levels, TG produced disorganization of the outgrowth zone, but the neurons remained unchanged; GTS caused total explant necrosis within 48 hours at 0.5 and 1 mg/ml. Thus, GTG causes pathological changes first in macrophages and glia, and later in neurons; its mode of action is different from that of GTS and TG.

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75.10 A TISSUE CULTURE MODEL FOR STUDIES OF REGENERATION AND FORMATION OF NEW FUNCTIONAL CONNECTIONS IN ADULT CNS. Stanley M. Crain and Edith R. PETERSON.* Depts. of Physiology and Neurology, Albert Einstein College of Medicine, Rose F. Kennedy Center, Bronx, New York 10461

Although fetal spinal cord explants can develop and be maintained in culture for many months, no attempts have been made to determine whether these mature cord neurons retain the capacity to regenerate a second time in vitro. After 2-4 months in culture cord explants were excised from mature cord-ganglion-skeletal muscle cultures (Peterson and Crain, Exp. Neurol. 36:136, '72) and transferred to fresh coverslips. Characteristic neuritic outgrowths developed around these explants, including formation of myelinated peripheral axons as well as many fine "CNS" neurites. Complex synaptically-mediated bioelectric discharges were recorded after 3-4 weeks in vitro, comparable to those in fetal cord explants after maturation without transfer. Electrophysiologic analyses of transferred cord paired with fetal cord explants demonstrate that these "mature" neurons can form functional interneuronal connections with newly explanted fetal neurons, and vice versa, after bridging gaps of 0.5-1 mm (as occurs between regular CNS explants (Crain et al., Ciba Symp: Growth of Nervous System, '68). Connections also formed between pairs of transferred cord explants, but only in 2 of 6 tests. Simultaneous recordings in one pair of cord transfers showed synchronized organotypic discharges occurring spontaneously (in low levels of strychnine) as well as in response to local stimuli, with latencies of the order of 10-100 msec between explants (as regularly observed in transfers paired with fetal cord). "Mature" cord neurons could, moreover, again innervate adult skeletal muscle fiber regenerates. This new model provides a valuable method for studies of trophic factors in regeneration of adult mammalian CNS (e.g., Guth and Windle, Exp. Neurol. 28:Suppl. 5, '70). (Supported by NINDS grants NS-06545 and NS-08770 and the Alfred P. Sloan Foundation.)

75.11 RHYTHMIC NEURAL ACTIVITY IN TISSUE CULTURE. Franklin D. Walker. Inst. of Psych. Res., Ind. Univ. Med. Ctr., Indianapolis, Ind. 46202.

Non-perturbing electrical recordings from assemblies of cultured cells have demonstrated patterns of spontaneous neuronal spike discharge which characterize the areas of brain from which the explants were taken. Explants from the cerebellum, midbrain, colliculi, and cerebrum of newborn rats were grown in roller tubes by the "flying cover slip" method of culturing mammalian neural tissue. The tissue was explanted over a hole measuring between 100 and 250 μm in diameter drilled through the coverslip. Cultures were maintained for at least two weeks by which time the tissue had proliferated and migrated into the hole in the slide. The tissue so grown formed an electrical barrier between two chambers across which the spontaneous activity of neurons was monitored as well as the steady potential and impedance change of the tissue containing both neurons and neuroglia. Cerebellar explants characteristically gave rapid bursts of spikes occurring every 100 msec and having a duration of 50 msec. Some cerebellar cultures were observed to have periodicities of a longer nature: every minute with bursts of 30 sec. The longest periods were observed in explants from the midbrain area having intervals of generally 4 to 7 min but as long as 10 min yielding a cascading firing pattern of over 1.0 min duration while the rest of the period remained essentially quiet. Explants from the colliculi gave peaks of activity having a serrated appearance to the spike discharge pattern with periods of approximately 4 min in length. Of the brain areas studied, the spikes generated in neocortical tissue alone did not yield a discrete pattern of activity. The recording from explants of rhythmic impedance changes having a time course similar to that for neuronal activity may suggest neuroglial participation in the phenomenon. (Supported by Grant-in-Aid from Eli Lilly & Co.).

75.12 ELECTROPHYSIOLOGICAL STUDIES ON SUPERIOR CERVICAL GANGLION NEURONS IN TISSUE CULTURE. Harold Burton, Chien-Ping Ko*, Richard Bunge and Rosemary Rees*. Dept. Anat. & Physiol., Sch. Med., Wash. Univ., St. Louis, Mo. 63110

Intracellular recordings have been made from dissociated superior cervical ganglion neurons (SCGNs) that were taken from newborn rats and subsequently grown in vitro together with explants of thoracic spinal cord from 15-day fetal rats. In this system axosomatic and axodendritic synapses are formed on SCGNs by outgrowing spinal cord neurites. In 2-5 week old cultures SCGNs showed resting potentials of 30-70 mV, action potentials of 30-80 mV, and thresholds of 7-12 mV to membrane depolarization. Anomolous rectification and multiple firing was observed by 2 1/2 weeks. Extracellular stimulation of processes of individual SCGNs showed that the action potentials could be fractionated into an early phase and a faster-rising late phase that resembled IS and SD fractionation of a motorneuron spike. In many SCGNs complex repetitive responses of 2-10 mV were noted and these could summate to trigger an all-or-none action potential. Graded steps of membrane polarization indicated that the size of the local potentials were directly and linearly related to the level of hyperpolarization. Spontaneous firing was blocked by high levels of $MgCl_2$ and was also not detected in mature cultures from which the spinal cord explants had been removed one week prior to the recording session. These results suggest that the local potentials represent chemically mediated post-synaptic potentials and that they arise because of the formation of synapses between spinal cord neurites and SCGNs in vitro. (Supported by Grants NS 09809 and NS 09923)

76.1 CONTROL OF SYNTHESIS AND RELEASE OF THYROTROPIN RELEASING FACTOR (TRF) BY HYPOTHALAMIC FRAGMENTS FROM NEWTS (TRITURUS VIRIDENSES) INCUBATED IN VITRO. Yvonne Grimm-Jorgensen* and Jeffrey F. McKelvy. Dept. of Physiology and Dept. of Anatomy, University of Connecticut Health Center, Farmington, Ct. 06032.

Hypothalamic fragments from newts were incubated in modified Ringer's solution in the presence of tritiated TRF precursor amino acids. Tritiated TRF was purified by successive chromatography and electrophoresis. All three precursor amino acids were incorporated into radioactive peaks corresponding to synthetic tritiated TRF. Newly formed TRF was detected in media and tissue extracts from hypothalamic incubates. Newt hypothalamic extracts effected release of TSH from rat pituitaries in vitro. The synthesis and release of radioactive TRF was not inhibited by the addition of 100 μg chloramphenicol or cycloheximide to the medium. These studies suggest: (1) that newt TRF is chemically identical to mammalian TRF, (2) that it is synthesized by adult newts in significant quantities, (3) that its synthesis can be measured under conditions where the majority of cytoribosomal and mitoribosomal protein synthesis is inhibited. Other approaches must be taken to rigorously rule out a ribosomal mechanism for the synthesis of the small amounts (2 - 3 pmoles) of TRF present in newt hypothalami.
This work was supported by NSF grant NSF-GB-31846.

76.2 NEUROTRANSMITTER REGULATION OF GROWTH HORMONE RELEASE. G.M. Brown, J.W. Chambers* and J. Feldmann*. Clarke Institute of Psychiatry and Department of Psychiatry, University of Toronto.

In order to clarify the nature of neurotransmitter control of Growth Hormone (GH) release, chair-adapted, unanaesthetized rhesus monkeys with a chronic indwelling intra-atrial cannula were given a thirty minute intravenous infusion of various agents that affect brain amines, and plasma samples were taken for GH determination. Administration of acid-saline vehicle alone had no effect on GH. Administration of the noradrenergic receptor stimulant, clonidine hydrochloride (150 ug/kg), produced a rapid increase in GH as did DL-threodops (90 mg/kg), the immediate precursor of norepinephrine suggesting that central noradrenergic neurons are excitatory to GH release. GH rise following clonidine occurred in the absence of a rise in cortisol indicating that the GH rise was not a stress response. L-Dopa (45 mg/kg) produced a rise in GH which was potentiated by disulfiram pretreatment suggesting that dopaminergic neurons also activate GH release. Apomorphine (0.3 mg/kg), a specific dopamine receptor stimulant, also produced a rise in GH; however, this was accompanied by emesis and by a rise in cortisol and could, therefore, be interpreted as a stress response. 5-hydroxytryptophan (45 mg/kg), the precursor of serotonin, also produced a prompt rise in GH suggesting that serotonin neurons can also activate GH release. In conclusion, these findings suggest the existence of central excitatory norepinephrine, dopamine and serotonin mechanisms in GH regulation in the primate.
(Supported by MRC MA 4749).

76.3 CYCLIC NUCLEOTIDE STIMULATED PROTEIN KINASE ACTIVITY IN THE HYPOTHALAMIC MEDIAN EMINENCE. Elizabeth Martin* and Jeffrey F. McKelvy (SPON: C. H. Phelps). Dept. of Anatomy, University of Connecticut Health Center, Farmington, Ct. 06032.

The median eminence of the hypothalamus is the site of convergence of neuronal, ependymal and vascular elements implicated in hypothalamic releasing factor regulation and is traversed by neurohypophysial neurosecretory neurons. As part of our studies on neuroendocrine regulatory mechanisms in this area, we have partially purified (through the DEAE cellulose step) a protein kinase from bovine stalk-median eminence tissue, employing the procedure of Kuo and Greengard (J. Biol. Chem. 244, 6395 (1969)) for whole brain. The partially pure enzyme is active in the absence of cAMP and shows a 2 to 4 fold increase in activity in the presence of optimal (10^{-6} M) cAMP, while higher concentrations ($> 10^{-4}$ M) inhibit activity below the unstimulated level. At optimal concentration cGMP is most effective, relative to unstimulated levels. cIMP is the least effective at its optimal concentration of the three cyclic nucleotides studied (cAMP, cGMP, cIMP). Median eminence constituents interact with the enzyme: thus, both histamine and epinephrine (10^{-6} M) stimulate both unstimulated and the cAMP stimulated kinase activity; while norepinephrine, dopamine, serotonin and thyrotropin releasing factor have no effect. Purified intact neurosecretory granules (NSG) serve as a substrate for the cAMP stimulated activity while NSG constituents (neurophysins I and II and oxytocin) do not. These findings suggest a role for protein kinase activity in neuroendocrine regulatory mechanisms in the hypothalamus.

This work was supported by NSF grant: NSF-GB-31846.

76.4 CYCLIC AMP INVOLVEMENT IN LUTEINIZING HORMONE RELEASING HORMONE (LRH) INDUCED LUTEINIZING HORMONE (LH) RELEASE? A. Ratner*, M. C. Wilson* and G. T. Peake* (Spon: L. S. Demski), Univ. New Mexico Sch. Med., Albuquerque, New Mexico 87106.

Although some evidence has recently indicated that the adenyl cyclase-cyclic AMP (AC-cAMP) system may play a role in the regulation of LH release from the pituitary, its precise role has not been clearly established. The present studies were performed to define more clearly the role of AC-cAMP in the mediation of LRH-induced LH release. Male rats were lightly anesthetized with ether and given saline, synthetic LH or prostaglandin E_1 (PGE_1) intravenously via the external jugular. The rats were killed 10 minutes later. Following administration of 100 ng LRH, serum LH values increased; however, pituitary cyclic AMP did not change significantly from control levels. Injection of 20 µg PGE_1 significantly increased pituitary cyclic AMP levels but LH values were not affected. Serum LH values were also not affected following administration of 2 mg dibutyryl cyclic AMP or pretreatment with 25 mg aminophylline. In vitro studies were carried out to substantiate the dissociation of LH release and pituitary cyclic AMP accumulation. Addition of 20 ng/ml LRH to incubated pituitary explants produced a significant rise in LH release following 30 and 60 minutes of incubation. However, pituitary cyclic AMP content did not rise until after 150 minutes of incubation. We conclude that LRH-induced LH release may not be mediated by activation of the pituitary AC-cAMP system. Although the significance of the delayed rise in cyclic AMP is unclear, a role for the AC-cAMP system in resynthesis of LH or release of LH from another pool may be indicated by this observation.

76.5 EFFECT OF SEPTAL LESIONS ON PLASMA LEVELS OF CORTICOSTERONE, GROWTH HORMONE, PROLACTIN AND MELANOCYTE STIMULATING HORMONE BEFORE AND AFTER STIMULATION. Jo A. Seggie*, Gregory M. Brown, Ivo V. Uhlir*, Andrew Schally*, and Abba J. Kastin (SPON: Oleg Hornykiewicz). Neuroendocrine Research Section, Clarke Institute of Psychiatry, Toronto; Endocrinology Labs, Veterans Administration Hospital and Department of Medicine, Tulane University, New Orleans.

Lesions of the septal nuclei in rats produce a state of behavioral hyperreactivity and adrenal overresponsiveness without altering the diurnal adrenal rhythm. Corticosterone levels were observed in septal lesion, sham operated and normal rats 0, 5, 15, 30 or 60 minutes after 5 seconds of handling or 3 minutes exposure to a novel environment at peak and trough of the adrenal rhythm. Stress responses in septal rats were significantly elevated compared to non-lesioned animals. At peak time in the adrenal cycle, resting and poststimulation levels of corticosterone, prolactin, growth hormone (GH), and melanocyte stimulating hormone (MSH) were examined. In controls, 3 minutes of novel environment produced significant elevations in corticosterone and prolactin levels, a drop in GH and no alteration of MSH suggesting the latter does not respond to this stress. In septal rats (in confirmation of the previous study), stress levels of corticosterone were elevated while no potentiation of prolactin responses were observed, GH responses were already maximal so that no potentiation was observed and MSH responses did not differ from those of non-lesioned animals. Result suggest that neural pathways regulating prolactin and corticosterone stress response differ.
(Dr. Jo Seggie is an Ontario Mental Health Foundation (O.M.H.F.) Scholar while Dr. Gregory Brown is an O.M.H.F. Associate. Additional support for these studies came from the Clarke Institute Research Fund).

76.6 IMMUNOHISTOLOGICAL LOCALIZATION OF MELATONIN IN THE PINEAL GLAND AND THE CEREBELLUM. G.A. Bubenik*, G.M. Brown and L.J. Grota* (SPON: D. Coscina). Neuroendocrinology Research Section, Clarke Institute of Psychiatry, Toronto, Ontario and the Department of Psychiatry, University of Rochester, Rochester, New York.

Using biochemical methods, melatonin has been localized only in the pineal gland and hypothalamus. Hydroxyindole-O-methyltransferase, the enzyme catalyzing formation of N-acetylserotonin (NAS), the precursor of melatonin, has been found in the pineal gland, habenula, retina and the Harderian gland. Radioactive melatonin is concentrated in the midbrain and the hypothalamus following intravenous or intraventricular administration. In the present study, immunological localization of melatonin (or NAS) in histological slices of the rat brain tissue has been performed using highly specific anti-melatonin serum (crossreactivity only to NAS). Frozen sections of brain tissue, 10 u thick were fixed in cold acetone, incubated with antimelatonin serum, washed and then exposed to anti-gamma-globulin labeled either by peroxidase or by fluorescein. After washing, visualization of bound peroxidase was performed using diaminobenzidine. Fluorescein labeled sections were investigated in UV light. Using both peroxidase and fluorescein techniques, melatonin was found homogenously distributed in the pineal gland and also in the outer part of the granular layer of the cerebellum. The highest concentration of melatonin was localized in the space just below the Purkinje cell layer. The localization of labeled structures corresponds with the localization of Golgi II cells in the cerebellum. Labeling in the cerebellum was found also in animals 6 weeks after pinealectomy. Our findings support the hypothesis that melatonin or NAS is produced elsewhere than in the pineal gland and also indicates the participation of melatonin (or NAS) in cerebellar activity.
(Supported by the Swiss Foundation for Alpine Research, Ontario Mental Health Foundation and National Institute of Mental Health).

76.7 LOCATION OF ACTION OF CENTRALLY ACTING DRUGS ON INHIBITION OF LH RELEASE IN RATS. Charles A. Blake. Dept. Anat., Sch. Med., Duke Univ., Durham, N.C. 27710.

In cycling rats, anterior afferents to the medial basal hypothalamus (MBH) are necessary to release pituitary LH on the afternoon of proestrus. Long-term ovariectomized (OVX) rats release LH in a pulsatile fashion and maintain high plasma LH levels without this anterior input (Anat. Rec. 175: 273, 1973). Nicotine tartrate (2 mg, sc) urethane (1.5 mg/kg, ip) or phenobarbital (75 mg/kg, ip), ovulation blocking agents, blocked spontaneous LH release (as indicated by radioimmunoassay of plasma LH) when the drugs were injected into 4-day cycling rats just prior to the onset of the 2 PM critical period on proestrus. Long-term OVX rats implanted with cardiac cannulas were bled at 10 min intervals before and after the injection of the same dosages of one of these drugs. In all 3 groups there was a rapid (within 20 min) and sustained (more than 1 hr) decrease in plasma LH concentration. None of these compounds were effective in inhibiting LH release in response to exogenous LH-releasing hormone. Anterior, anterior-lateral or posterior-lateral deafferentation of the MBH 6 wk prior to ovariectomy had no effect on the pulsatile discharge of LH. However, injection of any of the 3 drugs to these deafferented, OVX rats suppressed LH release. The data indicate that unlike cycling rats, OVX rats do not utilize a dual control mechanism for LH release and that at least 3 of the drugs known to block LH release and ovulation may do so at the level of the MBH. (Supported by UHS of N.C., Inc. and NIH HSAA 5 S04 RR 06148).

76.8 BLOCKADE OF CORTICAL SPREADING DEPRESSION'S EFFECTS ON PROLACTIN LEVELS IN FEMALE RATS BY SURGICAL ISOLATION OF THE AMYGDALA. Jorge A. Colombo*, Richard J. Krieg*, and Charles H. Sawyer, Dept. Anat., and Brain Res. Inst., UCLA, Los Angeles, 90024.

KCl-induced cortical spreading depression (SD) in PMS-HCG treated rats is followed by an increase in plasma prolactin levels (Colombo, J. A., C. A. Blake, C. H. Sawyer, 2nd Ann. Neurosci. Meet. Abst. #51.6, 1972). Attempting to analyze the possible role of subcortical extrahypothalamic structures in that response we have studied the effects of bilateral isolation of the amygdala and section of the fornix. Two weeks after surgery the animals were injected with PMS and HCG and tested one week later. Under continuous ether anesthesia blood samples for radioimmunoassay of prolactin were taken every 20 min from an indwelling femoral arterial cannula. After collection of two control samples, 25% KCl was applied to the dura overlying the frontal cortex to induce SD. No significant increase in plasma prolactin could be observed in rats in which the amygdala had been surgically isolated. However, animals with transected fornices still showed an increase in prolactin 40-60 min after KCl application. The results suggest that the amygdaloid nuclei or their connections are necessary for the increase in plasma prolactin following cortical SD in PMS-HCG treated animals. (Supported by NIH, FFRP and The Ford Foundation.)

76.9 EFFECT OF SEX ON THE NEUROENDOCRINE RESPONSE TO PSYCHOACTIVE AGENTS. James A. Clemens, E. Barry Smalstig*, and Barry D. Sawyer*. Dept. Physiological Research, Eli Lilly Research Labs., Indianapolis, Indiana, 46206.

Adult female, male and ovariectomized (OVX) female rats were treated with the following drugs: pimozide, 2.5 mg/kg; chlorpromazine (CPZ), 9.2 mg/kg; reserpine, 5.0 mg/kg; and alpha-methyltyrosine (AMT), 200 mg/kg. Rats were decapitated 4 hours after treatment and serum was assayed for prolactin by radioimmunoassay. Pimozide, an agent that blocks the dopamine-receptor interaction, and CPZ, an agent that appears to block both the dopamine and norepinephrine-receptor interaction stimulated prolactin secretion in male, intact female and ovariectomized female rats. Similar increases in prolactin were noted after administration of AMT or reserpine. These agents produced about a 5 fold increase in serum prolactin levels in OVX rats and about a 2-3 fold increase in serum prolactin in normal males. In the intact female rats increases in prolactin as high as 10-15 fold were noted after administration of all the agents. Addition of these agents to tissue culture medium containing male or female pituitaries did not cause prolactin to be released, but actually inhibited prolactin release. These studies indicate that the ovarian steroids are able to act on the CNS in such a way as to modify its response to psychoactive drugs. Possibly the interaction between sex steroids and the agents in this study was on a dopaminergic system, because pimozide was the most potent prolactin stimulator.

76.10 STIMULATION OF VASOPRESSIN BIOSYNTHESIS IN ORGAN CULTURES OF THE HYPOTHALAMO-NEUROHYPOPHYSIAL COMPLEX BY FETAL HYPOTHALAMIC FACTOR(S). David B. Pearson* and Howard Sachs* (SPON: C.Z. Neurath). Roche Institute of Molecular Biology, Nutley, New Jersey 07110.

It has been previously shown that either hypothalamic fragments (Sachs, et al. PNAS 68, 2782, 1971) or the entire hypothalamo-neurohypophysial complex (HNC) of adult guinea pigs can be maintained in organ culture for periods of several weeks under conditions where they retain their ability to synthesize vasopressin and the hormone-binding protein, neurophysin (Sachs, et al. Proc. IV Int. Cong. Endocrinology 1972, Excerpta Medica, in press). The rate of incorporation of ^{3}H-labeled amino acids into vasopressin in HNC cultures was stimulated 2-4 fold when the pulse-medium had been preconditioned by 24 hours of incubation with guinea pig fetal hypothalamo-neurohypophysial explants. Under the same conditions, the incorporation of ^{3}H-amino acids into total acid soluble proteins was unaffected. The fetal HNC cultures used to condition the medium were taken from animals at 40-45 days gestation; at this time the supraoptic neurosecretory cells have apparently differentiated as judged by the appearance of hormone and neurophysin and of the ability of the HNC to carry out the biosynthesis of these substances in vitro (R. Goodman and H. Sachs, unpublished). After 10 days in culture the fetal HNC could still be used to provide conditioned medium stimulatory for vasopressin biosynthesis with adult tissues. By contrast, no stimulatory effects on hormone biosynthesis were observed with media conditioned with equivalent cultures of either cerebral cortex or liver taken from 40-45 day-old fetuses or of the adult HNC. These data suggest the interesting possibility that the fetal HNC synthesizes a factor(s) which stimulates the functional activity of supraoptic neurosecretory neurons.

76.11 BINDING OF DEXAMETHASONE BY RAT BRAIN CYTOSOLS. W. Stevens,* D.J. Reed* and B.I. Grosser. Depts. of Anatomy, Pharmacology and Psychiatry, Univ. of Utah College of Medicine, Salt Lake City, Utah 84112.

Previous work has demonstrated "receptor" proteins for corticosterone (B_k) in brain cytosols and cellular nuclei. Since dexamethasone (Dx) has important central nervous system effects, it is important to determine if there are specific receptor molecules for Dx and whether these are the same as the receptors for B_k. Adult male adrenalectomized (adrex) or non-adrenalectomized (intact) rats were perfused ventriculocisternally with 1, 2,4-^{3}H-Dx (0.1 ug/ml, S.A. 30 Ci/mM). After a 1 h perfusion, the animals were sacrificed and brain cytosols were prepared. Binding was determined by chromatography on Sephadex G-25. In the adrex rats, 11,069 dpm/mg protein were bound whereas the comparable figure for intact rats was only 404 dpm/mg protein indicating that the available binding sites were filled by endogenous B_k. In in vitro experiments the binding of ^{3}H-B_k (S.A. 30 Ci/mM) and ^{3}H-Dx was compared by incubating equivalent amounts of these hormones at 4°C with brain cytosols from adrex animals injected with .28 x 10^{-6} moles non-radioactive B_k or Dx 30 min before sacrifice. After pretreatment with Dx, 3932 dpm ^{3}H-B_k and 1097 dpm ^{3}H-Dx were bound per mg protein. After pretreatment with B_k, the comparable figures were 1241 dpm ^{3}H-B_k and 657 dpm ^{3}H-Dx. These data appear to indicate a difference in the binding characteristics of "receptor sites" for ^{3}H-Dx and ^{3}H-B_k. Scatchard plots were made from data obtained by incubating cytosols with ^{3}H-Dx in vitro. The $K_{(dis)}$ was 4.2 x 10^{-13} and there were 2.4 x 10^{-13} moles of ^{3}H-Dx bound/mg protein. These binding properties were different from those obtained with ^{3}H-B_k. The regional distribution of the binding of ^{3}H-Dx was similar to that reported for ^{3}H-B_k in that the highest concentration of radioactive hormone was found in the hippocampus.

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77.1 **Trigeminal structures and feeding behavior in rat and pigeon.** **H. Philip Zeigler and H. J. Karten. Hunter College (CUNY) New York, N. Y. 10021 and Mass. Inst. Tech., Cambridge, Mass. 02139.**

Previous studies from our laboratories have shown that lesions of Principal Sensory Trigeminal Nucleus, Quinto-frontal tract and Nucleus Basalis produce feeding behavior deficits in the pigeon without impairing drinking. To clarify the implications of these findings in the pigeon for the neural control of feeding in mammals we placed bilateral lesions in Trigeminal lemniscus and in the medial portion of the ventrobasal thalamic complex in the rat. Lesions of these structures produced periods of aphagia and adipsia (2-4 days). Following the resumption of eating and drinking, recovery of ad-lib body weight was significantly retarded. No such effects were seen in control animals. Taken in conjunction with anatomical and electrophysiological studies of central trigeminal structures in rat and pigeon, the neurobehavioral findings suggest that the avian Quinto-frontal tract corresponds to the Trigeminal lemniscus of mammals. Accordingly, the Nucleus Basalis, despite its location in the telencephalon, may be the avian counterpart of the face portion (VBm) of the ventrobasal complex of the mammalian thalamus. The results help clarify previous reports of feeding behavior deficits after lesions of extrahypothalamic structures in the thalamus and midbrain of mammals. They are discussed in relation to neural mechanisms of mammalian feeding behavior.

77.2 AN ANATOMICAL CONNECTION BETWEEN THE ANTERIOR THALAMUS AND THE TELENCEPHALON IN THE FROG. Earl Kicliter* (SPON: John A. Jane) Dept. Anat., Upstate Med. Ctr., Syracuse, N.Y. and Dept. Neurol. Surg., University of Virginia School of Medicine, Charlottesville, Virginia 22901.

The dorsal anterior thalamus of the frog has been shown to be involved in wavelength discrimination. After lesions of this region, frogs are incapable of wavelength discrimination, but demonstrate normal prey-catching behavior. In order to establish the homology between this region of the frog brain and thalamic regions in other vertebrates it is necessary to know the pattern of anatomical connections as well as the functional similarities. For this purpose radio frequency coagulations were made in the dorsal anterior thalamus of 15 Rana pipiens. After survival times of 3-14 days at 20-23°C the frogs were sacrificed and sections of the brains were processed by modifications of Nauta and Fink-Heimer stains. Heavy terminal and pre-terminal debris was observed in the ipsilateral striatum. Lesser amounts of debris were seen bilaterally in medial portions of the telencephalon, including the medial pallium and the septal area. No degeneration was observed in the dorsal or lateral pallium. Hemisection of the thalamus at the thalamo-tectal border produced degeneration in medial portions of the telencephalon, and in nucleus accumbens, but the heavy pattern of degeneration in the striatum which was observed after anterior thalamic lesions was not seen after posterior thalamic hemisections.

77.3 TRANSECTION AND CHEMICAL LESION OF NIGRO-STRIATAL PATHWAYS: COMPARISON OF EFFECTS ON LEARNED BEHAVIOR. Ernest W. Kent, Michael Rezak* and S. P. Grossman. Dept. of Psychol., U. of Ill. at Chicago Circle, and U. of Chicago. Chicago, Ill. 60680

Kent and Grossman have reported severe and persistant deficits in several learned behaviors, as well as adipsia and aphagia, following transection of fiber pathways crossing the lateral border of the hypothalamic region. To further clarify the anatomical basis of this effect, 6 albino rats were subjected to small (1.5 mm^2) transections in the coronal plane immediately anterior to the zona compacta and ventral tegmental nucleus. These animals were rendered completely aphagic and adipsic until sacrificed (4 weeks post-surgery). During this time, they failed to perform or reacquire a previously learned lever press response to escape footshock, despite normal responses on tests of sensory and motor abilities. These animals thus closely resembled the animals with saggital transections at the lateral hypothalamic border. An additional 6 animals were subjected to injections of 6-hydroxy-dopamine into the zona compacta, using precisely the dosages and procedures reported by Ungerstedt to completely deplete striatal dopamine. These animals were also rendered completely aphagic and adipsic until sacrificed (4 weeks post-injection). During this period, tests of previously learned escape responding showed a decline to zero performance over a period of 3 to 6 days post-injection, followed by a recovery within 2 weeks post-injection. The effects of the injection thus mimicked the effects of the two transections with respect to food and water intake, but differed with respect to deficits in learned responding. These findings suggest that a pathway involved in learned escape responding may follow the course of the nigro-striatal bundle, and may interact with dopaminergic mehanisms, but may not itself be dopaminergic.

77.4 EFFECT OF SEPTAL LESIONS ON FEMALE SEXUAL BEHAVIOR IN THE RAT. Dwight M. Nance*, James Shryne* and Roger A. Gorski. Dept. Anat., Brain Res. Inst., Sch. Med., UCLA, Los Angeles, 90024

To study the possible influence of the septum on female sexual behavior, normal female (NF), androgen-sterilized female (ASF), neonatally castrated male (NCM), and normal male (NM) Sprague-Dawley rats were given bilateral lesions of the septum or sham operation. The animals were gonadectomized and tested for lordosis behavior under 3 conditions: tested without hormones, given 2 µg estradiol benzoate (EB) for 3 days and tested on the fourth day, or given EB plus 0.5 mg progesterone on the fourth day and tested. The animals were placed in a plexiglas arena with 2-3 sexually vigorous Long Evans male rats until mounted a total of 25 times. A lordosis quotient (LQ; # lordoses/# mounts x 100) was calculated for all animals under each hormonal condition. Histological examination of the brains indicated that the lesions were bilaterally symmetrical and generally included the entire lateral septum region while sparing the medial septum and fornix. No female sexual behavior was observed in the absence of gonadal hormones. The mean LQ for the sham-operated NF, ASF, NCM and NM rats, when given estrogen alone, was 24.6, 19.3, 63.2 and 10.0, whereas the mean LQ for the same groups of animals after destruction of the lateral septum were 74.1, 91.5, 77.3 and 78.0, respectively. Estrogen plus progesterone resulted in a mean LQ of 88.3, 29.3, 100.0 and 30.7 for the sham-operated NF, ASF, NCM, and NM groups, and septal-lesioned animals had mean LQ scores of 100.0, 92.5, 99.2, and 84.5, respectively. Thus, lesions of the lateral septum appear to increase behavioral responsiveness to estrogen, even in the ASF and NM animals which normally show very low levels of lordosis behavior in response to female gonadal steroids. The lordosis response in both the male and female rat is tonically inhibited; the septum and perhaps other extrahypothalamic structures may, at least in part, regulate this inhibition.(Support: USPHS HD01182 and Ford Found.)

77.5 SEPTUM AND HIPPOCAMPUS: FURTHER EVIDENCE FOR FUNCTIONAL COMMUNALITY. Jack D. Maser, Frank T. Dienst* and Edgar O'Neal*. Department of Psychology, Tulane University, New Orleans, Louisiana.

As a test of functional communality between septum and hippocampus, bilateral septal or sham lesions were administered to 16 New Zealand rabbits. Three others suffered bilateral dorsal hippocampal damage. All subjects acquired a conditioned eyeblink to a 2K tone (CS) which was paired with a .2 sec. electric shock to the lower eyelid. Septally damaged subjects met criterion (10 consecutive CRs) and attained the 10th CR significantly faster than sham operates. Extinction and eye opening responses were also examined. Hippocampectomized rabbits responded in a manner similar to the septal subjects and consistent with published reports. Although for some behaviors differential effects are known to be produced by septal or hippocampal damage, both limbic structures appear to participate in the elaboration of a conditioned response.

77.6 EFFECTS OF LIMBIC SYSTEM LESIONS DURING LATE GESTATION ON MATERNAL BEHAVIOR IN PRIMIPAROUS RATS. Lorraine Roth Herrenkohl. Psych. Dept., Temple Univ., Philadelphia, Pa., 19122

Late pregnant primiparous Sprague-Dawley rats were lesioned or sham-lesioned in the preoptic or arcuate-mammillary regions of the hypothalamus or in the hippocampus, and subsequently were observed for effects on labor, lactation and nursing behavior. Contrary to previous reports employing aspiration techniques (Kimble, Rogers & Hendrickson, JCPP 63: 401, 1967), bilateral electrolytic lesions in the hippocampus produced by 3 ma of current delivered for 15-sec did not affect nursing behavior. Nor were labor and lactation disturbed.

Anterior-preoptic lesioned rats, however, had great difficulty in maintaining young. Most of the lesioned rats attacked and cannibalized their own young and young with which they were housed. In standard nursing behavior tests employing foster young, they either cannibalized pups or else appeared finicky in their responses to them. In cases where lesioned females did crouch over young (show nursing behavior), they gave no milk. Thus in these animals effects on lactation did not appear independent of effects on nursing behavior.

It was possible in the arcuate-mammillary lesioned rats to dissociate an effect on labor and lactation from that on nursing behavior. In these rats, nursing behavior remained normal even though gestation was prolonged sometimes by as much as 4 days, and failure of milk-ejection occurred in most of the rats.

77.7 BRAIN LESION EFFECTS ON CONDITIONED VOCALIZATION IN RHESUS MONKEYS Dwight Sutton, Charles R. Larson* and Roger C. Lindeman*. Virginia Mason Research Center, Seattle, Wash. 98101

Five rhesus monkeys were trained to emit a clear call (koo) under stimulus control. Ablative lesions were placed in neocortex of three animals and in anterior cingulate-plus-subcallosal gyrus of two animals. Combinations of bilateral frontal and/or parietal neocortex damage in regions roughly analogous to Broca's area and Wernicke's area failed to affect the acoustical properties of the call or the performance criteria. Bilateral anterior cingulate-plus-subcallosal gyrus lesions impaired performance of the discriminative call, although the animals with such damage continued to phonate in the colony environment. The results indicate that learned vocalization in monkeys is not dependent upon intact neocortex. The outcome also shows that limbic structures may participate selectively in regulation of voluntary phonation.

77.8 MONOCULAR VISUAL PROCESSING CAPACITY LOSS IN THE SPLIT-BRAIN CAT: SENSORY OR CENTRAL? John S. Robinson. Brain-Behavior Research Center, Sonoma State Hospital, Eldridge, Ca. 95431.

We have shown in earlier reports (EN 26: 72, 1970; 33: 420, 1971) that the split-brain cat needs both hemispheres for optimal mediation of cognitively demanding 2-choice visual discrimination tasks; confinement of task inputs to one hemisphere results in a significant lowering of performance. We have also shown that differences in the individual hemispheres' capacities emerge when they have been isolated from each other by midline surgery (EN 38: 123, 1973). This report is concerned with determining the extent to which the above unilateral losses can be attributed to visual field defects. Following chiasm section we found that there was a transient depression of monocular performance, largely attributable to the subject's failure to approach the correct choice door when it was in his temporal visual field (i.e., the side affected by cutting the crossed fibers from the nasal hemiretina). When both chiasm and callosum were split, however, there was an enduring monocular loss which was still present even after training was carried to asymptote. At this point, however, there were no differences in accuracy for trials involving choice of a stimulus in the temporal field that had suffered the sensory loss and trials with the correct stimulus in the intact nasal field. This compensation for the fiber loss resulting from cutting the chiasm is in marked contrast to the monkey's failure to compensate for the blind temporal fields resulting from section of the chiasm. Some temporal field vision may survive in the chiasm-sectioned cat because of the overlap of ipsilateral fibers onto the nasal hemiretina. Ruling out visual field defect as an explanation for the unilateral loss of capacity increases the likelihood of its being a central phenomenon.

77.9 HEMISPHERIC SPECIFICITY, COMPLEMENTARITY, AND SELF-REFERENTIAL MAPPINGS. Joseph E. Bogen. (SPON: A. Smith). Ross-Loos Medical Group,Los Angeles, 90017

That most human attribute, cerebral hemispheric asymmetry, is inadequately characterized as modality specific or material specific; rather, the asymmetry is process specific. A geometric interpretation of process specificity is proposed--namely, that each hemisphere represents the other and the world in complementary mappings: the left mapping the self as a subset of the world and the right mapping the world as a subset of the self. It is argued that a rigorization of this complementarity requires an algebra which is not only non-commutative but also non-associative. The suggestion is offered that a mathematical modeling of the mind-brain relationship would do well to begin with the theory of operator loops, in which the identity element plays an exceptional role throughout.

77.10 A NON-VERBAL FORM OF THE STREET SILHOUETTE COMPLETION TEST. Santosh Kumar*, Murray Binder* and Joseph E. Bogen. Ross-Loos Medical Group, Los Angeles, 90017

There is considerable current interest in the design of psychometric instruments which will be differentially affected by lesions of the right cerebral hemisphere. Such tests should have sufficient range that they can be given to both brain damaged and normal populations. The Street silhouette completion test appears particularly promising in this regard except that it requires a verbal reply which disqualifies it whenever there may be significant left hemisphere malfunction, including cases of established or suspected aphasia. A multiple choice read out was developed which permits testing without verbalization. Data to date indicate that scores on this version of the test bear a regular relation to scores on the original test both in neurological hospital and college student populations.

78.1 NEUROMUSCULAR PATHOLOGY IN PSYCHOTIC PATIENTS. John W. Crayton and Herbert Y. Meltzer. Dept. of Psychiatry, Pritzker Sch. Med., Univ. Chicago, Chicago, Ill. 60637.

Previous studies (Meltzer, Arch. Gen. Psychiat. 27: 125, 1972) indicated that psychotic patients have histochemical and morphological abnormalities in muscle biopsies from the vastus lateralis muscle which are consistent with a neuropathic neuromuscular disorder. Further information on the validity of this hypothesis has been obtained by light and electron microscopic studies of muscle and intramuscular motor nerve endings in biopsies of peroneus brevis from 20 psychotic and 5 non-psychotic hospitalized patients and 14 normal volunteers. Six (30%) of the psychotic patients had more than 10 small angular fibers in sections examined with histochemical methods and 7 (35%) had extensive Z-band streaming in more than 2% of fibers, both of which are consistent with denervation. Of the 20 psychotic patients, 9 were abnormal by one or both of the two techniques. Only one (7%) volunteer exceeded these criteria ($Chi^2 = 4.943$, $p < 0.05$). Supravital staining of intra-muscular nerve terminals with methylene blue revealed, in the patient population, extensive neuronal sprouting and terminal branching with the innervation of as many as 18 end plates by a single axon. The terminal innervation ratio (number of end plates/number of axons) was greater than 1.4 in 11 (55%) psychotic patients and 1 (7%) control ($Chi^2 = 6.296$, $p < 0.01$). Patients with muscle fiber abnormalities consistent with denervation tended to have the highest terminal innervation ratios. The most extensive neuro-muscular pathology was found in 3 chronic schizophrenic patients. The amount of pathology could not be correlated with neuroleptic drug administration. These findings support the hypothesis that psychotic illness can be associated with a peripheral neuropathic process. Supported by grants USPHS MH-18, 396, MH-16, 127, RSDA MH-47, 808 (To H.Y.M.) and State of Illinois 231-12-RD.

78.2 EFFECT OF DANTROLENE SODIUM ON HUMAN SKELETAL MUSCLE. Nathaniel H. Mayer* and Richard Herman. Dept. Rehab. Med., Temple Univ. Hlth. Scs. Ctr., Philadelphia, 19140

Previous studies have shown that dantrolene sodium reduces the amplitude of human twitch and tendon jerk contractions and alters the EMG/torque ratio during voluntary contractions. The current study investigated the effect of dantrolene sodium on the contractile properties of human skeletal muscle. Hill's mechanical model of muscle consisting of a contractile component in series with an elastic element was adapted to determine the force-velocity relation of the triceps surae muscle before and after oral loading doses of dantrolene sodium. Percutaneous electrodes were used to stimulate the tibial nerve in the popliteal fossa. Torque developed by the contracting triceps surae muscle was measured by a force transducer. By assuming that the velocity of shortening depends only on the load, it follows that $V=dx/dt=(dx/dP)\cdot(dP/dt)$ where x=displacement of the series elastic component (eq.1). If an element with compliance C is inserted in series between muscle and transducer, then $V=d(x+CP)/dt=(d(x+CP)/dP)\cdot(dP/dt)_c$ (eq.2). This implies that for the same tension P: $dx/dP=C(dP/dt)_c/dP/dt-(dP/dt)_c$ (eq.3). The quantities on the right side of eq.3 were determined experimentally, thus enabling calculation of points on the force-velocity curve. Results showed that dantrolene sodium shifted the force-velocity relation of human muscle in the direction of decreased power output. It was also found that dantrolene sodium profoundly affects the maximal rate of rise of muscle tension $[(dP/dt)_{max}]$. These findings are consistent with the hypothesis that dantrolene sodium affects the contractile element of Hill's two component model.

78.3 MUSCLE PAIN AND POSTURE OR WHY MOSES NEEDED HELP. Patricia A. McGrath* and Robert M. Steinman. Dept. Psych., U. of Md., College Park, Md., 20742

Deep pain, occurring as a consequence of exercise of ischaemic muscle, was elicited and quantified in a simple reliable way. Observers (without prior experience) were able to consistently report the onset of muscle pain that arose from holding a weight in their outstretched arms. The mean times for pain to develop in the arm muscles varied as a function of the weight held. The heavier the weight, the shorter the time to pain-onset. The time-intensity function for each observer was linear on a semi-logarithmic plot. An analogous weight-holding experiment was performed with the tongue to assess the possible contribution of joint receptors to experimentally produced pain in the arm. Tongue time-intensity functions were similar to those obtained for the arm. The time-intensity relation for muscle pain measured in this manner supports and quantifies Lewis' (1942) earlier observations that muscle pain is caused by the accumulation of some physiochemical substance produced during normal muscle exercise when circulation is occluded. Pain results when the substance accumulates because normal circulation is reduced either by circulatory occlusion (as shown by Lewis) or by postural restrictions as shown in the present experiments. (ref. Lewis, T. Pain. New York: MacMillan Co., 1942.)

78.4 PROSTHETIC ARM CONTROL BY PATTERN RECOGNITION. F. Ray Finley*, Roy W. Wirta* and Donald Taylor* (SPON: R. Herman). Dept. Rehab. Med., Temple Univ. Hlth. Scs. Ctr., Philadelphia, 19140

Synergetic muscles of the chest, shoulder, and back are used by above-elbow amputees to control an externally powered engineering model prosthetic arm. Eight movements about four axes are controlled in simultaneous coordinated manner. No presently available arm prosthesis incorporates as many movements under the automatic control of its user. To mobilize the arm the amputee thinks of movement, not muscles, and thus control is quickly integrated into natural behavior. This control mode is possible owing to the presence of motor engrams which provide stereotyping in movement execution, and which persist in the neural repertoire even after amputation. Skin electrodes are used in connection with a pattern recognition circuit to provide movement control. Before developing the engineering system a series of investigations was planned to observe and correlate myoelectric activity with arm displacement under a variety of conditions including differences in load applied, movement velocity, and practiced execution. The results of these studies indicated augmentation of the signals, but constancy of their array regardless of load or velocity, and an enhancement of the synergy with practice. These results are presented and discussed together with a motion picture film displaying arm control quality gained after very brief practice by an amputee.

78.5 **THE EFFECTS OF 50 FT/MIN AND 100 FT/MIN COMPRESSION RATES IN EXCURSIONS FROM 870 FT TO 1000 FT ON FORCE MICROTREMOR AND TREMOR "SIGNATURES."** **Arthur E. Findling*, Arthur J. Bachrach, U.S. Naval Medical Research Institute, Bethesda, MD, and Peter B. Bennett, Dept. of Anesthesiology and Biomedical Engineering, Duke University Medical Center, Durham, NC**

In a hyperbaric chamber three divers saturated on a helium/oxygen breathing mix were compressed from the 870-ft level at which they were saturated to 1000 ft on excursion. Two different compression rates were used to determine possible effects of time of compression on tremor; these rates were 50 ft/min and 100 ft/min. No consistent changes over subjects were observed that could be attributed to depth, gas, or compression rate. Each subject was tested precompression at 870 ft, at reaching 1000 ft, and before decompression back to 870 ft. Within subjects, consistency was seen in the type of frequency spectrum produced at surface, 870 ft, and 1000 ft. These findings support the hypothesis that each person has a tremor "signature" which designates him under different conditions.

78.6 TEMPORAL SUMMATION AT THE ABSOLUTE THRESHOLD FOR WARMTH. Joseph C. Stevens. John B.Pierce Fndn.Lab. and Yale Univ., New Haven, Conn. 06519.

Threshold levels produced by infra-red irradiation of the forehead were measured in six subjects at 12 durations between 0.05 and 10 sec. Beyond a critical duration of approximately one second the threshold level is constant (independent of duration). Below the critical duration, time t can be traded for irradiance φ according to the hyperbolic equation $\varphi=kt^{-0.8}$ in order to preserve the absolute threshold. That these properties of the warmth sense are relatively independent of areal extent of stimulation was demonstrated by a study that compared temporal summation for two different areas of the same subject's skin. Psychophysically, temporal summation in the warmth sense behaves much as it does in audition, vision, vibration, taste, etc. The psychophysical findings are also examined in terms of changes in skin temperatures, using the Stolwijk-Hardy model for simulating the thermal state of the skin at various levels re the surface. Finally, individual variation in apparent absolute sensitivity was explored under the rubric of the theory of signal detection, leading to the conclusion that much, but not all, of the variation can be put down to the personal judgmental criterion of the subject.

78.7 COMPUTER ANALYSIS OF SERIAL EEGs FROM STROKE PATIENTS. B. A. Cohen*, E. J. Bravo-Fernandez*, and R. S. Hosek* (SPON: A. S. Wilson) Dept. of Biomedical Engineering, Marquette Univ., Neuroscience Research, Veterans Administration Center, Wood, Wis. 53193

Serial EEGs from stroke patients were computer analyzed in an effort to find significant quantitative indicators of these patients' prognoses. Zero-cross techniques were used to classify the analog EEG signal into its major periods or spectral bands. Computer plots as well as statistical analyses of the spectral band elements were obtained from acute cerebrovascular accident (CVA) patients and a control group. Results indicate that patient recovery may be accompanied by changes in the spectral makeup of the EEG which are not readily detectable by visual means. Acute CVA patient records show a tight clustering when one spectral band is plotted against another. However, clinical recovery is preceded and accompanied by a tendency for these same spectral band plots to become less clustered. This lack of clustering is similar to the diffuse patterns exhibited by the control group and may reflect a normal cyclic synchronous activity. In addition, the spectral elements in acute CVAs initially vary in a random fashion over time and become more organized with increasing degree of recovery as compared to spectral elements from the control group which continuously vary in an organized fashion as relative reciprocals of one another. These data prove promising in attempts to find an early indication of patient recoverability from CVA.

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79.1 PHOTORECEPTOR RESPONSES AND CENTRAL CONDUCTION IN THE EYE OF A NUDIBRANCH MOLLUSC. Ronald Chase. Dept. Biology, McGill Univ., Montreal, Quebec, Cda.

The two bilateral and internal eyes of the marine mollusc, Tritonia diomedia, each contain about 5 large (50μ) photoreceptors. Electrophysiological and morphological evidence indicates that the axons of these cells leave the eye to form the optic nerve, which travels 4.0 mm to the cerebral ganglia. Intracellular records obtained from the receptors reveal graded depolarizing responses to light with action potentials either highly attenuated or absent. The cells are coupled electrically and synaptically. The graded response of the receptors is decrementally conducted in the optic nerve where a positive DC shift is recorded with extracellular suction electrodes during light stimulation. Light-evoked action potentials are superimposed on the DC wave. With favorable electrode placements, a different extracellular spike waveform is recorded during light stimulation than in the dark, and the temporal relationship between paired receptor spikes and optic nerve spikes is also altered during light activation. It is concluded that only the axon membrane of the photoreceptors is electrically excitable, and that under the influence of the depolarization produced by light the site of spike initiation shifts from a region about 1.0 mm from the eye to higher threshold regions closer to the eye. Central conduction of action potentials under experimental conditions is severely rate limited and sensitive to accommodation and block.

79.2 INFORMATION CODING IN THE CRAYFISH OPTIC NERVE: MOTION DETECTOR ACTIVITY PREDICTS THE OCCURRENCE OF VISUALLY GUIDED BEHAVIOR. Raymon M. Glantz Dept. Biology, Rice Univ., Houston, Tx 77001

The behavioral response of a crayfish to a rapidly approaching object is either an escape (tail flip and swimming) reflex or defense (cheliped raising) response (DR). Target velocity, visual angle and contrast are important parameters in determining the DR probability of occurrence and the impulse frequency in cheliped muscles associated with the response. When these parameters are optimized the three classes of optic nerve interneurons (sustaining units, dimming units and motion detectors) exhibit an enhanced discharge frequency during the period of target motion. If a black target is presented against a white background the sustaining unit response latency equals or exceeds the DR latency (determined from discharge pattern of cheliped levatory muscles). Motion detector response latencies are 35-100 ms less than the DR latency which corresponds to the range of independently measured conduction times between the optic nerve and the muscles at the base of the cheliped. Mean conduction time is 44 ms. Dimming unit discharge precedes muscle response, by 100 to 150 ms. DR response amplitude and motion detector impulse frequency are identical functions of stimulus velocity. Simultaneously monitored motion detector and muscle spike trains elicited with rapidly approaching objects have been cross-correlated. The correlation function exhibits a marked peak between 35 and 50 ms. The occurrence of a correlated spike in the cheliped muscle is specifically contingent upon the previous occurrence of a high frequency burst in motion detector neurons. If data containing such a burst is partitioned out of the sample, the correlation function fails to exhibit a peak and the muscle fails to exhibit a stimulus dependent discharge.

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79.3 RETINAL PROJECTIONS IN THE LIZARD GEKKO gecko. Ann B. Butler and R. Glenn Northcutt. Dept. Neurosurg., Sch. Med., Univ. of Virginia, Charlottesville, Va. 22901 and Dept. Zool., Univ. of Michigan, Ann Arbor, Mich. 48104.

Retinal projections were studied experimentally in the lizard, Gekko gecko. Unilateral suction ablation of the retina was carried out under sodium pentobarbital anesthesia in 12 animals. Following survival times ranging from 10 - 74 days, the brains were sectioned and processed with Nauta silver methods. The retina projects contralaterally to nuclei geniculatus lateralis pars dorsalis (NGLpD) and pars ventralis (NGLpV) in the thalamus, nuclei geniculatus pretectalis (NGP), lentiformis mesencephali (NLM), and posterodorsalis (NPD) in the pretectum, nucleus opticus tegmenti (NOT) and to layers 8-14 of the optic tectum. NLM is present in Gekko only as a few, characteristically large cells, dorsal to the region of NGP. A few degenerated fibers also pass through the region of the supraoptic nucleus. Ipsilaterally, the retina projects to the dorsolateral portion of NGLpD and sparsely to NGLpV, NGP, NLM, and NPD. Degenerated fibers and terminal debris are also present in layers 8-14 of the ipsilateral optic tectum, particularly concentrated in layer 9. An ipsilateral retinotectal projection has not been previously demonstrated in reptiles, birds, or amphibians. This finding raises the question of whether such a condition was a generalized, ancestral one among vertebrates or is a mammalian characteristic which has been evolved independently in geckos. (This work was supported by NIH Grants 1 F10 NS 2568-02 to ABB and 1 R01 N508417-01A1 to RGN.)

79.4 RETINAL PROJECTIONS IN A TELEOST (MALAPTERURUS ELECTRICUS). Dorothy E. O'Donnell* and Sven O. E. Ebbesson. Dept. Neurosurg., UVa Sch.Med., Charlottesville, Virginia 22901.

Among the 40,000 species of teleosts, Malapterurus electricus was selected for having a poorly developed visual system. Unilateral eye enucleations on 6 adult electric catfish, 15 to 20 cm in length, were performed under anesthesia. After 2 to 26 days of postoperative survival, the fish were perfused with 10% formolsaline. The brains were embedded in egg yolk and frozen sections were cut at 33μ. Modifications of the Nauta and Fink-Heimer techniques were used in processing the tissue to specifically stain degenerating fibers and terminals. The degenerating fibers stained best after postoperative survival times of 16 to 26 days. Two day survival showed no degeneration and after 8 days only very fine degeneration was demonstrated.

The preliminary findings show the optic chiasm to be ventral to the anterior commissure. There is total decussation of the optic nerve. The right optic nerve passes dorsal and wedges into the left optic nerve. Fascicles of the optic tract are distributed to the fasciculus medialis nervi optici, area geniculata, nucleus preopticus magnocellularis, tractus marginalis lateralis and medialis. Fibers terminating in the optic tectum show coarse degeneration in narrow bands in the stratum fibrosum and griseum superficiale. The distribution of fibers in the thalamus is diffuse. Many of the nuclear cell groups seen in species with acute vision, are not differentiated in Malaperurus electricus.

79.5 RETINOGENICULATE PROJECTIONS OF C57BL/6J MICE. Irwin S. Westenberg* and Roland A. Giolli (SPON: J. Parnavelas). Dept. Psychobiol., Sch. Biol. Sci., UCI, Irvine, Cal. 92664

It has been hypothesized that the albino genes cause reduced uncrossed retinogeniculate projections (RGP) in mammals. A critical test of this hypothesis would involve a comparison of albino and pigmented animals that are otherwise genetically identical, e.g. albino (C57BL/6J-c^J) and normal C57BL/6J mice. In order to provide the basis for such a comparison, the RGP of normal C57BL/6J mice were mapped. The right eyes of three adult, male C57BL/6J mice were removed, and seven days later the mice were sacrificed. Brain sections were stained by variants of the Nauta-Gygax and Fink-Heimer techniques. In serial maps large crossed RGP and smaller, more localized uncrossed RGP were observed. The relatively large size and the localization of the uncrossed RGP suggest that the C57BL/6J mouse strain is ideal for testing the albinism hypothesis. Initial observations of normal-appearing uncrossed RGP in albino (C57BL/6J-c^J) mice suggest that the albinism hypothesis is incorrect. The technical assistance of T. Pickens, R. Morris, and A. Selvaggi is acknowledged.

79.6 DEPTH DISCRIMINATION IN THE CAT CONTINGENT UPON POSITIVE REWARD. Morton Gollender and Colin B. Pitblado*. Pacific University, College of Optometry, Forest Grove, Oregon 97116.

Three adult cats were trained to discriminate between near and far illuminated outline squares presented against a large background illuminated square. The randomly presented stimuli were enclosed in a dark viewing tunnel and controlled automatically. The cats were shaped to a nose-key response for food reward. Stimulus control was established by means of a "fading" technique in which other stimulus dimensions,(form and lateral separation) in addition to the depth difference, were initially available. Small images of the targets were projected upon the response keys. The target, forward and to the left, was projected upon the left key, the target back and to the right upon the right key. The cats solved the problem by pressing whichever key had the image. After reaching criterion (90% correct two days running), the illumination of the image was gradually faded until it was removed, leaving only the distant targets. After the large square was faded in, form and lateral separation differences were eliminated leaving the cats with a display consisting of a pair of concentric squares, with the small one lying either before or behind the large one. The angles subtended by the small squares were equal at the plane of the viewing ports. The discrimination was then transferred to a vectographic projection of 2 half-views, identical to those obtained with the real objects. One cat transferred immediately at criterion level, the others somewhat later. While we do not regard this as yet as a demonstration of stereopsis, we do infer performance under our conditions to be under the control of some stimulus dimension that varies with the targets displacement in depth. Planned is a final step which will transfer the discrimination to Julesz random-dot matrix and Kaufman letter-matrix stereograms in which the small square is not identifiable monocularly.

79.7 THALAMIC ELECTROENCEPHALOGRAPHIC CORRELATES OF DISCRIMINATIVE PERFORMANCE IN THE MONKEY. Anatol Costin and Samuel L. Moise, Jr. Dept. Anat., Sch. Med., UCLA, Los Angeles, 90024

In monkeys with chronic implanted electrodes in the brain the changes in the electrical activity of the thalamus (ventral anterior nucleus) were studied, during performance of color (red - green) discriminations. The animals were trained and tested with computer control (PDP-8) for presentation of stimuli selection of parameters, recording and evaluation of all behavioral data. The record for each trial was divided into the following segments: pre-stimulus, post-stimulus, pre-response, and post-response. 0.5 sec segments of EEG time-locked to stimulus or response events were chosen for analysis. The EEG data were evaluated by power density spectral analysis and non-parametric statistics. Statistical evaluation revealed significant differences in relative power spectra of thalamic EEG (primarily in the 2 - 6 Hz band) just prior to a discriminative response, when compared to spectra just prior or just after the stimulus onset. These patterns appeared mostly unilateraly. However, histology suggested similar bilateral placements and observation of the performing animals did not reveal biases in terms of head position and orientation during training.

(Supported by USPHS Grant GM 16058-08.)

79.8 VISUAL EVOKED RESPONSES AND SELECTIVE MASKING WITH PATTERN FLASHES OF DIFFERENT SPATIAL FREQUENCIES. Mario Musso* and M. Russell Harter. Dept. Psychol., UNC-Greensboro, Greensboro, N. C. 27412

Psychophysical and evoked cortical potential (EP) measures of visual masking were obtained to pairs of sequentially presented patterned light flashes (40 msec inter-flash interval) to ascertain 1) whether masking would be similarly reflected in both measures, and 2) whether the relationship between the spatial frequencies of pattern elements within the two flashes in a pair would influence both measures of masking. The pairs of flashes consisted of all combinations of four flashed displays: black and white checkerboards (checks subtending 7.5, 30, and 60 min) and diffuse light. EPs from four adult humans were recorded monopolarly over the occipital area (O_z to ear reference) and averaged. The contribution of the first and second flash to the complex EP elicited by the pair was assessed by a new variance analysis technique. Statistical analyses of the EP data indicated that the contribution of a light flash to the EP was reduced when the flash was either preceded or followed by a second patterned flash (indicating both forward and backward masking). The contribution of the second flash was always less than the first, forward masking being most pronounced. Forward masking was most pronounced when the first flash was the 30' checkerboard. When EPs to paired and single flashes were compared, the masking was greatest of that portion of the EP associated with the second flash in the pair when both flashes contained the same sized pattern. The EP data, therefore, indicated masking was influenced by the order of pattern, the absolute size of pattern, and the relationship between the size of pattern contained in the two flashes. Some discrepancies were evident between psychophysical and EP measures of visual masking. The data were interpreted within the framework of the spatial frequency analysis model of pattern coding.

79.9 TOPOGRAPHY OF LATE VISUAL EVOKED RESPONSES IN MAN. Merlin W. Donald, Psychology Dept., Queen's University, Kingston, Ontario, Canada.

Visual evoked responses (VER) were recorded from volunteer human subjects with patterned flash stimuli. Topography of each VER was estimated with posterior scalp electrodes placed in standard 10-20 locations. Stimuli were delivered binocularly to each retinal quadrant and to the upper and lower hemiretinae, at interstimulus intervals of 800 and 3500 msec. Small Ns were used in averaging (usually 16) to maximize the sensitivity of the VER to short term cortical excitability changes. Changes in VER topography in the 120-300 msec. latency range occurred both as a function of retinal locus and as a function of spontaneous fluctuations in late wave amplitude. Results are discussed in terms of parallel vs. serial stimulus processing models.

79.10 CHANGES IN THE LATE COMPONENTS OF VISUAL EVOKED POTENTIALS WITH VISUAL INFORMATION PROCESSING. Donald B. Lindsley, David M. Seales* and Glenn F. Wilson*. Depts. Psychol., Physiol., Psychiat. and Brain Res. Inst., UCLA, Los Angeles, 90024

Twenty-five college students participated in three experiments. AEPs were recorded from five sites: left and right visual association cortex, left and right Wernicke's area, and the vertex. AEPs were averaged off-line on a PDP-12 computer. In Exp. I, condition A, subjects viewed five three-line, non-meaningful patterns, each presented 20 times on a remote display scope. No task was involved in condition A. In condition B the same patterns were presented again, each followed in 0.5 sec by its respective code number. During this period the subject learned the pattern-number code. In condition C the patterns were presented a third time and the subject's task was to readout the code number of each pattern. Comparisons between AEPs for condition A before learning and condition C after learning showed a marked change in the P2 component--a reduction in amplitude and broadening of the wave. In Exp. II condition A was repeated three times to test for habituation effects--slight effects were noted but nothing like the changes observed in Exp. I after learning. In Exp. III the subject was required to note how many times a 6th pattern occurred among the other five. This less complex discrimination task also caused a reduction in amplitude and broadening of the P2 component, but the effect was enhanced by the additional task of learning the pattern-number code. Thus changes in P2 appear to be correlated with the complexity of the visual information processing task but mainly over visual association areas. The contrast between these changes and those observed under conditions of increased arousal, where late components are broadly enhanced, are interpreted in terms of specific and nonspecific sensory systems. Supported by USPHS grant NS-8552 to D. B. Lindsley.

79.11 CONCURRENT BEHAVIORAL AND LATERAL GENICULATE SPECTRAL RESPONSE FOR RHESUS MONKEY. M. L. J. Crawford and H. G. Sperling. University of Texas, Graduate School of Biomedical Sciences, Houston, Texas, 77025.

Fifty-four single units from the lateral geniculate nucleus (LGN) of the alert rhesus monkey have been recorded in response to colored test flashes delivered in Maxwellian view. Simultaneously, behavioral increment spectral thresholds show that when the animal's performance reaches chance levels, the LGN unit's response to the test flash has reached background discharge level. In the course of this experiment a question arose as to the variability of fixation of the test area by the monkey. Using a laser burn marking technique, it was concluded that in the increment threshold task, the rhesus monkey uses variable parafoveal retina for detection of stimuli which are as much as 0.5 log units intensity above threshold, placing only threshold level stimuli upon the fovea.

79.12 INTEROCULAR TRANSFER OF McCOLLOUGH EFFECT. Harutune H. Mikaelian. Dept. Psychol., U. of Ga., Athens, Ga. 30602

Orientation specific color after effects (McCollough aftereffects) were generated by alternate viewing of vertically and horizontally oriented square wave gratings projected through red and green (Wratten #25,58) filters respectively. Total viewing time was 5 min. An achromatic stimulus of concentric square band patterns, with alternate bands of horizontal and vertical edges was used to assess aftereffects. (Science, 1968, 162, 3861). The McCollough effect appeared as green and red bands (green on vertical edges and red on horizontal edges.) Twenty Ss were exposed monocularly (rt. eye) and tested for interocular transfer. Contrary to previous reports (Murch, JEP, 1972, 93, 30-34) 17 subjects reported the presence of color bands when viewing the achromatic stimulus with the contralateral eye. Nine Ss reported no immediate aftereffects with the contralateral eye but reported seeing color following 1-2 min. of viewing the achromatic stimulus with both eyes. A most notable observation was that in some cases the organization of the color bands between the two eyes was reversed; six out of the 17 Ss indicated that the bands were arranged orthogonally between the two eyes--the red band seen with one eye (ipsilateral) appeared green in the contralateral eye, with a similar reversal for the other color. The radical departure of the present data from those reported earlier may be due to the nature of the test stimulus, which contains highly redundant edges of vertical and horizontal orientation in a configuration that enhances the detection of hue differences. The orthogonal arrangement of the red and green bands between the two eyes has not been previously reported. These data implicate post-lateral geniculate structures in the generation of orientation specific hue aftereffects.

80.1 EFFECT OF PYRITHIAMINE INDUCED THIAMINE DEFICIENCY ON RAT MYELINATION. David McCandless* and Michael J. Malone. Depts. of Anat. and Neur., George Washington Univ. Med. Sch., Washington D.C., 20005

Myelination, a major developmental milestone in brain maturation, is affected by a variety of environmental, hormonal and nutritional factors. In order to determine the effect of a specific deficit in energy metabolism on the process of myelination, we studied, as an experimental model, the developing rat brain rendered thiamine deficient during the critical period. Pyrithiamine was administered in a low dose (50ug/d/6 days) and in a high dose (2000ug/d/12 days) to newborn nursing rats. The animals were observed for behavioral changes; histological and biochemical studies were made by sacrifice on alternate days. The brains were removed and split sagitally. One brain half was used for light microscopy and the other half was studied biochemically. The extent and degree of myelination was assessed in serially sectioned experimental and control brains stained with Weil's stain for myelin. Biochemical studies in cortex and subcortical white matter included tissue transketolase activity and pyruvic acid levels. There were no behavioral abnormalities between experimental animals and the controls. The process of myelination proceeded histologically in identical fashion between experimental and control brains. Biochemical studies indicated a major deficiency. Thiamine-dependant transketolase (TK) activities were depressed (> 50%) and tissue pyruvic acid levels were greatly increased. (> 75%)

We have found that a biochemical deficit, lethal in the adult rat brain, is not merely tolerated by the immature nervous system but is compatible with normal development. Alternative metabolic pathways are available to the immature brain and these pathways cannot be utilized by the mature, differentiated tissue.

80.2 THE NEUROCHEMISTRY OF PRENATAL MALNUTRITION IN RHESUS MONKEY. J. M. Davis and W. A. Himwich. Galesburg State Research Hospital, Galesburg, Ill., 61401 and Nebraska Psychiatric Institute, Omaha, Nebraska, 68105.

Pregnant rhesus females maintained at the Wisconsin Regional Primate Research Center were fed a control Similac formula the first 30 days of pregnancy, after which they were either continued on this diet as control subjects or were given Similac deficient in 3/4 of its normal protein content for the duration of pregnancy. The offsprings' diet, fed ad libitum, consisted of 18.2% protein (20 calories per fluid ounce). The brains of 1- and 2-year-old rhesus were sectioned into 17 different brain areas for analyses of protein, nucleic acids, amino acids and acetylcholinesterase (AChE). Brain and body weights were not affected by prenatal protein malnutrition. Protein content of the male temporal cortex was significantly lowered whereas the AChE activity of this same area was increased. Comparison of the nucleic acids indicate an increase in the DNA in temporal cortex, pons, medulla and thalamic areas and a decrease in the corpus callosum of the 3/4 protein deprived male rhesus. RNA on the other hand decreased in the occipital cortex and increased in the cerebellum and pons. Some amino acid and sex differences will be compared in the brain areas showing changes in the protein, AChE and nucleic acids, with a discussion on the significance of the prenatal protein deficiency alterations which occurred.

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80.3 CHRONIC PROTEIN MALNOURISHMENT AND THE DEVELOPMENT OF BRAIN FUNCTIONING IN RATS. William B. Forbes, Warren C. Stern, Joseph D. Bronzino* and Peter J. Morgane*. Neurophysiol. Lab., Worcester Fndn. Exp. Biol., Shrewsbury, Mass. 01545.

In order to evaluate the effect of chronic dietary restriction on development of brain functioning, three indices of neural activity were examined in the albino rat. Malnourished rats were born of mothers fed a restricted (8%) protein diet (normal=25%) beginning 3-6 wks. prior to mating and throughout gestation and lactation. After weaning, subjects were maintained on the diet fed their mothers. Development of frontal and parietal electrocorticograms (ECoG), as evaluated by hand-scoring of acute recordings, was unimpaired by the protein restriction at 4, 6, 8 and 14 days of age. In adulthood, visual evoked responses (VERs) in the lateral geniculate nucleus were studied by averaging 300 responses to flashes at 0.5 and 1.0 Hz in 6 normal and 6 deprived rats. The initial positive-negative deflection had a significantly greater latency and was of shorter duration in the deprived group. Further, the VERs of the deprived rats consistantly showed several long-latency secondary components of diminishing amplitude not seen in the normals. Sleep-waking behavior differed between deprived and normal adult rats in that three of five protein deprived rats showed less than 1% REM in an 8 hr. recording period (normal range: 4-13%). Based upon these initial findings it appears that protein restriction during development does not markedly affect the differentiation of the gross ECoG but in adulthood electrophysiological effects occur. (Supported by NICHHD grant 06364 and NIMH grant 10625.)

80.4 ESSENTIAL AMINO ACIDS AND PRENATAL BRAIN DEVELOPMENT. Sandra M. Hall*, Ludmila Grauel*, Edith van Marthens* and Stephen Zamenhof. Dept. Microbiol. & Immunol., Biol. Chem., Brain Research Institute and Mental Retardation Center, UCLA, Los Angeles, 90024.

In previous reports (Science, 160:322, 1968; J. Nutr., 101:1265, 1971) we have demonstrated that dietary protein restriction during pregnancy in rats results in offspring with lower neonatal cerebral weight, cerebral DNA (cell number) and cerebral protein. In many underdeveloped countries the primary source of protein is of plant origin and is often deficient in one or more essential amino acids. The purpose of this work was to establish the effects of a chemically defined amino acid maternal diet, and the omission of single essential amino acids, on the brain development of the progeny. A synthetic diet containing an L-amino acid mixture to replace protein was developed by one of us (E. van Marthens). Dams were maintained on this diet throughout gestation. It was found that this diet supported the weight increase of pregnant rats as well as the stock pelleted diet (controls). Food intake of the dams was not affected. The neonatal parameters, body weight, placental and cerebral weight, DNA, and protein were the same as for the control progeny. In another series of experiments, one of the essential amino acids was excluded singly from the diet either throughout the entire period of gestation (lysine) or from day 10 to 22 of gestation (methionine, tryptophan). Hormone supplementation was not given. These amino acid omissions resulted in inadequate weight gain and depressed food intake in the dams as well as differences in brain development of the progeny. (Supported by USPHS grants HD-05615, HD-05394 and HD-04612).

80.5 EFFECT OF FAT-FREE DIET ON THE DEVELOPING INFANT BRAIN. Harold B. White, Jr.*, M. Don Turner* and Richard C. Miller* (SPON: O. J. Andy). Depts. Biochem. and Surg., Sch. Med., Univ. Miss., Jackson 39216.

Extensive modifications of the lipid components have been found in the brains of two premature infants who received fat-free diets intravenously because of difficulties precluding oral feedings. There was a marked decrease (>50%) in total phospholipid concentration (mg/g wet brain) with the three major component phospholipids, ethanolamine phosphoglyceride (EPG), choline phosphoglyceride (CPG) and serine phosphoglyceride, each decreasing the same relative amount. Although the overall levels of unsaturation, as expressed by the UI notation (White, Galli and Paoletti, J. Neurochem. 18, 869, 1971) in brain EPG and CPG fatty acid mixtures were similar in control infants and those receiving the fat-free diet, there were major alterations in fatty acid constitution of the latter group. With brain EPG the level of 20:3ω9, which is an indicator of essential fatty acid deficiency, was elevated after only 12 days of intravenous fat-free alimentation. In addition, it was found that not all regions of the infant brain were affected to the same degree. The frontal and precentral lobes of the cerebrum showed elevated amounts of 20:3ω9 whereas the cerebellum did not. Two other fatty acids showing this same differential response were 22:5ω6 and 22:5ω3. However, the three brain locations studied each showed a decrease in amount of 22:4ω6. None showed diminished amounts of 20:4ω6 at this time. Changes in CPG fatty acids were generally in the same direction as those occurring in EPG but of lesser magnitude. (Supported by USPHS grants NS-08892 and K3-HL-18,345.)

80.6 DEVELOPMENTAL ASPECTS OF ACETYLCHOLINESTERASE. Anthony Donald Vanker* and Hiroshi Mizukami* (SPON: Duncan T. Kennedy). Dept. of Biology, Wayne State University, Detroit, Michigan 48202.

Kinetics of brain acetylcholinesterase (AChE) activity in several developmental stages of the mongolian gerbil (Meriones unguiculatus) were studied using the Ellman spectrophotometric assay and were analyzed using Lineweaver-Burk plots. Neonates (<72 hours old), young animals (11 and 30 days old) and adults were decapitated and the entire brain was used to isolate postsynaptic membranes. K_m was larger in the neonate than in the adult, while V_{max} was smaller. Intermediate values were obtained in the young animals. Inhibition of AChE with the local anesthetics, novocaine, xylocaine, and carbocaine was followed. Novocaine exhibited aspects of competitive inhibition in all four stages of development. The degree of inhibition at higher concentrations of novocaine was less in the neonate than in the adult. At lower concentrations, the effect was opposite. Again, intermediate values were obtained from the young animals. Xylocaine and carbocaine exhibited aspects of non-competitive inhibition which were similar in all stages. There is some evidence using another inhibitor, physostigmine sulfate in conjunction with novocaine that different isozymes of AChE are present depending upon the age of the animal.

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80.7 INDUCTION OF GLYCEROLPHOSPHATE DEHYDROGENASE (GPDH) BY HYDROCORTISONE (HC) IN PRIMARY RAT BRAIN CULTURES. Gail A. M. Breen*, Jean de Vellis & Ruth Cole*. Mental Retard. Res. Center, UCLA, Los Angeles, Ca., 90024

Previous studies in this laboratory have shown that the level of GPDH (EC1.1.1.8) is specifically regulated by HC in the rat brain and in the C-6 rat glial tumor cell line. This report concerns the hormonal regulation of GPDH in primary explant and reaggregating cultures of prenatal rat brain cortex. Explants, 0.5 to 1 mm^3, were sandwiched between 2 pieces of cellophane and maintained in a media of 50% BME, 25% Gey's BSS and 25% fetal calf serum with .6% glucose. Reaggregating cultures were placed on a rotating shaker at 70 rpm. Their media consisted of BME with 15% fetal calf serum and .6% glucose. The addition of 0.5 ug/ml of HC to both types of cultures resulted in a 3-5 fold increase in the specific activity of GPDH in 48 hours. This induction was blocked by Actinomycin D, cordycepin, cycloheximide and puromycin, indicating that RNA and protein synthesis are required. The induction was not blocked by cytosine arabinoside, an inhibitor of DNA synthesis. The inducer must be continuously present to maintain the induced level of the enzyme. Induction can be observed with cultures ranging from 1 to 4 weeks old. The basal level of the enzyme remains low at all times. The addition of HC for five days induced the enzyme to a new steady-state level which was approximately 8-10 fold higher than the basal level. This new level is approximately that reached in adult rat brain. Induction of GPDH can also be obtained in explants from other brain regions as well as in whole brain reaggregating cultures. These results are similar to those obtained in vivo and with the C-6 glial cell line. The data demonstrates that these neural tissue culture systems retain the ability to express a differentiated function, i.e. the brain-specific induction of GPDH. (Grants USPHS HD-04612 and USAEC AT-04 Gen 12.)

80.8 THE BLOCKING EFFECTS OF CYCLOHEXIMIDE ON THE SENSORY INDUCTION OF SUSCEPTIBILITY TO AUDIOGENIC SEIZURES. S. C. Maxson and P. Y. Sze*. Dept. Biobehavioral Sci., Univ. Conn., Storrs, Conn. 06268

During a sensitive period in development (between 16 and 19 days of age), exposure to a high intensity noise (105 to 115 db; re: 2×10^{-4} $dyne/cm^2$) will induce susceptibility to audiogenic seizures in otherwise resistent C57BL/6 mice. Pretreatment with cycloheximide (30 mg/Kg I.P.) at one-half hour prior to acoustic stimulation markedly reduced the acoustic sensitization whereas post-treatment one-half hour after the acoustic stimulation did not. Since maximum inhibition of protein synthesis takes place between one and three hours post injection, the inhibition of brain protein synthesis, which is crucial in blocking the acoustic sensitization, most likely occurs within one and one-half hours of the acoustic stimulation. Interestingly, this stimulation also produced a small and transient fall in the brain levels of γ-aminobutyric acid (GABA) at 15 to 20 minutes post stimulation. The levels of other amino acids as well as of the biogenic amines are unaffected by this treatment. Reversal of the fall in GABA by pretreatment (five hours prior to the acoustic stimulus) with aminooxacetic acid (AOAA, 25 mg/Kg sub "q") blocks this acoustic sensitization whereas pretreatment (one-half hour prior to the acoustic stimulus) either with dihydroxyphenylalanine (DOPA; 200 mg/Kg I.P.) or with 5-hydroxytryptophan (5-HTP; 200 mg/Kg I.P.) had no effect. These results suggest that for this genotype, sensory induction of susceptibility may be mediated by the fall in the level of GABA. Furthermore, the temporal relation between the changes in the level of this neurotransmitter and the changes in the level of protein synthesis are consistent with the hypothesis that long term behavioral modification may be initiated by the effects of neural transmitter on macromolecular synthesis.

80.9 THE EFFECT OF EARLY INPUT OF ETHANOL ON MICE ON THEIR SUSCEPTIBILITY TO AUDIOGENIC SEIZURES. Joseph Yanai and Benson E. Ginsburg*. Beh. Gen. Lab. Dept. Biobeh. Sci., Univ. of Conn., Storrs, 06268

A system was developed to study the effect of early input of ethanol in inducing behavioral changes. The alcohol intake of the mice was mediated by their mothers, who were fed alcohol from the time they were weaned until 14 days postparturition. The consumption and blood alcohol levels were monitored in the parents. The morphological development of the offspring was studied and appeared normal. Early ethanol input induced a susceptibility to audiogenic seizure in the offspring of normally nonsusceptible C57BL/10 mice (48.44%; $p < .001$; N-64). There was also an increase in seizure incidences in the genetically susceptible DBA/1 strain. The neonatal period was found to be the most sensitive one in producing this effect. Neuropharmacological studies involving the major neural transmitters and the alcohol metabolizing enzymes were conducted in order to determine the neurochemical systems that may be affected by the ethanol.

NONPROGRAMMED ABSTRACTS

PLASTICITY AND ELECTRICAL ACTIVITY OF THE LATERAL HYPOTHALAMIC AREA OF THE RAT. Michael J. Ackerman. Behavioral Sciences Dept., Naval Medical Research Institute, Bethesda, MD 20014

Behavioral and electroencephalographic observations were made on rats bearing electrodes chronically implanted bilaterally in the lateral hypothalamic area (LHA), to study stimulus-bound (SB) behavior. Electroencephalographic records were taken from the LHA electrodes: before any behavioral manipulation; while the Ss were hungry, thirsty, and satiated; and immediately after SB training sessions in which electrical stimulation of the brain (ESB) was made contingent on eating or drinking. These records underwent power spectral analysis. Differences between spectra were tested for statistical significance by multivariate T-tests. It was found that EEG spectra associated with hungry and thirsty Ss were different from those associated with satiated Ss, but not from each other. EEG spectra associated with Ss at the conclusion of the SB training sessions showed a "satiety" EEG pattern only on the nonstimulated side. The stimulated side showd a "deprivation" EEG pattern. A significant difference was also seen between EEG spectra taken before any behavioral manipulation from Ss that later became SB and Ss that did not become SB. These results indicate the presence of an integrative eating-drinking area within the LHA with specific eating and drinking outputs.

CHARACTERISTICS OF THE NEOMEMBRANE SURROUNDING THE SILASTIC DURAL SUBSTITUTE. T. Banerjee*, A. O. Humbertson, Jr. and W. E. Hunt. Dept. Anat., Sch. Med., Ohio State University, Columbus, Ohio, 43210.

Partial dura mater replacement is necessary during surgery when it is involved by a tumor or when severely lacerated by trauma. Various dural substitutes have been used in the past in elective operations. This paper is a report of our experience with Silastic dural substitute. An enveloping membrane forms about the dural substitute. This neomembrane is composed of dense connective tissue which completely surrounds the substitute. This membrane is adherent to the underlying brain when the pia-arachnoid has been injured, whereas, it is an easily separable tissue when the arachnoid is intact. However, the Silastic is relatively free within this newly formed membrane. Case histories of three patients who had hemorrhage within the space between the neomembranes will be discussed. The source(s) of bleeding was undetectable. The progression of neurological deficits was slower than in the usual cases of post-operative epidural hemorrhage. The relationship between the smooth surface of the neomembrane and the Silastic dural substitute appears to be conducive to the development of hematoma with minimal trauma. In our experience, Silastic has not met the optimal qualities of a dural substitute. Supported by General Research Support Grant Project 7207 NIH.

CAUDATE-PUTAMEN NEURONES: A CORRELATION OF EXTRACELLULAR UNIT ACTIVITY WITH CELL MORPHOLOGY. S.A. Deadwyler, G. Lynch, J. Haycock, C. Gall and C.W. Cotman. Dept. Psychobiology, UCI, Irvine, 92664

Rats anesthetized with urethane were used to study the response characteristics of striatal cells to thalamic, cortical, nigral and caudate stimulation. After collecting the neurophysiological data the individual cells were labelled and their morphological properties studied. Analysis of post-stimulus time histograms suggested that different types of cells in the striatum differentially respond to the various loci of stimulation. It appears that the various cell types in the caudate may be associated with different physiological functions.

A METHOD FOR CONVERTING NEURONAL PARAMETERS TO DIGITAL COORDINATE PAIRS FOR COMPUTER ANALYSIS. T. DeVoogd and W. T. Greenough (SPON: C. Trahiotis). Dept. Psychology and Behavioral Biology Program, University of Illinois, Urbana-Champaign, Ill. 61820

Direct measurement of neuronal parameters such as bouton area and length of postsynaptic thickening in electron micrographs, or dendritic length and spine density in Golgi preparations requires a large time expenditure. The fully automated systems available involve a substantial error rate and high initial cost. We have utilized a simple combination of a linear and a rotary potentiometer attached to a stylus controlled by a human operator. For EM work, negatives or prints are used. For light microscopy, the stylus can be controlled via a conventional camera lucida drawing attachment. Movement of the stylus is translated into voltage coordinates which are stored on FM tape. When processed by our computer system, the voltages are sampled and digitized at a rapid rate and are routed to one of several subprograms depending on the neuronal parameter being quantified. Advantages of such a system include low cost, direct operator control, and flexibility in that the same basic system is used for each of the above measurements with the changes made in the subsequent computer programing. The system reduces operator time and has a resolution equal or superior to any sort of direct measurement. (Supported by NIH grant HD 6862 and PHS grant PHFR 07030)

SEMANTICS AND BODY HOMEOSTASIS: ITCHING AND SCRATCHING. Wallace C. Ellerbroek, M.D., Metropolitan State Hosp., Norwalk, Calif 90650.

Clinical observation suggested that patients often scratched themselves when unpleasant subjects were discussed. This behavior was noted to be frequently associated with verbal statements so phrased as to deny the reality of the subject's own perceptions. Examples are: "he (she, they) shouldn't have acted that way" and "taxes should not be as high as they are." This led to a hypothesis that verbal statements contrary to reality as perceived by the subject initiate disturbances in homeostatic mechanisms. Sixteen naïve subjects were subjected to moderately severe emotional stress during instrumented and audiotaped interviews. A concealed event marker was used to record unequivocal scratching. During a post-interview session with audiotape playback, subjects were asked to discuss their thoughts at the moment the itching/scratching occurred. 170 items of scratching were recorded; ten could not be unambiguously reconstructed. 9 were temporally associated with overt speech which both subject and observer agreed was semantically invalid. In the remaining 151, the scratching was associated with thoughts so formulated as to be clearly semantically invalid. Thus in 160 of 170 scratching behaviors the hypothesis was confirmed. It may be worthy of note that in 151 of 160 items the subject apparently was not thinking something related to their ongoing speech content. This may be of considerable heuristic value in evaluating the results of other studies in human behavior. In spite of the problems of experimenter bias and verification of subject responses, this study may offer an approach to the murky problem of how the things we say and think affect our bodies.

EFFECTS OF LOW LEVEL CARBON MONOXIDE ON VISUAL DISCRIMINATION ACQUISITION AND RETENTION IN RATS. Sue Folk*, Douglas Burton*, Ralph Gunter, W. Jann Brown, and Robert T. Neher. Brain Lab, La Verne College, and Dept. of Path. (Neuropath.) UCLA, 90024

In order to determine the effects of realistically expected smog levels, we exposed 6 rats continuously for 14 days to 100 ppm CO mixed in ambient air for the effect on acquisition and retention in a discrimination active shock avoidance apparatus. It was found that after exposure, acquisition was adversely affected as compared with a normal unexposed control group, $p < .01$. The retention of the function, tested 14 days after criterion acquisition was less pronounced. In terms of percentage loss, acquisition is more severely affected than retention. Our data suggests that acquisition and retention abilities may be influenced by local smog levels. Relevant CNS structures are being investigated by the use of electronmicroscopy for possible correlated brain damage.

ANALGESIC PROPERTIES OF PHENYLETHYLAMINE AND PHENYLETHANOLAMINE IN MICE. W. J. Giardina. Dept. Pharm., Chgo. Med. Sch., Chicago, Ill. 60612.

2-Phenylethylamine (PEA) and phenylethanolamine (OHPEA) have been identified in brain (Inwang et al., Soc. Biol. Psychiat., 1972; J. Neurochem., 1973). Although PEA releases catecholamines (Fuxe et al., 1967), PEA as well as OHPEA have direct effects on CNS neurons (Giardina, et al., Life Sci., 1973). PEA probably functions as a precursor of OHPEA (Saavedra and Axelrod, Proc. Nat. Acad. Sci., 1973). The analgesic properties of PEA and OHPEA were studied in mice using the tail dip (water temperature 58°C; end point: tail movement) and hot plate (plate temperature 56°C; end point: paw lick) tests for analgesia. Saline, PEA (10 mg/Kg) and OHPEA (10 mg/Kg) were administered 15 min before testing. After inhibition of monoamine oxidase with pargyline (100 mg/Kg/24 hr), PEA and OHPEA produced analgesia on both the hot plate and tail dip tests. Neither PEA, OHPEA, or pargyline itself produced analgesia on these tests. In the following drug interaction studies, only the tail dip test was used. After pretreatment with pargyline (100 mg/Kg/24 hr) and the dopamine-β-hydroxylase inhibitor FLA-63 (50 mg/Kg/3 hr), OHPEA had a significant analgesic effect, but PEA had no analgesic effect, suggesting that the analgesia depends on a β-hydroxylated amine. Neither PEA nor OHPEA showed analgesic properties in mice treated with FLA-63 alone. FLA-63 did not influence pain threshold. Neither PEA nor OHPEA produced analgesia in mice pretreated with pargyline (100 mg/Kg/24 hr) and reserpine (10 mg/Kg/24 hr). OHPEA may have direct analgesic properties since its effects were not blocked by FLA-63, but they also require the inhibition of monoamine oxidase. However, the blockade of the analgesic effects of OHPEA (after pargyline) by reserpine suggests that the analgesia may be mediated by serotonin or dopamine.

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LESIONING BRAIN TO MODIFY HUMAN BEHAVIOR: THE CRITICAL ROLE OF NEUROSCIENTISTS. Robert J. Grimm. Department of Neurology, Good Samaritan Hospital and Medical Center, Portland, Oregon 97210.

Injury to specific areas of human brain can alter the control, expression, and content of emotional behaviors ranging from aggression to fear. Infarcts, tumors, metabolic insults, and paroxysmal disorders may express themselves in this way. Traditionally, it is the physician's role to diagnose and treat these disorders. The effort aims at preserving the integrity of existing normal brain and also to promote the recovery of the disordered part. Where aberrant behavior arises without an "organic" cause, it is argued by some--especially if we are dealing with criminal rage or an equally entrapping chronic anxiety state with repetitious behavior, e.g. compulsive hand washing--that such dysfunctional behavior derives from a faulty brain circuit or system involved in emotional expression. As concern for repairing the hypothesized faculty circuit frequently overrides, in the minds of the proponents of this theory, the matter of etiology, alternative explorations, or evidence for the existence of such dysfunctional physiology, the stage is set for the current and growing controversy over the return of psychosurgical procedures designed to effect a cure of these behaviors by lesioning. It is in the agenda of this paper to review the evidence for 1) assigning certain emotional behavior to specific brain structures by which their removal will 2) effect a restoration to more normal or sanctioned behavior, but 3) without alteration of personality or intellect. Amygdalotomies for rage reduction and cingulumotomies for anxiety will be considered. It is the interest of this review to provide guidelines for critical inquiry, decisions, and response by neuroscientists to advocates of such irreversible procedures.

CLINICAL EVIDENCE OF NEUROBEHAVIORAL RESPONSES CONDITIONED DURING EXPERIENCES IN ALTERED STATES OF CONSCIOUSNESS (ASC). Virginia Johnson, 1516 Westwood Boulevard, Los Angeles, California 90024.

Neurological processes and dependent behavioral patterns during ASC are well documented; but long term neurobehavioral effects and feedback circuits dependent upon learning and conditioning in such ASC are little understood. The present paper is concerned with findings from clinical protocols which suggest that characteristic variables of the ASC memory process include (1) state dependency; (2) correlation with an organismic (brain-behavior) continuum of such states; (3) ANS and motor feedback reflecting the neurophysiological responses in the prior ASC; and (4) the learning of disordered mental processes dependent on the perceptual distortions and varying degrees of impaired cerebral responsiveness typical of ASC. Such engrams can, in the presence of appropriate stimulation, reactivate ASC totally or in part, as well as the sensory, musculoskeletal, and autonomic responses experienced in such states. ASC learning is not amenable to cognitive recall as such and does not appear to be under voluntary control, but otherwise reflects fundamental learning processes such as association and reinforcement. Precipitation of a prior ASC, however, involves neurocerebral responses which differ from those learned during awake-aware states, and may result in behavior such as the sudden onset of impulsive acts, inappropriate responses, loss of consciousness, or mental processes noncontexted with respect to reality and immediacy. The paper will present findings from a clinical study of the experiential recall of ASC in terms of the precipitating factors of the original experience; the conditional variables present in the environment at that time; and the apparent persistence in terms of behavioral aftereffects including psychopathology.

MEASUREMENTS OF RESPIRATION IN ARNOLD-CHIARI MALFORMATION. Abbott J. Krieger, M.D. and John Detwiler, Ph.D.* University of Pittsburgh School of Medicine, Pittsburgh, PA, 15213 and Veterans Administration Hospital, University Drive C, Pittsburgh, PA, 15240

The Arnold-Chiari Malformation (ACM) is associated with respiratory distress in infants, most commonly with laryngeal stridor (LS). We have developed methods which allow continuous recording of resting respiration of infants, for study of such phenomena. Crucial to the method is the use of a specially designed nosepiece with an integral pneumotachograph screen. Virtually zero dead space is achieved with its flow-through configuration, and resistence to expiration is less than 1 mm H_2O. The low-resistence pneumotach necessitates an exceptionally stable and sensitive differential pressure recorder, achieved through our modification to a commercial instrument. Expired gas is sampled at the nostrils for conventional infrared CO_2 analysis.

Resting respirations have been measured in normal infants and those with ACM, while breathing various CO_2 mixtures. We find irregular rate and depth in ACM and steady-state CO_2 response normal or subnormal, while in normal infants our results confirm published averages. In ACM infants known to have episodes of LS, these findings are accentuated, suggesting that LS is merely the most dramatic manifestation of central respiratory nervous dysfunction in ACM. Our instrumentation appears to be a valuable and valid means for respiratory study in infants.

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GROOVE ELECTRODE ARRAYS FOR CHRONIC MULTICHANNEL RECORDING FROM DORSAL ROOT FIBERS. William B. Marks and W. Zev Rymer.*Johns Hopkins University, Baltimore, Md. 21218 and NIH, Bethesda, Md. 20014.

Arrays of 3 to 6 grooves in a chip of epoxy plastic with a teflon surface are cemented with tissue adhesive to the lumbar spinal cord of cats. The grooves are 5mm long and 75 to 150 microns wide and deep. Each groove has a midlength recording contact led out through a cable. The L7 dorsal root is dissected under oil into filaments by stroking and separating with micropipettes. The grooves are filled with saline before use, and this pulls the hydrophilic filaments from the oil into the grooves. Unit activity then appears. The array is covered to trap a layer of insulating oil, the remaining oil is removed, a metal shield is placed over the array, and the incision is closed. The emergence of the cable is protected by a saddle which mates with the cable and a preamplifier array or a 10 channel transmitter. Each channel carries 2 to 6 resolvable unit potentials of 50 to 600 microvolt amplitide, which are triphasic (+ - +) when the fibers are undamaged. Long term activity, often spontaneous, is recorded from cutaneous and muscle afferents of the hindlimb. The preparation will be used to study muscle control during normal locomotion.

VIRAL-INDUCED NEURONAL IMMUNOPATHOLOGY: LYMPHOCYTIC CHORIOMENINGITIS VIRUS INFECTION OF NEONATAL RATS. Andrew A. Monjan, Gerald A. Cole*, Neal Nathanson, and Manuel P. del Cerro. Dept. Epidemiology, Sch. Hyg. & Pub. Hlth., JHU, Baltimore, Md., 21205, and Center for Brain Research, Univ. Rochester, Rochester, N. Y., 14620.

Neurological disease established at or shortly after birth represents a major cause of chronic pediatric illness, presently classified under rubrics such as mental retardation and cerebral palsy. Obviously, a variety of etiologies are responsible, and established examples, such as rubella and cytomegalovirus, indicate that viral infections may be one cause. Thus, it is important to exploit newly discovered animal models of newborn or congenital central nervous system (CNS) disease produced by viruses. Infection of neonatal rats with lymphocytic choriomeningitis (LCM) virus is of particular interest since it produces a non-fatal and long lasting non-cytolytic infection of the CNS. Employing such methods as virus titration, serology, fluorescent antibody histochemistry, light and electron microscopy, and behavioral testing it was found that: (a) susceptibility is limited to the neonatal period, (b) animals regularly survive but are left with a permanent neurological deficit, (c) the selective vulnerability of the CNS to this virus is related to age at infection resulting in severe retinal or cerebellar pathology, (d) the lesions are a result of a viral-induced immunopathology, and (e) the infection is relatively acute, but the residual deficit is permanent.

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SIMULATION CLINICAL TRAINING AND ASSESSMENT IN NEUROLOGY - AN EXPERIMENTAL STUDY. F. C. Tinning* (SPON: M. Jones). Col. of Osteo. Med., MSU, East Lansing, MI. 48823

The general purpose of this study was to demonstrate that another approach for providing effective "hands-on" clinical training during the formative period of learning complicated clinical skills was available in medical education. The specific purpose was to ascertain the practical effectiveness of instructional simulation. This was demonstrated by comparing the use of simulated patients and real patients in clinical education. A comparison of the effects of the two training techniques in the development and transfer of total performance in clinical competency, psychomotor skills, affective behaviors of medical students, and cognitive medical knowledge was measured. A final Practical Neurological Evaluation History and Physical Examination on real patients was used to assess transfer in student performance. In general, it can be stated that simulated clinical training provided the learner with an opportunity to vary behavior, problem solve, and make decisions in an environment that was positive and free from distraction. The experiences provided relevant feedback on critical behaviors which were transferred to the real world in demonstrated learning outcomes. The experiment has demonstrated an alternative in medical education and has added to the body of knowledge of instructional methods in physician education as related to the training and transfer of psychomotor skills, affective behavior, cognitive knowledge, and clinical competency performance.