*Society*
*for*
*Neuroscience*

# PROGRAM and ABSTRACTS

*Second Annual Meeting*

October 8-11, 1972
The Shamrock Hilton, Houston, Texas

## Contents

# General Information

## REGISTRATION

Shamrock Hilton, Grand Ballroom Foyer

### Hours

Sunday, October 8 ..... 2:00 PM–9:00 PM
Monday, October 9 ..... 8:00 AM–5:00 PM
Tuesday, October 10 ..... 8:30 AM–5:00 PM
Wednesday, October 11 ..... 8:30 AM–1:30 PM

### Fees

Members ..... $20.00
Nonmembers ..... $25.00
Graduate Students ..... $ 5.00
(Any student working toward a degree in neuroscience or an allied field)

Social Registrants ..... $ 2.00
(Wives and other nonscientist family members of registrants)

## INFORMATION/TICKET DESK AND MESSAGE CENTER

Shamrock Hilton, Grand Ballroom Foyer

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 the 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 (713 668-9211) for the Neuroscience Information Desk.

## VISIBLE DIRECTORY OF REGISTRANTS

Shamrock Hilton, Grand Ballroom Foyer

Registration cards are filed in the Visible Directory, located adjacent to 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/ABSTRACTS

A Program was mailed to each Society member, and to nonmember advance registrants. An advance registrant, or a member who registers currently at the meeting, who does not bring his copy of the Program/Abstracts book may purchase another copy for $5.00 at the Annual Meeting Office.

## TICKETS

Annual Buffet Banquet tickets will be on sale at the Information/Ticket Desk located in the registration area, Grand Ballroom Foyer, Shamrock Hilton. Tickets are $10.50 per person and *must be purchased by 5:00* PM *on Monday.* The Buffet Banquet will begin with no-host cocktails at 6:30 PM, Tuesday, in the Grand Ballroom.

Tickets for the Monday morning tour of Houston, planned primarily for social registrants, will be sold in the registration area on Sunday. All other tickets for social registrant events will be sold in the Ladies' Hospitality Room, Shamrock Hilton, Venetian Room.

## ANNUAL MEETING OFFICE

Shamrock Hilton, Grand Ballroom Foyer

The office of the Annual Meeting staff and the Society is located in the checkroom, adjacent to the Grand Ballroom Foyer. It will be open on Sunday from 9 AM to 8 PM and daily thereafter from 8 AM to 6 PM. Registrants requiring assistance with housing, presentation of papers, etc., should consult this 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

Shamrock Hilton, Walnut Room

Members of the Press should register in the Walnut Room. Hours are 2 PM–5 PM on Sunday, 8 AM–5 PM on Monday and Tuesday, and 8:30 AM–11 AM on Wednesday.

## EXHIBITS

Shamrock Hilton, Hall of Exhibits

### Hours

Monday, October 9 . . . . . 8:30 AM–4:30 PM and 6:30 PM–7:30 PM
Tuesday, October 10 . . . . . 8:30 AM–5:30 PM
Wednesday, October 11 . . . . . 8:30 AM–1:00 PM

For alphabetical list of exhibitors see page 282.

Entrance to Hall of Exhibits in the Grand Ballroom Foyer.

On Wednesday morning, exhibits will include displays by exhibitors participating in the American Electroencephalographic Society meeting which follows the Annual Meeting.

## AIRLINES RESERVATIONS AND BUS TICKETS

The Shamrock Hilton Airlines Center is located off the main lobby. Airline representatives will assist registrants in arranging or confirming reservations with all airlines. Tickets for airport bus service may be purchased at the Airlines Center for $4, one way. The Shamrock Hilton is approximately one hour by bus from the Houston Intercontinental Airport.

## HOSPITALITY AND COFFEE LOUNGE/SNACK BAR

Shamrock Hilton, Hall of Exhibits

The Hospitality Lounge will be open during exhibit hours for coffee and light snacks. Information about Houston area attractions will be available. For the convenience of registrants, a moderately priced sandwich lunch will be served in the Hospitality Lounge from 11:30 AM to 1:00 PM, Monday through Wednesday.

## ANNUAL MEETING SOCIAL EVENTS

All registrants are invited to attend the three major social events which have been planned to provide opportunities for informal exchange and hospitality:

### Opening Reception

No-host cocktails, Sunday, October 8, from 8:00 PM to 10:00 PM, in the Grand Ballroom of the Shamrock Hilton. Admission by Annual Meeting badge.

### Exhibit Hall Reception

No-host cocktails, Monday, October 9, 6:30 PM to 7:30 PM, in the Hall of Exhibits, Shamrock Hilton.

### Annual Buffet Banquet

On Tuesday, October 10, the Annual Buffet Banquet will begin with no-host cocktails at 6:30 PM, in the Grand Ballroom of the Shamrock Hilton. Tickets for the Buffet Banquet are $10.50 per person *and must be purchased by 5:00 PM on Monday at the Information/Ticket Desk.* Tickets for those who made reservations in advance have been placed in Advance Registrant packets.

## SATELLITE FUNCTIONS AND MEETINGS

See listing of special interest group events on page 9.

## SOCIAL REGISTRANTS

The Ladies' Hospitality Room, located in the Venetian Room of the Shamrock Hilton, is open to all social registrants from 9:00 AM to 5:00 PM daily, Monday through Wednesday. Complimentary coffee will be provided. Hostesses will be on hand to greet guests and offer assistance as needed. Tickets for the Monday morning tour of Houston will be available in the registration area on Sunday; however, *all other tickets to social registrant events will be sold in the Venetian Room and will not be available in the registration area.* The social registrant badge and buffet ticket, if purchased in advance, have been placed in the registration packet of the sponsoring scientist.

### Social Registrant Program

In addition to the three major Annual Meeting social events, social registrants are invited to participate in the following activities:

*Slideview of Houston by Lady Hilton*—Monday, 10:00 AM, Venetian Room. An audio-visual presentation highlighting sights and sounds of Houston. Sponsored by the Ladies' Hospitality Committee and the Society.

*Bus tour of Houston*—Monday, 11:00 AM–4:00 PM.

Tour of cultural (old and new) Houston, with opportunity for shopping and lunch at the Galleria. Transportation $4. Tickets must be purchased by 8:00 PM on Sunday.

*Bayou Bend Collection and Museum/Campus Tour*—Tuesday, 1:00 PM–5:00 PM.

17th, 18th and early 19th century American furnishings and art. Visit to Garden Center for refreshments and tour of museums, campus, zoo, etc. Transportation and refreshments $5.50. Tickets must be purchased by 5:00 PM on Monday.

*Tour to NASA via San Jacinto Monument*—Wednesday, 10:30 AM–3:30 PM. Astronaut training facilities and collection of spacecraft. Lunch on own in NASA cafeteria. Transportation $6. Tickets must be purchased by 5:00 PM on Tuesday.

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

## HOTEL CHECK-OUT HOUR AND LUGGAGE STORAGE

Shamrock Hilton and Towers Hotels

The check-out hour is 3 PM. For their convenience, registrants may check-out on Wednesday morning and store their luggage until departure in an area near the entrance to the Grand Ballroom.

# Program Information

## SCIENTIFIC SESSIONS

Symposia, invited lectures, volunteer presentations and workshops will be scheduled daily, Monday through Wednesday, in the Shamrock Hilton Hotel. Morning sessions begin at 9:00 AM; afternoon sessions begin at 1:00 PM and at 3:15 PM.

A chart showing the four-day schedule is on pages 10 and 11.

## DEMONSTRATIONS

Physiological and behavioral demonstrations involving wet preparations such as tissue culture and organisms, as well as films, video tapes, graphic and photographic displays, are scheduled in the Multidisciplinary Laboratories North of the Baylor College of Medicine, Texas Medical Center, on Sunday beginning at 11:00 AM. The Texas Medical Center is located within a 10-minute walk of the Shamrock Hilton Hotel. For directions, refer to the area map on page 12. The Demonstration program begins on page 13.

## PUBLIC LECTURE

Sunday, 4:00 PM–5:00 PM, Continental Room, Shamrock Hilton

*Topic:* Neuroscience in the Public Interest

*Speaker:* Arthur A. Ward, Jr., Professor and Chairman, Department of Neurological Surgery, University of Washington School of Medicine, Seattle.

Dr. Ward will present information on aspects of the neurosciences which have important implications for public policy in the general interest of the nonscientific world.

## EXTENDED DISCUSSION GROUPS

To improve on the traditional 10-minute paper format, a series of experimental discussion opportunities is scheduled daily, Monday through Wednesday, at 3:15 PM and 4:15 PM. Authors of volunteer papers will be available during one of the two daily periods for further discussion with interested members of the audience.

Discussions will be on a personal and informal basis. Participating authors are indicated in each volunteer paper session listing, with the time and place each will be available.

## PRESIDENTIAL ADDRESS

Monday, 5:30 PM–6:30 PM, Emerald Room, Shamrock Hilton

*Topic:* Psychosomatic Effects of Learning

*Speaker:* Neal E. Miller, The Rockefeller University, New York, President of the Society for Neuroscience.

Open to all registrants.

## SOCIETY BUSINESS MEETING

Tuesday, 5:30 PM–6:30 PM, Emerald Room, Shamrock Hilton

Open to all members of the Society for Neuroscience.

## GRASS FOUNDATION LECTURE

Tuesday, 8:30 PM, Emerald Room, Shamrock Hilton

*Topic:* Microphysiology of the Synapse

*Speaker:* Stephen W. Kuffler, Professor and Chairman, Department of Neurobiology, Harvard Medical School, Boston.

# SATELLITE FUNCTIONS

### Sunday, October 8

### Society for Neuroscience Chapters Officers and Representatives

9 AM–12 noon, *Shamrock Hilton, Belvedere Room.* To encourage participation of the chapters in society activities, and provide a direct means of obtaining expressions of chapter opinions and needs.

### International Society for Developmental Psychobiology

9 AM–4 PM, *Shamrock Hilton, Azalea Room.* Morning session includes papers in the area of neural development; afternoon session, behavior. Luncheon in the Bluebonnet Room at 12 noon, followed by the Presidential Address: Professor William A. Mason, "How Baby Monkeys Construct Their Mothers and Vice Versa." Purchase tickets in advance from Dr. Williamina Himwich, Galesburg State Research Hospital, Galesburg, IL 61401.

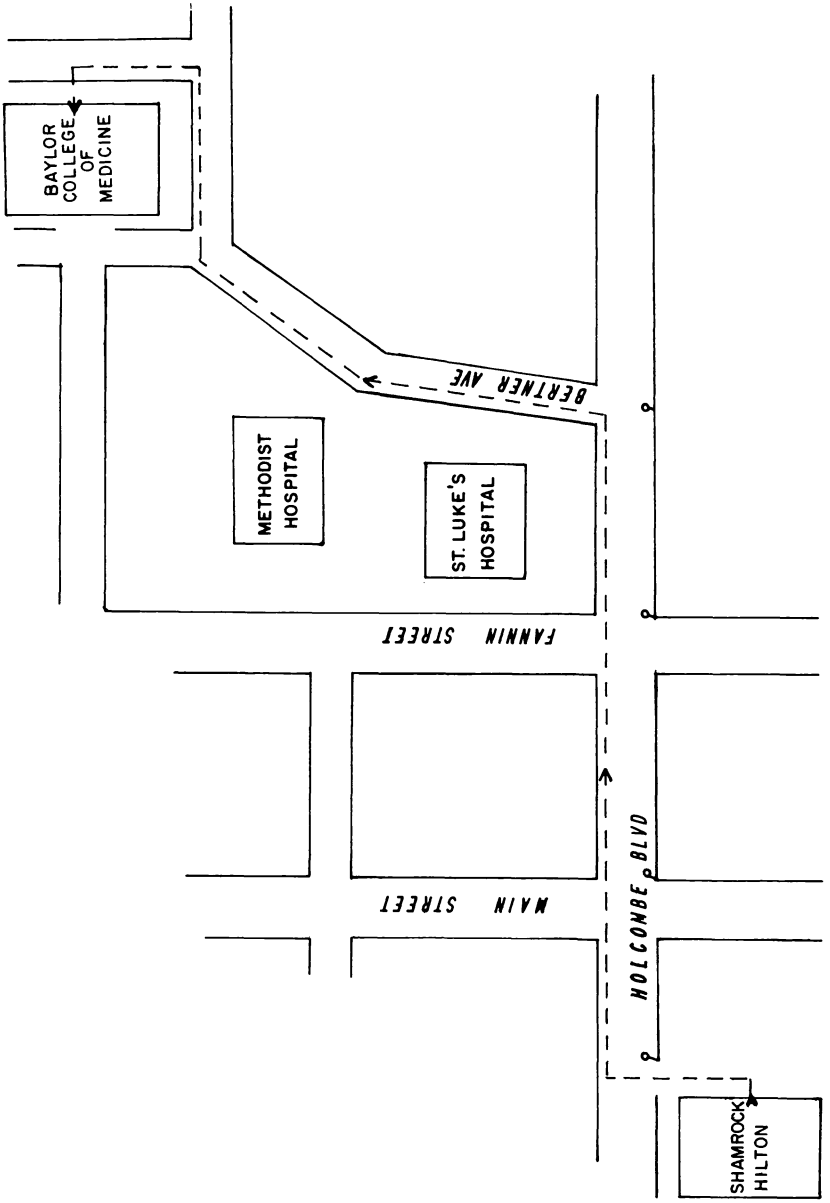
Unless otherwise noted, all sessions and events will take place at the Shamrock Hilton Hotel.

| | SUNDAY OCTOBER 8 | MONDAY OCTOBER 9 |
|---|---|---|
| MORNING | 11 AM–3:30 PM<br>Physiological and Behavioral Demonstrations<br>Baylor College of Medicine | 8 AM–5 PM<br>Registration and Information<br><br>8:30 AM–4:30 PM<br>Exhibits and Hospitality Lounge<br><br>9 AM–11:30 AM<br>Symposia and Volunteer Paper Sessions<br><br>*10 AM–10:30 AM<br>Slideview of Houston<br><br>*11 AM–4 PM<br>Tour of Houston |
| AFTERNOON | 2 PM–9 PM<br>Registration and Information<br>Grand Ballroom Foyer<br><br>4 PM–5 PM<br>Public Lecture<br>Continental Room | 1 PM–3 PM<br>Invited Lectures and Volunteer Paper Sessions<br><br>3:15 PM–5:15 PM<br>Workshops and Extended Discussion Groups |
| EVENING | 8 PM–10 PM<br>Opening Reception<br>Grand Ballroom | 5:30 PM–6:30 PM<br>Presidential Address<br>Emerald Room<br><br>6:30 PM–7:30 PM<br>Cocktail Party in the Hall of Exhibits |

## CALENDAR

* Events planned primarily for Social Registrants

| TUESDAY<br>OCTOBER 10 | WEDNESDAY<br>OCTOBER 11 |
|---|---|
| 8 AM–5 PM<br>Registration and Information | 8:30 AM–1:30 PM<br>Registration and Information |
| 8:30 AM–5:30 PM<br>Exhibits and Hospitality Lounge | 8:30 AM–1:00 PM<br>Exhibits and Hospitality Lounge |
| 9 AM–11:30 AM<br>Symposia and Volunteer Paper Sessions | 9 AM–11:30 AM<br>Symposia and Volunteer Paper Sessions |
| | *10:30 AM–3:30 PM<br>Tour of NASA |
| 1 PM–3 PM<br>Invited Lectures and Volunteer Paper Sessions | 1 PM–3 PM<br>Invited Lectures and Volunteer Paper Sessions |
| *1 PM–5 PM<br>Museum and Campus Tour | 3: 15 PM–5:15 PM<br>Workshops and Extended Discussion Groups |
| 3:15 PM–5:15 PM<br>Workshops and Extended Discussion Groups | |
| 5:30 PM–6:30 PM<br>Business Meeting<br>Emerald Room | |
| 6:30 PM–8 PM<br>Reception and Buffet<br>Banquet<br>Grand Ballroom | |
| 8:30 PM–9:30 PM<br>Grass Foundation Lecture<br>Emerald Room | |




Walking route—Shamrock Hilton to Baylor College of Medicine

# DEMONSTRATIONS

## 1. Physiological and Behavioral Demonstrations at the Baylor College of Medicine, Texas Medical Center

11:00 AM–3:30 PM

Demonstrations involving wet preparations such as tissue culture and organisms, as well as films, video tapes, graphic and photographic displays, are scheduled continuously in the Multidisciplinary Laboratories (2nd floor of the Cullen Building) of the Baylor College of Medicine. For walking directions, see the map on page 12. Directional signs will be posted at the building entrance. Lunch will be available from 11 AM to 2 PM at the cafeterias of nearby St. Luke's and Methodist Hospitals.

*Chairman:* **W. M. COWAN**

1.1 An independent study program in neuroscience with computer assistance. **G. WISE, R. BERAN** and **J. BURKHOLDER.** *Ohio State Univ. Col. of Med., Columbus, OH.*

1.2 Split-brain cats prepared by radiation. **C. T. GAFFEY** and **V. J. MONTOYA.** *Univ. of California, Berkeley, CA.*

1.3 Responses of tectal units to infrared stimuli in rattlesnakes. **P. H. HARTLINE.** *Univ. of California San Diego, La Jolla, CA.*

1.4 Effects of intoxicating doses of ethanol upon intermediary metabolite content of rat brain. **R. L. VEECH, D. VELOSO** and **J. V. PASSONNEAU.** *NIMH, St. Elizabeths Hosp., Washington, DC, and NIH, Bethesda, MD.*

1.5 The goldfish as a pharmacological and biobehavioral tool: a wet demonstration with illustrative data. **F. PETTY, R. C. BRYANT, N. N. SANTOS, L. A. KEPNER** and **W. L. BYRNE.** *Univ. of Tennessee Med. Units, Memphis, TN.*

1.6 Possible molecular coding for a learned motor adaptation in the goldfish. **J. A. HELTZEL, R. A. KING** and **G. UNGAR.** *Baylor Col. of Med., Houston, TX.*

---

The number preceding each paper title within the session listings refers to the corresponding abstract which appears in the abstracts section of this Program. There are no abstracts for Symposia. The author index includes participants who did not submit abstracts.

1.7 Sympathetic interneurons in organotypically cultured ganglia. **H. H. BENITEZ** and **M. R. MURRAY**. *Columbia Univ. Col. of Phys. and Surg., New York, NY.*

1.8 Synaptic and neuronal adjustment to the complexity of the rearing environment. **W. T. GREENOUGH, T. B. FLEISCHMANN, F. R. VOLKMAR** and **R. W. WEST**. *Univ. of Illinois, Champaign, IL, and Harvard Univ., Cambridge, MA.*

1.9 Cell dynamics in the olfactory mucosa of vertebrates. **P. P. C. GRAZIADEI, J. F. METCALF** and **R. S. DeHAN**. *Florida State Univ., Tallahassee, FL.*

1.10 Species differences in the synaptic organization of the vertebrate olfactory glomerulus. **E. L. WHITE**. *NIH, Bethesda, MD.*

1.11 A method for tracing the maturation of nervous pathways. **C. M. LEONARD**. *Rockefeller Univ., New York, NY.*

1.12 DMSO in the treatment of experimental head and spinal cord injuries. **J. C. de la TORRE, K. KAJIHARA, H. M. KAWANAGA, D. W. ROWED** and **J. F. MULLAN**. *Univ. of Chicago, Pritzker Sch. of Med., Chicago, IL.*

1.13 Computer analysis of Golgi impregnated neurons. **T. A. WOOLSEY, D. F. WANN, W. M. COWAN, M. L. DIERKER** and **C. M. SHINN**. *Washington Univ., St. Louis, MO.*

1.14 Experimental tests of a model system accounting for potassium accumulation in the periaxonal space. **W. J. ADELMAN, JR., Y. PALTI** and **J. P. SENFT**. *NIH, Bethesda, MD, Univ. of Maryland Sch. of Med., Baltimore, MD, Technion Med. Sch., Haifa, Israel, and Rutgers Univ., New Brunswick, NJ.*

1.15 Alumina in experimental cortical epileptic lesions, histochemistry and ultrastructure. **A. B. HARRIS**. *Univ. of Washington Sch. of Med., Seattle, WA.*

1.16 Uptake characteristics of $^{3}$H-GABA in structures of the basal ganglia by electron microscopic radioautography. **T. HATTORI** and **P. L. McGEER**. *Univ. of British Columbia, Vancouver, B. C., Canada.*

1.17 Optic tract regeneration in the adult rat. **A. F. MARKS**. *Johns Hopkins Univ., Baltimore, MD.*

1.18 Reversible cryogenic blockade of subcortical brain structures. **J. E. SKINNER**. *Methodist Hosp. and Baylor Col. of Med., Houston, TX.*

1.19 The use of push–pull perfusion techniques to examine CNS transmitter activity in several species. **R. D. MYERS** and **M. B. WALLER**. *Purdue Univ., Lafayette, IN.*

1.20 Demonstration of operant conditioning of 40HZ in humans. **D. E. SHEER, B. BIRD** and **F. NEWTON**. *Univ. of Houston, Houston, TX.*

## SYMPOSIUM

### 2. Pain

9:00 AM—*Grand Ballroom*

*Chairman:* **E. R. PERL**

**2.1** Overview of theories about pain and its mechanisms. **E. R. PERL.** *Univ. of North Carolina, Chapel Hill, NC.*

**2.2** Specificity in the neural systems for pain. **P. R. BURGESS.** *Univ. of Utah, Salt Lake City, UT.*

**2.3** Factors other than "specificity" in pain sensation. **P. D. WALL.** *University College London, London, England.*

**2.4** Persistent pain and its treatment. **F. W. L. KERR.** *Mayo Grad. Sch. of Med., Rochester, MN.*

## SYMPOSIUM

### 3. Central Adrenergic Mechanisms

9:00 AM—*Emerald Room*

*Chairman:* **S. S. KETY**

**3.1** Growth and plasticity of central adrenergic neurons. **R. Y. MOORE.** *Univ. of Chicago, Chicago, IL.*

**3.2** Cyclic AMP and the inhibition of cerebellar Purkinje cells. **F. E. BLOOM.** *St. Elizabeths Hosp., Washington, DC.*

**3.3** Cyclic AMP and the pharmacology of central catecholamines. **G. A. ROBISON.** *Univ. of Texas Med. Sch., Houston, TX.*

**3.4** Role and mechanism of action of cyclic AMP in neural function. **P. GREENGARD.** *Yale Univ. Sch. of Med., New Haven, CT.*

# VOLUNTEER PAPERS

## 4. Habituation and Conditioning

9:00 AM—*Continental Room*

*Chairman:* **J. BUCHWALD**

9:00 **4.1** Habituation and sensitization of interneuron activity in the reticular formation. **M. V. PARKER** and **P. M. GROVES.** *Univ. of Colorado, Boulder, CO.*

* 9:15 **4.2** Comparison of unit response decrements in the cochlear nucleus of decerebrate and intact paralyzed cats during repeated acoustic stimulation. **J. BUCHWALD, G. HUMPHREY** and **D. REGAN.** *Univ. of California Los Angeles, Los Angeles, CA.*

* 9:30 **4.3** Unit responses in the auditory system and posterior thalamus of rat during classical conditioning and extinction. **J. F. DISTERHOFT.** *California Inst. of Tech., Pasadena, CA.*

9:45 **4.4** Effects of predictability on neuronal responses to footshock. **C. E. OLMSTEAD.** *Univ. of Virginia, Charlottesville, VA.*

*10:00 **4.5** Rewarding and aversive brain stimulations have opposite effects on medial thalamic units. **J. J. KEENE.** *Univ. of Michigan, Ann Arbor, MI.*

10:15 **4.6** Topographical distribution of slow potential changes from monkey cortex. **J. J. HABLITZ** and **R. P. BORDA.** *Methodist Hosp. and Baylor Col. of Med., Houston, TX.*

*10:30 **4.7** Learned behavior: apparent elimination by a cut parallel to the median forebrain bundle. **E. W. KENT** and **S. P. GROSSMAN.** *Univ. of Illinois at Chicago Circle and Univ. of Chicago, Chicago, IL.*

*10:45 **4.8** Components of the intracranially reinforced bar-pressing response. **P. VRTUNSKI.** *Cleveland Psychiat. Inst., Cleveland, OH.*

11:00 **4.9** Effects of caudate nucleus stimulation on reactivity to noxious electrocutaneous stimulation. **C. G. LINEBERRY** and **C. J. VIERCK, JR.** *Univ. of Florida Col. of Med., Gainesville, FL.*

*11:15 **4.10** Direct cortical conditioning in macaques. **R. L. TESTERMAN, A. S. WILSON, A. SANCES, JR.** and **S. J. LARSON.** *Medtronic, Inc. and VA Center, Wood, WI.*

* Authors available for informal discussion at 3:15 PM in the Emerald Room.

# VOLUNTEER PAPERS

## 5. Developmental Neurobiology

9:00 AM—*Embassy Room*

*Chairman:* **W. A. HIMWICH**

* 9:00 **5.1** The fate of tracer proteins in the maturing nervous tissue. **M. P. del CERRO** and **R. S. SNIDER.** *Univ. of Rochester Med. Ctr., Rochester, NY.*

* 9:15 **5.2** Amino acids in the developing fetal brain. **J. M. DAVIS** and **W. A. HIMWICH.** *Galesburg State Res. Hosp., Galesburg, IL.*

* 9:30 **5.3** Changing relationships of mitotic Schwann cells to axons in newborn rat sciatic nerve. **J. R. MARTIN** and **H. deF. WEBSTER.** *NIH, Bethesda, MD.*

* 9:45 **5.4** Neuroembryology of the biogenic amine systems of the mouse brain. **G. S. GOLDEN.** *Montefiore Hosp., Bronx, NY.*

*10:00 **5.5** Quantitative variation of brain mass by prenatal and postnatal chemical treatment. **R. K. HADDAD** and **A. RABE.** *Bur. of Res. at the New Jersey Neuropsychiat. Inst., Princeton, NJ.*

10:15 **5.6** Developmental changes in the response properties of superior collicular neurons of the kitten. **B. E. STEIN** and **E. LABOS.** *Univ. of California, Los Angeles Sch. of Med., Los Angeles, CA.*

*10:30 **5.7** The behavioral onset of inhibitory mechanisms in the chick embryo. **R. W. OPPENHEIM, J. REITZEL** and **R. PROVINE.** *North Carolina Dept. of Mental Health, Raleigh, NC, and Washington Univ., St. Louis, MO.*

*10:45 **5.8** Biochemical and behavioral effects of administration of monosodium glutamate to the young rat. **H. K. BERRY** and **R. E. BUTCHER.** *Children's Hosp. Res. Fndn. and Univ. of Cincinnati Col. of Med., Cincinnati, OH.*

11:00 **5.9** Multivariate analysis of post maturity changes in behavior and the chemical morphological plasticity of the brain, pituitary and adrenals in C57Bl/10 mice. **J. M. ORDY.** *Northern Illinois Univ., DeKalb, IL.*

* Authors available for informal discussion at 3:15 PM in the Emerald Room.

# VOLUNTEER PAPERS

## 6. Membrane Biophysics

9:00 AM—*Azalea Room*

*Chairman:* **W. J. ADELMAN**

* 9:00 **6.1** Intracellular conductivity measurements in giant neurons, axons and muscle fibers. **D. O. CARPENTER, M. M. HOVEY** and **A. F. BAK.** *NIMH, Bethesda, MD.*

* 9:15 **6.2** Absence of accommodation in *Aplysia* giant neuron. **D. JUNGE.** *Univ. of California, Los Angeles Sch. of Dent., Los Angeles, CA.*

9:30 **6.3** Temperature effects on firing frequency and distribution in *Aplysia* pacemaker neurons. **J. A. WILLIS.** *Armed Forces Radiobiol. Res. Inst., Bethesda, MD.*

* 9:45 **6.4** Localization and geometry of fast extensor motoneurons in the crayfish abdomen. **S. N. TREISTMAN** and **M. P. REMLER.** *Univ. of North Carolina Sch. of Med., Chapel Hill, NC.*

*10:00 **6.5** Post-tetanic changes in membrane potential induced by repetitive stimulation of *Xenopus* single medullated nerve fibers. **G. M. SCHOEPFLE** and **C. R. KATHOLI.** *Univ. of Alabama Med. Ctr., Birmingham, AL.*

*10:15 **6.6** Electric organ discharge interactions in mormyrid fish. **P. MOLLER** and **R. BAUER.** *Hunter College, New York, NY, and Lab. de Neurophysiol. Sensorielle Comparée, CNRS, Paris, France.*

*10:30 **6.7** Short-distance electrical interaction in a mormyrid fish. **C. J. RUSSELL** and **C. C. BELL.** *Good Samaritan Hosp. and Med. Ctr., Portland, OR.*

*10:45 **6.8** Penicillin action on leech ganglia: production of "epileptic" invertebrate neurons. **J. W. PRICHARD.** *Yale Univ. Sch. of Med., New Haven, CT.*

*11:00 **6.9** Membrane properties of neuroglia in the chronic epileptogenic focus. **F. L. GLOETZNER, W. H. CALVIN** and **A. A. WARD, JR.** *Univ. of Washington Sch. of Med., Seattle, WA.*

*11:15 **6.10** Localized measurements of cerebral impedance and temperature in sensory relay nuclei during visual and auditory stimulation. **J. G. McELLIGOTT.** *Univ. of California Los Angeles, Los Angeles, CA.*

*11:30 **6.11** Chemical properties of tetrodotoxin binding sites in nerve membrane. **D. R. HAFEMANN.** *Marquette Univ., Milwaukee, WI.*

* Authors available for informal discussion at 3:15 PM in the Emerald Room.

# VOLUNTEER PAPERS

## 7. Visual Perception

9:00 AM—*Columbia Room*

*Chairman:* **P. PASIK**

* 9:00 **7.1** Unit and evoked potentials in cat optic tract to paired light flashes and their relationship to perceptual discrimination. **C. K. PECK** and **D. B. LINDSLEY.** *Pomona Col., Claremont, CA, and Univ. of California Los Angeles, Los Angeles, CA.*

9:15 **7.2** The suppression-recovery effect in optic tract responses in cat: psychological correlates and retinal mechanisms. **W. L. SALINGER.** *Univ. of North Carolina, Greensboro, NC.*

* 9:30 **7.3** Relationships between visual evoked potentials and reaction time in the monkey performing a visuo-motor task. **K. WATANABE.** *Univ. of California Los Angeles Sch. of Med., Los Angeles, CA.*

* 9:45 **7.4** Visual discrimination of random figures by Rhesus monkeys. **K. R. CARLSON.** *Univ. of Pittsburgh Sch. of Med., Pittsburgh, PA.*

10:00 **7.5** Effect of superior colliculi lesions on discrimination of luminous flux-equated figures by monkeys deprived of striate cortex. **J. WININGER, P. PASIK** and **T. PASIK.** *Mt. Sinai Sch. of Med., CUNY, New York, NY.*

*10:15 **7.6** The importance of telencephalic structures in visual discrimination learning in nurse sharks. **R. C. GRAEBER, D. M. SCHROEDER, J. A. JANE** and **S. O. E. EBBESSON.** *Univ. of Virginia, Charlottesville, VA, and Lerner Marine Lab., Bimini, Bahamas.*

*10:30 **7.7** Effects of sequential lesions of visual cortex and suprasylvian gyri on pattern discrimination in the cat. **P. D. SPEAR, C. C. WOOD** and **J. J. BRAUN.** *Yale Univ., New Haven, CT.*

*10:45 **7.8** Binocular summation and suppression: effects of contour density and disparity on monocular and binocular visually evoked cortical responses in humans. **M. R. HARTER** and **W. H. SEIPLE.** *Univ. of North Carolina, Greensboro, NC.*

*11:00 **7.9** Sensitization in scotomata symmetric with islands of blindness. **W. RICHARDS** and **E. POEPPEL.** *Massachusetts Inst. of Tech., Cambridge, MA, and Neurosciences Res. Program, Brookline, MA.*

11:15 **7.10** On the interpretation of the visual evoked response (especially in dyslexia). **J. de DIOS POZO-OLANO.** *Bedford, MA.*

* Authors available for informal discussion at 3:15 PM in the Emerald Room.

# VOLUNTEER PAPERS

## 8. Experimental Morphology and Ultrastructure

9:00 AM—*Nile Room*

*Chairman:* **L. KRUGER**

* 9:00 **8.1** Electron microscopy of non-neuronal events during thalamic degeneration. **M. A. MATTHEWS** and **L. KRUGER.** *Univ. of California, Los Angeles Sch. of Med., Los Angeles, CA.*

9:15 **8.2** Structure and function of the endoplasmic reticulum in the squid giant axon. **M. HENKART.** *NIH, Bethesda, MD.*

* 9:30 **8.3** Effects of hypertonic blood–brain barrier injury. **M. SPATZ, S. I. RAPOPORT, Z. M. RAP** and **I. KLATZO.** *NIH, Bethesda, MD.*

* 9:45 **8.4** Effect of serotonin on the blood–brain barrier to peroxidase in mice. **E. WESTERGAARD** and **M. W. BRIGHTMAN.** *NIH, Bethesda, MD.*

10:00 **8.5** Neuronal activity can alter glial cell metabolism. **H. BRACHO, P. M. ORKAND** and **R. K. ORKAND.** *Univ. of California Los Angeles, Los Angeles, CA.*

*10:15 **8.6** Cerebral secretion into the CSF ventricular system concomitant to electrocortical synchronization and desynchronization. **X. LOZOYA** and **M. VELASCO.** *Natl. Med. Ctr., Mexico City, Mexico.*

10:30 **8.7** Effects of water diuresis of infusions of transmitter substances into third cerebral ventricle. **E. E. CERNY.** *Univ. of Louisville Hlth. Sci. Ctr., Louisville, KY.*

*10:45 **8.8** Possible norepinephrine storage in heart atrial granules. **B. PETERS** and **B. HABER.** *Univ. of Texas Med. Br., Galveston, TX.*

*11:00 **8.9** New electron microscopic findings in subacute sclerosing panencephalitis. **M. G. HADFIELD, R. B. DAVID** and **W. I. ROSENBLUM.** *Med. Col. of Virginia, Richmond, VA.*

*11:15 **8.10** Serial EEG and clinical studies in squirrel monkeys inoculated with transmissible mink encephalopathy agent. **J. D. GRABOW, R. J. ECKROADE, G. M. ZuRHEIN, P. E. ZOLLMAN** and **R. P. HANSON.** *Mayo Clinic, Rochester, MN, Univ. of Delaware, Newark, DE, and Univ. of Wisconsin, Madison, WI.*

*11:30 **8.11** Fixation of developing rat cerebellum for electron microscopy: some experimental observations. **I. S. ZAGON** and **R. S. LASHER.** *Univ. of Colorado Med. Sch., Denver, CO.*

* Authors available for informal discussion at 3:15 PM in the Emerald Room.

## INVITED LECTURES

### 9. Pain

1:00 PM—*Grand Ballroom*

*Chairman:* **F. W. L. KERR**

1:00 **9.1** Ionic and physicochemical mechanisms underlying nonnarcotic analgesia. **J. L. BARKER** and **H. LEVITAN.** *NIH, Bethesda, MD.*

1:30 **9.2** Receptor representation in two trigeminal systems. **L. KRUGER, J. A. MOSSO** and **D. KIRKPATRICK.** *Univ. of California, Los Angeles Sch. of Med., Los Angeles, CA.*

1:50 **9.3** Interdependence of trigeminal primary relay nuclei. **R. B. KING.** *SUNY, Upstate Med. Ctr., Syracuse, NY.*

2:30 **9.4** Behavioral and pharmacological studies of analgesia from electrical stimulation of the periaqueductal gray matter in the rat. **H. AKIL, D. J. MAYER** and **J. C. LIEBESKIND.** *Univ. of California, Los Angeles, CA.*

## INVITED LECTURES

### 10. Central Adrenergic Mechanisms

1:00 PM—*Emerald Room*

*Chairman:* **T. W. RALL**

1:00 **10.1** Proliferation of cerebellar norepinephrine-containing fibers in response to peduncle lesions. **V. M. PICKEL, H. KREBS** and **F. E. BLOOM.** *St. Elizabeths Hosp., Washington, DC.*

1:30 **10.2** Studies on the interaction between noradrenaline and adenyl cyclase in the cerebral cortex. **N. LAKE** and **J. W. PHILLIS.** *Univ. of Manitoba, Winnipeg, Canada.*

2:00 **10.3** Effects of 6-hydroxydopamine on shuttle-box avoidance: involvement of brain dopamine. **B. R. COOPER, G. R. BREESE, J. L. HOWARD** and **L. D. GRANT.** *Child Develop. Inst. of North Carolina Sch. of Med., Chapel Hill, NC.*

2:30 **10.4** Role of central catecholamine neurons in feeding and drinking behavior: evidence from intrahypothalamic injections of 6-hydroxydopamine. **G. P. SMITH, G. N. ERVIN** and **D. J. REIS.** *Cornell Univ. Med. Col., New York, NY.*

# INVITED LECTURES

## 11. Neural Tissue Culture

1:00 PM—*Continental Room*

*Chairman:* **S. M. CRAIN**

1:00 **11.1** Tissue culture models of developing CNS functions. **S. M. CRAIN.** *Albert Einstein Col. of Med., Bronx, NY.*

1:30 **11.2** Development of organotypic spinal cord explants and interactions with adult skeletal muscle. **E. R. PETERSON.** *Albert Einstein Col. of Med., Bronx, NY.*

2:00 **11.3** Intracellular analysis of dissociated nerve cell tissue culture. **M. DICHTER.** *Beth Israel Hosp., Boston, MA.*

2:30 **11.4** Neuroblastoma: a model system for studying encoding and decoding of neural information. **M. NIRENBERG.** *NIH, Bethesda, MD.*

# VOLUNTEER PAPERS

## 12. Action of Hallucinogenic Drugs

1:00 PM—*Embassy Room*

*Chairman:* **W. H. BRIDGER**

* 1:00 **12.1** Subcellular studies on the effect of LSD on rat brain serotonin (5-HT). **A. E. HALARIS, R. A. LOVELL** and **D. X. FREEDMAN.** *Univ. of Chicago, Pritzker Sch. of Med., Chicago, IL.*

1:15 **12.2** Stress changes the action of mescaline from behavioral inhibition to excitation. **W. H. BRIDGER, D. M. STOFF** and **D. A. GORELICK.** *Albert Einstein Col. of Med., Bronx, NY.*

* 1:30 **12.3** Effect of $\Delta^9$ tetrahydrocannabinol on infant rat brain nucleic acid and protein synthesis in vivo. **A. JAKUBOVIC** and **P. L. McGEER.** *Univ. of British Columbia, Vancouver, B.C., Canada.*

* 1:45 **12.4** Effects of prolonged amphetamine administration on ad libitum self-stimulation, eating and drinking in rats. **T. ROGGE, G. F. KOOB** and **Z. ANNAU.** *Johns Hopkins Univ., Baltimore, MD.*

* 2:00 **12.5** Effect of the amphetamine derivative, 2,5-dimethoxy-4-methylamphetamine, on the spontaneous locomotor activity in mice. **J-T. HUANG** and **B. T. HO.** *Texas Res. Inst. of Mental Sci., Houston, TX.*

2:15 **12.6** Differential actions of *d*-amphetamine and *l*-amphetamine in mice. **C. M. QUIRCE.** *Indiana Univ., Bloomington, IN.*

* 2:30 **12.7** Suppression of the visual placing response by 6 hydroxydopamine: restoration with amphetamine. **J. A. SECHZER, G. N. ERVIN** and **G. P. SMITH.** *Cornell Med. Ctr., White Plains, NY.*

2:45 **12.8** Effects of *d*-amphetamine, chlordiazepoxide, and chlorpromazine on signalled shock avoidance. **M. E. RISNER** and **K. A. KHAVARI.** *Univ. of Wisconsin, Milwaukee, WI.*

* Authors available for informal discussion at 4:15 PM in the Emerald Room.

## VOLUNTEER PAPERS

### 13. Chemistry and Behavior I

1:00 PM—*Azalea Room*

*Chairman:* **W. L. BYRNE**

* 1:00 **13.1** Opposite effects on behavior in the goldfish of β-MSH and MSH-inhibiting factor. **R. C. BRYANT, F. PETTY** and **A. J. KASTIN.** *Univ. of Tennessee Med. Units, Memphis, TN, and VA Hosp. and Tulane Univ. Sch. of Med., New Orleans, LA.*

* 1:15 **13.2** Melanocyte-stimulating hormone affects learning and extinction in normal and brain-damaged rats. **L. O. STRATTON, A. J. KASTIN** and **A. V. SCHALLY.** *Louisiana State Univ., VA Hosp., and Tulane Univ. Sch. of Med., New Orleans, LA.*

* 1:30 **13.3** Comparative ability of pentadecapeptides to induce dark avoidance in naive rats, mice, and goldfish. **H. N. GUTTMAN, M. A. WEILER** and **G. MATWYSHYN.** *Univ. of Illinois at Chicago Circle, Chicago, IL.*

1:45 **13.4** Synthetic scotophobin in the rat: effects of intraventricular and intraperitoneal administration in several behavioral procedures. **B. M. KULIG, P. S. D'ENCARNACAO, G. LITTLE** and **R. C. BRYANT.** *Univ. of Tennessee Med. Units and Memphis State Univ., Memphis, TN.*

* 2:00 **13.5** Dark-avoidance factor from trained fish brain: comparison in goldfish with synthetic learning-linked rat peptide scotophobin. **W. L. BYRNE, R. C. BRYANT, N. N. SANTOS, F. PETTY, L. S. BRADHAM** and **L. A. KEPNER.** *Univ. of Tennessee Med. Units, Memphis, TN.*

* 2:15 **13.6** Use of mass spectrometry to elucidate the structure of oligopeptides of brain origin. **D. M. DESIDERIO** and **K. HAGELE.** *Baylor Sch. of Med., Houston, TX.*

2:30 **13.7** Further studies of the effects of extracts from brains of trained donor goldfish: effects of performance level of donors and injection-testing interval. **W. G. BRAUD** and **P. V. LAIRD.** *Univ. of Houston, Houston, TX.*

* Authors available for informal discussion at 4:15 PM in the Emerald Room.

# VOLUNTEER PAPERS

## 14. Memory

1:00 PM—*Columbia Room*

*Chairman:* J. L. McGAUGH

* 1:00 **14.1** Retention of escape training and activity changes in single paramecia. J. C. HUBER, W. B. RUCKER and C. G. McDIARMID. *Mankato State Col., Mankato, MN.*

* 1:15 **14.2** Possible circadian factors in the retention of a passive avoidance response. F. A. HOLLOWAY and R. A. WANSLEY. *Univ. of Oklahoma Health Sci. Ctr., Oklahoma City, OK.*

* 1:30 **14.3** Biphasic retention curves support the two-store theory of memory. A. CHERKIN. *VA Hosp., Sepulveda, CA, and Univ. of California, Los Angeles Sch. of Med., Los Angeles, CA.*

* 1:45 **14.4** Evidence for matched filter retrieval of interactive memory traces. J. A. ANDERSON. *Rockefeller Univ., New York, NY.*

* 2:00 **14.5** Conditions for stimulus-induced recovery from experimental amnesia in rats. R. R. MILLER, A. D. SPRINGER and D. C. VEGA. *Brooklyn Col., Brooklyn, NY.*

* 2:15 **14.6** Retrograde amnesia thresholds and gradients: role of localized cortical stimulation and its electrophysiological consequences. P. E. GOLD and J. L. McGAUGH. *Univ. of California, Irvine, CA.*

* Authors available for informal discussion at 4:15 PM in the Emerald Room.

# VOLUNTEER PAPERS

## 15. Neurobiology: Peripheral Central Interactions

1:00 PM—*Nile Room*

*Chairman:* **F. CALARESU**

* 1:00 **15.1** Role of the central nervous system in cardiac fibrillation: an experimental model in chronic pig preparations. **J. E. SKINNER, J. S. ARTHUR, D. N. MOHR** and **M. POWERS.** *Methodist Hosp. and Baylor Col. of Med., Houston, TX.*

1:15 **15.2** Inhibition of chemoreceptor reflex bradycardia by hypothalamic stimulation in the cat. **M. R. THOMAS** and **F. R. CALARESU.** *Univ. of Western Ontario, London, Ont., Canada.*

* 1:30 **15.3** Development rates of autonomic and skeletal concomitants of conditioned suppression. **A. R. ZEINER, L. MARSHALL** and **O. A. SMITH, JR.** *Univ. of Washington, Seattle, WA, and Univ. of Oklahoma Health Sci. Ctr., Oklahoma City, OK.*

* 1:45 **15.4** Recovery from apneustic breathing produced by vagotomy two days after pontine pneumotaxic area destruction. **R. L. GLASSER, R. A. KING, J. A. PAGET, JR., J. W. PENDILL, JR.** and **G. M. McCLAIN.** *Univ. of North Carolina, Chapel Hill, NC.*

* 2:00 **15.5** Activity of bulbar respiratory neurons during alterations in the duration of inspiration. **W. D. BARBER.** *Univ. of California Los Angeles, Los Angeles, CA.*

* 2:15 **15.6** Reflex and behavioral withdrawal responses to tooth pulp stimulation. **K. H. REID.** *Univ. of Louisville Sch. of Med., Louisville, KY.*

2:30 **15.7** Monoamines and behavioral tests of affect: effect of catecholaminergic lesions, chronic serotonin depletion, and both on emotional behavior. **D. BRESLER** and **G. ELLISON.** *Univ. of California, Los Angeles, CA.*

2:45 **15.8** Avoidance learning in adult rats treated prenatally with chlorpromazine. **M. GOLUB** and **C. KORNETSKY.** *Boston Univ. Sch. of Med., Boston, MA.*

* Authors available for informal discussion at 4:15 PM in the Emerald Room.

# VOLUNTEER PAPERS

## 16. Monoamines and Behavior

1:00 PM—*Castilian Room*

*Chairman:* **S. GILMAN**

1:00 **16.1** Localization of lateral geniculate spikes in awake, sleeping and reserpine-treated cats. **J. B. MUNSON** and **R. B. GRAHAM.** *Univ. of Florida, Gainesville, FL.*

1:15 **16.2** Effects on isolation induced aggression in mice of monoamine precursors in combination with a peripheral decarboxylase inhibitor. **G. K. HODGE** and **L. L. BUTCHER.** *Univ. of California Los Angeles, Los Angeles, CA.*

* 1:30 **16.3** Effects of L-dopa and reserpine on evoked responses from basal ganglia of freely behaving rats. **N. DAFNY** and **S. GILMAN.** *Columbia Univ. Col. of Phys. and Surg., New York, NY.*

1:45 **16.4** CNS catecholamine and serotonin inhibition of muricide: evidence for monoamine interactions. **L. D. GRANT, G. R. BREESE** and **J. L. HOWARD.** *Univ. of North Carolina Sch. of Med., Chapel Hill, NC.*

2:00 **16.5** Effects of amygdaloid administration of two beta-adrenergic drugs on the timing behavior (DRL-20) of rats. **P. D. STACEY, J. S. RICHARDSON, W. R. SAXBY** and **R. E. MUSTY.** *Univ. of Vermont, Burlington, VT.*

* Authors available for informal discussion at 4:15 PM in the Emerald Room.

## Extended Discussion Groups

3:15 PM—*Emerald Room*

Authors of volunteer papers presented in 9:00 AM sessions will be available for informal discussion.

# WORKSHOP

## 17. Tissue Culture

3:15 PM—*Continental Room*

*Chairman:* **S. M. CRAIN**

**17.1** Selective depression of organotypic bioelectric discharges of CNS explants by glycine and γ-aminobutyric acid. **S. M. CRAIN.** *Rose F. Kennedy Ctr., Albert Einstein Col. of Med., Bronx, NY.*

**17.2** Uptake of γ-aminobutyrate, glutamate and glycine by a cloned line of astrocytoma cells in culture. **H. T. HUTCHISON** and **B. HABER.** *Human Genetics and the Marine Biomed. Inst., UTMB, Galveston, TX.*

**17.3** Uptake of $^{3}$H-gamma-aminobutyric acid by neurons in cultures of dissociated postnatal rat cerebellums. **R. S. LASHER** and **S. ZAGON.** *Univ. of Colorado Med. Sch., Denver, CO.*

**17.4** Dissociated cell cultures of mouse spinal ganglia. **E. TYSZKA, C. RAIBORN** and **S. VARON.** *Univ. of California, San Diego Sch. of Med., La Jolla, CA.*

# WORKSHOP

## 18. Cutaneous Sensation

3:15 PM—*Embassy Room*

*Chairman:* **B. WHITSEL**

**18.1** Somatosensory coding in single cells of cat mesencephalic reticular formation. **K. B. BRADEN.** *Sch. of Med., Case Western Reserve Univ., Cleveland, OH.*

**18.2** Characteristic properties of mammalian cutaneous mechanoreceptors. **P. R. BURGESS, M. C. CORNWALL** and **K. W. HORCH.** *Univ. of Utah Col. of Med., Salt Lake City, UT.*

**18.3** Cutaneous mechanoreceptors: problems in the classification of units on the basis of temporal discharge patterns. **J. M. GIBSON, R. E. BEITEL** and **W. I. WELKER.** *Univ. of Wisconsin, Madison, WI.*

**18.4** First-order trigeminal neurons responding to movement of mystacial vibrissae of opossum. **B. H. PUBOLS, JR., P. J. DONOVICK** and **L. M. PUBOLS.** *Hershey Med. Ctr., Pennsylvania State Univ., Hershey, PA.*

**18.5** Tactile deficits resulting from dorsal column lesions in monkeys. **C. J. VIERCK, JR.** *Ctr. for Neurobiol. Sci., Univ. of Florida Col. of Med., Gainesville, FL.*

**18.6** Evidence for the contributions of different spinal pathways to S-1. **B. L. WHITSEL, D. A. DREYER** and **R. J. SCHNEIDER.** *Univ. of North Carolina Sch. of Med., Chapel Hill, NC, and Univ. of Pittsburgh Sch. of Med., Pittsburgh, PA.*

# WORKSHOP

## 19. Single Neuron Activity and Behavior

3:15 PM—*Azalea Room*

*Chairman:* **N. A. BUCHWALD**

**19.1** Functional chaining of frequency-independent elements in spontaneous brain activity. **H. AHN** and **S. S. FOX.** *Univ. of Iowa, Iowa City, IA.*

**19.2** Dopamine depletion and striatal unit firing. **N. A. BUCHWALD, M. S. LEVINE, C. D. HULL** and **A. HELLER.** *Univ. of California Los Angeles, Los Angeles, CA, and Univ. of Chicago, Chicago, IL.*

**19.3** Single cell discharge in the nucleus medialis dorsalis of the thalamus during delayed response performance. **J. M. FUSTER** and **G. E. ALEXANDER.** *Brain Res. Inst., Univ. of California, Los Angeles Sch. of Med., Los Angeles, CA.*

**19.4** Operantly conditioned single unit activity of rats maintained during paralysis. **D. E. HIATT.** *California Inst. of Tech., Pasadena, CA.*

**19.5** Inhibition of polysensory responses by striato-nigral stimulation. **G. KRAUTHAMER** and **M. DALSASS.** *Rutgers Med. Sch., New Brunswick, NJ.*

**19.6** Prefrontal cortical unit activity during delayed alternation in monkeys. **H. NIKI.** *NIMH, Bethesda, MD.*

# WORKSHOP

## 20. Neuromuscular Junction

3:15 PM—*Columbia Room*

*Chairman:* **J. P. SEGUNDO**

**20.1** Pattern sensitivity of crustacean neuromuscular junctions. **G. D. BITTNER** and **J. P. SEGUNDO.** *Univ. of Texas, Austin, TX, and Univ. of California Los Angeles, Los Angeles, CA.*

**20.2** Neuromuscular junctions in the leech. **R. E. COGGESHALL.** *Marine Biomed. Inst., Univ. of Texas Med. Br., Galveston, TX.*

**20.3** Developmental changes in the time course of synaptic potentials at an amphibian neuromuscular junction. **M. W. COHEN** and **R. W. KULLBERG.** *McGill Univ., Montreal, Que., Canada.*

**20.4** Effect of lead on the electrophysiology of neuromuscular transmission in the frog. **R. S. MANALIS** and **G. P. COOPER.** *Univ. of Cincinnati Col. of Med., Cincinnati, OH.*

**20.5** Sympathetic ganglion: release of acetylcholine elicited by black widow spider venom. **D. W. PUMPLIN** and **W. O. McCLURE.** *Univ. of Illinois, Urbana, IL.*

**20.6** EPR measurements of muscle intracellular viscosity. **F. SACHS** and **R. LATORRE.** *NIH, Bethesda, MD.*

# WORKSHOP

## 21. Vestibular System and Eye Movements

3:15 PM—*Nile Room*

*Chairman:* **V. WILSON**

**21.1** Organization of vestibular nystagmus in the oblique oculomotor system. **R. BAKER** and **A. BERTHOZ.** *Univ. of Iowa, Iowa City, IA, and Lab. de Physiologie du Travail, Paris, France.*

**21.2** Optokinetic nystagmus in goldfish. **S. S. EASTER, JR.** *Univ. of Michigan, Ann Arbor, MI.*

**21.3** Examination of the normal and deafferentated lateral vestibular nucleus in the rat by electron microscopy. **J. E. JOHNSON, JR.** and **T. H. WILLIAMS.** *Tulane Univ. Sch. of Med., New Orleans, LA.*

**21.4** Neural activity in the vestibular nuclei. **J. H. RYU** and **B. F. McCABE.** *Univ. of Iowa Col. of Med., Iowa City, IA.*

**21.5** Visual-vestibular interaction: effects of vision in suppressing vestibular nystagmus. **S. TAKEMORI** and **B. COHEN.** *Mt. Sinai Sch. of Med., New York, NY.*

# WORKSHOP

## 22. Albinism

3:15 PM—*Castilian Room*

*Chairman:* **C. L. SHERIDAN**

**22.1** Differences in the visual cortical projection area in albino and pigmented guinea pigs. **D. J. CREEL** and **R. A. GIOLLI**. *VA Hosp. and Arizona State Univ., Phoenix, AZ, and Univ. of California Sch. of Med., Irvine, CA.*

**22.2** Anatomical organization of the primary optic projections in pigmented and albino guinea pigs. **R. A. GIOLLI** and **D. J. CREEL**. *Univ. of California Sch. of Med., Irvine, CA, and VA Hosp., Phoenix, AZ.*

**22.3** Abnormal retinogeniculate and geniculocortical projections in the albino allelomorphic series of mammals. **K. J. SANDERSON, J. H. KAAS** and **R. W. GUILLERY**. *Univ. of Wisconsin, Madison, WI.*

**22.4** The structure of albino visual systems in relation to behavior. **C. L. SHERIDAN**. *Univ. of Missouri and VA Hosp., Kansas City, MO.*

## WORKSHOP

### 23. Brain Stem Morphology

3:15 PM—*Belvedere Room*

*Chairman:* **W. J. NAUTA**

**23.1** Synaptic organization of somatosensory afferent projections to the squirrel monkey thalamus. **D. J. FORBES.** *Univ. of Wisconsin Med. Sch., Madison, WI.*

**23.2** Quantitative structural organization in brain stem nuclei. **F. J. FRY.** *Indiana Univ. and Purdue Univ., Indianapolis, IN.*

**23.3** A Golgi study of the nucleus gracilis in the rat. **R. L. GULLEY.** *Harvard Med. Sch., Boston, MA.*

**23.4** Projections of the subnuclear areas of the periaqueductal gray matter in the cat. **B. L. HAMILTON.** *Georgetown Univ. Sch. of Med. and Dent., Washington, DC.*

**23.5** Maturative processes in dendrites of spinal cord and brain stem in the cat. **M. E. SCHEIBEL, A. B. SCHEIBEL** and **T. L. DAVIES.** *Univ. of California, Los Angeles Sch. of Med., Los Angeles, CA.*

### Extended Discussion Groups

4:15 PM—*Emerald Room*

Authors of volunteer papers presented in 1:00 PM sessions will be available for informal discussion.

## SYMPOSIUM

### 24. Amphetamines

9:00 AM—*Grand Ballroom*

*Chairman:* **D. X. FREEDMAN**

**24.1** Behavioral pharmacology of the amphetamines. **V. G. LATIES.** *Univ. of Rochester Sch. of Med., Rochester, NY.*

**24.2** Biochemical pharmacology of the amphetamines. **S. H. SNYDER.** *Johns Hopkins Sch. of Med., Baltimore, MD.*

**24.3** Neurophysiological studies of amphetamines. **F. E. BLOOM.** *St. Elizabeths Hosp., Washington, DC.*

## SYMPOSIUM

### 25. Genetic Neuroembryology and Behavioral Development

9:00 AM—*Emerald Room*

*Chairman:* **R. SIDMAN**

**25.1** Somatic cell genetic approach to the analysis of cytodifferentiation. **F. RUDDLE.** *Yale Univ., New Haven, CT.*

**25.2** Neurophysiological genetics: new approaches to behavior and development in *Drosophila melanogaster.* **K. IKEDA.** *City of Hope Med. Ctr., Duarte, CA.*

**25.3** The albino genetic locus and organization of the visual system in mammals. **R .W. GUILLERY.** *Univ. of Wisconsin Med. Sch., Madison, WI.*

# VOLUNTEER PAPERS

## 26. Limbic System and Behavior

9:00 AM—*Continental Room*

*Chairman:* **J. H. NAUTA**

* 9:00 **26.1** Electrophysiology of hippocampal input to the septum of the cat. **J. F. DeFRANCE, C. CHRISTENSEN, K. HATADA** and **S. T. KITAI.** *Wayne State Univ., Detroit, MI.*

* 9:15 **26.2** Perirhinal afferents to the dentate fascia. **L. E. WHITE, JR.** and **R. B. CHRONISTER.** *Univ. of Florida Col. of Med., Gainesville, FL.*

* 9:30 **26.3** Contrasts in mammillary body fluorescence following septal or hippocampal lesions. **E. W. POWELL, C. G. WINTER, M. E. KIRBY** and **B. AUSTIN.** *Univ. of Arkansas Sch. of Med., Little Rock, AR.*

9:45 **26.4** Release of norepinephrine and serotonin from the amygdala during rewarding median forebrain bundle stimulation. **J. A. HOLLOWAY.** *Univ. of Oklahoma Hlth. Sci. Ctr., Oklahoma City, OK.*

*10:00 **26.5** Correlation of latency to drink and unit activity following cholinergic stimulation of medial septal nucleus in rats. **J. BUGGY, Z. KHACHATURIAN** and **A. E. FISHER.** *Univ. of Pittsburgh and Univ. of Pittsburgh Sch. of Med., Pittsburgh, PA.*

*10:15 **26.6** Role of the septum in the regulation of consummatory responding in rats. **L. W. HAMILTON.** *Rutgers Univ., New Brunswick, NJ.*

*10:30 **26.7** Effect of sex reversal on sex differences in emotionality following septal lesions in rats. **A. G. PHILLIPS.** *Univ. of British Columbia, Vancouver, B.C., Canada.*

*10:45 **26.8** Effect of limbic injury on tonic immobility in chickens. **J. D. MASER, J. W. KLARA** and **G. G. GALLUP, JR.** *Tulane Univ., New Orleans, LA.*

11:00 **26.9** Stimulus-induced mating: peripheral vs. intracranial stimulation. **J. H. McLEAN** and **M. KENNEY.** *Louisiana State Univ., New Orleans, LA, and Natl. Ctr. for Primate Biol., Davis, CA.*

*11:15 **26.10** Anosmia and mouse killing by rats: a nonsensory, limbic role for the olfactory bulbs. **E. M. HULL, H. D. HOMAN** and **S. A. SPECTOR.** *State Univ. of New York at Buffalo, Amherst, NY.*

* Authors available for informal discussion at 3:15 PM in the Emerald Room.

# VOLUNTEER PAPERS

## 27. Motor Neurons and Motor Units

9:00 AM—*Embassy Room*

*Chairman:* **E. HENNEMAN**

* 9:00 **27.1** Effects of inactivity and programmed stimulation on feline skeletal muscle fibers. **D. A. RILEY.** *NIH, Bethesda, MD.*

* 9:15 **27.2** Accommodation versus adaptation in motoneuron rhythmic firing mechanisms. **W. H. CALVIN.** *Univ. of Washington, Seattle, WA.*

* 9:30 **27.3** Behavior and histochemistry of functionally isolated ankle extensors in the chronic cat. **M. C. WETZEL, R. L. GERLACH** and **L. Z. STERN.** *Univ. of Arizona and Univ. of Arizona Med. Ctr., Tucson, AZ.*

* 9:45 **27.4** Bilateral effects of VIIIth nerve stimulation on the lumbar cord. **A. H. HASSEN** and **C. D. BARNES.** *Indiana State Univ., Terre Haute, IN.*

10:00 **27.5** Activation of the gamma motor system in the cat following selective stimulation of the motor cortex and the pyramidal tract. **J. FORBES** and **A. J. SZUMSKI.** *Medical Col. of Virginia and Commonwealth Univ., Richmond, VA.*

*10:15 **27.6** Evaluation of spinal cord injury using cortical evoked responses. **S. H. MARTIN** and **J. R. BLOEDEL.** *Univ. of Minnesota Sch. of Med., Minneapolis, MN.*

*10:30 **27.7** Recovery of function after partial denervation of the spinal cord: a behavioral and anatomical study. **M. E. GOLDBERGER** and **M. MURRAY.** *Univ. of Chicago Sch. of Med., Chicago, IL.*

*10:45 **27.8** Relationship of twitch and metabolic properties of muscle fibers to recruitment patterns in various kinds of movements in animals. **V. R. EDGERTON** and **H. HEWITT.** *Univ. of California Los Angeles, Los Angeles, CA.*

*11:00 **27.9** Differential recruitment patterns of soleus and gastrocnemius motor units. **J. L. SMITH** and **N. L. HERNDEN.** *Univ. of California Los Angeles, Los Angeles, CA.*

*11:15 **27.10** The frequency response of extraocular motoneurons to intracellular stimulation. **N. H. BARMACK.** *Good Samaritan Hosp. and Med. Ctr., Portland, OR.*

* Authors available for informal discussion at 3:15 PM in the Emerald Room.

# VOLUNTEER PAPERS

## 28. Neurometabolism

9:00 AM—*Azalea Room*

*Chairman:* J. V. PASSONNEAU

* 9:00 **28.1** Control of glycogen metabolism in brain. **J. V. PASSONNEAU, H. WATANABE** and **D. A. ROTTENBERG.** *NIH, Bethesda, MD.*

9:15 **28.2** Isolation and properties of an inhibitor of tetrazolium reductase and related proteins. **R. FRIED.** *Creighton Univ. Med. Sch., Omaha, NB.*

* 9:30 **28.3** Relationship of folate metabolism and the anticonvulsant efficacy of phenobarbital. **D. B. SMITH** and **L. C. RACUSEN.** *Univ. of Vermont Col. of Med., Burlington, VT.*

9:45 **28.4** Intracellular electrical events and nicotinamide adenine dinucleotide levels of dorsal root ganglion neurons. **C. RODRIGUEZ-ESTRADA.** *Central Univ. of Venezuela, Caracas, Venezuela.*

10:00 **28.5** Disordered mitochondrial respiration in a human neurodegenerative disorder. **J. H. FRENCH, D. HOLTZMAN** and **C. L. MOORE.** *Montefiore Hosp., Bronx, NY.*

*10:15 **28.6** Activity of monoamine oxidase in purified brain mitochondria. **F. M. ACHEE, G. TOGULGA** and **S. GABAY.** *VA Hosp., Brockton, MA.*

10:30 **28.7** Regional variations in brain tissue gas tensions. **B. BURNS.** *Johns Hopkins Univ., Baltimore, MD.*

10:45 **28.8** Metabolic and electroencephalographic effects of acute ischemia in gerbil brain. **D. C. HOWSE** and **T. E. DUFFY.** *Cornell Univ. Med. Col., New York, NY.*

*11:00 **28.9** Postischemic metabolic activity of neurons and glia. **D. H. HINZEN** and **U. MULLER.** *Univ. of Cologne, Cologne, Germany.*

11:15 **28.10** Effect of X-irradiation and vitamin A alcohol on four lysosomal enzymes in normal rat brain and experimental brain tumors. **N. R. CLENDENON, H. ABE, N. ALLEN** and **W. GORDON.** *Ohio State Univ. Col. of Med., Columbus, OH.*

11:30 **28.11** Origin of cerebral temperature changes evoked by sensory stimulation. **M. A. BAKER, F. McFRYE** and **V. E. MILLET.** *Univ. of Southern California Sch. of Med., Los Angeles, CA.*

* Authors available for informal discussion at 3:15 PM in the Emerald Room.

# VOLUNTEER PAPERS

## 29. Visual Receptors

9:00 AM—*Columbia Room*

*Chairman:* **H. WAGNER**

* 9:00 **29.1** Effect of temperature on pattern firing in *Limulus* optic nerve. **G. D. LANGE** and **J. F. McCLEARY**. *Univ. of California, San Diego Sch. of Med., La Jolla, CA.*

* 9:15 **29.2** Temperature coefficient for spontaneous and light induced discrete waves in the *Limulus* photoreceptor. **R. SREBRO** and **M. BEHBEHANI**. *State Univ. of New York, Buffalo, NY.*

9:30 **29.3** Light adaptation of discrete waves in the *Limulus*. **M. BEHBEHANI** and **R. SREBRO**. *State Univ. of New York, Buffalo, NY.*

* 9:45 **29.4** Retinal sensitivity in the mudpuppy (*Necturus maculosus*). **L. M. PROENZA**. *Univ. of Georgia, Athens, GA.*

10:00 **29.5** Ionic basis of hyperpolarizing receptor potential in an invertebrate photoreceptor. **J. S. McREYNOLDS** and **A. L. F. GORMAN**. *NIH, Bethesda, MD.*

10:15 **29.6** Circadian rhythm in *Aplysia* optic nerve activity: effect of calcium and chloride substitution. **J. W. JACKLET**. *State Univ. of New York, Albany, NY.*

*10:30 **29.7** Fourier analysis of the cat's electroretinograms. **R. F. QUICK, W. M. KOZAK** and **T. W. CALVERT**. *Carnegie-Mellon Univ., Pittsburgh, PA.*

*10:45 **29.8** Visual function in rats without photoreceptors. **W. K. O'STEEN** and **K. V. ANDERSON**. *Emory Univ., Atlanta, GA.*

*11:00 **29.9** Visual discrimination performance in rats without photoreceptors or pigment epithelial cells. **K. V. ANDERSON** and **W. K. O'STEEN**. *Emory Univ., Atlanta, GA.*

* Authors available for informal discussion at 3:15 PM in the Emerald Room.

## VOLUNTEER PAPERS

### 30. Human Neuropsychology

9:00 AM—*Nile Room*

*Chairman:* J. ZUBIN

* 9:00 **30.1** Electrophysiological correlates of pattern preferences in human infants. **B. Z. KARMEL, R. F. HOFFMANN** and **M. J. FEGY.** *Univ. of Connecticut, Storrs, CT.*

9:15 **30.2** Average evoked potential correlates of information processing in schizophrenics, psychotic depressives and normals. **R. A. LEVIT, S. SUTTON** and **J. ZUBIN.** *New York State Dept. of Ment. Hyg., New York, NY.*

* 9:30 **30.3** Hemispheric sharing between verbal and manual performance after callosal section. **M. KINSBOURNE.** *Duke Univ. Med. Ctr., Durham, NC.*

* 9:45 **30.4** Hemispheric asymmetry in slow cortical potentials as a function of verbal or nonverbal set. **G. R. MARSH** and **L. W. THOMPSON.** *Duke Univ. Med. Ctr., Durham, NC.*

10:00 **30.5** Cardiorespiratory mechanism in plateau waves among head-injured patients. **C. P. McGRAW, G. T. TINDALL, K. IWATA** and **R. W. VANDERVEER.** *Univ. of Texas Med. Br., Galveston, TX.*

10:15 **30.6** Cocaine: clinical effects in depressed patients. **R. M. POST, J. KOTIN** and **F. K. GOODWIN.** *NIMH, Bethesda, MD.*

*10:30 **30.7** A comparative study of mental status. **I. F. SMALL, V. MILSTEIN** and **J. G. SMALL.** *Larue D. Carter Mem. Hosp., Indianapolis, IN.*

*10:45 **30.8** Electron-transfer factors in psychosis and dyskinesia. **P. H. PROCTOR.** *M. D. Anderson Hosp., Houston, TX.*

*11:00 **30.9** The schizexperience: a learning and feedback model for schizophrenia and schizoid process. **V. JOHNSON.** *Los Angeles, CA.*

*11:15 **30.10** A clinical services system representing the "TOTE" model. **M. N. OZER.** *George Washington Univ. Med. Sch., and Child. Natl. Med. Ctr., Washington, DC.*

* Authors available for informal discussion at 3:15 PM in the Emerald Room.

# INVITED LECTURES

## 31. Amphetamines

1:00 PM—*Grand Ballroom*

*Chairman:* **D. X. FREEDMAN**

1:00 **31.1** Amphetamine: direct evidence for an action on dopaminergic neurons. **B. S. BUNNEY, G. K. AGHAJANIAN, R. H. ROTH** and **J. R. WALTERS.** *Yale Univ. Sch. of Med. and Connecticut Mental Hlth. Ctr., New Haven, CT.*

1:30 **31.2** Predictors of response to stimulant drug treatment in MBD children. **J. H. SATTERFIELD, G. E. ATOIAN** and **R. E. SAUL.** *Gateways Hosp., Los Angeles, CA.*

2:00 **31.3** Recent advances in the biochemical pharmacology of amphetamine and its chlorinated derivatives. **F. SULSER** and **E. SANDERS-BUSH.** *Vanderbilt Univ. Sch. of Med., Nashville, TN.*

2:30 **31.4** Provocation of psychotic symptoms in schizophrenics by methylphenidate. **J. M. DAVIS, D. S. JANOWSKY, M. K. EL-YOUSEF** and **H. J. SEKERKE.** *Vanderbilt Univ. Sch. of Med. and Tennessee Neuropsychiat. Inst., Nashville, TN.*

# INVITED LECTURES

## 32. Genetic Neuroembryology and Behavioral Development

1:00 PM—*Emerald Room*

*Chairman:* **R. SIDMAN**

1:00 **32.1** Histofluorescent and electron microscopic studies of the developing substantia nigra in the rabbit. **V. M. TENNYSON, C. MYTILINEOU** and **R. BARRETT.** *Columbia Univ., Col. of Phys. and Surg., New York, NY.*

1:30 **32.2** Proliferation rate and latency between final cell division and onset of differentiation of cerebellar stellate and basket neurons. **P. RAKIC.** *Harvard Med. Sch., Boston, MA.*

2:00 **32.3** Effect of olfactory bulbectomy on nursing behavior in the Wistar (DAB) rat pup. **P. J. SINGH** and **E. TOBACH.** *American Museum of Natural History, New York, NY.*

2:30 **32.4** Development of species-specific auditory perception in duck embryos: behavioral analysis. **G. GOTTLIEB** and **M. B. HEATON.** *North Carolina Dept. of Mental Hlth., Raleigh, NC.*

## INVITED LECTURES

### 33. Social Issues

1:00 PM—*Continental Room*

*Chairman:* **F. PLUM**

1:00 **33.1** Nutritional research and mental retardation. **M. WINICK.** *Columbia Univ., New York, NY.*

**33.2** DISCUSSANT: Unmet responsibilities of neuroscience in mental retardation. **H. G. BIRCH.** *Albert Einstein Col. of Med., New York, NY.*

2:00 **33.3** Psychopharmacological contributions to patient care in psychiatry. **S. H. SNYDER.** *Johns Hopkins Univ. Sch. of Med., Baltimore, MD.*

**33.4** DISCUSSANT: How basic science might solve social problems in drug abuse. **A. GREEN.** *Special Action for Drug Abuse Prevention, c/o White House, Washington, DC.*

## INVITED LECTURES

### 34. Inhibitory Processes

1:00 PM—*Embassy Room*

*Chairman:* **E. ROBERTS**

1:00 INVERTEBRATE: AT THE CELLULAR LEVEL

**34.1** Inhibition in the function of the stomatogastric ganglion in the spiny lobster. **D. M. MAYNARD** and **K. WALTON.** *Univ. of Oregon, Eugene, OR.*

1:30 VERTEBRATE: AT THE CELLULAR LEVEL

**34.2** Inhibitory effects of imidazole and some derivatives on cortical neurones. **K. KRNJEVIC, J. M. GODFRAIND** and **R. PUMAIN.** *McGill Univ., Montreal, Canada.*

2:00 VERTEBRATE: AT THE SUBSYSTEM LEVEL

**34.3** Synaptic properties of striatal and pallidal neurons. **C. D. HULL, M. S. LEVINE** and **N. A. BUCHWALD.** *Univ. of California, Los Angeles, CA.*

2:30 VERTEBRATE: AT THE ORGANISMIC LEVEL

**34.4** Disinhibition of frog tectal units after pretectal lesions. **D. INGLE.** *McLean Hosp. and Harvard Med. School, Belmont, MA.*

# VOLUNTEER PAPERS

## 35. Tissue Culture

1:00 PM—*Azalea Room*

*Chairman:* **M. R. MURRAY**

* 1:00 **35.1** Morphological transformation of dissociated embryonic brain cells in the presence of brain extracts. **R. LIM, W. K. P. LI** and **K. MITSUNOBU.** *Univ. of Chicago, Chicago, IL.*

* 1:15 **35.2** Biochemical correlates of inhibition of oligodendrocyte differentiation in tissue culture. **G. M. LEHRER, J. M. FRY** and **M. B. BORNSTEIN.** *Mt. Sinai Sch. of Med., New York, NY, and Albert Einstein Col. of Med., Bronx, NY.*

* 1:30 **35.3** Differential effects of inhibitors of RNA synthesis on the catecholamine and cortisol inductions of enzymes at a rat glial cell line. **J. de VELLIS** and **D. INGLISH.** *Univ. of California Los Angeles, Los Angeles, CA.*

* 1:45 **35.4** Responses of sympathetic chain-ganglia isolated in long-term culture to agents affecting adrenergic neurons. **H. H. BENITEZ** and **M. R. MURRAY.** *Columbia Univ. Col. of Phys. and Surg., New York, NY.*

2:00 **35.5** Effects of maple syrup urine disease metabolites on L-strain mouse fibroblasts. **M. G. BISSELL, K. G. BENSCH** and **M. M. HERMAN.** *Stanford Univ. Sch. of Med., Stanford, CA.*

* 2:15 **35.6** Intracellular changes resulting from exposure to morphine sulfate. Phase contrast and electron microscopic study of tissue culture line derived from glioblastoma multiforme. **L. LISS.** *Ohio State Univ. Col. of Med., Columbus, OH.*

* 2:30 **35.7** Developmental and biosynthetic studies on the guinea pig hypothalamoneurohypophysial complex, in vivo and in organ culture. **R. GOODMAN, J. OSINCHAK** and **H. SACHS.** *Roche Inst. of Molecular Biol., Nutley, NJ.*

* Authors available for informal discussion at 4:15 PM in the Emerald Room.

# VOLUNTEER PAPERS

## 36. Somatosensory Mechanisms

1:00 PM—*Columbia Room*

*Chairman:* **V. B. MOUNTCASTLE**

* 1:00 **36.1** Trigeminal pain projections to the bulbar lateral reticular formation. **S. G. NORD** and **G. S. ROSS.** *State Univ. of New York, Upstate Med. Ctr., Syracuse, NY.*

1:15 **36.2** Sensory organization of the mesencephalic pontine reticular formation in rats. **S. W. MILLER** and **P. M. GROVES.** *Univ. of Colorado, Boulder, CO.*

1:30 **36.3** Dynamic transfer characteristics of thalamic sensory neurons. **T. C. T. YIN** and **W. J. WILLIAMS.** *Univ. of Michigan, Ann Arbor, MI.*

1:45 **36.4** The importance of cerebral cortex for the central processing of temporally ordered somesthetic afferent input. **R. H. LaMOTTE** and **V. B. MOUNTCASTLE.** *Johns Hopkins Univ. Sch. of Med., Baltimore, MD.*

* 2:00 **36.5** Long duration sequence of responses in sensorimotor cortex. **N. R. KREISMAN** and **I. D. ZIMMERMAN.** *Tulane Univ. Sch. of Med., New Orleans, LA, and Med. Col. of Pennsylvania, Philadelphia, PA.*

* 2:15 **36.6** Regulatory influences on the laryngeal input to the solitary tract nucleus. **B. J. SESSLE.** *Univ. of Toronto, Toronto, Ont., Canada.*

2:30 **36.7** Modification of unit activity in hypothalamus and reticular formation by sensory and central stimulation. **G. DAUTH, N. DAFNY, L. MARCO, M. GLUSMAN** and **S. GILMAN.** *Columbia Univ. Col. of Phys. and Surg., New York, NY.*

2:45 **36.8** Dynamic responses of primate warm fibers. **C. LAMOTTE, K. JOHNSON, I. DARIAN-SMITH, M. GOSWELL** and **R. LONG.** *Johns Hopkins Univ. Med. Sch., Baltimore, MD.*

* Authors available for informal discussion at 4:15 PM in the Emerald Room.

# VOLUNTEER PAPERS

## 37. Reflex Control of Movements

1:00 PM—*Nile Room*

*Chairman:* **J. E. SWETT**

* 1:00 **37.1** Mechanical mechanisms of transduction in the Golgi tendon organ. **J. E. SWETT** and **T. W. SCHOULTZ.** *Univ. of Colorado Med. Ctr., Denver, CO.*

* 1:15 **37.2** Significance of the silent period during muscular contraction. **A. M. IANNONE** and **L. T. ANDREWS.** *Med. Col. of Ohio, Toledo, OH.*

* 1:30 **37.3** Neural control of the cat step cycle: nature and role of lengthening contractions. **G. E. GOSLOW, JR.** and **D. G. STUART.** *Northern Arizona Univ., Flagstaff, AZ, and Univ. of Arizona, Tucson, AZ.*

1:45 **37.4** Slowly developing hyperreflexia in the crayfish abdomen following nerve cord transection. **J. J. WINE.** *Stanford Univ., Stanford, CA.*

2:00 **37.5** Paradoxical changes in a motor reflex response to reticular formation stimulation during active sleep. **M. H. CHASE** and **M. BABB.** *Univ. of California Los Angeles Sch. of Med., Los Angeles, CA.*

* 2:15 **37.6** Aversive conditioning of contact placing in cats and its developmental aspects. **C. T. WERTENBAKER, R. J. ROSS** and **V. E. AMASSIAN.** *Albert Einstein Col. of Med., New York, NY.*

* Authors available for informal discussion at 4:15 PM in the Emerald Room.

# VOLUNTEER PAPERS

## 38. Chemistry and Behavior II

1:00 PM—*Castilian Room*

*Chairman:* **S. H. BARONDES**

* 1:00 **38.1** Alterations in the pattern of RNA synthesis in goldfish brain during training. **V. E. SHASHOUA.** *Harvard Med. Sch., Boston, MA, and McLean Hosp. Res. Lab., Belmont, MA.*

* 1:15 **38.2** Changes in radioactivity in brain uridine nucleotide pools during active avoidance learning. **D. ENTINGH, T. ENTINGH, E. GLASSMAN** and **J. E. WILSON.** *Univ. of North Carolina Sch. of Med., Chapel Hill, NC.*

* 1:30 **38.3** Gradient and permanence of amnesia of a passive avoidance task in cycloheximide treated mice as a function of the number of training trials. **E. E. QUINTON.** *Univ. of Louisville, Louisville, KY.*

* 1:45 **38.4** Evidence that memory depends on protein synthesis within minutes after the beginning of training. **L. R. SQUIRE, G. A. SMITH** and **S. H. BARONDES.** *Univ. of California, San Diego Sch. of Med., La Jolla, CA.*

* 2:00 **38.5** Potentiating effect of adrenocorticotrophic hormone on cycloheximide-induced amnesia in mice. **A. M. GOLUB** and **R. H. McCLUER.** *Eunice Kennedy Shriver Ctr., Waltham, MA.*

* 2:15 **38.6** The learning-enhancing drug UCB 6215: effects in goldfish. **G. BARNETT, R. C. BRYANT, F. PETTY, L. A. KEPNER** and **W. L. BYRNE.** *Univ. of Tennessee Med. Units, Memphis, TN.*

2:30 **38.7** Effects of magnesium pemoline on the habituation of an immobility response in *Carassius auratus.* **R. D. OLSON, S. T. ELDER** and **J. G. MAY.** *Louisiana State Univ. at Lakefront, New Orleans, LA.*

2:45 **38.8** Effects of carbon dioxide and flurothyl upon retention of one-trial learning in goldfish. **W. H. RIEGE** and **A. CHERKIN.** *VA Hosp., Sepulveda, CA, and Univ. of California Los Angeles Sch. of Med., Los Angeles, CA.*

* Authors available for informal discussion at 4:15 PM in the Emerald Room.

# VOLUNTEER PAPERS

## 39. Audition

1:00 PM—*Belvedere Room*

*Chairman:* S. D. ERULKAR

* 1:00 **39.1** A mathematical description of thresholds for electrical stimulation of subcortical auditory structures. **G. M. GERKEN.** *Callier Hearing and Speech Ctr., Dallas, TX.*

* 1:15 **39.2** Bullfrog inner ear receptors: structural differences related to function. **E. R. LEWIS.** *Univ. of California, Berkeley, CA.*

* 1:30 **39.3** A neural model of the laterality effect in dichotic listening. **K. E. ACHENBACH.** *Univ. of South Florida, Tampa, FL.*

* 1:45 **39.4** Anatomical connections of the inferior colliculus of the tree shrew (*Tupaia glis*). **J. H. CASSEDAY** and **J. K. HARTING.** *Duke Univ., Durham, NC.*

* 2:00 **39.5** Effects of unilateral and bilateral ablations of auditory cortex in the cat on binaural masking and unmasking. **J. L. CRANFORD.** *Indiana Univ., Bloomington, IN.*

2:15 **39.6** Responses of neurons in the auditory cortex of squirrel monkeys to acoustically similar vocalizations. **J. D. NEWMAN** and **Z. WOLLBERG.** *NIH, Bethesda, MD.*

* 2:30 **39.7** Motivational factors influencing auditory cortical evoked potentials in the cat. **G. KARMOS.** *Univ. of Illinois Med. Ctr., Chicago, IL, and University Med. Sch., Pécs, Hungary.*

* 2:45 **39.8** "Mirror-images" in hearing. **M. L. PINHEIRO** and **L. T. ANDREWS.** *Medical Col. of Ohio, Toledo, OH.*

* Authors available for informal discussion at 4:15 PM in the Emerald Room.

## Extended Discussion Groups

3:15 PM—*Emerald Room*

Authors of volunteer papers presented in 9:00 AM sessions will be available for informal discussion.

## WORKSHOP

### 40. Social Issues

3:15 PM—*Continental Room*

*Chairman:* **F. PLUM**

A forum for the discussion of important social issues and the purposes and functions of the Society for Neuroscience Committee on Social Responsibility.

**40.1** INTRODUCTION: **D. MAX SNODDERLY, JR.** *The Retina Foundation, Boston, MA.*

**40.2** DISCUSSION MODERATOR: **ETHEL TOBACH,** *American Museum of Natural History, New York, NY.*

## WORKSHOP

### 41. Cerebellar and Vestibular Function

3:15 PM—*Embassy Room*

*Chairman:* **W. T. THACH**

**41.1** Visual–vestibular interaction: effect of vision on pre- and post-rotatory nystagmus. **B. COHEN.** *Mt. Sinai Sch. of Med., New York, NY.*

**41.2** Responses of interpositus cells to stimulation of cutaneous mechanoreceptors. **J. C. ECCLES, I. ROSEN, P. SCHEID** and **H. TABORIKOVA.** *State Univ. of New York at Buffalo, Amherst, NY.*

**41.3** Activity of dentate neurones during the performance of a pattern movement. **R. J. GRIMM, D. S. RUSHMER, R. WEAR** and **R. NEWTON.** *Good Samaritan Med. Ctr., Portland, OR.*

**41.4** Single cell responses from the cerebellum of rhesus preceding voluntary vestibular and optokinetic saccadic eye movements. **R. LLINAS** and **J. W. WOLFE.** *Univ. of Iowa, Iowa City, IA, and USAF Sch. of Aerospace Med., San Antonio, TX.*

# WORKSHOP

## 42. Adrenergic Mechanisms

3:15 PM—*Azalea Room*

*Chairman:* **D. J. REIS**

**42.1** Alteration in catecholamine fluorescence after local freeze lesions in cerebral cortex of rabbits. **F. P. BOWEN.** *Columbia Univ. Col. of Phys. and Surg., New York, NY.*

**42.2** Effects of monoamine precursors on enchancement of the spinal monosynaptic reflex by para-methoxyphenylethylamine. **J. D. COULTER, A. M. BIRD, J. C. WILLIS** and **W. D. WILLIS.** *Marine Biomed. Inst., Univ. of Texas Med. Br., Galveston, TX.*

**42.3** Radioautographic studies on noradrenergic axon terminals of rat frontal cortex. **L. DESCARRIES** and **Y. LAPIERRE.** *Univ. of Montreal, Montreal, Que., Canada.*

**42.4** Dynamic changes in dopamine-$\beta$-hydroxylase activity in cortex, brainstem, and cerebellum after hypothalamic lesions in rat. **R. A. ROSS** and **D. J. REIS.** *Cornell Univ. Med. Col., New York, NY.*

**42.5** Disruption of physiologic function by 6-hydroxydopamine. **R. D. SMITH, R. A. MUELLER** and **G. R. BREESE.** *Univ. of North Carolina Sch. of Med., Chapel Hill, NC.*

# WORKSHOP

## 43. Neural Plasticity

3:15 PM—*Columbia Room*

*Chairman:* **A. A. WARD, JR.**

**43.1** Fixation of inhibition of a spinal reflex by electrical stimulation of the medulla. **V. C. ABRAHAMS** and **J. DAYNES.** *University College, London, and Queen's Univ., Kingston, Ont., Canada.*

**43.2** Facilitation of a flexion reflex in the spinal cat using classical conditioning techniques. **R. G. DURKOVIC.** *Upstate Med. Ctr., Syracuse, NY.*

**43.3** Operantly conditioned patterns of epileptic cell activity. **E. E. FETZ, A. R. WYLER** and **A. A. WARD, JR.** *Primate Ctr., Univ. of Washington Sch. of Med., Seattle, WA.*

**43.4** Conceptual impediments in the study of biochemical correlates of neural plasticity. **L. IRWIN.** *Columbia Univ., New York, NY.*

**43.5** CNS inhibitory and facilitatory effects on peripherally mediated habituation of gill withdrawal in *Aplysia.* **B. PERETZ** and **D. BLACK.** *Univ. of Kentucky Med. Ctr., Lexington, KY.*

**43.6** Mechanisms of conditioning in the limbic telencephalic system of the rat. **M. SEGAL.** *California Inst. of Tech., Pasadena, CA.*

**43.7** Role of calcium in potentiation at the neuromuscular junction of frog sartorius. **S. G. YOUNKIN.** *Univ. of Pennsylvania Sch. of Med., Philadelphia, PA.*

# WORKSHOP

## 44. Central Synaptic Transmission

3:15 PM—*Nile Room*

*Chairman:* **L. MENDELL**

**44.1** Effectiveness of cat motoneuron dendritic synapses. **J. N. BARRETT** and **W. E. CRILL.** *Univ. of Washington, Seattle, WA.*

**44.2** Effects of hyperventilation on the plantar cushion reflex in cats. **M. D. EGGER, J. W. BISHOP, E. W. CLARK** and **C. H. CONE.** *Yale Univ. Sch. of Med., New Haven, CT.*

**44.3** Membrane effects-analysis of cerebral 5HT, LSD and CPZ interaction. **C. C. HUANG** and **A. S. MARRAZZI.** *Univ. of Missouri Inst. of Psychiatry, St. Louis, MO.*

**44.4** Effect of microelectrophoretically applied para-methoxy-phenyl-ethylamine on cat spinal cord neurons. **L. M. JORDAN.** *Univ. of Manitoba, Winnipeg, Man., Canada.*

**44.5** Convergence of pairs of group Ia fibers to spinal motoneurons in the cat. **L. MENDELL** and **R. WEINER.** *Duke Univ. Med. Ctr., Durham, NC.*

**44.6** Acetylcholine-induced responses measured under voltage clamp and their dependence on membrane potentials. **M. SATO** and **J. MARUHASHI.** *Univ. of Oregon Med. Sch., Portland, OR.*

**44.7** A molecular mechanism of depolarization generated by acetylcholine. **C. TORDA.** *Mt. Sinai Sch. of Med., New York, NY.*

# WORKSHOP

## 45. Sensorimotor Integration

3:15 PM—*Castilian Room*

*Chairman:* **P. S. G. STEIN**

**45.1** Motor cortex activity in association with quick reflex movements. **E. V. EVARTS.** *NIMH, Bethesda, MD.*

**45.2** Sensory alteration of walking in land crabs. **W. H. EVOY** and **C. R. FOURTNER.** *Univ. of Miami, Coral Gables, FL.*

**45.3** A neuronal basis for interappendage phase delay during locomotion. **P. S. G. STEIN.** *Washington Univ., St. Louis, MO.*

**45.4** Neural control of the cat step cycle: nature and role of proprioceptive input. **D. G. STUART** and **G. E. GOSLOW, JR.** *Univ. of Arizona, Tucson, AZ, and NAU, Flagstaff, AZ.*

**45.5** Utility of a limb following unilateral deafferentation in monkeys. **E. TAUB, G. BARRO, B. PARKER** and **T. GORSKA.** *Inst. of Behavioral Res., Silver Spring, MD.*

# WORKSHOP

## 46. Chemical Senses I: Smell

3:15 PM—*Belvedere Room*

*Chairman:* **B. M. WENZEL**

**46.1** The impregnable olfactory transduction code and its solvability. **R. G. DAVIS.** *Univ. of Northern Iowa, Cedar Falls, IA.*

**46.2** Role of the habenular nuclei in simple vs. complex olfactory discrimination learning. **L. J. RAUSCH, R. RAUSCH** and **C. J. LONG.** *Memphis State Univ., Memphis, TN.*

**46.3** A corticomedial amygdalobulbar centrifugal system in olfaction in the male rat. **G. K. RIEKE** and **M. H. BENNETT.** *Univ. of California Los Angeles Sch. of Med., Los Angeles, CA, and Univ. of Pittsburgh, Pittsburgh, PA.*

**46.4** Odor detection and discrimination in rats following section of lateral olfactory tract. **B. M. SLOTNICK.** *NIMH, Bethesda, MD.*

## Extended Discussion Groups

4:15 PM—*Emerald Room*

Authors of volunteer papers presented in 1:00 PM sessions will be available for informal discussion.

## SYMPOSIUM

### 47. Chemical Senses

9:00 AM—*Grand Ballroom*

*Chairman:* **C. PFAFFMANN**

**47.1** Evidence on receptor sites and mechanisms of mammalian gustatory receptors. **L. BEIDLER.** *Florida State Univ., Tallahassee, FL.*

**47.2** Invertebrate chemoreception: receptor mechanism and behavioral responses. **R. O'CONNELL.** *Rockefeller Univ., New York, NY.*

**47.3** Olfactory communication in mammals. **R. P. MICHAEL.** *Bethlem Royal Hosp., Beckenham, Kent, and Univ. of London, London, England.*

## SYMPOSIUM

### 48. Structure and Function of the Membrane

9:00 AM—*Emerald Room*

*Chairman:* **J. D. ROBERTSON**

**48.1** Protein–lipid interaction. **C. TANFORD.** *Duke Univ., Durham, NC.*

**48.2** Rhodopsin–phospholipid coupling in recombinant membranes. **W. HUBBELL.** *Univ. of California, Livermore, CA.*

**48.3** Alpha-bungarotoxin and nicotinic acetylcholine receptors. **L. T. POTTER.** *Univ. College of London, London, England.*

**48.4** Particulate arrays in unit membranes. **J. D. ROBERTSON.** *Duke Univ. Med. Ctr., Durham, NC.*

# VOLUNTEER PAPERS

## 49. Neurochemistry: Transmitters

9:00 AM—*Continental Room*

*Chairman:* **R. E. McCAMAN**

9:00 **49.1** Temporal changes in enzyme activities after brain hemisection or 6-hydroxydopamine administration. **E. G. McGEER** and **H. C. FIBIGER.** *Univ. of British Columbia, Vancouver, B.C., Canada.*

9:15 **49.2** Electron microscopic and enzyme marker studies in areas of bovine brain with special emphasis on MAO. **E. KOCH, B. TABAKOFF, F. UNGAR, L. MEYERSON, R. ANDERSON** and **S. G. A. ALIVISATOS.** *Chicago Med. Sch., Chicago, IL.*

* 9:30 **49.3** Metabolism of $^{3}H$-normetanephrine and $^{14}C$-norepinephrine in brain and peripheral tissue homogenates. **H. DEKIRMENJIAN** and **J. W. MAAS.** *Illinois State Psychiat. Inst., Chicago, IL.*

9:45 **49.4** Behavioral correlates of brain histamine levels and levels and uptake of brain catecholamines. **D. AURES, M. K. MENON** and **W. G. CLARK.** *VA Hosp., Sepulveda, CA, and Univ. of California Col. of Med., Irvine, CA.*

*10:00 **49.5** A new mechanism of action of diphenylhydantoin: effect on norepinephrine uptake and binding in synaptosomes. **M. G. HADFIELD** and **M. E. BOYKIN.** *Med. Col. of Virginia, Richmond, VA.*

10:15 **49.6** Phenylethylamine-like substances(s) in mammalian brain and their increase by repeated electroshock seizures. **A. D. MOSNAIM, E. E. INWANG** and **H. C. SABELLI.** *Chicago Med. Sch., Chicago, IL.*

*10:30 **49.7** Depression of acetylcholine release from cerebral cortical strips by cholinesterase inhibition. **J. C. SZERB** and **G. SOMOGYI.** *Dalhousie Univ., Halifax, N.S., Canada.*

*10:45 **49.8** Choline: high affinity uptake into cholinergic nerve terminals in the brain and periphery. **H. I. YAMAMURA, C. B. PERT, T. L. GARDNER** and **S. H. SNYDER.** *Johns Hopkins Univ. Sch. of Med., Baltimore, MD.*

*11:00 **49.9** An enzymatic assay for the determination of picomole amounts of acetylcholine. **A. M. GOLDBERG** and **R. E. McCAMAN.** *Johns Hopkins Univ., Baltimore, MD, and City of Hope, Duarte, CA.*

*11:15 **49.10** Acetylcholinesterase: recovery in brain tissue, cerebrospinal fluid and plasma following pinacolyl methylphosphonofluoridate. **T. L. YAKSH, L. A. FEDELE, T. L. GARDNER** and **H. I. YAMAMURA.** *Biomedical Lab., Edgewood Arsenal, MD.*

* Authors available for informal discussion at 3:15 PM in the Emerald Room.

# VOLUNTEER PAPERS

## 50. Brain Lesions and Behavior

9:00 AM—*Embassy Room*

*Chairman:* **M. C. TRACHTENBERG**

9:00 **50.1** Effect of methylmercury on performance of mice on a multiple schedule. **J. A. HUGHES.** *Johns Hopkins Univ., Baltimore, MD.*

9:15 **50.2** Corticofugal fiber degeneration following lesions of the insular cortex in *Macaca mulatta.* **J. ASTRUC.** *Med. Col. of Virginia and Virginia Commonwealth Univ., Richmond, VA.*

9:30 **50.3** Projections from the orbital cortex in the marmoset (*Saquinus oedipus*). **G. R. LEICHNETZ** and **J. ASTRUC.** *Med. Col. of Virginia and Virginia Commonwealth Univ., Richmond, VA.*

9:45 **50.4** Age-independent effects of orbital prefrontal lesions in infant monkeys. **E. A. MILLER** and **P. S. GOLDMAN.** *NIMH, Bethesda, MD.*

*10:00 **50.5** Spatial learning in monkeys with dorsolateral prefrontal lesions. **R. W. BUDDINGTON, P. S. GOLDMAN** and **H. E. ROSVOLD.** *NIMH, Bethesda, MD.*

10:15 **50.6** Some consequences of one- and two-stage lesions of the ventrobasal complex. **R. REYES, S. FINGER** and **J. FRYE.** *Washington Univ., St. Louis, MO.*

*10:30 **50.7** Impaired acquisition of classically conditioned eye blink to click-CS after ablation of cortical motor areas in cats. **C. D. WOODY, P. YAROWSKY** and **J. OWENS.** *Univ. of California Los Angeles, Los Angeles, CA.*

*10:45 **50.8** Somatosensory and auditory behavioral function of cats' orbital, anterior sylvian and anterior ectosylvian cortex. **R. B. GLASSMAN.** *Lake Forest Col., Lake Forest, IL.*

11:00 **50.9** The trigeminal system and hunger in the pigeon: differential role of central and peripheral trigeminal structures in the control of appetitive and consummatory behavior. **H. P. ZEIGLER.** *Hunter Col., New York, NY.*

11:15 **50.10** Terminal degeneration and behavioral changes due to thalamic lesions in anurans. **M. C. TRACHTENBERG.** *McLean Hosp., Belmont, MA.*

* Authors available for informal discussion at 3:15 PM in the Emerald Room.

# VOLUNTEER PAPERS

## 51. Hormones and the Nervous System

9:00 AM—*Azalea Room*

*Chairman:* **R. Y. MOORE**

* 9:00 **51.1** In vitro reversal by diphenylhydantoin of the electrophysiological effects of steroid-induced myopathy. **R. GRUENER** and **L. Z. STERN.** *Univ. of Arizona Sch. of Med., Tucson, AZ.*

* 9:15 **51.2** Inhibition of radioactivity uptake in brain and peripheral tissues after the injection of 1,2-$^{3}$H testosterone by cyproterone acetate or progesterone. **M. SAR** and **W. E. STUMPF.** *Univ. of North Carolina, Chapel Hill, NC.*

* 9:30 **51.3** Effect of adrenal secretion on midbrain tryptophan hydroxylase activity in rats. **E. C. AZMITIA, JR.** and **B. S. McEWEN.** *Rockefeller Univ., New York, NY.*

* 9:45 **51.4** The organization of tubero-hypophysial and reticulo-infundibular catecholamine neuron systems in the rat brain. **A. BJORKLUND, R. Y. MOORE, A. NOBIN** and **U. STENEVI.** *Univ. of Lund, Lund, Sweden, and Univ. of Chicago, Chicago, IL.*

*10:00 **51.5** Effect of acute starvation on the sleep–growth hormone response. **I. KARACAN** and **R. L. WILLIAMS.** *Univ. of Florida, Gainesville, FL.*

*10:15 **51.6** Release of rat pituitary prolactin and LH following application of KCl to the cerebral cortex. **J. A. COLOMBO, C. A. BLAKE** and **C. H. SAWYER.** *Univ. of California Los Angeles, Los Angeles, CA.*

10:30 **51.7** Effect of an antipsychotic tranquilizer on the secretion of prolactin in vivo and in vitro. **R. BLACKWELL, W. VALE, C. RIVIER** and **R. GUILLEMIN.** *Salk Inst., La Jolla, CA.*

*10:45 **51.8** Increased sensitivity of the cyclic 3′,5′-AMP system of rat pineal gland induced by decreased sympathetic nerve activity. **S. J. STRADA** and **B. WEISS.** *NIMH, St. Elizabeths Hosp., Washington, DC.*

*11:00 **51.9** Electrophysiological correlates of experimental hyperthyroidism. **L. Z. STERN** and **R. GRUENER.** *Univ. of Arizona Sch. of Med., Tucson, AZ.*

11:15 **51.10** Intense lordosis in the absence of ovarian hormones after septal ablation in rats. **B. R. KOMISARUK, K. LARSSON** and **R. COOPER.** *Rutgers—The State Univ., Newark, NJ.*

* Authors available for informal discussion at 3:15 PM in the Emerald Room.

# VOLUNTEER PAPERS

## 52. Central Visual Mechanisms

9:00 AM—*Columbia Room*

*Chairman:* **I. T. DIAMOND**

* 9:00 **52.1** Basis of electrically evoked potentials from the goldfish optic tectum. **G. C. OFFUTT.** *City College of New York, New York, NY.*

9:15 **52.2** Formation of anomalous projections from the retina to the pulvinar following removal of the superior colliculus in neonatal tree shrews. **V. A. CASAGRANDE, W. C. HALL** and **I. T. DIAMOND.** *Duke Univ., Durham, NC.*

9:30 **52.3** Ultrastructure of the accessory optic tract nucleus in the monkey. **T. PASIK, P. PASIK, J. HAMORI** and **J. SZENTAGOTHAI.** *Mt. Sinai Sch. of Med., New York, NY, and Semmelweis Univ. Med. Sch., Budapest, Hungary.*

9:45 **52.4** Identification of Golgi type II interneuron profiles in lateral geniculate nucleus of monkeys. **P. PASIK, T. PASIK, J. HAMORI** and **J. SZENTAGOTHAI.** *Mt. Sinai Sch. of Med., New York, NY, and Semmelweis Univ. Med. Sch., Budapest, Hungary.*

*10:00 **52.5** Effects of saccadic image motion on the geniculo-stria system of chronic cats. **H. NODA** and **W. R. ADEY.** *Univ. of California Los Angeles Sch. of Med., Los Angeles, CA.*

10:15 **52.6** A retinotopic projection area in the hyperstriatum of the burrowing owl. **J. W. GRAY** and **A. M. REVZIN.** *Oklahoma Univ. Sch. of Med. and Civil Aeromed. Inst., Oklahoma City, OK.*

10:30 **52.7** Pharmacological properties and receptive fields of neurons of the primary visual cortex of the cat. **E. WALLINGFORD, R. OSTDAHL, P. ZARZECKI, R. GLENDENNING** and **G. SOMJEN.** *Duke Univ., Durham, NC.*

10:45 **52.8** Correlation between potentials photically evoked in pre-cruciate cortex and behavioral recovery from visual deprivation. **J. GLASS.** *Univ. of Rochester, Rochester, NY.*

*11:00 **52.9** Area 17: Layer I as the termination site of a topographically organized fiber projection from Area 18. **J. TIGGES, M. TIGGES** and **W. B. SPATZ.** *Emory Univ., Atlanta, GA, and Max-Planck-Inst. f. Hirnforschung, Frankfurt/M., Germany.*

11:15 **52.10** Electrophysiological effects of a chelating ion exchange resin (Chelex 100) introduced into the lateral geniculate body of the cat. **A. COSTIN, E. M. ROVNER** and **I. M. SABBOT.** *Univ. of California Los Angeles, Los Angeles, CA.*

* Authors available for informal discussion at 3:15 PM in the Emerald Room.

## INVITED LECTURES

### 53. Chemical Senses

1:00 PM—*Grand Ballroom*

*Chairman:* **C. PFAFFMAN**

1:00 **53.1** Taste as a model for the neurogenesis of receptor properties and synaptic connections. **B. OAKLEY.** *Univ. of Michigan, Ann Arbor, MI.*

1:30 **53.2** Central gustatory pathways. **R. E. NORGREN, C. M. LEONARD** and **C. PFAFFMANN.** *Rockefeller Univ., New York, NY.*

2:00 **53.3** Synaptic organization of the olfactory pathway of mammals. **G. M. SHEPHERD.** *Yale Univ. Sch. of Med., New Haven, CT.*

2:30 **53.4** Communicative behavior in stressed aquatic environment. **J. TODD.** *Woods Hole Oceanographic Institution, Woods Hole, MA.*

## INVITED LECTURES

### 54. Structure and Function of the Membrane

1:00 PM—*Emerald Room*

*Chairman:* **J. D. ROBERTSON**

**54.1** Proteolipids from membrane systems. **J. FOLCH-PI.** *Harvard Med. Sch. and McLean Hosp., Belmont, MA.*

**54.2** Evidence for conformational change in axonal membrane during excitation. **I. TASAKI, M. HALLETT** and **E. CARBONE.** *NIH, Bethesda, MD.*

**54.3** Membrane actions of the excitability-controlling drugs (or the "hydrophobic expansion theory of anesthesia"). **P. SEEMAN.** *Univ. of Toronto, Toronto, Canada.*

# INVITED LECTURES

## 55. Neural Plasticity

1:00 PM—*Continental Room*

*Chairman:* **L. GUTH**

1:00 **55.1** Synaptic complex formation and axonal growth rostral to site of hemisection in monkey spinal cord. **J. J. BERNSTEIN** and **M. E. BERNSTEIN.** *Univ. of Florida Col. of Med., Gainesville, FL.*

1:20 **55.2** Ultrastructure of intensely stimulated preganglionic nerve endings with and without recovery. **J. J. PYSH** and **R. G. WILEY.** *Northwestern Univ.-McGaw Med. Ctr., Chicago, IL.*

1:40 **55.3** Neuronal adjustments in the hippocampus following lesions of the entorhinal cortex. **G. S. LYNCH** and **C. W. COTMAN.** *Univ. of California, Irvine, CA.*

2:00 **55.4** Physiological and histochemical properties of the soleus muscle after denervation of its antagonists. **L. GUTH** and **J. B. WELLS.** *NIH, Bethesda, MD.*

2:10 **55.5** DISCUSSANT: **PATRICIA S. GOLDMAN.** *NIMH, Bethesda, MD.*

2:20 General discussion.

# VOLUNTEER PAPERS

## 56. Neurochemistry

1:00 PM—*Embassy Room*

*Chairman:* **C. F. BAXTER**

1:00 **56.1** Amino acids in mammalian CNS: biochemical synaptic properties. **W. J. LOGAN, A. ARREGUI, J. P. BENNETT** and **S. H. SNYDER.** *Johns Hopkins Univ., Baltimore, MD.*

1:15 **56.2** Amino acid incorporation by synaptosomes isolated from the teleost (*Galeichthys felis*). **P. MAXCY, JR.** and **D. A. RAPPOPORT.** *Univ. of Texas Med. Br., Galveston, TX.*

* 1:30 **56.3** Intrinsic inhibitor of glutamic acid decarboxylase (glutamic carboxyl-lyase) in the cockroach (*Periplaneta americana*). **C. F. BAXTER, G. F. TORRALBA** and **J. L. EMGE.** *VA Hosp., Sepulveda, CA.*

* 1:45 **56.4** Chlorpromazine induced inhibition of glutamate uptake by insect nerve. **I. R. FAEDER** and **M. M. SALPETER.** *Duke Univ. Med. Sch., Durham, NC, and Cornell Univ., Ithaca, NY.*

* 2:00 **56.5** Polyamines in the brain: enzymatic-isotopic assay of putrescine and blockade of its synthesis by $\alpha$-hydrazino-ornithine. **S. I. HARIK, G. W. PASTERNAK** and **S. H. SNYDER.** *Johns Hopkins Univ. Sch. of Med., Baltimore, MD.*

* 2:15 **56.6** *N*-Acetylneuraminic acid in the developing optic tectum of the chick embryo. **D. B. GRAY.** *Columbia Univ., New York, NY.*

* 2:30 **56.7** Uptake and accumulation of $^{3}$H-6,7-dihydroxytetrahydroisoquinoline by sympathetic nerves in vivo. **G. COHEN** and **S. E. LOCKE.** *Columbia Univ. Col. of Phys. and Surg., New York, NY.*

2:45 **56.8** Relationship between nuclear and cytosol binding of $^{3}$H-corticosterone in the rat brain. **R. W. RHEES, W. STEVENS** and **B. I. GROSSER.** *Univ. of Utah Col. of Med., Salt Lake City, UT.*

* Authors available for informal discussion at 4:15 PM in the Emerald Room.

# VOLUNTEER PAPERS

## 57. Mechanisms of Action of Addicting Drugs

1:00 PM—*Azalea Room*

*Chairman:* **W. G. CLARK**

1:00 **57.1** Blockade of brain dopamine release by gamma-hydroxybutyric acid and its use as a tool in studying mechanisms of action of psychotropic drugs. **W. G. CLARK** and **M. K. MENON.** *VA Hosp., Sepulveda, CA, and Univ. of California Los Angeles, Los Angeles, CA.*

* 1:15 **57.2** Effects of depressant drugs on deprivation-induced fluid consumption in rats. **G. J. MALONEY** and **R. P. MAICKEL.** *Indiana Univ., Bloomington, IN.*

1:30 **57.3** Effect of antidiuretic hormone on the level of pentazocine in the brain of rodents. **W. L. DEWEY, T-T. CHAU** and **L. S. HARRIS.** *Univ. of North Carolina, Chapel Hill, NC.*

* 1:45 **57.4** Aspects of alkaloid involvement in alcoholism. **M. J. WALSH.** *Bowman Gray Sch. of Med., Winston-Salem, NC.*

* 2:00 **57.5** Effects of ethanol and acetaldehyde in brain tissue: serotonergic correlates. **B. TABAKOFF, W. O. BOGGAN, F. UNGAR** and **S. G. A. ALIVISATOS.** *Chicago Med. Sch. and Univ. of Chicago, Chicago, IL.*

2:15 **57.6** Modification of physical dependence to morphine by aversive stimuli in rats. **S. N. DUTTA, P. T. BAILEY** and **S. N. PRADHAN.** *Howard Univ. Col. of Med., Washington, DC.*

* 2:30 **57.7** Tolerance effects of direct morphine stimulation of the anterior thalamus and ventral medial nucleus of the hypothalamus of the rat. **J. MASSERANO, G. LITTLE, PAT D'ENCARNACAO** and **PAUL D'ENCARNACAO.** *Memphis State Univ., and VA Hosp., Memphis, TN.*

* 2:45 **57.8** Effects of repeated morphine administration on lateral hypothalamic self-stimulation in rats. **S. A. LORENS** and **C. L. MITCHELL.** *Univ. of Iowa Col. of Med., Iowa City, IA.*

* Authors available for informal discussion at 4:15 PM in the Emerald Room.

# VOLUNTEER PAPERS

## 58. Epilepsy

1:00 PM—*Columbia Room*

*Chairman:* **A. A. WARD**

* 1:00 **58.1** Spontaneous seizure frequency and avoidance conditioning in monkeys. **J. S. LOCKARD, W. WILSON** and **V. UHLIR.** *Univ. of Washington Sch. of Med., Seattle, WA.*

* 1:15 **58.2** A quantitative analysis of the anatomical and electrophysiological correlates of chronic epileptogenic foci in cats. **M. VELASCO, F. VELASCO** and **X. LOZOYA.** *I.M.S.S., Mexico, D.F., Mexico.*

* 1:30 **58.3** Suppression of photically elicited cortical hypersynchrony in rats by trimethadione. **C. E. WILSON** and **D. J. CREEL.** *VA Hosp., Phoenix, AZ.*

* 1:45 **58.4** Multiple unit activity of specific and nonspecific systems during experimental nonfocal epilepsy. **F. VELASCO** and **M. VELASCO.** *Natl. Med. Ctr., I.M.S.S., Mexico, D.F., Mexico.*

* 2:00 **58.5** Low level X-radiation and audio-sensitization seizures. **W. B. ITURRIAN** and **L. J. PEACOCK.** *Univ. of Georgia, Athens, GA.*

* 2:15 **58.6** Unequal participation of neuronal dendrites and soma in seizure activity generated by different concentrations of epileptogenic agents. **E. C. ZUCKERMANN.** *Yale Univ. Sch. of Med., New Haven, CT.*

* 2:30 **58.7** Drug effects of epileptiform activity in chronically isolated slabs of cerebral cortex. **A. J. VAZQUEZ** and **G. KRIP.** *Chicago Med. Sch., Chicago, IL, and Univ. of Manitoba, Winnipeg, Man., Canada.*

* 2:45 **58.8** Brainstem section and propagation of focal paroxysmal discharge in rabbit. **M. L. WOODRUFF, F. H. GAGE III** and **R. L. ISAACSON.** *Univ. of Florida, Gainesville, FL.*

* Authors available for informal discussion at 4:15 PM in the Emerald Room.

## Extended Discussion Groups

3:15 PM—*Emerald Room*

Authors of volunteer papers presented in 9:00 AM sessions will be available for informal discussion.

# WORKSHOP

## 59. Axonal Transport

3:15 PM—*Grand Ballroom*

*Chairman:* **B. GRAFSTEIN**

**59.1** Actomyosin-like protein in brain: a postulated function in transmitter release. **S. BERL, S. PUSZKIN** and **W. J. NICKLAS.** *Columbia Univ. Col. of Phys. and Surg., New York, NY.*

**59.2** Neurofilament-interspace in frog sciatic nerve. **P. H. COOKE, R. E. LINDBERG** and **F. E. SAMSON, JR.** *Univ. of Kansas, Lawrence, KS.*

**59.3** Axonal transport of dopamine in nigra striatal neurons of rats. **H. C. FIBIGER** and **E. G. McGEER.** *Univ. of British Columbia, Vancouver, Canada.*

**59.4** Neuronal and glial iontophoresis of $^{3}H$ amino acids in leech ganglion. **A. GLOBUS, H. D. LUX** and **P. SCHUBERT.** *Univ. of California, Irvine, CA.*

**59.5** Axonal transport of RNA in goldfish optic system. **N. A. INGOGLIA, B. GRAFSTEIN, B. S. McEWEN** and **I. G. McQUARRIE.** *Cornell Univ. Med. Col., New York, NY, New Jersey Col. of Med. and Dent., Newark, NJ, and Rockefeller Univ., New York, NY.*

**59.6** Calcium requirement for axoplasmic flow. **J. B. KIRKPATRICK** and **R. E. ROSE.** *Univ. of Arizona Col. of Med., Tucson, AZ.*

**59.7** Membrane properties (excitability and osmoticity) and fast axoplasmic transport in vitro. **S. OCHS.** *Indiana Univ. Med. Sch., Indianapolis, IN.*

# WORKSHOP

## 60. Structure–Function Considerations in Electrophysiological Modeling

3:15 PM—*Continental Room*

*Chairman:* **G. SHEPHERD**

**60.1** Relationship of anatomy and function in CNS: a neuronal model study. **P. A. ANNINOS** and **R. ELUL.** *Mental Retard. Ctr., NPI, Univ. of California Los Angeles, Los Angeles, CA.*

**60.2** Dendritic organization of stellate cells in layer IV of cat striate cortex. **N. B. CANT** and **L. T. RUTLEDGE.** *Univ. of Michigan, Ann Arbor, MI.*

**60.3** Parkinsonian behavior in artificial neural nets. **R. A. CYRULNIK** and **P. A. ANNINOS.** *Mental Retard. Ctr., NPI, Univ. of California Los Angeles Sch. of Med., Los Angeles, CA.*

**60.4** Periodicity and metachronism in nervous system ensembles? **D. A. GOODMAN** and **C. L. RICHARDS.** *Newport Neuroscience Ctr., Irvine, CA.*

**60.5** Spike interval distribution coding in the mammalian visual pathway. **A. C. SANDERSON, W. M. KOZAK** and **T. W. CALVERT.** *Carnegie-Mellon Univ., Pittsburgh, PA.*

**60.6** A step in the analysis of retinal circuitry by means of extensive three-dimensional reconstructions from electron micrographs of serial sections. **F. S. SJOSTRAND.** *Univ. of California, Los Angeles, CA.*

**60.7** Evidence against a strong relationship between dendritic tree patterning and differences in physiology. **R. W. WEST** and **J. E. DOWLING.** *Harvard Univ., Cambridge, MA.*

## WORKSHOP

### 61. Unit Discharge, Slow Potentials and Sleep

3:15 PM—*Embassy Room*

*Chairman:* **B. L. JACOBS**

**61.1** Hippocampal neural activity: regional differences in sleep and waking. **P. J. BEST.** *Univ. of Virginia, Charlottesville, VA.*

**61.2** Septal unit responses to hippocampal stimulation. **H. M. EDINGER, R. A. TROIANO** and **A. SIEGEL.** *Col. of Med. and Dent. of New Jersey and New Jersey Med. Sch., Newark, NJ.*

**61.3** The temporal relationships of brain stem and cortical unit activity to the eye movements of desynchronized sleep. **J. A. HOBSON, R. W. McCARLEY** and **R. T. PIVIK.** *Harvard Med. Sch., Boston, MA.*

**61.4** The neurochemical bases of ponto-geniculate-occipital cortex waves. **B. L. JACOBS, S. J. HENRIKSEN** and **W. C. DEMENT.** *Princeton Univ., Princeton, NJ, and Stanford Univ. Med. Sch., Stanford, CA.*

**61.5** Brain stem neurons: firing during repeated sleep–waking cycles. **R. W. McCARLEY, J. A. HOBSON** and **R. T. PIVIK.** *Harvard Med. Sch., Boston, MA.*

**61.6** Continuous Markov processes modelling single neuron's activity. **L. M. RICCIARDI.** *Univ. of Chicago, Chicago, IL.*

# WORKSHOP

## 62. Cerebellar Function

3:15 PM—*Azalea Room*

*Chairman:* **R. R. LLINAS**

**62.1** Role of cerebro-ponto-cerebellar and cerebro-reticulo-cerebellar pathways in the early mossy fiber response. **G. I. ALLEN, G. B. AZZENA** and **T. OHNO**. *State Univ. of New York at Buffalo, Buffalo, NY.*

**62.2** Behavioral, electrophysiological, and ultrastructural effects of cooling on the goldfish cerebellum. **N. KOTCHABHAKDI** and **C. L. PROSSER**. *Univ. of Illinois, Urbana, IL.*

**62.3** Rhythmic activation of the cerebellar climbing fiber input by harmaline. **Y. LAMARRE** and **C. de MONTIGNY**. *Univ. of Montreal, Montreal, Que., Canada.*

**62.4** Cerebello-hippocampo-cerebellar interrelationships. **J. MITRA** and **R. S. SNIDER**. *Univ. of Rochester Med. Ctr., Rochester, NY.*

**62.5** Synaptic currents produced in cerebellar cortex by proprioceptive inputs. **J. T. MURPHY** and **H. KWAN**. *Univ. of Toronto, Toronto, Ont., Canada.*

# WORKSHOP

## 63. Chemical Senses II: Taste

3:15 PM—*Columbia Room*

*Chairman:* **J. C. BOUDREAU**

**63.1** Taste of water: neural recordings from rat, hamster, cat and squirrel monkey. **L. M. BARTOSHUK** and **M. K. FRANK.** *John B. Pierce Fndn. Lab., New Haven, CT, and Rockefeller Univ., New York, NY.*

**63.2** Classification of cat geniculate ganglion tongue units. **J. C. BOUDREAU** and **N. ALEV.** *VA Hosp., Pittsburgh, PA.*

**63.3** A solution to the problem of cerebral cortical localization of taste in the cat. **P. J. HAND, A. R. MORRISON** and **M. I. RUDERMAN.** *Univ. of Pennsylvania Sch. of Vet. Med., Philadelphia, PA.*

**63.4** Stimulus-dependent modification of taste cell membrane potentials by electrical stimulation of sensory nerve fibers. **F. A. KUTYNA** and **R. A. BERNARD.** *Michigan State Univ., East Lansing, MI.*

**63.5** Taste bud innervation and lateral interactions. **I. J. MILLER, JR.** *Bowman Gray Sch. of Med. of Wake Forest Univ., Winston-Salem, NC.*

**63.6** Survival and trophic function of neurons in homografts of Ag-B histocompatible rats. **A. A. ZALEWSKI.** *NIH, Bethesda, MD.*

## WORKSHOP

## 64. Thermal Sensitivity

3:15 PM—*Belvedere Room*

*Chairman:* **J. STEVENS**

**64.1** Thermosensitivity of the medulla oblongata: influence on thermoregulatory behavior and body temperature. **J. M. LIPTON.** *Univ. of Texas Southwestern Med. Sch., Dallas, TX.*

**64.2** Temporal summation in the warmth sense. **L. E. MARKS.** *John B. Pierce Fndn. Lab. and Yale Univ., New Haven, CT.*

**64.3** Spatial summation in the warmth sense. **J. C. STEVENS.** *John B. Pierce Fndn. Lab. and Yale Univ., New Haven, CT.*

**64.4** Response to heat of vibration-sensitive mechanoreceptors. **I. WEXLER** and **R. F. MAYER.** *Univ. of Maryland Hosp. Sch. of Med., Baltimore, MD.*

## Extended Discussion Groups

4:15 PM—*Emerald Room*

Authors of volunteer papers presented in 1:00 PM sessions will be available for informal discussion.

## ANNOUNCEMENT

The Society for Neuroscience is pleased to announce the funding of a Traveling Lectureship Program by the Grass Foundation of Quincy, Massachusetts. The program, to begin in early 1973, will send speakers on pre-arranged tours to those chapters of the Society that wish to be included in the program.

We would like to take this opportunity to express publicly our gratitude to the Grass Foundation for their generous support.

# ABSTRACTS

**1.1** AN INDEPENDENT STUDY PROGRAM IN NEUROSCIENCE WITH COMPUTER ASSISTANCE
Gary Wise, Robert Beran*, James Burkholder*. Ohio State University, College of Medicine, Columbus, Ohio 43210

An independent study program for pre-clerkship medical education has been developed by the OSU College of Medicine. Comparisons between this program and the lecture-oriented curriculum are being made. Many of the features of this program can be adapted for undergraduate, graduate, and post-graduate neuroscience studies. This neuroscience curriculum has been designed by both basic scientists and clinical neurologists. Study objectives and assignments are provided. Videotape patient demonstrations and neuroanatomical prosections are provided for clinical-anatomical-pathologic correlations. The student progresses at his own rate. Self-evaluation is then accomplished by a computer test. The computer programming flexibility provides a student-computer dialogue with either immediate feedback to the student answers or additional questions which develop an approach to the problem. The computer gives study prescriptions in the weak areas identified. Faculty tutorial assistance is available after additional study. Conventional written and oral tests are then given for certification. It is hoped that the development of skills and attitudes necessary for self-education will be beneficial for the student's continued professional development. The curriculum is easy to evaluate, easy to change, and can be utilized in developing schools at a low cost. Adaptations of this program should have special importance in the education of both superior students and students with a less-than-ideal background since each can progress at his own rate.

**1.2** SPLIT-BRAIN CATS PREPARED BY RADIATION. C. T. Gaffey and V. J. Montoya*
Donner Lab., Lawrence Berkeley Lab., Univ. Calif., Berkeley, Calif. 94720

Interhemispheric transfer of information between hemispheres occurs via commissural nerve fibers. Interruption of commissural transmission produces an organism that performs as if it had two separate brains. These "split-brain" animals are uniquely useful in CNS research. We have attempted to produce split-brain cats by a radiation procedure that appears rewarding in comparison to surgery.

The technique consists in passing a narrow beam of focused, cyclotron radiation (910 MeV helium ions) along the interhemispheric fissure. Only the volume of brain tissue along the midsaggital plane intercepts high-energy radiation. The non-scattering property of this radiation is of special advantage.

The efficiency of radiation in blocking interhemispheric transmission was tested using electrophysiologic criteria. The corpus callosum (CC) on either side of the interhemispheric fissure was chronically implanted with stimulating and recording electrodes. Action potentials initiated in one hemisphere were detected in the contralateral hemisphere. The dose-time relationship to block electrically-evoked transcallosal action potentials was determined, as well as the effectiveness of various sizes of radiation beams. The genu, body, splenium of the CC, or combination of these, could be selectively blocked. Surgical bisection of the CC frequently caused irrepairable damage along the brain's medial surface due to retraction of one hemisphere. Radiation treatment involved no retraction, or threat of brain infection. The gradual adaptation of the CNS to suppression of interhemispheric transmission also appeared advantageous.

This work was supported by the U.S. Atomic Energy Commission and the National Aeronautic and Space Administration.

**1.3** RESPONSES OF TECTAL UNITS TO INFRARED STIMULI IN RATTLESNAKES. Peter H. Hartline. Dept. of Neurosciences, Univ. of Calif. San Diego, La Jolla, Calif. 92037

Receptive fields of infrared sensitive tectal units have been mapped in blindfolded, anesthetized pit vipers (Crotalidae). Objects warmer or cooler than background were introduced or moved within the receptive cones of the facial pits at a distance of 30 cm. Responses were recorded as a function of object position and motion. Most units had central areas 10°-30° in diameter, in which introduction of a warm object or removal of a cold object caused a phasic or phasic-tonic response. The phasic component gave a strong impression of motion sensitivity. Introduction of a cold object into the center caused inhibition of the irregular background firing, as did removal of a warm object. The size of receptive field center is unexpectedly small, since primary units have fields with diameters of 45°-90°. There are some units which show an opposing surround, where introduction of a warm object suppresses background activity and introduction of a cold object evokes a weak response. There is a spatiotopic mapping relating receptive field location to position of the electrode on the tectal surface. More rostral receptive fields are represented rostrally and laterally; more ventral fields are represented caudally and laterally, (contralateral mapping).

The crotalid pit organ does not form a point image on the sensory epithelium of each point source of infrared radiation (as the eye does for light). This study suggests that by processing information about the shadows of the pit borders, the snake's central nervous system is able to reconstruct such an "image", albeit one of low resolution.

**1.4** EFFECTS OF INTOXICATING DOSES OF ETHANOL UPON INTERMEDIARY METABOLITE CONTENT OF RAT BRAIN. R. L. Veech*, D. Veloso* and J. V. Passonneau* (SPON:Philip G. Nelson). NIMH, St. Elizabeths Hospital, Washington, D. C. 20032 and NINDS, Bethesda, Md. 20014.

Acute intoxication of 72 hr starved, 400g, male Sprague-Dawley rats was produced 6 minutes after intraperitoneal injection of ethanol (3.5ml of 7 M in 0.15 M NaCl). In a second group of rats intoxication was prolonged for 13 hours by repeated ethanol injections. Intoxication was judged by loss of righting reflex. The brain substance between the osmic bulbs and the superior colliculus was removed and frozen within a second using a new rapid brain freezing apparatus which minimizes anoxic changes. A number of intermediary metabolites were then measured by standard enzymatic analysis. Arterial $pCO_2$ and pH were measured under similar conditions. The results of metabolite assays showed that acute ethanol intoxication is associated with increased concentrations of glucose, glucose-6 P and citrate. Prolonged intoxication was associated with elevation of brain glycogen, glucose, glucose-6 P, and decreased concentrations of pyruvate, lactate, malate, α-ketoglutarate, glutamate and aspartate. It is concluded that the early changes in metabolite concentration following ethanol intoxication result from a primary alteration of nerve cell membrane, not from interference with the cells energy producing mechanisms. Changes after prolonged intoxication result from an elevation of arterial $pCO_2$ acting in conjunction with a remarkably constant redox and phosphorylation state to produce changes in metabolite concentration. There is no evidence that metabolism of ethanol by brain alcohol dehydrogenase plays a physiologically significant role in either short or long-term alcohol intoxication.

**1.5** THE GOLDFISH AS A PHARMACOLOGICAL AND BIOBEHAVIORAL TOOL: A WET DEMONSTRATION WITH ILLUSTRATIVE DATA.
F. Petty, R. C. Bryant, N. N. Santos, L. A. Kepner and W. L. Byrne. Brain Research Institute, Univ. of Tenn. Med. Units, Memphis 38103.

In this demonstration session with live goldfish, ethanol and d-amphetamine are used in performing techniques of drug administration by intra-cranial injection and incubation. Intra-cranial injection and incubation are two routes of administration that are somewhat peculiar to fish; when used properly, they provide specific advantages in the investigation of certain problems. Evans blue is used to demonstrate spread and penetration of injectant. A simple modification and improvement of the intra-cranial injection technique is presented. Data are described implicating state-dependent effects on learning with ethanol but not with d-amphetamine. In recognition of the increasing use of goldfish by laboratories interested in various areas of neuroscience, we describe several factors pertinent to their routine use. Data relating intra-cranial injection volume and behavioral disturbances, neurological abnormalities, and mortality are presented. Data are presented on the effect of room light level with respect to dark-avoidance and light-avoidance learning in fish; on the effect of oxygen tension and home-tank density on activity and spontaneous light avoidance; on feeding in relation to general activity and health; on the relative difficulty of light- and dark-avoidance learning in fish; and on the spontaneous increase in shuttle response (characteristic of goldfish) which mimics a "learning curve." THIS WILL BE A LIVE "HANDS ON" DEMONSTRATION OF BASIC TECHNIQUES.

**1.6** POSSIBLE MOLECULAR CODING FOR A LEARNED MOTOR ADAPTATION IN THE GOLDFISH.
J. A. Heltzel, R. A. King* and G. Ungar. Baylor Coll. of Med., Houston, Texas 77025.

Goldfish (Carassius auratus) were trained to adapt their swimming to the conditions created by a float made of polystyrene foam attached by an elastic thread to their ventral surface close to the first pair of lateral fins (Shashoua, Nature, 217, 238, 1968). The float must be of such size as to assure sufficient buoyancy to pull the fish toward the surface of the water but not make it impossible for the fish to overcome the difficulty and eventually swim normally. The adaptation was learned by most fish in 3 to 4 hours but the float was left on for four days. A brain extract, a crude RNA preparation (according to Ungar et al., Nature, in press), taken from the trained donors was injected intracranially into groups of recipient fish at a dose equivalent to 80 mg of wet weight of brain. Control fish were injected with the same dose of an identically prepared extract from untrained donors. Twenty-four hours after the injection, the fish were provided with a float and observed for swimming behavior. The results, expressed in terms of the time (min $\pm$ S.D.) necessary to swim horizontally in the correct upward position without visible effort, were as follows: controls 200 $\pm$ 33 ($N = 35$); experimentals 138 $\pm$ 38 ($N = 36$). The difference was significant to $p < .001$ (t-test). After dialysis of the crude RNA at pH 3.7, the diffusible fraction contained all the activity (136 $\pm$ 32; $N = 28$). Incubation of the extract with proteases showed that the behavioral activity was abolished by trypsin but not by chymotrypsin. Preliminary results with gel filtration on Sephadex G-25 suggest a peptide of about 20 amino acid residues. Material is being accumulated for isolation and identification of the active substance. (Supported by HEW grant No. OEG-0-72-0699.)

**1.7** SYMPATHETIC INTERNEURONS IN ORGANOTYPICALLY CULTURED GANGLIA. Helena H. Benitez and Margaret R. Murray. Dept. Surg., P and S., Columbia Univ., New York City, 10032

In living, long-term cultures of newborn rat stellate and superior cervical ganglia, groups of small cells believed to be interneurons can be identified with the light microscope in many ganglia, as they develop against a background of adjacent principal neurons. These distinctive cell groups fulfil in general the criteria put forward by Matthews and Raisman (J. Anat. 105, 1969) and by Williams and Paley (Brain Res. 15, 1969) for cells of the rat superior cervical ganglion which these authors and others designate "interneurons".

Observations by scanning and conventional electron microscopy as well as by fluorescence histochemistry further confirm this relationship, with regard to size, arrangement, fine structure and other cytological properties of the neuron groups identifiable in the living state.

Supported by H.E.W. Grant No. 2 R01 NS00858.

**1.8** SYNAPTIC AND NEURONAL ADJUSTMENT TO THE COMPLEXITY OF THE REARING ENVIRONMENT. William T. Greenough, T. Blaise Fleischmann, Fred R. Volkmar*, Dept. Psychol., Univ. Illinois, Champaign, 61820, and Roger W. West, Biological Laboratories, Harvard Univ., Cambridge, Mass. 02138.

Following original findings that the post-synaptic thickenings of asymmetric round-vesicle synapses are longer, on average, in some occipital cortical layers of rats reared in "enriched" environments than in littermates reared in isolation, detailed examination with light and electron microscopy has revealed:

1. A reliable tendency towards increased numbers of synapses with gaps or "holes" in the post-synaptic thickening following social or enriched rearing;
2. No reliable differences in the number of synapses in which a portion of the post-synaptic spine intrudes into, or invaginates, the presynaptic bouton;
3. No effect of differential housing on post-synaptic thickenings in layer 3 of occipital cortex when the environmental treatment began at 90 days of age (this contrasts with reported differences in cortical weight and may indicate a critical period for the synaptic alterations);
4. Significant and large differences in the pattern of dendritic branching in occipital cortex, as seen in Golgi-stained sections, depending upon the complexity of the rearing environment.

These findings, and others to be discussed, provide further evidence for regulation of neuronal maturation by "use", in terms of the amount of stimulation provided by the rearing environment.

**1.9** CELL DYNAMICS IN THE OLFACTORY MUCOSA OF VERTEBRATES. P. P. C. Graziadei, J. F. Metcalf* and R. S. DeHan*. Dept. Biological Science, Unit I, Florida State University, Tallahassee, Florida 32306.

The modalities of neuronal turnover in the olfactory neuro-epithelium of various vertebrates, including mammals, is presently under investigation. It has been shown, by means of autoradiographic techniques at the light (LM) and electron microscope (TEM) levels, that olfactory receptor neurons undergo turnover in adult frogs (Graziadei & Metcalf, Z. Zell. 116: 305-18, 1971). The basal cells of the olfactory epithelium serve as a source of new olfactory neurons, replacing those lost by degeneration. When the olfactory nerve of the frog is sectioned, all of the mature olfactory receptors and the fila olfactoria degenerated within one to two weeks. There are no obvious morphological changes (TEM) in the supporting cells as a result of nerve section. The basal cells undergo active cell division, as evidenced by the appearance of numerous mitotic figures. Subsequently, the rate of cell division decreases and new olfactory neurons complete with olfactory rod, vesicle and cilia differentiate from the former basal cells. The centripetal growth of new axons following nerve section has been demonstrated in the dove, and the possibility of the re-establishment of synaptic contacts in the glomeruli of the olfactory bulb is being investigated. Following olfactory bulb ablation in the gerbil, all of the olfactory neurons degenerated within one week, leaving the supporting and basal cells intact. Further studies of the turnover, degeneration and regeneration of olfactory neurons in these animals is presently underway. The role of the supporting cells in elimination of degenerating olfactory neurons, and the presume survival of 50% of the olfactory neurons following ablation of the bulb (LeGros Clark, Proc. Roy. Soc. B 146: 299-319, 1957) is not confirmed by present observations. (USPHS NS 08943)

**1.10** SPECIES DIFFERENCES IN THE SYNAPTIC ORGANIZATION OF THE VERTEBRATE OLFACTORY GLOMERULUS. Edward L. White* (SPON: M. Henkart). Lab. of Neuropathology and Neuroanatomical Sciences, NIH, Bethesda, Md. 20014.

A previous study of the mouse olfactory glomerulus in serial thin sections (White, '72) showed that presumed mitral and tufted cell dendrites are postsynaptic to afferent axons, while dendrites thought to arise from periglomerular cells are not. These findings imply that the activity of mouse periglomerular cells is not affected directly by input from the olfactory receptors. In contrast, Pinching ('71) concluded that in the rat periglomerular cell dendrites are postsynaptic to afferent axons. The results of the present study of the rat olfactory glomerulus have confirmed that periglomerular cell dendrites are postsynaptic to afferent axons; however, our preliminary findings suggest that these axo-dendritic synapses may be infrequent. In addition, reciprocal synapses between periglomerular cell dendrites and mitral and tufted cell dendrites are more frequent in the rat than in the mouse. These findings indicate that the synaptic organization, and hence the processing of olfactory information, may be different even in closely related vertebrates. Studies are in progress to determine the types and frequencies of glomerular synapses in other species, specifically those commonly used in physiological investigations of the olfactory system. (Supported by NIH postdoctoral fellowship 1 F2 NS 53, 124-01 NSRA)

1.11 A METHOD FOR TRACING THE MATURATION OF NERVOUS PATHWAYS. Christiana Morison Leonard. Rockefeller Univ., New York, N.Y. 10021

Golden hamsters are born after only 16 days gestation. Although many neurones in the forebrain are then still in the migratory phase, the mid and hind brain are mature enough to permit the animals' independent existence. On the day of birth, the hamster can perform a directed locomotor response. This response is impaired by tectal but not forebrain lesions. When tectal-lesioned brains are stained with the Fink-Heimer technique, degenerating fibers are seen in the tectobulbar tracts. By contrast, after large (but behaviorally ineffective) forebrain lesions, no degenerating fibers can be seen in the corticofugal pathways (1-4 days survival). Further experiments of this type suggest that the onset of visible degeneration argyrophilia may be a reliable indicator of the acquisition of behavioral function by nervous pathways. Evaluation of neonatal brain lesions using combined behavioral and degeneration techniques should prove useful for correlating structural and functional changes in development.

Supported by grant NS08902 from USPHS to Carl Pfaffmann and NIH Training Grant GM1789 from USPHS to Rockefeller University.

1.12 DMSO IN THE TREATMENT OF EXPERIMENTAL HEAD AND SPINAL CORD INJURIES. J.C. de la Torre, K. Kajihara*, H.M. Kawanaga*, D.W. Rowed*, and J.F. Mullan*. University of Chicago, Pritzker School of Medicine, Chicago, Illinois 60637.

The role of the structural and functional aspects of the cell membrane in head injury has been the object of much investigation in this laboratory. Neuropharmacological data on the blood-brain barrier indicated some activity of the drug dimethyl sulfoxide (DMSO) at the membrane level.

The present study demonstrates that DMSO when compared to urea can modify the survival rate in monkeys subjected to experimental head injury and to accelerate the recovery of function in dogs following spinal cord compression.

Ten control monkeys died after reaching a critical end point (E.P.) subsequent to balloon compression of the brain. Ten of 15 monkeys receiving urea at E.P. survived; three animals showed various neurological deficits. Fourteen of 15 DMSO-treated monkeys survived, only one had a transient right arm paresis. Ten control dogs subjected to spinal cord compression suffered flaccid paraplegia. Ten dogs treated with DMSO could maintain the erect posture 24 hours after injury and regained a spastic walking ability by day 16. Treatment of 10 dogs by urea or dexamethasone also accelerated the return of function following spinal cord injury but to a lesser extent when compared to DMSO (film).

**1.13** COMPUTER ANALYSIS OF GOLGI IMPREGNATED NEURONS. T. A. Woolsey, D. F. Wann*, W. M. Cowan, M. L. Dierker* and C. M. Shinn*. Depts. Anat. and Elec. Engr., Washington Univ., St. Louis, Mo. 63110

Rapid and accurate measurements of neuronal processes in Golgi preparations are possible with the aid of a small computer (Glaser & Van der Loos 1965). We have recently developed a system for doing this using a PDP-12 computer which controls stepping motors (0.5μ steps) attached to the stage (x,y axes) and fine focus (z axis) of a Zeiss microscope. The observer tracks the processes, and topological information, such as the location of the soma, dendritic origins, branch points and ends of processes, are signaled to the computer by special controls and the x,y and z coordinates of each are stored in digital format. The computer print-out yields: (a) individual x, y and z coordinates with associated topological identifiers; (b) quantitative data for each dendritic segment in order (i.e., primary, secondary branches, etc.); and (c) computes the actual linear dimensions of each segment in microns. An associated oscilloscope display can: (a) display the whole neuron, or individual processes, by connecting recorded points by vectors; (b) identify each dendrite; (c) rotate (continuously or by a specified angle) the whole cell, or individual dendrites, around any selected point or axis; and (d) indicate spatial relationships by dynamic rotation, intensity modulation or stereo pairs. Following a software correction, for mechanical backlash, deviations in length of less than 3% were obtained when several observers traced the same dendrites. Descriptions of the system hardware and software will be presented and its performance illustrated by print-outs and computer generated movies of neocortical stellate and pyramidal cells and a cerebellar Purkinje cell. The system thus permits the rapid accumulation of detailed quantitative data about the processes of neurons and their graphic reconstruction and display. (Supported by Contract NIH-NEI-71-2289 and NIH Grant 1 RO1 NS 10244-01.)

**1.14** EXPERIMENTAL TESTS OF A MODEL SYSTEM ACCOUNTING FOR POTASSIUM ACCUMULATION IN THE PERIAXONAL SPACE. W. J. Adelman, Jr., Y. Palti* and J. P. Senft*. Laboratory of Biophysics, NINDS, NIH, Bethesda, Md. 20014; Dept. Physiol., Sch. Med., U. of Md., Baltimore, Md. 21201; The Technion Med. Sch., Haifa, Israel; and Rutgers Univ., New Brunswick, N.J. 08903.

In voltage clamping squid giant axons, current flows outward through the potassium conductance, $g_K$, upon membrane depolarization to $E_1$. This current was isolated by using TTX which blocks the initial transient (sodium) current. Upon stepping the membrane potential from $E_1$ to a more polarized value ($E_2$), $g_K$ turns off and a decaying tail current flows. The initial value of this tail is determined by the product of $g_K$ just before repolarizing and the difference between the membrane potential after the step ($E_2$) and the value of the potassium reversal potential ($E_K$). In agreement with Frankenhaeuser and Hodgkin (1956), tail currents following very short depolarizing pulses were outward; following longer depolarizing pulses these were inward having reversed at some finite pulse duration. As any $E_1$ pulse was constant in amplitude, it was concluded that $E_K$ is a function of the duration of $E_1$. By taking many $E_1$ values, it was shown that $E_K$ is a function of the amplitude of $E_1$. The kinetics of $E_K$ changes were related to the time course of $I_K$. These $E_K$ changes were modeled by assuming an imbalance between membrane and external barrier ionic fluxes resulting in periaxonal K accumulation. The external diffusion barrier assumption was tested by exposing axons to hypertonic or hypotonic solutions to shrink or swell the Schwann cells and the giant axon. In accord with model predictions, periaxonal K accumulation was altered in the right direction and magnitude. Modifications in the Hodgkin and Huxley equations were made incorporating the model system. The role of perineuronal space in modifying CNS neuron behavior is compared with that of periaxonal space. (Supported in part by USPHS grant NS 04601 to the U. of Md.)

**1.15** ALUMINA IN EXPERIMENTAL CORTICAL EPILEPTIC LESIONS, HISTOCHEMISTRY AND ULTRASTRUCTURE. A. Basil Harris. Dept. Neurosurg., Sch. Med., U. Wash., Seattle, Wash. 98195

Aluminum hydroxide gel, alumina, sensorimotor intracortical injections cause clinical recurrent convulsions in monkeys. Pure crystals and their reactions with serum and the products of brain cellular injury from injection at acute, intermediate and chronic phases are studied to examine the mechanisms of action of this compound. Aluminum histochemistry depends upon formation of bright red aurine lakes for identification. Positive histochemical reactions occur in granuloma, perivascular encrustaceons, and glia but not in neurons. Moderate electron density alumina crystals, ~15 Å wide and 500 Å long, are enhanced in opacity by tenaciously adhered proteins which become visible after fixation by osmium and staining with uranyl and lead. Ultrastructurally, phagocytosis of crystals is first seen in monocytic macrophages and later in fibroblasts, pericytes and astrocytes but not in polymorphonuclear leucocytes or neurons. Endocytosed alumina phagosomes, joined by lysosomes and autophagosomes, are dense bodies and complex cytosegresomes. Many crystals are sequestered in membrane bound vacuoles but some appear in cytoplasm associated with fibrils and microtubules. Phagocytes are not injured by ingested alumina, as they are by silicon, but continue to form new cytosegresomes and secondary lysosomes containing crystals in chronic animals with seizures. Although alumina crystals are protected from dilute acids by protein coatings, intracellular digestive processes may cause crystal degradation into soluble compounds which inflict sublethal injury. Neurofibrillary changes are not present, as with some soluble aluminum salts, but increased fibrils are present in macrophages and prominent fibrils are in astrocytes. This may indicate local or intracellular slow soluble compound formation. Supported by PHS Grant 11-8244.

**1.16** UPTAKE CHARACTERISTICS OF $H^3$-GABA IN STRUCTURES OF THE BASAL GANGLIA BY ELECTRON MICROSCOPIC RADIOAUTOGRAPHY. T. Hattori* and P.L. McGeer. Kinsmen Laboratory, University of British Columbia, Vancouver, Canada.

An electron microscopic study employing the combined techniques of serial ultra thin sections and $H^3$-GABA radioautography has been carried out to investigate the characteristics of GABA uptake in various structures of the basal ganglia. In the substantia nigra, 72% of all silver grains from radioautographic exposure were located over pre-synaptic terminal boutons, 13% were over dendritic structures and the remainder were over other elements such as glial cells and myelinated or unmyelinated axons. In the globus pallidus only 34% of the grains were over boutons, while 43% were over the cell soma and 10% were over dendrites. In the caudate nucleus, 56% were over boutons, 24% were over the cell soma and 6% were over dendrites. The nerve endings in the substantia nigra, globus pallidus and caudate which took up the $H^3$-GABA were characterised by dark type mitochondria. They also contained pleomorphic vesicles ranging in size from 200-1200 A, some of which were granulated. Serial sections of the substantia nigra showed that all nerve endings contained large granulated vesicles. However, only about 10% of the boutons in the caudate nucleus contained such vesicles. The high preference of GABA uptake for terminals in the substantia nigra is consistent with biochemical evidence suggesting a descending gabaminergic pathway to the substantia nigra (McGeer & Fibiger, Abstract). (Supported by a grant from the Medical Research Council of Canada, MA-4013).

**1.17** OPTIC TRACT REGENERATION IN THE ADULT RAT. Anne F. Marks* (SPON: William B. Marks). Johns Hopkins Univ., Baltimore, Md. 21218.

A cut through the brain was made with the 1.0-1.5mm crossbar of a U-shaped loop of paraffin-coated 89μ wire with squared corners. Its parallel arms were used to push the loop from the top of the cortex to the floor of the skull. The cut was marked by leaving the wire in the living brain. After sacrifice, the ventral skull was removed and the brain was impregnated by the Ranson pyridine silver method. After the pyridine step had dissolved the wire's paraffin coating, the loop's crossbar, visible at the ventral surface of the brain and protruding through the optic tract near the midline, was pulled out to remove its arms from the fixed tissue. The parallel holes remaining in the brain marked the boundaries of the cut. Paraffin sections were counterstained with Luxol Fast Blue and Nuclear Fast Red. In brains fixed at zero time, optic axons in the path of the crossbar had been cut except for a slight tract displacement around the arms of the loop. By 3 days the lateral two thirds of the cut contained axons oriented toward and around its boundaries. Retinofugal fibers showed terminal enlargements and rings oriented toward the middle third of the cut. By 18 days there was no such contingent of retinofugal fibers perpendicular to the middle of the cut: instead, an orderly interweaving pattern of axons approaching the cut became parallel to the middle of the cut, distributed around each end as gross accumulations of densely packed axons, and continued a straight retinofugal path within the optic tract. The appearance of this interweaving pattern, which could not have been formed by lateral drift of uncut fibers, after the disappearance of axons showing 'abortive regeneration', indicates rapid, path-specific axon regrowth around a small incision. Completely severed optic tracts, after 6 and 12 days, continue to exhibit terminal enlargements on fibers facing the entire cut. The rats weighed 400+g and were mature.

**1.18** REVERSIBLE CRYOGENIC BLOCKADE OF SUBCORTICAL BRAIN STRUCTURES. J. E. Skinner, Neurophysiol. Dept., Methodist Hosp., and Physiol. Dept., Baylor Coll. Med., Houston, Texas 77025

Cryoprobes for use in small animal brains will be demonstrated. A 5-minute video tape will be shown illustrating the behavioral and electrophysiological effects of cryogenic blockade in the mesencephalic reticular formation and nonspecific thalamocortical system, and the subsequent reversibility of these effects following the cessation of cooling. A combination cryo-heat probe will be demonstrated for use in human stereotaxic surgery. The reversibility of the functional blockade produced by the cooling allows the search for the optimum neural target before permanent heat lesions are created. A teflon-jacketed tip prevents coagulated tissue from sticking to the probe tip, a problem encountered in radio-frequency and electrolytic lesioning methods.

**1.19** THE USE OF PUSH-PULL PERFUSION TECHNIQUES TO EXAMINE CNS TRANSMITTER ACTIVITY IN SEVERAL SPECIES. R. D. Myers and M. B. Waller*. Lab. Neuropsych. Purdue Univ., Lafayette, In., 47907.

Until recently, the relative inaccessibility of many structures in the CNS has hindered the investigation of the turnover or release of a putative transmitter within the brain. Recently developed methods for microperfusion now provide the capability of examining, at discrete morphological sites, the resting levels of certain transmitter substances, as well as the enhancement or suppression of their release following a physiological change. The original push-pull cannula system devised by Fox and Hilton (J. Physiol. 142: 219-232, 1958) consisted of two parallel needles 1.5-2.0 cm apart which were used to perfuse subcutaneous tissue in the forearm. Although the technique has been developed further to study neural events, its application has been somewhat limited by the occurrence of tissue damage at the site of the perfusion. Our demonstration presents different types of push-pull cannulae used for the rat, cat and monkey as well as other advances in perfusion technology which minimize the incidence of expansion lesions. Morphological mapping of sites and pathways within the diencephalon and mesencephalon of the conscious monkey will be illustrated in terms of the evoked release of acetylcholine following peripheral heating or cooling. Included are other results on the use of the push-pull perfusion technique in order to maintain an imbalance in the ratio of sodium to calcium to alter the temperature "set-point" as well as other vital diencephalic functions.

**1.20** DEMONSTRATION OF OPERANT CONDITIONING OF 40HZ IN HUMANS. Daniel E. Sheer, Bruce Bird*, and Fred Newton*. Dept. Psych., University of Houston, Houston, 77004

The conditioning of EEG activity, particularly alpha, has now been clearly established. A low voltage, high frequency EEG rhythm with a narrow band centering at 40Hz presents considerable problems for conditioning from scalp leads in the human. In addition to the low voltage, the 40Hz frequency band also overlaps with muscle activity. Procedures have been developed for detecting 40Hz EEG, independent of muscle, as a reinforcement contigency. Recordings are made from both standard 10-20 EEG leads and neck and temporal muscles. These EEG and muscle recordings are sent through identical coincidence detector units. The units consist of 23% 40Hz and 70Hz filters, the outputs of which are integrated with adjustable time constants and threshold levels set with amplitude comparators. An anion gate circuit allows the 40Hz output to trigger a light reinforcement when it is not coincident with the 70Hz output, used as an index of the polyphasic muscle. For each subject, the time constants and threshold levels for the 40Hz and 70Hz are empirically determined to maximize the discrimination of the 40Hz independent of the 70Hz. As an additional control, the 40Hz output on the muscle leads are at a minimum at the same settings used on the EEG leads. Whenever the 40Hz outputs on the muscle leads come through coincident with the 40Hz EEG outputs, the contingency is set so that the reinforcement is not triggered. The demonstration will show the conditioning of 40Hz in subjects in 30 minute sessions where arousal state is maintained by using complex lighted slides as reinforcers. The instructions to the subjects are that the money they will be able to make in each session depends upon the number of slides they can accurately describe at the end of each session.

**4.1** HABITUATION AND SENSITIZATION OF INTERNEURON ACTIVITY IN THE RETICULAR FORMATION. M. Virginia Parker* and Philip M. Groves. Dept. Psych., Univ. Colo., Boulder, 80302

Activity of neurons in the mesencephalic-pontine reticular formation of locally anesthetized rats was recorded using extracellular tungsten microelectrodes. Sensory responsiveness and the effects of repeated peripheral stimulation were noted. Response decrement (habituation) and response increment (sensitization) occurred reliably in reticular elements. Parameters of these labile processes were similar to those of behavioral lability in intact animals. Polysensory units (cells responsive to more than one sensory stimulus--light flash, auditory click, foot shock) often showed different forms of plasticity to repetition for different modalities. Habituation did not transfer across modalities for polysensory cells, but habituation to one modality could be dishabituated by another. Although the response to a repeated dishabituation stimulus remained constant, its effect on the response to the habituation stimulus showed marked decrement as a result of repetition. These results strengthen the notion that behavioral habituation may be in part mediated by the reticular formation of the brain stem and that this process may result from the effects of both increments and decrements in cellular activity.

Supported by Grant MH 19515 from NIMH.

**4.2** Comparison of Unit Response Decrements in the Cochlear Nucleus of Decerebrate and Intact Paralyzed Cats during Repeated Acoustic Stimulation. J. Buchwald, G. Humphrey* and D. Regan*. Departments of Physiology and Psychiatry, University of California, Los Angeles, California.

Monaural acoustic stimuli presented repeatedly at 5 sec intervals to the mid-collicular-decerebrate, paralyzed cat resulted in a progressive decrement of cochlear nucleus (CN) unit responses. Regardless of whether the initial response was accelerated discharge or an inhibition of discharge (as occurred in the dorsal cochlear nucleus with contralateral tone presentations), the initial response decremented 10 to 45% in all 21 CN preparations studied. Concurrent recordings of the round window microphonic potential (an index of receptor discharge) showed no significant change. Recovery of response to pre-stimulus levels spontaneously occurred after approximately 10 min of rest; only a slight, transient reversal of the response decrement was induced by somatic stimulation of the paw. In contrast to these data, the responses recorded from the cochlear nucleus of intact paralyzed cats showed smaller and more erratic decrements to a similar habituation procedure with significant decrements ranging from 6 to 15% of the initial response level. Moreover, paw stimulation induced a rather marked reversal of the decremented response. In neither preparation was the decremental phenomenon blocked with strychnine. These data suggest that response decrements in the cochlear nucleus do not reflect incrementing inhibition mediated by higher levels, but rather a local loss of excitation, in accord with the synaptic depression hypothesis of habituation. Based on current data, an indirect excitatory influence of the reticular activating system on the cochlear nucleus is proposed; in the absence of this excitation, synaptic depression in the CN is enhanced. (Supported by USPHS Grants NB 05427 and GM00448).

**4.3** UNIT RESPONSES IN THE AUDITORY SYSTEM AND POSTERIOR THALAMUS OF RAT DURING CLASSICAL CONDITIONING AND EXTINCTION. John F. Disterhoft. Div. of Biology, California Institute of Technology, Pasadena, Cal. 91109.

Previous mapping of chronically recorded unit changes in rat brain indicated that responses during classical conditioning, both in response latency from CS onset and in the trial sequence from the start of training, were focused in thalamic regions when compared to cortex (Disterhoft & Olds, J. Neurophysiol., in press; Olds et al., J. Neurophysiol., 1972, 35, 202-219). However, it was not possible to assign functional primacy within the thalamic regions on the basis of the available data except to note that responses were particularly numerous and large in posterior nucleus units. The purpose of the present work is to attempt to determine where, within thalamus, initial changes occur during classical conditioning. Also, since it is possible that conditioned changes occur in more peripheral regions of the auditory system, units in inferior colliculus are being examined. The paradigm being used involves pairing one of two tones ($CS^+$) with food. Another tone serves as the $CS^-$. Unit and behavioral responses to the tones during successive pseudoconditioning, conditioning and extinction periods are examined. The data gathered thus far indicates that functionally significant learned changes are seen in medial geniculate with a latency of 7.5 msec. and in posterior nucleus with a 12.5 msec. latency. Detectable but small changes have been seen in inferior colliculus with a latency of 4.5 msec. but their importance remains in doubt. Very interesting increases in firing have been detected in medial geniculate and posterior nucleus neurons after the beginning of extinction. This phenomenon has not been seen in inferior colliculus.

**4.4** EFFECTS OF PREDICTIBILITY ON NEURONAL RESPONSES TO FOOTSHOCK. Charles E. Olmstead* (SPON: P. J. Best). Dept. of Psychol., Univ. of Virginia, Charlottesville, Va. 22901

Single unit activity in the hippocampus and midbrain reticular formation (MRF) was recorded from chronically implanted electrodes (62.5u) in unrestrained rats during fixed (FI) or variable (VI) interval presentation of footshock (FS). The presentations were either tone signalled (SS) or unsignalled (USS). A highly significant number of units in both areas responded to FS with an increased rate of firing. In both areas, however, the duration of the increase was highly dependent upon the schedule of shock presentation with the order being FI-SS < FI-USS < VI-SS < VI-USS. An analysis of the schedule effects indicates that regularity of presentation (i.e., FI) has a more pervasive effect on the level of arousal seen than does the presence of a signal. In both areas only the FI groups showed significant decrements across the first twenty seconds following FS. This modulation of neural activity is consistent with that predicted by a safety signal interpretation of the effects of non-contingent FS and indicates that in addition to the dynamic arousal effects of the stimuli presented it is necessary to consider the non-specific arousal induced by the schedule of stimulus presentation.

**4.5** REWARDING AND AVERSIVE BRAIN STIMULATIONS HAVE OPPOSITE EFFECTS ON MEDIAL THALAMIC UNITS. James J. Keene* (SPON: K. L. Casey). University of Michigan, Ann Arbor, Mich. 48104

Medial thalamus receives fibers from both medial forebrain bundle (MFB) and hind- and midbrain reticular formation (RET). In unanesthetized cerveau isole and awake, unrestrained, behaving rats, over 250 units were recorded. MFB and RET effects converge on 66% of these units in the dorsal medial and paracentral nuclei of thalamus and are opposite in the following ways:

| | MFB stimulation | RET stimulation |
|---|---|---|
| 1. Post-stimulus pattern during 7 Hz stimulation | short latency excitation followed by inhibition | mixed effects followed by excitation |
| 2. Slow-wave recruiting during 7 Hz stimulation | yes | no |
| 3. Rates with 20 Hz compared to 7 Hz stimulation | decreased discharge | increased discharge |
| 4. Post-train (60 Hz,.2 sec) effects lasting seconds | decreased discharge | increased discharge |

Non-MFB and parafasicular sites do not elicit these responses to MFB and RET stimulation respectively. In the habenular and ventral basal nuclei, MFB stimulation does not elicit the excitation-inhibition post-stimulus (7 Hz) pattern or decreased firing with increased stimulus frequency. Threshold currents for opposite MFB and RET effects are similar to those eliciting self-stimulation and escape respectively in several chronic rats tested both behaviorally and neurophysiologically. These opposite neural responses in single units parallel the opposite behavioral and motivational properties of the brain stimuli and may play a role in integrating reward and pain mechanisms.

**4.6** TOPOGRAPHICAL DISTRIBUTION OF SLOW POTENTIAL CHANGES FROM MONKEY CORTEX. John J. Hablitz* and Robert P. Borda Neurophysiol. Dept., Methodist Hosp., and Physiol. Dept., Baylor Coll. Med., Houston, Texas 77025

The present study attempted to obtain information concerning the distribution of slow potential (SP) changes from monkey cortex in order to delineate the source and functional significance of these previously described potentials. Two modes of reinforcement were employed in separate groups of animals in an attempt to determine the relationship of SPs with behavior. Subjects with chronically implanted electrodes were trained to respond in order to either receive food reinforcement or avoid shock. A warning stimulus (click) was followed one second later by the imperative stimulus (1500 Hz tone, 500 msec duration); subjects were required to respond during the tone period by pressing a lever. Approximately 100 trials were given a day, five days a week, for a two-month period. Brain electrical activity was suitably amplified and recorded on magnetic tape for subsequent computer analysis. The most marked finding of the study was the demonstration of the existence of two independent SPs related to the conditioning task. A frontal dominant potential developed gradually with training, while the central dominant SP was of significant magnitude from the onset of training. Each SP was of equal magnitude bilaterally and persisted for the duration of the two-month testing period. Type of reinforcement was a significant variable in determining SP distribution.

**4.7** LEARNED BEHAVIOR: APPARENT ELIMINATION BY A CUT PARALLEL TO THE MEDIAN FOREBRAIN BUNDLE. Ernest W. Kent and S. P. Grossman. U. of Illinois at Chicago Circle, Chicago, Ill. 60680, and U. of Chicago, Chicago, Illinois, 60637.

A cut (made with a wire knife through an implanted needle) was made to separate the lateral hypothalamus from areas lateral to it. The cut occupies a vertical plane along the lateral border of the hypothalamus in the AP direction, extending from the base of the brain to the top of the hypothalamus. When properly placed (6 of 11 animals), the cut eliminates acquisition and/or retention of learned behaviors such as lever press to escape foot shock, step-down passive avoidance, lever pressing and straight alley running for rewarding brain stimulation, habituation of exploration in a novel environment, etc. Eating and drinking are also eliminated, but not lapping and swallowing of liquid diet placed in the mouth. Unlearned or stimulus-bound behaviors such as grooming, righting, exploration, climbing, negative phototropism, and thigmotaxis are unaffected. Slightly misplaced cuts (5 of 11 animals) produce varying degrees of partial decrement in performance of learned responses. In neither case is there any detectible deficit in motor ability ( balancing on a rotating rod, swimming, etc.), sensory detection thresholds ( flinch and jump to shock, orienting to light or sound), or general activity (jiggle cage). The underlying mechanism of the effect is not yet clear, and could include motivational deficits, failure of reinforcement, inability to inhibit competing responses, or other processes, as well as direct effects on learning or recall. Our animals were maintained for one month without signs of recovery of function.

**4.8** COMPONENTS OF THE INTRACRANIALLY REINFORCED BAR-PRESSING RESPONSE. Predrag Vrtunski. Laboratory of Neuropsychology, Cleveland Psychiatric Institute, Cleveland, Ohio 44109.

Twelve Holtzman rats were implanted with stimulating electrodes aimed at posterolateral hypothalamus. Animals were trained to bar-press for hypothalamic reinforcement for fifteen 10-minute daily sessions. Following the training period, tests included varying reinforcing stimulus intensities, threshold of bar-pressure, extinction and food deprivation conditions. Throughout the training and test sessions, an on-line computer (PDP-12) averaged the analog of the bar pressing response. In order to analyze observed changes, the average analog of the response was divided into four components. Those were initial depression of the bar, transition from the depression to release, release of the bar and initiation of the succeeding response. Duration of each component was measured in milliseconds and maximum force emission was measured in grams. Results indicated that response components may be differentially affected by test procedures, e.g., certain test conditions may increase duration of one component without affecting the others. Findings are discussed in terms of possible role of at least two feedback loops, one being defined by proprioceptive mechanisms involved in response emission and the other being defined by reinforcing stimulus occurrence.

**4.9** EFFECTS OF CAUDATE NUCLEUS STIMULATION ON REACTIVITY TO NOXIOUS ELECTROCUTANEOUS STIMULATION. Charles G. Lineberry and Charles J. Vierck, Jr. Center for Neurobiological Sciences and Dept. of Neuroscience, Univ. of Fla. Col. of Med., Gainesville, Fla. 32601.

Macaca speciosa monkeys were trained to escape repetitive, 10 msec trains of 200/sec pulses ranging in intensity from 4 to 40 mA. Each trial consisted of a maximum of 15 trains of leg stimulation presented at a rate of 1 per sec. The force exerted in terminating shock was an increasing function of stimulation intensity. On half the trials of each session, 50 msec trains of 200/sec pulses were delivered to the caudate nucleus at various intervals preceding each 10 msec train of cutaneous stimulation. Stimulation of the caudate nucleus reduced escape force maximally when a delay of 50 msec between brain and leg stimulation was used, indicating reduction of reactivity to painful input. Delays of 500 msec or greater were ineffective in reducing escape force, eliminating the possibility that the decrease in force observed with a 50 msec delay resulted from direct motor inhibition. Other response measures suggested that caudate stimulation produced a generalized calming that was independent of the delay between brain and leg stimulation.

**4.10** DIRECT CORTICAL CONDITIONING IN MACAQUES. R. L. Testerman, A. S. Wilson, A. Sances, Jr., and S. J. Larson. Medtronic, Inc. and V. A. Center, Wood, Wisconsin 53193.

Electrical stimuli delivered directly to several cortical areas were tested as substitutes for peripheral discriminative stimuli. Stumptail macaques were originally trained in a two-choice visual pattern situation for food reward. Flashing of one choice pattern identified it as the correct choice, whereas the absence of flash required selection of the other pattern for reward. Subsequently, cortical stimulation was paired with the flash cue and the flash was gradually faded. Correct responding was maintained by the cortical stimulation. Furthermore, both frontal and occipital cortex provided effective sites for conditioning. A titration procedure was used for threshold determination, revealing behavioral as well as electrical parameters to be important.

**5.1** THE FATE OF TRACER PROTEINS IN THE MATURING NERVOUS TISSUE. M. P. del Cerro and R. S. Snider. Center for Brain Research, Univ. of Rochester Medical Center, Rochester, N.Y. 14642

Ferritin and horseradish peroxidase were injected in the cerebellum of 7 day old rats and the animals sacrificed between 15 minutes and 24 hours afterwards. Control animals were injected with the same tracers i.v. or i.m. and the cerebellar cortices studied under the electron microscope. Regardless of the time elapsed, both tracers were simultaneously found at intra and extracellular locations, although there is a clear time-related increase into the intercellular compartment. Both molecules readily permeate intercellular gaps and synaptic clefts, and only the vascular and pial limiting membranes retain large amounts of either tracer. However, those membranes do not constitute a barrier since the proteins do cross them to become in contact with and be incorporated by pial and endothelial cells, and a few molecules even reach the vascular lumina. Germinal cells, young neurons and glia avidly incorporate both proteins in their somas. The uptake is carried out by coated and non-coated vesicles that open into the plasma membrane. Similar vesicles, devoid of tracer, are often seen in contact with Golgi cisternae; thus, it is conceivable that they could form in this organoid, migrate to the cell surface, and be retrieved taking pinocytized material to be discharged into lysosomes. Few synaptic terminals in the developing cortex incorporate tracer and even those in minimal amounts, indicating lack of pino and exo-cytosis at this level. Axonal and glial growth cones differ in their incorporation behavior--the first incorporate no tracer, while the latter show intense uptake. Comparison of the fate of exogenous proteins in the mature and developing nervous tissue offers a means of exploring their physiological differences. (Supported in part by Grant No. NS-06827-06)

**5.2** AMINO ACIDS IN THE DEVELOPING FETAL BRAIN. Jimmie M. Davis and Williamina A. Himwich. Galesburg State Research Hospital, Galesburg, Illinois 61401.

We have previously studied in several mammalian species the simultaneous biochemical changes and structural and functional alterations occurring during postnatal ontogenesis. This report describes the continuation of our efforts to establish in detail the biochemical patterns present during the full spectrum of development. For the prenatal phase of our investigations we have chosen the rat, dog, cat and guinea pig. The pregnancies of the mothers were carefully controlled to eliminate large discrepancies in the estimations of the actual age of the fetus. The body and brain weights, crown-rump measurements, water content and levels of free amino acids in whole brain will be reported. Due to their unique role in intermediary metabolism and their neurotransmitting capabilities, special consideration will be given to glutamic and aspartic acids, GABA, glutamine and glycine. Prenatal levels of these amino acids exhibit varying patterns of changes which occur at different interspecies ages during ontogeny. The biochemical values observed during these periods will therefore be viewed on an age-equivalent basis for the various species. In the guinea pig, whose brain develops the most rapidly of the species studied, a correlation of the changes in the amino acid levels of the postnatal brain with the physiological and functional maturation of the central nervous system will be attempted.

**5.3** CHANGING RELATIONSHIPS OF MITOTIC SCHWANN CELLS TO AXONS IN NEWBORN RAT SCIATIC NERVE. John R. Martin* and Henry deF. Webster. Lab. Neuropath. Neuroanat. Sci., NINDS, NIH, Bethesda, Md. 20014

Schwann cells divide rapidly as they surround bundles of axons and segregate those destined to become myelinated (Asbury, 1967). In order to study the shape of mitotic Schwann cells and their axon relationships, three dimensional reconstructions were prepared from electron micrographs of transversely and longitudinally sectioned sciatic nerves of newborn rats. Sheet-like processes of interphase Schwann cells surrounded bundles of axons and segregated others in individual cytoplasmic furrows. Schwann cells in prophase had smaller processes that enveloped fewer axons; they were spindle shaped in metaphase and neighboring Schwann cells surrounded all of the adjacent axons. In telophase, thin processes reappeared and enlarged rapidly to reclaim nearby axons. The retraction and re-extension of Schwann cell processes that occurs during mitosis may facilitate surface interaction with axons during a sorting process that remains poorly understood.

**5.4** NEUROEMBRYOLOGY OF THE BIOGENIC AMINE SYSTEMS OF THE MOUSE BRAIN. Gerald S. Golden. Montefiore Hospital, Bronx, N. Y. 10467.

The development of the biogenic amine containing neurons and nerve terminals in the fetal mouse was studied by the fluorescence histochemistry technique of Falck et al. (J. Histochem. Cytochem.10:347, 1962) Catecholamine and indolealkylamine containing cells are first visualized in the mesencephalon on the 13th gestational day. The catecholamine cells are predominantly dopaminergic and project to the striatum (Golden and Commede Broth, Abstract, Amer. Acad. Neurol 1972). Other catecholamine containing cells first appear in the locus coeruleus after the 16th fetal day. Only scattered catecholamine cells are seen elsewhere. The serotonergic cells of the raphe system rapidly develop in number, and form well organized groups during the remaining gestational period following their initial appearance on day 13. Scattered nerve terminals begin to appear by day 16, and at the end of gestation well defined terminals are present in the hypothalamus and other areas of the forebrain and in the brainstem. Nerve terminals first appear in the striatum on the 15th day, and by the 19th day, it is densely packed with discrete terminals. These findings of the extensive prenatal development of biogenic amine systems in an animal that is quite immature at birth support the concept that functional competence of these systems may be important to even the very immature animal. (Supported by The Grant Foundation.)

**5.5** QUANTITATIVE VARIATION OF BRAIN MASS BY PRENATAL AND POSTNATAL CHEMICAL TREATMENT. R. K. Haddad and Ausma Rabe*. Bureau of Research at the New Jersey Neuro-Psychiatric Institute, Princeton, N. J. 08540

Graded reduction of brain mass in otherwise normal rats was produced by exposing them on day 15 of gestation to a single intraperitoneal injection of the appropriate dose of methylazoxymethanol acetate (MAM). Brain weights showed a monotonic decrease with increased dose of MAM. Regional dissection revealed a rostral-caudal gradient of decreasing sensitivity, both in terms of the smallest dose required to produce a detectable loss of mass, as well as the amount lost. The mass of the telencephalon was reduced by the smallest dose used (11 mg/kg), the diencephalon was first affected by a higher dose (17 mg/kg), and the mass of the mesencephalon was reduced only by the highest dose (30 mg/kg). At 28 days of age, animals that had been exposed to the 30 mg/kg dose showed a 64% reduction in the mass of the telencephalon, a 46% loss of the diencephalon, and a 24% loss of the mesencephalon. The mass of the hindbrain, including that of the cerebellum, was not affected. The reduction in brain mass by prenatal exposure to MAM can be produced reliably, has been shown in animals of several different species, and has demonstable behavioral consequences. These facts suggest potential usefulness of the treatment for producing a model of certain kinds of mental deficiency.

In contrast, postnatal treatment (on the day of birth) with MAM produced permanent hypoplasia of the cerebellum without any grossly apparent damage to other regions of the brain. This effect was also dose-dependent, and could be produced in a variety of species. (Supported, in part, by NIH Grants MH-16610, NS-08856, and 5-S01-FR-05553-08,-09,-10.)

**5.6** DEVELOPMENTAL CHANGES IN THE RESPONSE PROPERTIES OF SUPERIOR COLLICULAR NEURONS OF THE KITTEN. Barry E. Stein* and Elemér Lábos* (SPON: L. Kruger). Dept. Anat., Sch. Med., UCLA, Los Angeles, 90024

The response properties of neurons in the superior colliculus of neonatal (ages 1-30 days) and adult cats under gaseous anesthesia were studied with moving and stationary visual stimuli. Movement was usually the most effective stimulus in the adult, whereas stationary light proved most effective in young kittens. Slow velocity sensitivity predominates in young kittens and the range of effective velocities increases with age. Responses in kittens were usually elicited only via the contralateral eye and were sluggish, with unusually long latencies (often exceeding 0.5 sec) as compared with adults. These neurons of the immature cat often required long stimulus duration and long interstimulus intervals. The "on" and "off" components were studied at different stimulus durations, intensities and repetition rates. A small number of "tonic" units were located in kittens which were inhibited by change in ambient illuminations for periods of 20-90 sec followed by a return to "resting" activity. At later stages of development, latencies shorten, sensitivity to stationary stimuli decreases, and responsiveness to rapid movement and ipsilateral eye stimulation becomes evident. (Supported by USPHS Grant EY-571)

**5.7** THE BEHAVIORAL ONSET OF INHIBITORY MECHANISMS IN THE CHICK EMBRYO. Ronald W. Oppenheim, John Reitzel* and Robert Provine.* Div. of Research, N. C. Dept. of Mental Health, Raleigh, N. C. 27611 and Dept. of Psychol., Wash. Univ., St. Louis 63130

Inhibitory mechanisms have been examined in the chick embryo by injecting into the egg various pharmacological antagonists to putative inhibitory neurotransmitters (e.g. strychnine, picrotoxin), and evaluating the embryos' overt movements before and after such a treatment. Beginning at about 15-16 days of incubation strychnine produces a significant increase in embryonic movement. Prior to this time strychnine either has no effect, or it has the paradoxical effect of greatly reducing overt movements. Picrotoxin has a similar effect as strychnine; increasing overt movements slightly earlier (on day 14), and depressing overt movements prior to this time. Both drugs produce a progressively greater excitatory effect with age, after the initial onset of sensitivity. Results from electrophysiological recording of burst activity in the spinal cord after strychnine injections agrees quite well with the behavioral data. The onset and subsequent development of the excitatory effects of these drugs appear to be related to the drastic reduction of overt movements in normal embryos during this time, as well as, with the first overt occurrence of clear coordinated patterns of motor behavior at 17 days.

**5.8** BIOCHEMICAL AND BEHAVIORAL EFFECTS OF ADMINISTRATION OF MONOSODIUM GLUTAMATE TO THE YOUNG RAT. Helen K. Berry and Richard E. Butcher. Children's Hospital Research Foundation and the Dept. of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, Oh 45229

The effect of glutamic acid and its salts on the central nervous system has been the subject of controversy for over 25 years since reports of beneficial effects of glutamic acid administration to mentally retarded children appeared. More recent reports implicated the sodium salt of glutamic acid as a specific central nervous system intoxicant in infant animals, based on finding of neuroanatomic lesions in retina and/or hypothalamus. If administration of monosodium glutamate (MSG) results in structural or functional damage to the developing nervous system, effects should be evident in psychological testing. The present study was undertaken to test this hypothesis and to investigate the biochemical consequences of MSG administration in the young rat. MSG (4 mg/g) was administered to Sprague-Dawley rats on each of the first 10 days of life. When tested at 50 days of age animals receiving MSG were less able than littermates receiving saline injections to learn a swimming maze or a brightness discrimination task. Amino acid analyses were performed on tissues from animals sacrificed on day 10. Results showed that aspartic and glutamic acids, taurine, urea, and glutathione were consistently increased in brain, liver, and blood in MSG animals, while histidine and tyrosine were consistently decreased in all three tissues. Other amino acids showed variable changes. While the biochemical changes cannot be specifically related to observed behavioral deficits, they form grounds for speculation on the mechanism leading to interference with the tricarboxylic acid cycle during a period when the rat brain is developing at a rapid rate, prior to myelination.

**5.9** MULTIVARIATE ANALYSIS OF POST MATURITY CHANGES IN BEHAVIOR AND THE CHEMICAL AND MORPHOLOGICAL PLASTICITY OF THE BRAIN, PITUITARY AND ADRENALS IN C57BL/I0 MICE. J. Mark Ordy, Northern Illinois University, DeKalb, Ill., 60115.

Previous studies have shown a chemical and morphological "plasticity" of the brain and endocrines in response to environmental stimulation and stress during maturation. The specific aims of this study were to examine post maturity changes in behavior in relation to changes in chemical and morphological plasticity of the brain and endocrines. Mice at 4, 8, 16 and 24 months were exposed for 1 month to electric foot shock, tested in behavioral tests and sacrificed for chemical and morphological evaluations. There was a significant age decline in learning, running speed, maze exploration and motor activity. Brain DNA, RNA and protein increased in response to stress. Brain acetylcholinesterase and norepinephrine differed with sex, declined with age and norepinephrine decreased in response to stress. Brain, pituitary and adrenal weights increased with age and stress. Superimposed on post maturity changes, there occurred changes in chemical and morphological plasticity of the brain and endocrines. Contrary to expectations, decreases in age specific mortality and increases in mean life span were observed after stress. In addition to 15 separate factorial analyses, a multivariate analysis of principal components was performed to identify a set of 5 factors generated by the covariance relationships among the 4 behavioral, 6 chemical and 5 morphological dependent variables.

**6.1** INTRACELLULAR CONDUCTIVITY MEASUREMENTS IN GIANT NEURONS, AXONS AND MUSCLE FIBERS. D. O. Carpenter, M. M. Hovey* and A. F. Bak*. Lab. Neurophysiology, NIMH, Bethesda, Md. 20014

In previous studies we have reported a technique which measures local conductivity with a single metal microelectrode, and found the intracellular conductivity of Aplysia neurons to be equivalent to a solution of only 5% sea water in distilled water. Similar values of intracellular conductivity were obtained with a completely independent technique utilizing a fixed array of 4 microelectrodes and measuring the voltage drop across the center pair on passage of constant current pulses between the outer pair. We have now extended these measurements to several other marine tissues. The neuronal somata of Navanax inermis (15 cells) had an average conductivity equivalent to 4% sea water (range 2-8%), while neurons from Anisodoris nobilis (20 cells) showed a conductivity equivalent to 2% sea water (range 1-3%). In contrast the giant axon of the squid, Loligo opalescens (12 axons) had an average conductivity equivalent to 81% sea water (range 71-100%), and the giant axon of the annelid, Myxicola infundibulum (13 axons) had a conductivity equivalent to 45% sea water (range 39-60%). In 15 giant muscle fibers of the barnacle, Balanus nubilus, the internal conductivity was equivalent to 15% sea water (range 13-16%). From the available information it would appear that the concentrations of intracellular ions in these tissues are reasonably similar. Furthermore, there is no good evidence that a major fraction of intracellular K+, the predominant cation, is bound. We attribute the lower than expected conductivity of all these tissues except squid axon to an extensive structuring of cellular water.

**6.2** ABSENCE OF ACCOMMODATION IN APLYSIA GIANT NEURON. Douglas Junge. Sch. of Dent. and Dept. of Physiol., UCLA, Los Angeles, Calif. 90024.

Responses to linearly-rising currents were studied in the R2 cell in the visceral ganglion of Aplysia, using separate intracellular stimulating and recording electrodes. When current ramps were applied to the cell soma, the threshold current for the spike always decreased with decreasing rate of rise of the stimulus. With slowly-rising ramps, the critical depolarization for the spike was independent of rate of rise of the stimulus. When currents were injected into the giant-cell axon at 1 cm. from the soma, the threshold current also decreased with decreasing rate of rise of the stimulus. Thus, neither the soma nor the axon showed accommodation to subthreshold current ramps. Analysis of the voltage response to inward steps of current applied to the soma indicated that the passive properties of the neuron resembled a single-section RC circuit. The response of such a model to linear current ramps was close to the ramp response of the neurons, except that predicted potential changes just before the spike were smaller than those observed. In this model, if the critical depolarization, $\Delta V_c$, was assumed to be constant, then the variation of the current threshold, $I_{th}$, with the time of occurrence of the spike, t, was

$$I_{th} = t\Delta V_c/R(t - \tau + \tau e^{-t/\tau}),$$

where R = membrane resistance and $\tau$ = time-constant. Using measured values of R and $\tau$, this curve agreed with the observed variation of current threshold with time of occurrence of spike in the R2 cell.

**6.3** TEMPERATURE EFFECTS ON FIRING FREQUENCY AND DISTRIBUTION IN APLYSIA PACEMAKER NEURONS. James A. Willis* (SPON: D. O. Carpenter). Armed Forces Radiobiology Research Institute, Bethesda, Md. 20014

Intracellular recordings from Aplysia visceral ganglion pacemaker neurons subjected to an environmental temperature range of 10°C to 26°C have been analyzed using computer techniques. Interval histograms and autocorrelations were done on each cell as the environmental temperature was varied in 2°C steps. Cells firing in bursting and regular patterns were included in the population studied.

Interspike interval during pacemaker discharge was found to decrease with increased temperature. These results agree with those reported by Carpenter (j.Gen.Physiol. 50(6): 1469, 1483, 1967). The interburst interval in bursting neurons was found to decrease with increasing temperature, independent on the number of spikes in the burst. The distribution of both interspike and interburst intervals indicated less variability with increased temperature.

These results suggest that similar ionic mechanisms may control the interspike and interburst intervals, that these mechanisms exhibit a positive temperature coefficient, and that the mechanisms become more effective in regularizing the cell as temperature is increased.

**6.4** LOCALIZATION AND GEOMETRY OF FAST EXTENSOR MOTONEURONS IN THE CRAYFISH ABDOMEN. Steven N. Treistman and Michael P. Remler. Neurobiology Program, Sch. Med., Univ. of North Carolina, Chapel Hill, N.C. 27514

The present work is an attempt to locate, in the third abdominal ganglion of the crayfish, Procambarus clarkii, the motoneurons controlling the fast extensor muscles. It is these muscles which operate to extend the tail during the series of quick tail flips which characterize the escape response. Injection of Procion Yellow dye was utilized to study cell geometry.

The ventral nerve cord, containing the second through fourth ganglia, was isolated, along with the extensor musculature. The positions of the motoneurons within the ganglion were relatively consistent from preparation to preparation. There was some minor variability, but the identified neurons could be located in almost all preparations. The cell bodies are non-excitable, and isolated from integrative activity. A small (less than 15 mv.) depolarization is characteristically seen in the soma, in association with an antidromically-initiated action potential. In most of the cells, the neurite was long and thin, as evidenced by a difficulty in direct activation of the cell via an intracellular soma electrode, and by dye injections. Physiological interactions among the extensor neurons, and between extensor and flexor neurons are currently under study.

**6.5** POST-TETANIC CHANGES IN MEMBRANE POTENTIAL INDUCED BY REPETITIVE STIMULATION OF XENOPUS 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 35233

Post-tetanic depolarization is followed by a transient hyperpolarization consisting of a relatively sharp 3 to 6 mv spike-like component of several seconds duration and a subsequent slow creep over many seconds to a normal voltage level. While both components vary with duration of tetanic stimulation interval, the ratio of the slow creep to the faster spike tends to vanish as stimulation interval is reduced. The transient hyperpolarization is reversibly abolished by cyanide and by lithium replacement of sodium in the manner obtained by Ritchie and Straub (J. Physiol. 136:80, 1957) from whole nonmyelinated nerve trunks. Insofar as these phenomena may be attributed to changes in external K ion concentration it is apparent that only the slow creep can be explained in terms of a neutral pump and K ion diffusion, either in the presence or absence of an external diffusion barrier. The spike itself introduces an apparent discontinuity which cannot be accounted for by a variety of pump transient configurations, including those of very brief and quite prolonged decay times. In the course of cyanide depression a brief hyperpolarization spike component is followed by a prolonged phase of depolarization before return to the resting level. This in itself precludes the possibility of an annular diffusion barrier enclosing a shell of trapped K ions. An analogue heat flow device was employed to simulate the diffusion system with appropriate boundary conditions. Supported by NIH Grant (5R01 NS0917 03) and NIH Grant (FR00-145).

**6.6** ELECTRIC ORGAN DISCHARGE INTERACTIONS IN MORMYRID FISH. Peter Moller* and Richard Bauer*(SPON: R.L.Thompson). Hunter College of the City University, New York and Laboratoire de Neurophysiologie Sensorielle Comparee, C.N.R.S., Paris.

The electric organ discharges of pairs of weakly electric fish (Gnathonemus petersii) were recorded to study the significance of the EOD's as intraspecific communication signals. In a 100 gallon tank a larger fish (12-15cm) was passively moved within a shelter tube toward a smaller specimen (6-9cm) either in steps or in a continuous move. The movement was stopped at that distance when at least one fish stopped its discharge activity. From this "threshold" interfish distance the spatial range of a possible "communication field" was found to extend about 30 to 40 cm from the fish. At threshold distances an EOD frequency increase of the fish demonstrating the stronger electrical field strength to the other fish temporarily stopped the EOD activity of the electrically weaker fish.

**6.7** SHORT-DISTANCE ELECTRICAL INTERACTION IN A MORMYRID FISH. C. J. Russell* and C. C. Bell. Neurophysiology Laboratory, Good Samaritan Hospital and Medical Center, Portland, Oregon 97210

The electric organ discharge of minimally-restrained Gnathonemus petersii was recorded during stimulation by strong, brief electrical pulses delivered to the surrounding water. Post-stimulus time histograms show a response of the electric organ at 12-14 milliseconds. Above threshold, the probability of response increases with stimulus amplitude and decreases with stimulus frequency, but the latency remains constant. The significance of this phenomenon in the normal interaction between fish was examined by recording from freely-moving pairs of fish. Each fish responded to the other's discharge with an "echo" discharge of its own at this same 12-14 millisecond latency. The echo discharge was a short-distance interaction; it disappeared when the animals were separated more than a few centimeters by plastic screens. This behavior may play a role in species recognition, social dominance, or avoidance of synchrony. (USPHS NIH NS06728 and Gertrude Cammack Foundation)

**6.8** PENICILLIN ACTION ON LEECH GANGLIA: PRODUCTION OF "EPILEPTIC" INVERTEBRATE NEURONS. James W. Prichard, Dept. of Neurol., Yale Univ. Sch. Med., New Haven, 06510

Intracellular electrophysiological techniques were used to investigate a characteristic kind of discharge caused in the Retzius cells of leech segmental ganglia by 10 mM citrate-free benzylpenicillin sodium. The discharge appeared in 75% of 108 cells and consisted of bursts of rapidly repeating action potentials associated with excitatory synaptic potentials and usually followed by a longer lasting hyperpolarization. These bursts could be triggered easily by shocks to the segmental nerves or interganglionic connectives but only rarely by intense depolarizing current pulses passed across the cell membrane from the recording electrode. Both spontaneous and triggered bursts were entirely suppressed by 20 mM magnesium sulfate and by 0.1 mM atropine sulfate. The excitatory synaptic potentials were increased in amplitude and eventually caused to occur without action potentials when the bursts were produced against a background of membrane hyperpolarization. The response was reversible and could usually be repeated once or twice in the same cell but was progressively less likely to appear with subsequent exposures to the drug. The incidence and persistance of the bursts were not affected by variations of pH from 7.0 to 8.0.

Discharges of this sort occurred in leech ganglia only as responses to penicillin and certain other drugs. In form and physiological behavior they resemble the "depolarization shifts" seen in some mammalian neurons in or near epileptic foci produced by penicillin, freezing and alumina cream. The similarity encourages the view that invertebrate preparations can be effectively used to study some of the basic vulnerabilities of nervous tissue which underlie epilepsy.

**6.9** MEMBRANE PROPERTIES OF NEUROGLIA IN THE CHRONIC EPILEPTOGENIC FOCUS. F. L. Gloetzner*, W. H. Calvin and A. A. Ward, Jr. Dept. Neurological Surg., Sch. Med., Univ. of Wash., Seattle, Wash. 98105.

In cats injection of aluminum hydroxide into the motor cortex produced EEG spiking about 6 weeks later. Intracellular micropipette studies were performed about 12 weeks after the injection in the awake animal using an implanted chamber. Glial cells were identified by a stable resting potential up to 90 mv, which showed a typical "graded response" to direct cortical stimulation. A striking difference in membrane properties was found for glial scar cells compared to normal glial cells. In the focus the "glial" membrane time constant is about 200 microseconds and the input resistance ($R_i$) about 1.5 Megohm. These values equal one half and one tenth respectively of the normal values of Trachtenberg and Pollen (Science 167: 1248 and 1252, 1970). Following the equation $R_m = R_i \times S$, in which $R_m$ is the specific membrane resistance and S the equivalent spherical surface area of the cell, a ten times decrease of $R_i$ may be due to a ten times larger surface of the scar cell or to a ten times smaller specific membrane resistance or to a change in both, $R_m$ and S. In fact, electron microscopy of the focus (Harris, Westrum, personal communication) shows an increase of glial surface area and an increase of the number of "tight junctions", which might provide low resistance pathways. The changes in specific membrane resistance and surface area would mean a marked increase of the glial "safety factor" (glial potassium uptake versus neuronal potassium release). Thus, in the focus the neuroglial buffering system seems to transport even more potassium away from sites of potassium release than it does under normal conditions. The deterioration of this system as proposed by Pollen and Trachtenberg does not seem to occur in focal epilepsy.

**6.10** LOCALIZED MEASUREMENTS OF CEREBRAL IMPEDANCE AND TEMPERATURE IN SENSORY RELAY NUCLEI DURING VISUAL AND AUDITORY STIMULATION. James G. McElligott. Space Biology Lab, BRI, UCLA, Los Angeles, Calif. 90024

Localized measurements of impedance and temperature have been separately used to estimate various aspects of neurophysiological activity in discrete populations of nerve cells. Changes in cerebral tissue impedance (at 1000 Hz) have been measured during learned discrimination tasks, hypothermia, asphyxiation and during the micro-injection of various chemicals. On the other hand, localized thermal changes have been produced in relay nuclei during sensory stimulation. The purpose of this experiment was to measure impedance shifts in sensory relay nuclei during periods of natural stimulation and to correlate them with localized thermal activity. Low frequency flashing light (10/sec) produced temperature increases (.01°C) in the lateral geniculate nucleus of the anesthetized and also the awake cat. There was also a concomitant increase in neural spike activity. Similar results were obtained in the inferior colliculus when auditory clicks (10 to 15/sec) were presented. Simultaneous recording of the impedance produced no localized changes that could be correlated with sensory stimulation. Previous results have indicated that these temperature changes are due both to neural metabolic heat and to local blood flow alterations. In as much as there were no impedance changes under these conditions, then previously reported impedance shifts cannot be attributed to these factors. In addition, the concomitant change in neural spike activity without an impedance shift would also obviate this as a factor. (This work supported by USAF Grant #F44620-70-C-0017)

**6.11** CHEMICAL PROPERTIES OF TETRODOTOXIN BINDING SITES IN NERVE MEMBRANE. Dennis R. Hafemann, Department of Biology, Marquette University, Milwaukee, Wisconsin 53233.

The binding of tritium-labelled tetrodotoxin (TTX*) has been used to study the chemical properties of TTX binding sites in homogenates of bovine brain. At 27°, these sites have a half life of 29 hours, but they are stable for long periods when frozen. The sites tolerate the pH range 5-10 quite well, but are rapidly inactivated outside this range. Saxitoxin displaces TTX* from its binding sites, but procaine does not, showing that there must be at least two separate binding sites capable of inactivating the sodium channel. The alkali metal ions also displace TTX* from its binding site, but the relative displacing abilities of the ions are quite similar, implying that competition for this site does not explain the high selectivity of the sodium channel. The binding site is insensitive to phospholipases, neuraminidase, hyaluronidase, and lysozyme, but it is degraded by pronase, indicating the importance of a protein constituent. (This work was done under NIH Grant NS-09985.)

**7.1** UNIT AND EVOKED POTENTIALS IN CAT OPTIC TRACT TO PAIRED LIGHT FLASHES AND THEIR RELATIONSHIP TO PERCEPTUAL DISCRIMINATION. Carol K. Peck* and Donald B. Lindsley. Dept. Psychol., Pomona College and Depts. Psychol., Physiol., Psychiat. and Brain Res. Inst., UCLA, Los Angeles, 90024

Simultaneous or successive recordings of single unit response patterns and of gross evoked potentials were obtained from the optic tract of barbiturate anesthetized cats in response to paired and single flashes of light. The shortest interflash interval at which a unit responded separately to each of a pair of flashes (unit "recovery") was compared to the shortest interflash interval at which evoked potentials responded separately to both flashes (evoked potential "recovery"). Under light adapted conditions, about one-half of the units tested showed paired-flash "recovery" within the same range of interflash intervals which yielded evoked potential recovery. Under dark adapted conditions, only one-third of the units paralleled the evoked potentials. Since the evoked potentials to paired flashes, recorded under these conditions, were sufficiently similar to those recorded in a previous study of behaviorally alert cats and since a correspondence between evoked potentials and perceptual discrimination of paired flashes was established, the unit responses can be indirectly related to perceptual responses. Thus, the present results suggest that an appreciable number of retinal units fail to play a significant role in temporal discrimination between paired and single flashes.

**7.2** THE SUPPRESSION-RECOVERY EFFECT IN OPTIC TRACT RESPONSES IN CAT: PSYCHOLOGICAL CORRELATES AND RETINAL MECHANISMS. W. L. Salinger* (SPON: D. B. Lindsley). Dept. Psychol., Univ. North Carolina, Greensboro, 27410.

The visual system from eye to cortex manifests a transient suppression of its responses following the response to the first flash of a train of repetitive light flashes above 8 to 10 Hz, depending upon stimulus and background luminance levels. After initial suppression there is a gradual recovery to a stabilized level less than that of the response to the first flash in the train. Salinger and Lindsley (Vis. Res. 11: 1435, 1971) referred to this phenomenon as the suppression-recovery effect (S-R effect). This effect has been studied further in the optic tract of cats under Nembutal with both macro- and micro-electrodes with the following results. The S-R effect has two psychological correlates: 1. threshold changes during rapid light adaptation, and 2. a progressive increase in critical fusion frequency during the initial exposure to flickering light. The S-R effect appears to be due to a sustained on-effect and a delayed off-effect which occur in photoreceptors in response to high intensity flashes.

7.3 RELATIONSHIPS BETWEEN VISUAL EVOKED POTENTIALS AND REACTION TIME IN THE MONKEY PERFORMING A VISUO-MOTOR TASK. Kyozo Watanabe* (SPON: J. M. Fuster). Dept. Psychiatry and Brain Research Institute, Sch. Med., UCLA, Los Angeles, 90024

Rhesus monkeys were trained to perform a motor response (lever-press) to presentation of a brief and difuse flash of light preceded at variable intervals (2-6 sec.) by an acoustic warning signal (click). Evoked potentials (EP's) elicited by the flash were recorded from the lateral geniculate body and from the surface of the striate cortex by means of chronically implanted gross electrodes. The reaction time (RT) was electronically measured between the flash and the animals' motor response. In the geniculate, RT's shorter than the median for a given animal were accompanied by lower voltage EP's than those accompanying RT's longer than the median. The inverse relationship was observed for the EP's from the visual cortex (shorter RT with larger EP, longer RT with smaller EP). EP's preceding responses with RT close to the median, - as analyzed after excluding trials giving extreme measures of RT -, conformed best to the expressed relationships. The paradoxically inverse EP - RT functions obtained from the lateral geniculate and from the visual cortex may reflect differences of neuronal organization between the two structures.

7.4 VISUAL DISCRIMINATION OF RANDOM FIGURES BY RHESUS MONKEYS. Kristin R. Carlson. Dept. Pharm., Sch. Med., U. of Pittsburgh, Penna. 15213

Random figures are constructed by randomly assigning points to coordinates in a matrix and connecting the points to form closed polygons, and have been used extensively in studies of human discrimination processes. In the present experiment, five Rhesus monkeys were taught successive discriminations between 24 pairs of random planometric figures, both figures in a pair having either 4, 6, 8, 10, 12, or 14 sides. A statistically significant U-shaped function was found between trials to criterion and the number of sides comprising the figures, with most efficient learning at intermediate sidedness levels. These data are consistent with the performance of humans. There was no relation between number of sides and latency to choice, however, suggesting that this measure is insensitive to variations in learning speed in the monkey. For two monkeys, after criterion performance was attained on each problem, both figures were rotated 180° and an additional 20 trials were given. Errors after rotation bore no consistent relation to sidedness level. However, across all sidedness levels, errors in the 20 trials after rotation were intermediate between, and significantly different from, errors on the first 20 trials of that problem and the last 20 trials before rotation. This suggests that rotation of the figures only partially disrupts discrimination performance; subjects neither treated the rotated figures as comprising an entirely new problem, nor were they unaffected by the change in orientation.

**7.5** EFFECT OF SUPERIOR COLLICULI LESIONS ON DISCRIMINATION OF LUMINOUS FLUX-EQUATED FIGURES BY MONKEYS DEPRIVED OF STRIATE CORTEX. Jon Wininger*, Pedro Pasik and Tauba Pasik. Dept. Neurol., Mount Sinai Sch. Med., CUNY, New York 10029.

Monkeys without striate cortex can master visual tests in the absence of total luminous flux cues (Pasik et al, Exp. Neurol. 1969; Schilder et al, Brain Res. 1971, Exp. Brain Res. 1972). This capacity is abolished by complete ablation of striate and circumstriate cortex (Pasik et al, Neurology 1972). In the attempt to find critical structures for conveying visual information into circumstriate cortex in the absence of area 17, 3 monkeys were trained to a criterion of 90% correct responses in 200 trials, using a pulling-in situation with movable transilluminated stimuli. In test 1, targets differed in total luminous flux and brightness. In tests 2, 3 and 4, targets were flux-equated and differed in brightness and area with or without perimeter differences. Training was repeated after total bilateral ablation of area 17 with partial damage to 18 and 19. Testing was again attempted following additional bilateral destruction of the superior colliculi. Normal monkeys mastered all problems with significant decrease in error scores in the last three tests. After striate cortex removal, all subjects had significant deficits, but succeeded in all discriminations with transfer effects across the tests. After collicular ablations, the animals solved the first problem but failed to reach the established criterion in the second test within 7500 trials. Training was discontinued at this stage. Findings confirm that monkeys deprived of striate cortex can master visual problems without luminous flux cues. The superior colliculi are crucial for this capacity but not for discrimination of figures differing in total luminous flux. It is conceivable that retino-collicular input is relayed to circumstriate cortex via the pulvinar. (Aided by U.S.P.H.S. Grants # MH-02261 and K3-EY-16,865).

**7.6** THE IMPORTANCE OF TELENCEPHALIC STRUCTURES IN VISUAL DISCRIMINATION LEARNING IN NURSE SHARKS. R. Curtis Graeber*, Dolores M. Schroeder, John A. Jane and Sven O. E. Ebbesson. Depts. Psych. and Neurol. Surg., Univ. of Virginia, Charlottesville, Va. 22901, and Lerner Marine Lab., Bimini, Bahamas.

Previous work in our laboratory has shown that bilateral tectal ablation does not impair the nurse shark's (Ginglymostoma cirratum) ability to learn black-white (BW) or pattern discriminations. This result, coupled with recent anatomical findings (Ebbesson & Schroeder, Sci., 173:254, 1971), suggests the possible involvement of the shark's telencephalon in visual function. To investigate this possibility subjects (2-4 ft.) were trained on BW and then on horizontal vs. vertical stripes using food rewards in a modified Y-maze. Initial training either preceded or followed surgery. Bilateral lesions were made by aspiration in the presumably nonvisual regions of the anterior forebrain or in the rostral portion of the posterior forebrain. Anterior lesions had no effect on the sharks' ability to learn the discriminations or on the ability to retain them when learned preoperatively. Conversely, subjects could not learn even the BW discrimination following posterior lesions which severely damaged the nucleus intermedius. Moreover, such sharks with preoperative training could not retain nor relearn the tasks. The visual nature of the deficit is emphasized by the low post-operative response latencies and the animals ability to learn a position task. The results provide additional evidence for the encephalization of visual function to sharks. SUPPORTED BY: 1R01-EY00154-01A1; 1K04-NS-46292-01A1; Lucille Sebrell Memorial Fund and James A. Bauer Research Fund.

**7.7** THE EFFECTS OF SEQUENTIAL LESIONS OF VISUAL CORTEX AND SUPRASYLVIAN GYRI ON PATTERN DISCRIMINATION IN THE CAT. Peter D. Spear, Charles C. Wood* and J. Jay Braun*. Dept. Psychol., Yale Univ., New Haven, Conn. 06510

Eight cats were trained on a pattern discrimination between horizontal and vertical stripes, which had no differences in total luminous flux or total amount of contour, and in which consistent local luminous flux cues were eliminated. They then received, in different orders, a four-part sequence consisting of lesions of: a) visual cortex (areas 17, 18, and 19); b) middle suprasylvian gyri; c) posterior suprasylvian gyri; and d) a control retention period in which no lesion was administered. Following each manipulation in the sequence, cats were tested on the pattern discrimination and retrained to criterion if necessary. The following results were obtained: 1) Discrimination performance immediately following the retention period was equal to or greater than criterion; thus, retention was perfect. 2) Little or no performance deficit was produced by suprasylvian gyrus lesions in normal cats. 3) In cats having previously undergone removal of visual cortex and retrained to criterion, suprasylvian gyrus lesions produced a significant disruption of the discrimination. 4) Cats lacking both visual cortex and suprasylvian gyri were significantly more impaired than cats lacking visual cortex alone, both in their average postoperative performance level and in the maximum level attained after extensive retraining. These results suggest that although the suprasylvian gyrus appears to have little or no role in pattern discrimination by normal cats, this region is involved in the residual pattern discrimination ability of cats lacking visual cortex. Finally, despite their profound impairment, cats with complete lesions of visual cortex and suprasylvian gyri were eventually able to perform the pattern discrimination at levels significantly above chance.

**7.8** BINOCULAR SUMMATION AND SUPPRESSION: EFFECTS OF CONTOUR DENSITY AND DISPARITY ON MONOCULAR AND BINOCULAR VISUALLY EVOKED CORTICAL RESPONSES IN HUMANS. M. Russell Harter and William H. Seiple*. Dept. Psychol., U. North Carolina at Greensboro, 27412

All combinations of crossed grid line transparency patterns (between line distance of diffuse, 15, 30, and 60 min of arc subtense) were continuously presented to the two eyes with a stereoscope. One eye was presented a given pattern while the other was presented various patterns. Monopolar averaged evoked cortical responses (VERs), recorded 2.5 cm above the inion on the midline, were obtained under these conditions by back illuminating (10 microsec flash) the transparencies viewed by the right or left eye (monocular flash condition) or both eyes (binocular flash condition). Greater amplitude VERs were obtained when 15 and 30 min patterns were flashed for both monocular and binocular flash conditions. The effects of pattern presented to one eye depended on the pattern presented to the other eye. The wave-form of monocular VERs to a given pattern shifted progressively more negative as the pattern continuously presented to the contralateral eye was varied from diffuse to 60 min of arc (particularly with VERs to diffuse flashes). With binocular stimulation, if pattern is presented to one eye and diffuse light to the other, the diffuse flash contributed little to the binocular VER (suppression of eye receiving diffuse light); if pattern was presented to both eyes, both eyes contributed significantly to the binocular VER (binocular summation of pattern responses). The results indicate a hierarchy of pattern dominance in terms of binocular interaction, pattern light dominating over diffuse light and 15 to 30 min patterns dominating over 60 min patterns.

**7.9** **SENSITIZATION IN SCOTOMATA SYMMETRIC WITH ISLANDS OF BLINDNESS.** Whitman Richards and Ernst Pöppel*. Dept. Psych., Mass. Inst. of Tech., Cambridge, Mass. 02139 and Neurosciences Research Program, 280 Newton Street, Brookline, Mass. 02146

In 1966 Sprague[1] demonstrated in cat that visually guided behavior could be restored following unilateral ablation of occipito-temporal neocortex if the contralateral superior colliculus was subsequently removed. (An analogous effect in the sensory-motor system has been observed by Twitchell[2].) Sprague interpreted his result as the release of intercollicular inhibition. To seek a similar visual effect in Man, we have examined brain-injured patients with various visual field defects. On occasion, visual fields are found that include a small scotoma in the intact field across the midline from a quadrant or hemifield defect. In such a case, visual function (detection of flashes or moving lights) appears as an island in the quadrant scotoma at a symmetrical position across the midline. This result is analogous to Sprague's finding, but restricted to a local portion of the visual field. A similar, but more complex result is also observed in blind regions symmetric with the optic disc, where again, sensitization is observed in a region roughly symmetrical across the midline: often movement detection is present or eye movement responses (saccades) have an affinity for this portion of the blind field when stimulated by flashed targets[3]. Our results suggest that interhemispheric interactions in Man are organized with a symmetric topography.

1. J. M. Sprague, Science, 153, 1544 (1966).
2. T. Twitchell, Conference on Mechanisms in Restitution of Function after Brain Damage. NINDB., (1967), pp. 147-157.
3. E. Pöppel, D. Frost and R. Held, ARVO Spring Meeting, Sarasota, April 26, 1972

**7.10** ON THE INTERPRETATION OF THE VISUAL EVOKED RESPONSE (ESPECIALLY IN DYSLEXIA). Juan de Dios Pozo-Olano. Bedford, Massachusetts 01730.

Attempts have been made to correlate anomalies in the visual evoked response (VER) to perceptual deficiencies and specific learning disabilities. This may be eventually proven to be true, provided certain considerations on the spatio-temporal neurophysiological correlates and experimental conditions are carefully observed when recording and interpreting the VER. The configuration of the VER in relation to its spatial coordinates is a valid argument against any topographic generalization. The total evolution of a VER takes approximately 750 milliseconds, a time much longer than other repetition rates of stimulation that the visual system can normally handle. Thus, one stimulus presented during the development of a VER does not stop its temporal evolution, but actually generates another VER which is summed (superimposed) algebraically with the remaining components of the previous one. Hence, the position (in time) of each component of the VER would therefore depend on the actual physiological latencies (events triggered at whatever nervous structure involved in the processing of visual inputs), and their analog projection onto the surface of the scalp; and, on the frequency of stimulation. This means that by using different repetition periods of stimulation, especially below those of the latencies of the early components, different temporal configurations of a VER can be seen. These arguments point in the direction of how inadequate an observation can be if one considers the anomalous (or spurious) experimental physical events, rather than the anomalous neural responses. Or, the imposition of incoherent after-effect signals at the level of the surface of the scalp do not necessarily reflect neurological function or dysfunction.

**8.1** ELECTRON MICROSCOPY OF NON-NEURONAL EVENTS DURING THALAMIC DEGENERATION
M. A. Matthews and L. Kruger. Department of Anatomy and Brain Research Institute, UCLA, Los Angeles, California 90024.

The ablation of cortical projection fields provides a suitable model for addressing the problem of a mesodermal contribution to thalamic "gliosis" in a circumscribed zone distant from the lesion site. Electron microscopic examination of several thalamic nuclei in the rabbit from one day to 34 weeks after surgical removal of limbic, striate and somatosensory cortex reveals a rapid loss of neurons within the first two weeks associated with the abnormal accumulation of a variety of indigenous perivascular and hematogenous elements within the external basal lamina of some venules and large capillaries in the zone of degeneration. Agranular leukocytes comprise the majority of accumulated blood elements and are characterized by heterochromatin nuclei and moderately dense cytoplasm containing numerous free ribosomes. Non-neuronal elements distinct from astrocytes and normal oligodendrocytes simultaneously appear in the neuropil and increase in numbers as neuronal degeneration progresses. Some resemble agranular leukocytes and examples of such cells were sometimes seen bridging the external basal lamina. Other reactive elements display some free ribosomes but more numerous arrays of polysomes, rosettes and endoplasmic reticulum in addition to electron-lucent lipid vacuoles and lysosomes. After longer survival periods, astrocytes and enlarged, lipid-laden cells represent the predominant non-neuronal entities in the zones of degeneration. Several morphological criteria suggest that a significant proportion of the reactive "glia", particularly those laden with lipids and lysosomes, are of mesodermal origin.

(Supported by NIH grants EY 571 and NS6594)

**8.2** STRUCTURE AND FUNCTION OF THE ENDOPLASMIC RETICULUM IN THE SQUID GIANT AXON.
Maryanna Henkart. NINDS, NIH, Bethesda, Md. 20014.

An electron microscopic study of the giant axon of the squid Loligo irridescens shows that there is an endoplasmic reticulum (ER) composed of narrow tubules often seen to be continuous with expanded cisternae. "Dense cored vesicles" about 80nm in diameter sometimes can be shown to be sections either through areas of tubules which contain a dense material or through outpocketings from cisternae. Some cisternae of the ER form close associations with the surface membrane in structures which resemble the subsurface cisternae (SSC) described by others in cell bodies of nerve cells. The sites of apposition between the surface membrane and SSC are characterized by approach of the two membranes to within 10nm and increased electron opacity in the space between. The opacity of the contents of the tubules, and the frequency and opacity of the "dense cored vesicles" are increased by addition of Ca to the fixative, although the fixation of the cell components is otherwise adequate without the addition of Ca. Baker, et al.,(J. Physiol. 218, 709, 1971) have presented evidence of an internal store of Ca in the squid giant axon (suggested to be associated with mitochondria). Our working hypothesis is that the ER in the squid axon may function as a Ca accumulating system because of its structural similarity to the sarcoplasmic reticulum of certain muscles and because it undergoes similar changes subsequent to the addition of Ca to fixation solutions (Hagiwara, et al., J. Physiol. 219, 233, 1971). The analogy with muscle may be extended to include the suggestion that the junctions between the surface membrane and SSC which are continuous with the ER may be involved in coupling the electrical activity of the surface membrane to intracellular activities, the coupling being mediated by Ca released from the ER. A survey of the literature shows a widespread incidence of similar SSC, ER, and dense cored vesicles in neurons.

**8.3** EFFECTS OF HYPERTONIC BLOOD-BRAIN BARRIER (BBB) INJURY. Maria Spatz*, Stanley I. Rapoport, Zbigniew M. Rap* and Igor Klatzo. National Institute of Neurological Diseases and Stroke, NIH, Bethesda, Md. 20014

Injury of BBB by direct application of hypertonic solutions to the cerebral vasculature was studied in the rabbits in order to elucidate aspects of reversibility of barrier damage and to assess some effects of barrier opening on brain parenchyma. The reversibility of BBB damage was investigated in topical applications of circular filter paper pledgets soaked in various salt solutions to the exposed pial surface of the rabbit. Intravenously injected Evans Blue dye served as the BBB indicator. Observations revealed that electrolytes and nonelectrolytes which have little or no lipid solubility produce a reversible BBB damage with intensity directly related to their concentration. In other experiments using hypertonic solutions via internal carotid perfusion of one hemisphere osmotic opening of the tight junctions between endothelial cells was observed using horseradish peroxidase in electron microscopic investigations. Application of double isotope technic of Oldendorf in rabbits subjected to hyperosmotic BBB injury via internal carotid revealed an increased brain uptake index for glucose following the BBB injury. The demonstrated competitive inhibition of 2-deoxy-D-glucose uptake by unlabeled 2-deoxy-D-glucose suggests that hyperosmotic BBB injury produces an increase in facilitated glucose transport rather than passive diffusion of glucose from blood to brain.

**8.4** THE EFFECT OF SEROTONIN ON THE BLOOD-BRAIN BARRIER TO PEROXIDASE IN MICE. E. Westergaard* and M. W. Brightman* (SPON: H. Webster). Lab. Neuropath. Neuroanat. Sci., NINDS, NIH, Bethesda, Md. 20014

Horseradish peroxidase (HRP; MW 40,000) was injected (10 mg.) intravascularly after which the cerebral ventricles were perfused for 3 to 30 minutes with 0.1 ml balanced salt solution containing 50 to 1000 µg serotonin creatinine sulfate (ST). The brains were fixed with aldehydes perfused through the aorta or cerebral ventricles and pieces were incubated for HRP activity and examined electronmicroscopically. Creatinine sulfate (100 µg), when perfused by itself through the cerebral ventricles, was without any effect. However, a few minutes after perfusion with ST, forced respirations and solitary convulsions appeared, followed by more rapid respirations and generalized convulsions. HRP reaction product occurred in the basement membrane of large subependymal vessels and in the extracellular spaces of adjacent neuropil, but not in the basement membrane around subependymal capillaries. In the walls of the large vessels with a muscle coat, extracellular pockets between consecutive tight junctions connecting their endothelial cells were penetrated by HRP and no protein was freely dispersed in the endothelial cytoplasm. Thus, the protein moved through opened tight junctions and not across a damaged endothelium. Since capillaries were not penetrated, ST might act either directly on the smooth muscle of large vessels and only indirectly on their endothelium, or the amine might act on these endothelial junctions directly without affecting those of capillaries.

**8.5** NEURONAL ACTIVITY CAN ALTER GLIAL CELL METABOLISM. H. Bracho* P.M. Orkand* and R.K Orkand. Dept. Biol. and Anat., UCLA Los Angeles, 90024

Metabolic interactions between neurons and glia require processes whereby glial cells detect nervous activity and respond. Previously, Orkand, Nicholls and Kuffler (J. Neurophysiol. 29: 788, 1966) found that potassium released from active axons accumulates in the intercellular clefts and depolarizes the adjacent glial cells. In the present experiments we find that relatively small increases in extracellular potassium are sufficient to alter glial cell metabolism, as indicated by changes in the level of reduced nucleotides. The observations are made in 'all glia' optic nerves of Necturus (obtained after axon degeneration) using sensitive fluorometric techniques developed by Chance and his colleagues (Sci. 137: 499, 1962). These results suggest a mechanism for the coupling of glial cell metabolism and neuronal activity.

(Supported by USPHS Research Grants No. NS-09521 and NS-08346 and Training Grant NS-05670).

**8.6** CEREBRAL SECRETION INTO THE CSF VENTRICULAR SYSTEM CONCOMITANT TO ELECTROCORTICAL SYNCHRONIZATION AND DESYNCHRONIZATION. Xavier Lozoya* and Marcos Velasco. Scientific Research Dept. National Medical Center, Mexico Cy. (P.O. Box 73-032).

The present investigation attempted to determine cerebral secretions into the CSF ventricular system by means of animals in parabiosis. Experiments were performed on 15 couples of male cats. One cat of each couple (receptor) received intraventricular injections of 0.03 ml/30 min. CSF from other cat (donnor) coursing with EEG synchronization and desynchronization, induced by electrical stimulation of the intralaminar thalamic nuclei (8/sec) and reticular formation (50/sec) respectively. EEG synchronization sustained for 30 min. of the receptor animal was observed only when the CSF was obtained from and was injected to the third ventricle. A sustained EEG desynchronization of the receptor animal occurred only when the CSF was obtained from the lateral ventricle and injected into an homologous region. CSF perfusions obtained or injected from or into other regions of the ventricular or cisternal systems were unable to produce such effects. These results suggest that sustained synchronization and desynchronization are partially mediated by neurohumoral secretions with a regional topographic distribution within the ventricular system.

**8.7** EFFECTS ON WATER DIURESIS OF INFUSIONS OF TRANSMITTER SUBSTANCES INTO 3RD CEREBRAL VENTRICLE. Eva E. Cerny*. Dept. Anat., U. of Louisville Health Sciences Center, Louisville, Ky, 40201. SPON: L. A. Carr.

Eleven female cats weighing 2-4 kg. each were anesthetized with intravenous injections of Na pentabarbital and placed in Kopf stereotaxic holder. 70 mls of tap water were introduced into the stomach via a stomach tube, the urinary bladder was catheterized and urine was collected at hourly intervals. The osmolarity of these samples was measured on an Advanced Osmometer. The scalp was then incised, and a cannula positioned (A=14 L=0 H=9) so it would reach the third ventricle. The muscles were cleaned from the occipital region of the skull, exposing the foramen magnum, the dura below which was then punctured and a 4 cm piece of polyethylene tubing with a 2 mm outer diameter was carefully inserted thru fourth ventricle up to the cerebral aqueduct. A perfusion pump was filled with sterile saline to deliver 0.1 ml/min, and connected via a long piece of polyethylene tubing to a needle which was inserted into the cannula in the third ventricle. In this manner, the third cerebral ventricle was perfused with saline. The first hour following surgery served as a control period of urine volume. 50 µg of one of 3 different neurotransmitter type substances was then injected into the third ventricle, and urine collected over following 2 hours to see what, if any, effect each substance exerted. The mls of urine following each injection were compared to the control volume using Wilcoxon-T test. It was found that both norepinephrine ($p < .01$), and acetylcholine ($p < .05$) exerted a significant increase in urine output. The effect of epinephrine was statistically insignificant. It was suggested that possibly ADH was released by these two neurotransmitters, and that in a concentration which causes diuretic response rather than the customary antidiuretic one.

**8.8** POSSIBLE NOREPINEPHRINE STORAGE IN HEART ATRIAL GRANULES. B. Peters and B. Haber. Marine Biomedical Institute and Division of Neurology, University of Texas Medical Branch, Galveston, Texas 77550

Atrial muscle cells contain 0.2-0.4 micron membrane bound vesicles or granules. These juxtanuclear granules can be visualized by an electron microscopic histochemical technique for unsubstituted catecholamines, following L-Dopa administration. The simultaneous administration of disulfiran or reserpine abolishes the staining seen with L-Dopa alone. The atrial NE level is increased twofold with L-Dopa, and markedly reduced by reserpine. The disulfiran effects strongly suggest that norepinephrine and not dopamine may be stored in heart atria. Atrial granules are found primarily in the 3000-14,000xG fraction ($P_2$) of atrial homogenates. $P_2$ is free of microsomes and is further subfractionated on discontinuous sucrose gradients, yielding a fraction (AGF) markedly enriched in granule content. AGF binds $H^3NE$ to a greater extent than either the starting homogenate or the $P_2$ fraction. This uptake is temperature and concentration dependent and is blocked by reserpine. The possible storage of NE by heart atrial granules may be involved in the arrythmias frequently seen during L-Dopa therapy. Supported by PHS grant 5R01 MH 19502, grant MSRDP 602333, and by the Moody Foundation of Galveston.

**8.9** NEW ELECTRON MICROSCOPIC FINDINGS IN SUBACUTE SCLEROSING PANENCEPHALITIS (SSPE), M.G. Hadfield*, R.B. David*, and W.I. Rosenblum. Dept. Path., Div. Neuropath., Dept. Med., Div. Neurol., Med. Coll. Va., Richmond 23219

Electron microscopy (EM) has demonstrated the presence of filamentous nuclear bodies and of tubular material in subacute sclerosing panencephalitis (SSPE). The tubular material is thought to represent the nucleocapsids of a measles-like virus. Although others have suggested that nucleocapsids are formed from the filamentous nuclear bodies, EM evidence for such a transition has not yet been generally accepted. In the present case additional EM evidence of a transition between nuclear bodies and nucleocapsids was observed. We will demonstrate a previously unreported whorled or fingerprint pattern of nucleocapsids. This configuration mimicked that of the filaments in the nuclear bodies, a finding best explained by a transformation of nuclear bodies into nucleocapsids or a synthesis of the latter by the former. Further evidence supporting a relationship between filamentous nuclear bodies, and the nucleocapsids, is the unusual demonstration of a closely associated filamentous and tubular material within the nucleus of a single cell. Additional findings of interest include an intranuclear striated rod, reported only once before in SSPE, and degeneration of neuronal processes, not previously reported in EM studies of SSPE.

**8.10** SERIAL EEG AND CLINICAL STUDIES IN SQUIRREL MONKEYS INOCULATED WITH TRANSMISSIBLE MINK ENCEPHALOPATHY (TME) AGENT. J. D. Grabow, R. J. Eckroade*, G. M. ZuRhein*, P. E. Zollman* and R. P. Hanson*. Mayo Clin., Rochester, Minn.; Univ. Delaware, Newark; and Univ. Wisconsin, Madison.

In the anticipation of developing a single primate model for a comparative study of the neurologic, pathologic, and immunochemical responses to different "slow virus" agents, an extensive EEG and clinical investigation was initiated with squirrel monkeys. The present study of 12 squirrel monkeys intracerebrally inoculated with TME agent and 6 controls included 562 serial EEG tracings (2-week interval) and 2 depth studies made during a 20-month period. All inoculated monkeys had significant EEG changes prior to observable clinical findings. Decrease in frequency or in voltage (or in both) of the background alpha activity was noted 288 days (mean) after inoculation--80 days (mean) before clinical "signs." Other abnormalities recorded during the course of the disease included epileptiform activity (in 7 monkeys), photosensitivity and pattern sensitivity (in 1), periodic complexes (in 2), and myoclonic jerks (in 3). Clinical findings included behavioral changes (in 11), gait disturbances (in 11), balance disorders (in 11), tremors (in 7), myoclonus (in 3), seizures (in 2), visual agnosia (in 1), increased deep tendon reflexes (in 10), hypotonia (in 8), extensor toe signs or fanning of toes (in 5), and hypothermia (in 7). Death occurred 383 days (mean) after inoculation, which was 14 days (mean) after clinical symptoms began. Presently, the controls are healthy and have normal EEGs. Postmortem examinations confirmed the presence of spongiform encephalopathy. These findings suggest that TME agent behaves in primates as Jakob-Creutzfeldt agent behaves in humans and therefore suggest that the agents may be closely related. (Movie)

**8.11** FIXATION OF DEVELOPING RAT CEREBELLUM FOR ELECTRON MICROSCOPY: SOME EXPERIMENTAL OBSERVATIONS. Ian S. Zagon*and Robert S. Lasher. Dept. Anat., Univ. Colo. Med. Sch., Denver, CO220.

Fixation of developing neural tissues has proven difficult and few experimental studies of an extensive nature have been reported. In conjunction with a light and electron microscopic examination of the developing rat cerebellum, a comparative study of fixation techniques was conducted in order to determine optimal fixation. Different primary fixatives, in combination with several procedures, that included variations of buffers, duration of fixation, temperature, pH, osmolarity, and en bloc staining (aqueous 2% uranyl acetate), were evaluated. All tissue was fixed by immersion, postfixed with 1% $OsO_4$ in buffer for $\frac{1}{2}$ hour, dehydrated in an ethanol series, and embedded in Epon. Fixation times between 1-4 hours, temperatures from 0°C to ambient, and pH ranges from 6.8 to 8.0 were not critical. Osmolarities below 250 mOsM were hypotonic and membrane systems were fragmented; 320 mOsM and above produced a hypertonic situation with visible shrinkage. Glutaraldehyde (glut.) buffered with cacodylate or s-Collidine, half-strength Karnovsky's fixative, or Zamboni's fixative, all gave inadequate fixation. Acrolein (0.5%-10%) in combination with glut. and any of the buffers used, resulted in hypertonic fixation which was visible under the light microscope. En bloc staining for 1-2 hours resulted in a lack of crisp structural definition. In summary: 1.6% glut. in 0.05M Sorensen's phosphate buffer (290 mOsM) proved to be the most reliable primary fixative and gave the best cytological preservation. Support:NIH Grants NS-09641, GM-01981.

**9.1** IONIC AND PHYSICO-CHEMICAL MECHANISMS UNDERLYING NON-NARCOTIC ANALGESIA. J. L. Barker and H. Levitan, NIH, NICHD, Bethesda, Md. 20014.

The relative ability of the non-narcotic analgesic salicylate and its analogues to increase the potassium permeability and decrease the chloride permeability of identified invertebrate neurons was correlated with some physico-chemical properties of these compounds. Activity in this system was directly correlated with octanol-water partition coefficient (P) and inversely correlated with pKa (correlation coefficient = 0.992). That is, a compound's ability to alter neuronal membrane permeability increased with increasing membrane solubility (P value) and decreased with decreasing pKa. This latter observation reflects the percentage of organic anions available at the pH of the experimental conditions. These results indicate that the degree of increase in cation permeability and decrease in anion permeability is determined by the number of negatively charged organic anions adsorbing to the membrane. The observed changes in membrane permeability decrease both the probability of action potential output and the efficacy of synaptic input. Since a compound's activity in this system correlates well with its reported analgesic potency, these results not only strengthen the hypothesis that similar ionic mechanisms underlie non-narcotic analgesia, but may also provide a physico-chemical basis for predicting analgesic activity. With this insight it should be possible to predict the analgesic potency of as yet untested drugs and to design new agents of any desired potency.

**9.2** RECEPTOR REPRESENTATION IN TWO TRIGEMINAL SYSTEMS. *Lawrence Kruger, James A. Mosso and Douglas Kirkpatrick, Depts. Anat. & Neurosurg., Sch. Med., UCLA, Los Angeles, 90024.

Clinical findings have demonstrated that anterolateral cordotomy and interruption of the caudal portion of the sensory trigeminal complex results in analgesia, thermanesthesia and a poorly defined tactile defect. Interruption of the lemniscal path, including its trigeminal component, also results in a tactile defect but without loss of recognized specific cutaneous modalities. In order to understand the modality basis for sensory dissociation, a study of cutaneous receptor categories in the two principal components (lemniscal and anterolateral) of the trigeminal sensory complex was undertaken in a series of decerebrate cats.

The findings indicate that the principal varieties of low-threshold mechanoreceptors, including those with thin axons, are represented in both lemniscal and anterolateral components. In the spinal V nucleus caudalis, specific nociceptor and thermoreceptor representation is predominant in the marginal zone, whereas all modalities appear to be represented in the nucleus proprius.

Receptive field size, thresholds and graded discharge characteristics of sensitive mechano-receptors appear comparable in both systems. This finding fails to provide a basis for the concept of a poorly organized "protopathic" system subserving "crude touch". The remarkable specificity of the anterolateral component indicates that those aspects of pain subserved by receptors other than specific nociceptors (e.g., corneal receptors) remain obscure. (Supported by U.S.P.H.S. Grant NS-5685)

*

**9.3** **INTERDEPENDENCE OF TRIGEMINAL PRIMARY RELAY NUCLEI.** **R.B.King (SPON: F.G.Worden) Dept. Neurosurg., SUNY, Upstate Med. Cent., Syracuse, N.Y. 13210.**

**Perception of a noxious facial stimulus as painful is dependent upon neural mechanisms in the caudal portion of the trigeminal primary relay nuclei in the brain stem. However, a population of neurones in this location which respond in some characteristic way to a noxious stimulus have been difficult to identify. This apparent paradox has suggested that interruption of neural mechanisms which link rostral and caudal elements of the trigeminal primary relay nuclei may contribute at least in part to the facial analgesia which follows trigeminal spinal tractotomy. Changes in the excitability of primary afferent preterminals at nucleus oralis can be demonstrated following its isolation from nucleus caudalis and by altering the excitability of neural elements in nucleus caudalis. Noxious and non-noxious conditioning stimuli influence the excitability of these rostral relay preterminals differentially. Altered information transfer at rostral relay nuclei secondary to their isolation from nucleus caudalis, therefore, may, in addition to the interruption of classical relays at nucleus caudalis, contribute to the altered perception of a noxious facial stimulus which follows trigeminal spinal tractotomy.**

**9.4** BEHAVIORAL AND PHARMACOLOGICAL STUDIES OF ANALGESIA FROM ELECTRICAL STIMULATION OF THE PERIAQUEDUCTAL GRAY MATTER IN THE RAT. H. Akil, D. J. Mayer, and J.C. Liebeskind. Department of Psychology, UCLA, Los Angeles, Calif. 90024

Electrical stimulation of periaqueductal gray matter (PGM) of the rat results in powerful and sometimes long-lasting analgesia to various noxious stimuli (Mayer et al., Science 174: 1351, 1971). Spinal nociceptive reflexes are inhibited as much by PGM stimulation as by large doses of morphine (Mayer, doct. diss., UCLA, 1971). Others have suggested PGM as a possible site of action of morphine. We have thus looked for other comparisons between analgesia from morphine and PGM stimulation. Drugs which decrease brain monoamine levels are known to block the antinociceptive action of morphine. We find such drugs have a similar action on analgesia from PGM stimulation. In one study PCPA (a 5-HT synthesis inhibitor) blocked analgesia only from stimulation near the 5-HT cells of dorsal raphe in posteroventral PGM. In another study, TBZ (a depletor of all 3 brain monoamines) blocked analgesia from stimulation in a wider area of PGM; and original levels of analgesia were restored by injection of monoamine precursors 5-HTP or L-DOPA. We have most recently found that Naloxone, a specific morphine antagonist, also blocks brain-stimulation analgesia. It appears that a neural system for the active inhibition of pain exists in the brainstem, that this system can act upon spinal cord mechanisms of the pain response, and that this system can be excited by electrical as well as pharmacological stimulation. (Supported by USPHS grant NS 07628)

**10.1** PROLIFERATION OF CEREBELLAR NOREPINEPHRINE-CONTAINING FIBERS IN RESPONSE TO PEDUNCLE LESIONS. V. M. Pickel*, Helmut Krebs* and F. E. Bloom. Lab of Neuropharmacology, NIMH, St. Elizabeths Hosp., Wash., D.C. 20032

Regenerative axon sprouting and plastic changes of catecholamine neurons in response to denervation have been shown in the mesencephalon and septal region of the rat (see Moore et al., Brain Res. 33:13, 1971). The present study attempted to ascertain this phenomenon for recently demonstrated cerebellar norepinephrine-containing (NE) fibers (Bloom et al., Brain Res. 25:501, 1971). In 43 rats the superior (SP), inferior (IP) and middle (MP) peduncle were cut as follows: unilateral IP or SP; IP and SP; IP, SP and MP; as well as total bilateral transection. Seven sham-operated rats served as controls. The short- and long term effects (approx. 7 days and 40 days) of these transections were then studied employing the Fink-Heimer procedure for terminal degeneration and the histofluorescence technique for the NE-containing pathway, respectively. The NE fibers were traced from their origin in the Locus Coeruleus to the cerebellar cortex, i.e., Purkinje cells (P), via the SP. Only following transection of IP and/or partial SP, which removed a portion of the climbing and NE-containing fiber input, terminal axon proliferation of the NE pathway was consistently observed throughout areas of innervation, specifically proximal to P cells. Silver impregnation revealed terminal fiber degeneration patterns closely paralleling the fluorescent NE fiber reinnervation in the cerebellar cortex. The proliferation in this neuronal network of known origin and termination corroborates earlier reports of regeneration in the central nervous system and, in addition, may provide a model system for an elucidation of its physiological role.
(Supported by NIH postdoctoral fellowship GM52391-01 and Canadian Med. Res. Council postdoctoral fellowship.)

**10.2** STUDIES ON THE INTERACTION BETWEEN NORADRENALINE AND ADENYL CYCLASE IN THE CEREBRAL CORTEX. N. Lake* and J.W. Phillis, Department of Physiology, University of Manitoba, Winnipeg, Canada.

It has been proposed (Hoffer et al, Ann. N.Y. acad. Sci.(1971) 185, 531-549) that the depressant effects of noradrenaline (NA) on Purkinje neurones in the rat cerebellar cortex are intermediated by cyclic AMP. This is consistent with the finding that exogenous NA stimulates the formation of cyclic AMP in brain slices in vitro. NA also depresses cerebral cortical neurones. However the amount of stimulation of cyclic AMP formation by NA in cerebral cortical slices is ten times greater in slices from rats than that observed in slices from guinea pigs, and two fold greater than that seen in slices from cats. The actions of NA (pH 5.0) on cerebral cortical neurones of rats, guinea pigs and cats anaesthetized with methoxyflurane and nitrous oxide were compared using the microiontophoretic technique. The most usual action was depression of the firing rate (approx. 65% of neurones); only 2 cells of the population showed an elevation of the firing rate. There were no significant differences between species as to the number of responsive neurones. There was no apparent difference in the depressant potency of NA in the cortices of these species in vivo to parallel the marked differences in cyclic AMP formation observed in vitro. Preliminary trials of the microiontophoretic application of aminophylline (one action of which is to inhibit the phosphodiesterase that breaks down cyclic AMP) in rats and guinea pigs have revealed that a prior application of aminophylline potentiates the depression produced by NA on 77% of rat neurones and 39% of guinea pig neurones. For the remaining 23% of rat neurones and 61% of guinea pig neurones there was no change in the response to NA. Studies with cyclic AMP and prostaglandins are in progress.

**10.3** EFFECTS OF 6-HYDROXYDOPAMINE (6-OHDA) ON SHUTTLE-BOX AVOIDANCE: INVOLVEMENT OF BRAIN DOPAMINE. B.R. Cooper*, G.R. Breese, J.L. Howard and L.D. Grant. Child Develop. Inst., UNC Sch. of Med., Chapel Hill, N.C., 27514

Previous work has suggested that catecholamines are of importance to conditioned avoidance responding. Utilizing intracisternal (IC) injections of 6-OHDA, we have examined the relationship of catecholamine neurons to the acquisition and performance of a shuttle-box avoidance response. Male Sprague-Dawley rats were treated with (1) 25 + 25 + 25 μg 6-OHDA I.C. to preferentially deplete NE (NE↓) (2) 200 μg 6-OHDA I.C. 1 hr after 25 mg/kg desipramine to preferentially deplete dopamine (DA↓) or (3) 200 μg of 6-OHDA I.C. given 30 min after pargyline (P + 6-OHDA). When tested for shuttle-box avoidance acquisition during a 100 trial session 3 weeks after injection, P + 6-OHDA treated rats failed to show acquisition. In contrast, the rats given NE↓ treatment showed significantly facilitated acquisition, while the DA↓ group did not differ from controls. Rats previously trained to perform in the shuttle-box were also given the P + 6-OHDA treatment. When tested 2 weeks later, no differences in performance were evident, although 25 mg/kg alpha-methyltyrosine (α-MPT), which did not affect performance in control subjects, significantly reduced performance of the P + 6-OHDA group. To further examine the contribution of NE and DA to avoidance acquisition and performance, rats given NE↓ and DA↓ treatments were injected with α-MPT four hours before testing. α-MPT markedly reduced acquisition and performance in the DA↓ group. Acquisition and performance in NE↓ treated rats was reduced to slightly below that of control animals. These data support the view that brain catecholamines are important in avoidance responding. Our results emphasize the role of dopamine. (Supported by USPHS Grants MH-16522, HD-24585 and HD-03110).

**10.4** ROLE OF CENTRAL CATECHOLAMINE NEURONS IN FEEDING AND DRINKING BEHAVIOR: EVIDENCE FROM INTRAHYPOTHALAMIC INJECTIONS OF 6-HYDROXYDOPAMINE. Gerard P. Smith, Gregory N. Ervin* and Donald J. Reis. Depts. of Psychiat. and Neurol., Cornell Univ. Med. Coll., New York, N.Y. 10021.

To establish if the syndrome of aphagia and adipsia induced by bilateral electrolytic lesions of lateral hypothalamus (LH) results from damage of axons of catecholamine (CA) neurons, 6-hydroxydopamine (6-OHDA, 8 to 32 μg/4μl) was microinjected bilaterally into LH at 3 sites: anteriorly at level of optic chiasm; posteriorly at caudal edge of ventromedial nucleus (VM) and at an intermediate site across from mid-VM. Of 43 rats injected, 36 became aphagic and adipsic, 3 became anorexic and adipsic. Bilateral 6-OHDA injections at any one of these 3 sites also produced aphagia and adipsia, but less consistently. Injection of 6-OHDA in the anterior site alone decreased hypothalamic norepinephrine (NE), but not striatal dopamine (DA); all other injections decreased both hypothalamic NE and striatal DA. Rats were resistant to strong stimuli for feeding (insulin hypoglycemia) and drinking (IM NaCl or isoproterenol). If rats were maintained by tube feeding, some ate and drank again. Their behavioral recovery differed from that described by Teitelbaum and Epstein (1962) after LH electrolytic lesions in 3 ways: recovered rats 1) drank water in the absence of food, 2) drank water in response to IM NaCl or isoproterenol, and 3) ate dry food in the absence of water. The disruption of feeding and drinking after 6-OHDA is consistent with the hypothesis that central CA axons in LH are part of the neural networks for feeding and drinking behavior in rats. (Supported by NS-08402, NS-06911 and Harris Foundation.)

**11.1** TISSUE CULTURE MODELS OF DEVELOPING CNS FUNCTIONS.[1] Stanley M. Crain. Dept. Physiol. & Rose F. Kennedy Ctr., Albert Einstein Coll.Med.,Bx.,N.Y.

Cultures of immature central nervous tissues provide a powerful model system for studies of developing brain functions. Microelectrode recordings in "pre-synaptic" explants of embryonic mammalian CNS tissues have shown that these neurons possess intrinsic "self-organizing" properties since they can still develop *in vitro* the capacity to generate complex patterned bioelectric discharges resembling activity of synaptic networks of the CNS (Crain and Peterson, Science 141, 1963). Similar organotypic bioelectric activity develops in small clusters of neurons which reaggregate *in vitro* even after dissociation and random dispersion of fetal mouse cerebral cortex, brainstem or spinal cord cells (Crain and Bornstein, Science 176, 1972). Complex spontaneous bioelectric discharge patterns which may occur at intervals of the order of 1-10 sec in cultures of organized CNS tissues (Corner and Crain, J. Neurobiol. 3, 1972) show remarkable mimicry of rhythmic polyneuronal burst discharges recorded in the chick embryo spinal cord *in ovo* (Provine *et al*, PNAS 65, 1970). Demonstration that these cord discharges *in situ* are neural correlates of embryonic motility (Provine, Brain Res. 29, 1971) provides strong support for the relevance of CNS tissue culture models to behavioral studies. The culture model is strengthened by observation of similar relations *in vitro* between spontaneous rhythmic, bioelectric discharges in fetal rodent spinal cord explants and coordinated contractions of innervated skeletal muscle fibers. Further analyses of the cellular and molecular mechanisms which control generation and spread of organotypic patterned discharges in embryonic CNS explants maintained in rigidly restricted environments may therefore provide valuable insights into some aspects of early behavioral development. ([1]Supported by NINDS grant NS-06545, The Alfred P. Sloan Foundation, and a Kennedy Scholar Award.)

**11.2** DEVELOPMENT OF ORGANOTYPIC SPINAL CORD EXPLANTS AND INTERACTIONS WITH ADULT SKELETAL MUSCLE.[1] Edith R. Peterson. Dept. Neurol. and Rose F. Kennedy Center, Albert Einstein Coll. Med., Bronx, New York.

Fetal rodent spinal cord adapts well to long-term maintenance in vitro. In order to encourage optimal development of both the CNS and the peripheral nerve complex, cross-sections of spinal cord are explanted with their meningeal covering and attached dorsal root ganglia (Peterson et al, Zeit. Zellforsch., 66, 1965). Onset and development in vitro of complex bioelectric activity (Crain & Peterson, Brain Res. 6, 1967) correlates with the appearance and elaboration of synaptic ultrastructure (Bunge et al, Brain Res. 6, 1967). As the explants mature, large motor neurons become visible among the abundant small cord neurons. Myelination begins after about 7 days in vitro and extends rapidly over the entire explant. An abrupt transition from CNS myelin to peripheral Schwannian-type myelin occurs at the meningeal boundary where dorsal and ventral roots are clearly defined. Myelination of peripheral nerve fascicles increases gradually for several weeks. The concurrent differentiation of CNS and peripheral nerve elements is essential to development and function of an organotypic neuromuscular model. Adult skeletal muscle regenerates after incorporation into a 4-5 day old spinal cord culture. Early regeneration can be enhanced by neural as well as non-neural cell contacts, but continued neural deprivation leads to regressive changes. Full muscle differentiation and long-term maintenance are dependent on innervation in vitro, as in vivo. Maturation of motor endplate structures - increased complexity of nerve terminals and postsynaptic specializations - proceeds during weeks in vitro, as shown by light microscopy (Peterson & Crain, Exp. Neurol., in press) and electron microscopy (Pappas et al, Ann. N.Y. Acad. Sci., 18, 1971). ([1] Supported by NINDS Grant #NS08770.)

**11.3** INTRACELLULAR ANALYSIS OF DISSOCIATED NERVE CELL TISSUE CULTURE
Marc Dichter*, Beth Israel Hospital, Boston, Massachusetts

Over the past few years there has been increasing interest among neurobiologists in the study of the physiological properties and synaptic connectivity of nerve cells grown in dissociated cell culture. In such systems neurons and nerve nets can develop and be studied under controlled conditions. These preparations lend themselves to studies which attempt to correlate physiological properties with anatomical, developmental and genetic analysis.

The range of preparations currently being investigated varies widely: primary cultures of vertebrate muscle, spinal cord, sensory and sympathetic ganglia, cerebellum and cortex; invertebrate ganglia; continuous lines of neuroblastoma; hybrids between neurons and dividing somatic cells. Such preparations can be used to study passive membrane properties of neurons and the development of, and mechanisms responsible for, active responses.

Both excitatory and inhibitory chemical synapses from de novo in vitro and appear to be similar to those in the CNS. Analysis of these synapses may provide answers to the many unresolved questions about vertebrate CNS chemosensitivity, receptor properties, and transmitters. Complex nerve networks, including recurrent synaptic connections, are quite abundant. Where analysis has been possible, a large degree of "appropriateness" of synaptic connections has been seen. Neurons do not necessarily form synapses with their nearest neighbors in cultures. Glia are not needed for synapses formation.

12.1 SUBCELLULAR STUDIES ON THE EFFECT OF LSD ON RAT BRAIN SEROTONIN (5-HT). Angelos E. Halaris, Richard A. Lovell and Daniel X. Freedman. Dept. of Psychiatry, Pritzker Sch. Med., Univ. of Chicago, Chicago, Ill., 60637

Three particulate fractions (synaptosomal, mitochondrial, microsomal) are involved in the LSD-induced increase in rat brain 5-HT (Rosecrans et al., Biochem. Pharm. 16, 2011, 1967). We have undertaken to determine a) whether the 5-HT increase in each fraction is real or due to cross-contamination; b) the nature of the binding of 5-HT in these fractions; and c) the subcellular localization of LSD. Subcellular fractionation of sucrose homogenates of whole brains from male Sprague-Dawley rats (200-300 g) was accomplished as by Rosecrans et al., except that density-gradient subfractionation was done at 100,000 g for 30 min instead of 50,000 g for 120 min. The shorter spin at higher g resulted in less loss of 5-HT in particulate fractions without any change in protein content and, as verified by electron microscopy, a higher yield of synaptosomes with less mitochondrial contamination and a very small degree of myelin contamination. Thus, by this different centrifugation and a different separation method for 5-HT, we confirmed both qualitatively and quantitatively the results of Rosecrans et al. Experiments to explore the nature of the 5-HT binding to synaptosomal substructures, the significance of the binding in mitochondrial and microsomal fractions and the effect of tolerance to LSD are in progress. First results on the subcellular localization of LSD, using $^{3}$H-LSD of high specific activity injected i.p., have shown that maximum $^{3}$H-LSD in all subcellular fractions is found at 10 min with a steady decline thereafter in particulate $^{3}$H-LSD and a corresponding rise in the supernatant fractions. The same amount of $^{3}$H-LSD added to brain homogenates in vitro binds to all the particulate fractions, but to a lesser extent than is seen after injection of $^{3}$H-LSD in vivo. Supported by a F.F.R.P. postdoctoral fellowship (to A.E.H.) and U.S.P.H.S. research grant 13,186-06 from N.I.M.H.

12.2 STRESS CHANGES THE ACTION OF MESCALINE FROM BEHAVIORAL INHIBITION TO EXCITATION. Wagner H. Bridger, David M. Stoff* and David A. Gorelick*. Depts. of Psychiatry and Pharmacology, Albert Einstein College of Medicine, Bronx, N. Y. 10461.

Two experiments were performed which demonstrate that the action of mescaline on the behavior of rats depends on the amount of stress present in the paradigm. In the first experiment animals were given 12½, 25, or 50 mg/kg mescaline (ip) or 2 mg/kg amphetamine (ip) prior to being placed on a raised platform in the center of a cage. When the animal stepped off the platform he received electric shock and was returned to the platform. Step down latency (SDL) prior to shock administration revealed dose dependent inhibition (increased SDL) by mescaline and excitation (decreased SDL) by amphetamine. All drug groups showed excitation (decreased mean SDLs) both over 15 shock trials and on a 24 hour retention test, with amphetamine producing more excitation than mescaline on retention. In the second experiment, rats were trained in two-way shuttlebox avoidance for 11 days. Mescaline (50 mg/kg ip) given prior to daily session caused excitation (increased % avoidance) in all rats on day 1 and in poor avoiders on day 11. Good avoiders showed inhibition (decreased % avoidance) on day 11. Amphetamine (2 mg/kg ip) caused excitation in all rats on both days. On day 1, amphetamine rats, compared to saline, showed more intertrial crossings (ITCs) and more shuttlebox crossings during a 5 minute presession period. Mescaline rats showed the same number of ITCs and fewer presession crossings. These experiments suggest that mescaline causes behavioral excitation when rats are stressed (shocked) and inhibition when they are not, whereas amphetamine causes excitation in both situations.

**12.3** THE EFFECT OF $\Delta^9$TETRAHYDROCANNABINOL ON INFANT RAT BRAIN NUCLEIC ACID AND PROTEIN SYNTHESIS IN VIVO. A. Jakubovic and P.L. McGeer. Kinsmen Laboratory, University of British Columbia, Vancouver 8, Canada.

Previous investigations have shown that some cannabinoids decrease the incorporation of uridine-2-$^{14}$C as well as L-leucine-U-$^{14}$C into the nucleic acid and protein fractions, respectively, of infant and adult rat brain cortex slices in vitro (Can. J. Biochem., in press). In order to detect any effect on brain metabolism in vivo, infant rats received simultaneously a single s.c. dose of Tetrahydrocannabinol (20 mg/kg) and a one microliter intra-cerebral injection containing uridine-2-$^{14}$C (0.05 µc) or L-leucine-U-$^{14}$C (0.05 µc). With uridine-2-$^{14}$C as the tracer metabolite the results show that: (a) between 75-90 min there is an apparent increase of radioactivity in the acid soluble as well as the nucleic acid fractions of the brains of THC-treated rats (b) after 3-4 h there is a significant decrease of radioactivity in both fractions and (c) after 5-6 h there is no difference in the radioactivity of the fractions. With L-leucine-U-$^{14}$C as the tracer metabolite, there is a decrease in incorporation into brain proteins 3 h after the injection in the THC-treated rats. The radioactivity in the liver fractions is not affected by THC when uridine is the tracer metabolite injected into brain, suggesting the inhibition is a direct effect on brain and not mediated by the liver.

**12.4** EFFECTS OF PROLONGED AMPHETAMINE ADMINISTRATION ON AD LIB SELF-STIMULATION, EATING AND DRINKING IN RATS. T. Rogge*, G.F. Koob* and Z. Annau. Dept. Environ. Med. Johns Hopkins Univ., Baltimore, Md. 21205

Two groups of 4 male hooded rats each were implanted with bipolar electrodes in the posterior lateral hypothalamus. Following recovery from surgery, each rat was trained to self-stimulate and then placed in a Skinner box where it had ad lib access to self-stimulation, food and water. Stable baseline rates of self-stimulation were established for at least three days. Intraperitoneal injections of d-amphetamine sulfate, 5 mg/kg, every eight hours for either 3 or 6 days were associated with 100% or greater increase in the daily rate of self-stimulation in both groups. In some rats, the drug induced self-stimulation, was preceded by a period of stereotyped sniffing and licking that decreased from an initial 3.5 hours duration to 1.5 hours by the fourth day. Cessation of drug administration was associated by a profound depression of self-stimulation that lasted from 24 to 72 hours. Food intake decreased by 50% during drug administration and rebounded to 150% of baseline when the drug was discontinued. Results indicate that the post amphetamine depression is specific to neural systems mediating self-stimulation behavior, and further, that the effectiveness of amphetamine in inducing stereotyped behavior decreases with continued treatment.

**12.5** EFFECT OF THE AMPHETAMINE DERIVATIVE, 2,5-DIMETHOXY-4-METHYLAMPHETAMINE, ON THE SPONTANEOUS LOCOMOTOR ACTIVITY IN MICE. Jen-Tzaw Huang* and Beng T. Ho. Texas Research Institute of Mental Sciences, Houston, Tex. 77025

A characteristic effect of amphetamine on laboratory animals is the increase of spontaneous locomotor activity (SLA). Several hypotheses correlate SLA with brain norepinephrine (NE) and dopamine (DA). 2,5-Dimethoxy-4-methylamphetamine (STP or DOM), a hallucinogen and derivative of amphetamine, decreased the motor activity in neonatal chicks (Europ. J. Pharmacol. 17: 259, 1972). With a photocell activity cage, the present study showed STP in a dose of 25 mg/kg, i.p., decreased SLA in Yale-Swiss mice to below 50% of the control values at both 30 and 60 min, while 5 mg/kg of the compound did not have significant effect on SLA. This increased SLA by STP was reversed by pretreating with *d*-amphetamine sulfate (3 mg/kg, i.p.) 30 min prior to STP. Cinanserin [2-(3-dimethylaminopropylthio)cinnamanilide HCl], which was found to block STP pressor action in rats, was evaluated on the effect on SLA in STP-treated mice. The results showed that cinanserin at the doses which either had no effect or decreased SLA failed to block SLA in STP animals, but did block the increased SLA by amphetamine. The effects of STP on brain NE and DA were also studied in mice. The compound neither caused any significant alteration in NE or DA level nor did it exert an effect on the disappearance of NE or DA formed from $^{14}$C-tyrosine in mouse brains. Our results indicate that STP differs from amphetamine in both the effects on SLA and brain catecholamines in mice.

**12.6** DIFFERENTIAL ACTIONS OF d-AMPHETAMINE AND l-AMPHETAMINE IN MICE. Carlos M. Quirce* (SPON: R.P. Maickel). Dept. of Pharmacology, Med. Sci. Program, Indiana Univ., Bloomington, Indiana 47401.

The therapeutically used preparations of amphetamine generally consist of the racemic d,l-mixture (Benzedrine$^{R}$) or the pure d-isomer (Dexedrine$^{R}$). The pure l-isomer has been discarded because of its low activity. We have begun to examine the comparative effects of d- and l-isomers of amphetamine on various behavioral tests and biochemical parameters in mice. When tested on gross motor activity (actophotometer), d-amphetamine had a stimulatory effect at doses from 0.5 to 4.0 mg/kg, i.p., with a decrement in activity occurring at 8.0 mg/kg, i.p., presumably reflecting the onset of sterotyped behavior. With l-amphetamine, a dose of 0.5 mg/kg evoked slight stimulation, while 1.0-4.0 mg/kg caused a decrease in motor activity. At 8.0 mg/kg, increased activity was once again observed. All doses of d-amphetamine tested increased blood glucose for 1 hour after dosage; the effects of comparable doses of l-amphetamine were similar in initial potency but more prolonged in duration of action, lasting for 4 hours at 2.0-8.0 mg/kg. Plasma levels of free fatty acids were significantly elevated only by doses of d-amphetamine of 2.0 or 4.0 mg/kg and by doses of l-amphetamine of 4.0 mg/kg. In the light of the hyperglycemia evoked by both isomers, the effects on fatty acids presumably reflect the net differential between increased lipolysis and increased triglyceride synthesis. These differential effects of d- and l-amphetamine will also be compared in animals with altered levels of norepinephrine. (Supported by USPHS grants MH-18852 and KO2-MH-41083 to R.P. Maickel and by a grant from Strasenburgh Pharmaceutical Division, Pennwalt Corporation.)

**12.7** SUPPRESSION OF THE VISUAL PLACING RESPONSE BY 6 HYDROXYDOPAMINE: RESTORATION WITH AMPHETAMINE. Jeri A. Sechzer, Gregory N. Ervin* and Gerard P. Smith. Dept. Psychiat., Cornell Med. Ctr., White Plains, N.Y. 10605

Visual placing responses in rats were completely suppressed after bilateral injections of 6 hydroxydopamine (6 OHDA) into the medial forebrain bundle. These deficits have persisted after recovery from the post 6 OHDA effects on feeding and drinking. On a behavioral scale from 0-6 (0=no visual placing; 6=excellent visual placing) the dopamine treated rats rated 0 and normal rats rated 4-6. Intraperitoneal amphetamine administration restored visual placing in the defective rats to 4-6. These responses then gradually deteriorated to preamphetamine levels in approximately 72 hrs. The amphetamine effect was repeated at least 3 times. Although pathways in the medial forebrain bundle have been associated with generalized motor function and feeding and drinking, our experimental results provide evidence that severe and persisting visual deficits may be an additional consequence of destruction of catecholaminergic neurons by 6 OHDA in this system.

**12.8** EFFECTS OF D-AMPHETAMINE, CHLORDIAZEPOXIDE, AND CHLORPROMAZINE ON SIGNALLED SHOCK AVOIDANCE. M. E. Risner and K. A. Khavari. Dept. of Psychology, University of Wisconsin-Milwaukee, Milwaukee, Wisconsin 53201

Twelve, male, albino rats were initially trained to bar press for 0.5 ml drops of 10% sucrose. Following acquisition of the response, the reinforcement was discontinued and the Ss were trained in a signalled shock avoidance paradigm until a stable baseline was reached. The rats were then intraperitoneally injected with d-amphetamine (1, 2, and 4 mg/kg), chlordiazepoxide (10, 20, and 40 mg/kg), and chlorpromazine (1, 2, and 4 mg/kg) in a randomized procedure such that six animals received each dose of each drug. At least 7 days intervened between successive drug injections, and a no-drug session was included in this 7 day period. There were both drug-dependent and dose-dependent changes in each of several behavioral indices collected throughout the 6-hour sessions. Shock avoidance behavior was disrupted in all cases with chlorpromazine exhibiting the greatest dose-dependent decrease. Both chlordiazepoxide and d-amphetamine also showed dose-dependent decreases in shock avoidance responses. Although light avoidances increased in all cases, there were no significant differences among the three drugs used in this study. In general, total bar presses decreased for both chlorpromazine and chlordiazepoxide, whereas there was an increase in total bar presses for d-amphetamine, significant only at the highest dose. Finally, shock escapes/opportunity showed a dose-dependent decrease following injections with chlordiazepoxide. Chlorpromazine also produced a decrease in shock escapes/opportunity at the lowest and highest doses. Shock escapes/opportunity were not affected by the three doses of d-amphetamine.

**13.1** OPPOSITE EFFECTS ON BEHAVIOR IN THE GOLDFISH OF $\beta$-MSH AND MSH-INHIBITING FACTOR. Rodney C. Bryant, Frederick Petty, and Abba J. Kastin. Brain Res. Inst, Univ. of Tenn. Med. Units, Memphis 38103; and VA Hosp. and Tulane Univ. School of Medicine, New Orleans, La. 70146.

The finding (Kastin and Schally, Gen. Comp. Endocrinol., 7, 452, 1966) of an inhibiting factor (MIF) for melanocyte-stimulating hormone (MSH) coupled with increasing evidence that MSH may have important effects on behavior and centrally mediated phenomena in rats and humans, prompted the examination of the behavioral effects of MSH and MIF in a lower vertebrate, the common goldfish (Carrasius auratus). Fish were kept in continuous light or darkness and were given five daily sessions of active light-avoidance training. On day six, they were given one test session in extinction, immediately followed by intra-cranial injection of $\beta$-MSH, synthetic MIF, or the vehicle. On succeeding test sessions in extinction, conditioned responses and general activity were recorded. No effect among groups on extinction of the conditioned response was found. General activity during test sessions showed marked differences among groups, with MIF elevating and MSH depressing general shuttling activity; these differences varied over sessions and according to whether the fish had been kept in light or darkness. This is apparently the first time the administration of these pituitary and hypothalamic substances has been shown to affect behavior in the goldfish.

**13.2** MELANOCYTE-STIMULATING HORMONE (MSH) AFFECTS LEARNING AND EXTINCTION IN NORMAL AND BRAIN-DAMAGED RATS. Lois O. Stratton, Abba J. Kastin, and Andrew V. Schally*. Louisiana State Univ. in New Orleans, 70122; VA Hosp. and Tulane Univ. Sch. of Med., New Orleans, 70146.

Previous studies showed that MSH, which produces pigmentary changes in amphibians, affects learning and extinction of aversive and appetitive habits in mammals. One hypothesis suggested that MSH increases emotional arousal which leads to increased attention to environmental cues. The present study examined the effects of synthetic $\alpha$-MSH (10 $\mu$g/rat) and saline on learning and extinction of two T-maze tasks involving discrimination of brightness. The first task involved escape from electric shock by entry into a lighted goal box; in the second task, avoidance of shock required the rat to change direction depending upon the presence or absence of lights in the maze. The behavior of pigmented rats with large and small lesions of the posterior neocortex was compared with that of intact rats. Results of the first problem showed a significant effect of the lesion, but no learning differences between rats treated with MSH or saline. When switched to the second problem, animals receiving MSH took longer to learn than the controls; rats with larger lesions were more severely affected than those with the smaller lesions. In the second task, rats injected with MSH made significantly more repeated erroneous responses, exhibited more vicarious trial-and-error behavior at the choice point, and took longer to extinguish. This part of the study confirms previous work using different models which found resistence to extinction in albino rats and extends the finding to a pigmented strain. MSH had the greatest effect upon rats with the large cortical lesions, making them less likely to respond adaptively to the new behavior required by the altered stimulus. The results suggest that MSH produced a temporary emotional arousal state which led to delayed extinction of the first task and thus slower learning of the second task.

**13.3** COMPARATIVE ABILITY OF PENTADECAPEPTIDES TO INDUCE DARK AVOIDANCE IN NAIVE RATS, MICE, AND GOLDFISH. Helene N. Guttman, Martin A. Weiler* and George Matwyshyn*. Dept. Biol. Sci., Univ. Illinois at Chicago Circle, Chicago, 60680 Ill.

Naturally dark preferring rodents and fish can be trained to avoid dark portions of a shuttle box. Ungar et al. have isolated, and purified the rat principle, a pentadecapeptide named scotophobin (SCOTO). Rat SCOTO was synthesized by Parr and Holzer. Using similar methods, we isolated and characterized mouse and goldfish SCOTO.

Synthetic rat SCOTO (synthesized by Parr and Holzer and donated by Ungar), deamidoSCOTO(DESCOTO), N-acetylDESCOTO, and the 8-15 AA fragment of DESCOTO (synthesized and donated by Weinstein) were tested for stability and bio-activity. SCOTO, synthesized by the Merrifield solid state procedure, is very labile whereas the Weinstein molecules, synthesized by classical methods, are much more stable. In all cases, degradation was followed by the appearance of additional spots on two dimensional TLC chromatograms of microdansylated peptides. One can speculate that traces of contaminating reagents from the solid state synthesis labilizes the product.

All compounds were bio-assayed by our previously published passive avoidance methods. Ability of peptides to induce active dark avoidance was also tested. SCOTO induces dark avoidance in both active and passive tests thus ruling out a mode of action based upon reduction in gross animal activity. The nature of the transient activity of the SCOTO analogues will be discussed.

Aided in part by grants from UICC Research Board and Sigma Xi.

**13.4** SYNTHETIC SCOTOPHOBIN IN THE RAT: EFFECTS OF INTRAVENTRICULAR AND INTRA-PERITONEAL ADMINISTRATION IN SEVERAL BEHAVIORAL PROCEDURES. B.M. Kulig, P.S.D'Encarnacao, G. Little*, and R.C. Bryant. Brain Research Institute, Univ. of Tenn. Med. Units, Memphis 38103; and Dept. of Psychology, Memphis State Univ., Memphis 38111.

Despite the fact that the natural peptide was originally isolated from brains of rats trained to avoid the dark, synthetic scotophobin has never been shown to be active in the rat, although activity in the mouse and the goldfish has been reported. Results are described from several procedures in which rats were administered synthetic scotophobin intraperitoneally or intra-ventricularly. Rats learned to lever-press for a water reinforcer on a VI 30" schedule. All illumination in the experimental chamber was periodically eliminated for short periods to adapt out effects of dark-onset on rate of lever-pressing. Rats then received scotophobin or control solution either intra-peritoneally or intra-ventricularly, and "suppression ratios" were computed for subsequent dark periods. In another procedure, rats were tested before and after injection with scotophobin or control solution, in an "Animex" activity chamber, lighted or darkened. The general effects on activity are the first reported for scotophobin. Finally, results are presented from a sensory reinforcement procedure in which rats pressed a lever for light or for dark, with scotophobin administered intra-peritoneally.

**13.5** DARK-AVOIDANCE FACTOR FROM TRAINED FISH BRAIN: COMPARISON IN GOLDFISH WITH THE SYNTHETIC LEARNING-LINKED RAT PEPTIDE SCOTOPHOBIN. William L. Byrne, Rodney C. Bryant, Nelson N. Santos, Frederick Petty, Laurence S. Bradham*, and Larry A. Kepner. Brain Res. Inst. and Dept. of Biochemistry, Univ. Tenn. Med. Units, Memphis 38103.

It has been previously reported that synthetic rat scotophobin is active in goldfish (Bryant, 1971; Guttman et al., 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 appear to produce little change in general shuttling activity. Differences were found in response of fish to SP and DFF according to whether fish were naive or partially pretrained, possibly indicating differences between the rat peptide and the comparable fish factor. Work on the effect of puromycin on the development of the behavioral effects of SP and DFF is reviewed.

Bryant, R.C. Paper presented at Annual Meeting, Society for Neuroscience, 1971.
Guttman, H.M., et al. Nature New Biology, 235:26 (1972).

**13.6** THE USE OF MASS SPECTROMETRY TO ELUCIDATE THE STRUCTURE OF OLIGOPEPTIDES OF BRAIN ORIGIN. Dominic M. Desiderio and Klaus Hägele*. Institute for Lipid Research and Department of Biochem., Baylor Sch. Med., Houston, Tex., 77025.

Within the past few years, there have been reports of structural elucidation studies of oligopeptides by mass spectrometry. This "non-classical" approach was taken in some cases due to the presence of protected termini and/or an extremely small amount of material available. The derivatives which must be formed in order to provide sufficient volatility include N-acetylation, N,O,S-peralkylation and the conversion of arginine to a dimethyl pyrimidyl ornithine. The instrumentation employed includes electron impact and chemical ionization mass spectrometry, high and low resolution techniques and the use of computers. Use was made of the above techniques in the elucidation of scotophobin. That initial work illuminated the procedure's limitations (mass range of 1-2000 units, volatility, combinations of certain amino acids). The availability of synthetic C-terminal peptides has permitted us to methodically investigate each individual peptide's behavior in order to be better able to apply these techniques to oligopeptides of natural origin.

**13.7** FURTHER STUDIES OF THE EFFECTS OF EXTRACTS FROM BRAINS OF TRAINED DONOR GOLDFISH: EFFECTS OF PERFORMANCE LEVEL OF DONORS AND INJECTION-TESTING INTERVAL. William G. Braud and Porter V. Laird*. Dept. Psychol., Univ. of Houston, Houston, Tex. 77004

RNA- and protein-rich extracts from brains of trained donor goldfish have yielded specific behavioral changes in naive recipient goldfish; these changes are quite similar to the behavioral changes produced in the donor fish by direct training. Two studies were conducted to determine: (a) whether the magnitude of this biochemical modification of recipient behavior would vary systematically with performance level of trained donors and (b) the effect of injection-testing interval in recipients. In Experiment 1, separate RNA-protein extracts were prepared from brains of goldfish that had shown high levels of performance, low levels of performance, or did not perform at all (control) during seven days of shuttle-box active avoidance training. The resulting three extracts were injected intracranially into three groups of naive recipient goldfish which were given three days of nonreinforced testing in the shuttle-box. Recipients of extract from high performance donors performed during testing at a level significantly higher than that of recipients of extract from low performance donors; the latter recipients in turn performed at a level significantly higher than that of recipients of control extract. In Experiment 2, the time course of this biochemical transfer effect was assessed. (Previous within-subject time course determinations have been confounded with practice effects.) Independent groups of goldfish injected with brain extracts from either trained or control donors were tested once and only once either 1, 2, or 3 days after injection. Although recipients of "trained" extract consistently outperformed recipients of "untrained" extract at all three nonreinforced test sessions, the effect was maximal and was significant at 3 days. This between-subjects time course is consistent with within-subject time courses previously assessed in this laboratory.

**14.1** RETENTION OF ESCAPE TRAINING AND ACTIVITY CHANGES IN SINGLE PARAMECIA. Joseph C. Huber*, William B. Rucker, and Colin G. McDiarmid*. Department of Psychology, Mankato State College, Mankato, Minnesota 56001.

Paramecia sucked individually into a capillary tube and allowed to swim back into a drop of their own culture medium escape more rapidly over successive trials (French: J. of Exp. Psych. 26: 609, 1940). Hanzel and Rucker reported in these proceedings in 1971 that neither variations in intertrial interval, inner diameter of the capillary tube, nor time in the drop prior to training affected the rate at which escape speed increased over trials, and that escape speed was asymptotic within ten trials. They also reported, contrary to French, that activity in the drop was greater after training. Changes in activity, however, could not be shown to contribute to increased escape speed. In the present experiment, 108 subjects were trained for ten trials and after either 0, 6, 30, or 150 minutes were tested for retention over ten trials, according to a split-plot design. During the intertrial intervals, activity in the drop was measured and used as a covariate adjuster for escape speed. Escape speed increased reliably in the training session ($p=.001$) and was retained at all intervals ($p=.001$), though retention scores were highest in the six minute group ($p=.05$). Activity was not correlated with escape speed within trials and across subjects ($r=.013$), though the means for the two measures were parallel across trials and across retention intervals. Several ad hoc multivariate analyses of variance were conducted to investigate the commonality and independence of the two measures. Further, room temperature and culture pH at running time had no effect on escape speed. Supported in part by a grant to W. B. R. from the Mankato State College Faculty Research Council.

**14.2** POSSIBLE CIRCADIAN FACTORS IN THE RETENTION OF A PASSIVE AVOIDANCE RESPONSE. Frank A. Holloway and Richard A. Wansley.* Dept. Psychiat. & Behav. Sci. Univ. Okla. Health Sci. Center, Oklahoma City, 73190.

A one-trial, step-through passive avoidance response (PAR) was used to evaluate various training-testing intervals through-out the 24-hr cycle on retention. Impairment of the retention of conditioned avoidance responses has been noted at training-testing intervals ranging from 1 to 8 hrs with nearly perfect retention immediately after training and at intervals of 24- or 48-hrs (e.g., Kamin, 1957). In preliminary experiments, we replicated this U-shaped retention curve with the PAR task, showing a maximal deficit at 6-hrs. However, by examining other training-testing intervals intermediate to 8- and 24- hrs and 24- and 48- hrs, we have found in independent groups of rats that retention deficits on the PAR tasks also appear at 12hr intervals after initial deficit at 6 hrs (i.e., at 6-, 18-, 30-, 42- and 54-hrs) while little or no retention impairment occurred at 12 hrs after training or at successive 12 hr intervals (i.e., at 24-, 36-, 48-, 60-, or 72 hrs). Since these animals were trained during the 12 hr light cycle, we replicated the finding controlling for both light-dark cycle and time of day. In this second experiment, we again found a retention deficit at 6 hrs after training irrespective of time of training. Performance was always perfect 15 minutes and 24 hrs after training. The degree of impairment at 12- or 18- hrs after training depended upon the time of training during the 24-hr cycle. These results appear to indicate that retention performance of the PAR is related to some circadian factor but not in any simple direct manner. Rather, it appears that a significant change in the "state", perhaps as reflected by a variable like activity of the animal, may account for the periodic occurance of retention deficits. Whether or not these effects would qualify as "state-dependent" learning phenomenon is still unclear.

**14.3** BIPHASIC RETENTION CURVES SUPPORT THE TWO-STORE THEORY OF MEMORY. Arthur Cherkin. Psychobiology Research Laboratory, VA Hospital, Sepulveda, Ca. 91343 and UCLA School of Medicine, Los Angeles, Ca. 90024.

Theories which invoke two forms of memory imply that biphasic retention curves should be demonstrable under appropriate conditions, with a retention minimum between a peak of short-term memory (STM) and a peak of long-term memory (LTM). Biphasic retention with a minimum at 1-22 min post-training has been observed in the mouse (Psychopharmacologia 12: 286, 1968), chick (Comm. Behav. Biol. 5: 379, 1971), goldfish (Science 172: 966, 1971), sepia (Nature 232: 202, 1971), and Poecilia formosa (Riege and Cherkin, in preparation). In the mouse, chick and goldfish, high initial retention of one-trial avoidance learning fell to a minimum 1-5 min post-training, rose to a second peak within the next 3-85 min, then approached baseline in 24 hr. In sepia, initial retention of habituation remained high for 15 min, fell at 22 min post-training, recovered at 60 min and fell at 90 min. In Poecilia, low initial retention of one-trial avoidance rose to a peak at 1 min, fell at 4 min post-training, rose at 16 min, and fell after 64 min. We found that weakening the aversive training of chicks accelerated the fall of the first peak and slowed the rise of the second peak. A parsimonious interpretation is that the first peak reflects the rapid formation and decay of STM and the second peak reflects the slower formation and decay of LTM. Other interpretations, such as time-dependent changes in level of apprehension, stress or motivation, appear less satisfactory. Biphasic retention is easily missed. Its detection requires intermediate training strengths, to avoid floor and ceiling effects that obscure fluctuations in learned performance, and retention testing of large independent groups at closely-spaced intervals, to disclose rapid fluctuations. The growing evidence for biphasic memory retention and its generality in the mollusc, fish, bird and mammal support the argument that biphasic retention may directly demonstrate two forms of memory.

**14.4** EVIDENCE FOR MATCHED FILTER RETRIEVAL OF INTERACTIVE MEMORY TRACES. James A. Anderson. Rockefeller University, New York, New York, 10021.

If synaptic junctions change in strength with use, many reasonable assumptions about the details of the change generate automatically a type of memory in which (1) memory traces correspond to large patterns of individual neuron activities and (2) distinct memory traces interact with each other in storage. Formally, if traces are represented by N element vectors (where N is large, elements corresponding perhaps to activities of individual neurons, or to strengths of single synapses), and there are K traces to be stored, $(\overline{f}_1, \overline{f}_2, \cdots \overline{f}_K)$, a storage vector (the memory) is formed by

$$\overline{s} = \Sigma\, \overline{f}_k .$$

Recent experiments (Hirsh and Spinelli, Exp. Brain Res. 13, 509) found that kittens exposed to a restricted visual environment (three horizontal stripes to one eye, three vertical to the other) have visual cortical cells whose receptive fields reproduce aspects of the environment. It can be argued that such a finding is in accord with the theoretical result that the optimum retrieval system for an interactive memory is the spatial matched filter formed from the sensory input to the system. Their result also agrees with the kind of synaptic modification required to generate an interactive memory. The theoretical result states that if we wish to know whether an input to memory, $\overline{f}$, is present in $\overline{s}$, the optimal linear filter (in the sense of largest output signal to noise ratio (s/n))is formed by the vector dot product, $\overline{f}\cdot\overline{s}$. The (s/n) of the system is then given, subject to some assumptions, by (s/n) = N/K, an expression which represents a lower bound for these models.

**14.5** CONDITIONS FOR STIMULUS-INDUCED RECOVERY FROM EXPERIMENTAL AMNESIA IN RATS[1]. Ralph R. Miller, Alan D. Springer* and Diana C. Vega*. Dept. Psychol., Brooklyn College of CUNY, Brooklyn, N.Y. 11210

Experimental amnesia induced by such diverse treatments as antimetabolites and electrical stimulation of the brain has recently been found to be reversible with the aid of select recovery agents. Such data indicate that some or all experimental amnesia is due to retrieval failure, one that is most readily established soon after information acquisition. We have examined recovery agent parameters in rats rendered amnestic with electroconvulsive shock after one-trial passive avoidance training. The UCS presented noncontingently was found to be a highly effective recovery agent. Similarly, the CS presented noncontingently facilitated retrieval, but was less effective as a recovery agent than the UCS in that a longer exposure to the CS than the UCS was required to induce memory restoration. This suggests an explanation of why "spontaneous recovery" from experimental amnesia is sometimes observed to occur after repeated test trials, but is rarely seen in paradigms specifying only one test trial per subject. Memory restoration was attenuated with increasing stimulus dissimilarity between the recovery agent and the CS or UCS, and was facilitated by increments in the intensity of the recovery agent. Preliminary data indicate that restoration of one-trial appetitive training memories from electroconvulsive shock-induced amnesia is subject to the same constraints as recovery from amnesia for aversive events.

[1]Supported by USPHS Grant MH19497 & Research Foundation of CUNY Grant 1385

**14.6** RETROGRADE AMNESIA THRESHOLDS AND GRADIENTS: ROLE OF LOCALIZED CORTICAL STIMULATION AND ITS ELECTROPHYSIOLOGICAL CONSEQUENCES. Paul E. Gold* and James L. McGaugh. Dept. Psychobiology, Univ. Calif., Irvine, 92664.

Electrical stimulation (2-8 mA) was delivered bilaterally to either frontal cortex (2 mm anterior to Bregma, 2 mm lateral) or posterior cortex (7 mm posterior to Bregma, 2 mm lateral) in rats at various times, from immediately to 4 hr, after rats received a training trial on an inhibitory avoidance task. As indicated by a retention test given 24 hr later, the length of the retrograde amnesia gradient ranged from less than 5 sec to more than 30 min, varying both with the brain region stimulated and the intensity of the stimulating current.

These results support an hypothesis that retrograde amnesia thresholds change with time after training and that retrograde amnesia gradients reflect these changing thresholds. Such data suggest that a retrograde amnesia gradient does not directly represent a fixed "memory consolidation" period; rather, the data suggest that there is decreasing susceptibility of memory to disruption during a period following training.

Electrocorticographic responses to the brain stimulation were observed for each experimental animal. Brain seizure thresholds and RA thresholds coincided only when the stimulation immediately followed the training trial. Brain seizure thresholds did not coincide with RA thresholds at later footshock-brain stimulation intervals. Brain seizure patterns did not vary as a consequence of different footshock-brain stimulation intervals.

**15.1** ROLE OF THE CENTRAL NERVOUS SYSTEM IN CARDIAC FIBRILLATION: AN EXPERIMENTAL MODEL IN CHRONIC PIG PREPARATIONS. J. E. Skinner, J. S. Arthur,* D. N. Mohr,* and M. Powers.* Neurophysiol. Dept., Methodist Hosp., and Physiol. Dept., Baylor Coll. Med., Houston, Texas 77025

Complete denervation protects the heart against fibrillation following occlusion of the left descending coronary artery (LDCA) and electrical stimulation in the brain stem and hypothalamus will produce paroxysmal contractions that facilitate fibrillation. In anesthetized preparations a large variability exists for the time of onset of fibrillation (TOF) following occlusion of the LDCA, a finding supported by the results of Porter and French (Amer. J. Surg. 100: 354, 1960), who showed that the amplitude of the vagal afferent evoked potential recorded in the brain stem was markedly affected by the level of barbiturate anesthesia. Present results in chronic pig preparations implanted with reversible LDCA occluders and bilateral cryorings for reversible blockade of the cervical vagus trunks show: 1) the TOF is highly predictable between subjects and has a small variance; 2) strain differences exist for the TOF (Landrace (L) pigs, 5 min; Hampshire (H) pigs, 12 min); 3) adaptation to the experimental situation before the first occlusion and repeated experiments in the same subjects result in monotonic increases in TOF until it reaches the maximum period for reversible myocardial ischemia; 4) bilateral vagal blockade in adapted H pigs markedly increases heart rate (HR) and markedly reduces TOF, but in L pigs only slightly increases HR and does not reduce TOF; 5) TOF is indepependent of increased HR produced by electric pacing; and 6) TOF in adapted H pigs could be reduced by anxiety due to periodic electric shock but not in L pigs.

**15.2** **Inhibition of chemoreceptor reflex bradycardia by hypothalamic stimulation in the cat.** M. R. Thomas and F. R. Calaresu. Dept. of Physiology, Univ. of Western Ontario, London, Ontario, Canada.

To investigate the mechanism of the bradycardia elicited by carotid chemoreceptor activation experiments were done in nine chloralosed cats. Injection of sodium cyanide (NaCN, 50-100 µg) into the common carotid artery via a cannula in the medial thyroid artery consistently elicited a marked bradycardia (32 ± 9.5 bpm) and an increase in mean arterial pressure (31 ± 4 mmHg). These cardiovascular responses were independent of respiratory changes as they could still be elicited in artificially ventilated cats. The magnitude of the bradycardia was not affected, but the arterial hypertension was abolished by spinal transection at $C_7$; the bradycardia was shown to be purely of vagal origin as it was not altered by administration of propranolol (1.5 mg/kg, I.V.), but was reduced by ipsilateral vagotomy and eliminated by bilateral vagotomy. As it is known that hypothalamic stimulation inhibits the vagal bradycardia due to baroreceptor excitation, the possibility that the chemoreceptor bradycardia was similarly affected by hypothalamic stimulation was investigated. In ten chloralosed cats transected at $C_7$ electrical stimulation of 22 ipsilateral and 17 contralateral sites histologically located in the postero-medial hypothalamus consistently inhibited the chemoreceptor induced bradycardia (from 36 ± 4.0 to 11 ± 2.4 bpm). It is concluded that the bradycardia elicited by chemoreceptor activation is due exclusively to vagal excitation and that the arterial hypertension is mediated by increased sympathetic vasoconstrictor activity. In addition, it has been shown that the chemoreceptor induced vagal bradycardia is inhibited by stimulation of a discrete hypothalamic region. (Supported by the Medical Research Council of Canada).

**15.3** DEVELOPMENT RATES OF AUTONOMIC AND SKELETAL CONCOMITANTS OF CONDITIONED SUPPRESSION. Arthur R. Zeiner, Leslie Marshall*, and Orville A. Smith, Jr. Regional Primate Research Center, University of Washington, Seattle, 98105 and University of Oklahoma Health Sciences Center, OKC. 73190.

In eleven chaired male adolescent monkeys (Macaca mulatta), blood flow velocity in the terminal aorta, pulsatile blood pressure in the ascending aorta, heart rate, lever pressing and activity were concurrently monitored over daily discriminated conditioned emotional response (CER) sessions. The conditional (CS) and discriminative (DS) stimuli were blue and red lights of 60 seconds duration. CS termination was followed by a 12.0 ma pulsed shock, 2 seconds in duration, to the buttocks. The question asked of the data was, would evidence of CER discrimination occur before, at the same time as, or after discrimination occurred with the lever press measure. The ordering of the various indices at which statistically reliable discrimination occurred was determined, in part, by the type of data reduction and analyses employed. In the case where comparisons were made within subjects across response measures, there was no difference in the rate at which skeletal and autonomic indices showed discrimination. In the case where group means were employed, reliable conditioned lever press suppression tended to occur on an earlier trial block than did discrimination with autonomic indices. The results are relevant for mediational views of learning.

**15.4** RECOVERY FROM APNEUSTIC BREATHING PRODUCED BY VAGOTOMY TWO DAYS AFTER PONTINE PNEUMOTAXIC AREA DESTRUCTION. Richard L. Glasser, Richard A. King, Joe A. Paget, Jr.*, John W. Pendill, Jr.*, and Gary M. McClain*. Department of Physiology and the Neurobiology Program, University of North Carolina at Chapel Hill, N. C., 27514.

Bilateral lesions were placed by stereotaxic procedures in the pontine pneumotaxic areas in cats anesthetized with Nembutal. Two days later the vagal nerves were sectioned under Brevital anesthesia. The marked prolongation of inspiration characteristic of apneustic breathing was exhibited by all of the experimental animals. Recovery of the awake condition required several hours. Some animals did not make purposeful movements, sit or stand until the seventh or eighth hour after vagotomy. Respiratory changes occurred in parallel with the increasing signs of arousal. Inspiratory phase durations, maximal in the first hour, diminished slowly but progressively. After four to eight hours most of the animals exhibited a background pattern of normal respiration frequently interrupted by apneustic inspirations of moderately long duration. In an earlier report from this laboratory, Glasser, St. John and King (Physiologist 13: 207, 1970) described a much more rapid and a greater degree of recovery in cats vagotomized one or three months after the placement of lesions in the pneumotaxic areas. These data indicate that the time interval between the pneumotaxic lesion phase and the vagotomy phase of this two-step procedure significantly affects the course of recovery. Histological examination of the brains revealed that the most effective pneumotaxic area lesions were concentrated within frontal planes P 2.5 to P 5.0, from 2.5 to 5.5 mm. lateral to the midline and from 9.0 to 5.0 mm. dorsal to the interaural zero. This pneumotaxic region placement corresponds closely to that described by Bertrand and Hugelin (J. Neurophysiol. 34: 189-207, 1971).

**15.5** ACTIVITY OF BULBAR RESPIRATORY NEURONS DURING ALTERATIONS IN THE DURATION OF INSPIRATION. William D. Barber*, (SPON: W. Ross Adey). Dept. Anat., UCLA, Los Angeles, 90024.

The response of single-unit activity of bulbar respiratory neurons was observed during induced alterations in the duration of inspiration in anesthetized cats. The parameters monitored under halothane and nitrous oxide anesthesia were blood gases, diaphragmatic EMG, intrapleural pressure, and airway pressure. Single-unit activity was recorded during changes in the duration of inspiration from neurons which exhibited rhythmical bursting patterns that were phase-locked to some aspect of the respiratory cycle. The onset of inspiration was initiated when the animal triggered a volume-cycled modified Bourns Infant Ventilator by decreasing the airway pressure approximately 0.5 cm of water. The duration of the inspiratory cycle was altered by 1) changing the flow rate at a constant tidal volume, or 2) changing the tidal volume with the flow rate remaining constant. Reducing the flow rate at a constant tidal volume resulted in an increase in the burst duration of both inspiratory and expiratory neurons. The increased burst duration which occurred at this reduced flow rate could then be decreased by a reduction in tidal volume. Conversely, inspiratory and expiratory units under the influence of increased flow rates at a constant tidal volume showed a decrease in the burst duration and this decrease associated with the higher flow rate was reversed by increasing the tidal volume. Some inspiratory neurons were inhibited when high respiratory rates were imposed upon the animal by manually cycling the ventilator. In contrast, expiratory units faithfully followed the cycling of the ventilator with pronounced bursting activity. The burst duration of both inspiratory and expiratory neurons was thus shown to be related to the length of the inspiratory phase.

**15.6** REFLEX AND BEHAVIORAL WITHDRAWAL RESPONSES TO TOOTH PULP STIMULATION. Kenneth H. Reid. Dept. of Physiology & Biophysics, School of Medicine, University of Louisville, Louisville, Kentucky 40201.

In studies of experimental pain in man, three levels of stimulus intensity are customarily recognized: threshold, reflex withdrawal, and tolerance limit. However, in animal studies escape responses are commonly used to define "threshold". Using electrical stimulation of tooth pulp as the pain source, it has been found possible to show three corresponding levels of pain in the cat, with the responses - arousal, reflex jaw opening, and escape - occurring at well separated stimulus intensities. Bipolar stimuli to tooth pulp were applied using the technique of Mitchell & Kaelber (Am. J. Physiol. 210: 263, 1966); the awake cat sat in a low box and terminated the stimulus by stepping out. Jaw opening responses were reliably produced by stimuli of 0.05, 0.5, and 5 msec duration presented at 0.3, 3, and 30 stimuli/sec. With presentation rates of 0.3 and 3/sec, escape did not occur until stimulus current reached 2-5 times that required to induce reflex jaw opening. At 30/sec, escape occurred before palpable activation of the digastric muscles was present. Arousal from the drowsy state preceded visible jaw opening in most cases. Escape is inferred to be equivalent to a tolerance limit rather than a threshold because it represents a judgement: warm cosy box plus contact with experimenter (digastric palpation) plus pain VS open floor with no pain; this is comparable to the judgement made when a human volunteer withdraws from an experiment. Failure to escape does not mean an animal is free from pain.

**15.7** MONOAMINES AND BEHAVIORAL TESTS OF AFFECT: EFFECT OF CATECHOLAMINERGIC LESIONS, CHRONIC SEROTONIN DEPLETION, AND BOTH ON EMOTIONAL BEHAVIOR. David Bresler* and Gaylord Ellison* (SPON: L.L. Butcher). University of California, Los Angeles, California 90024.

Rats were given multiple 25 ug intraventricular injections of 6-hydroxydopamine (6-OHDA), chronic subcutaneous injections of p-chlorophenylalanine (PCPA) (100 mg/kg every four days), or both and compared to normal controls using a variety of tests designed to measure affectual or emotional behavior including activity, open field, avoidance, startle, tail flick (pain), aggression, and gustatory affect. Complex interactive effects of monoaminergic depletion on behavior were found. On some tasks, the two treatments summate (e.g., in open field tests, animals receiving PCPA appear more fearful than controls, as do animals with 6-OHDA lesions, and animals receiving both are the most fearful). But on a variety of other tests, the doubly depleated animals show behaviors more similar to the controls than to the singly depleated animals suggesting that the relative balance between the catecholamines and serotonin is more important than their absolute levels for behavioral output.

**15.8** AVOIDANCE LEARNING IN ADULT RATS TREATED PRENATALLY WITH CHLORPROMAZINE (CPZ). Mari Golub and Conan Kornetsky* Boston Univ. Sch. of Med. Boston, Mass. 02118

Pregnant Charles River rats were given 2 daily injections of saline or CPZ (2 mg/kg) on days 5-8 of gestation. Offspring of saline and CPZ-treated mothers were cross-fostered at birth. At 90 days of age, all offspring were trained in shock avoidance. The conditioned stimulus was 3100 cps tone and the escape-avoidance response was a quarter-turn of a wheel mounted on the box. Compared to controls, CPZ-treated rats showed (1) higher numberof avoidance responses during training; (2) higher final level of avoidance; (3) higher and more consistent rate of inter-trial responding; (4) shorter response latency. These results indicate that prenatal treatment of rats with the tranquilizing agent chlorpromazine can produce a hyper-responsiveness stressful situation in adulthood. (Supported by NIMH Grant MH 12568 and Research Scientist Award (CK) 1759).

**16.1** LOCALIZATION OF LATERAL GENICULATE SPIKES IN AWAKE, SLEEPING AND RESERPINE-TREATED CATS. John B. Munson and Robert B. Graham. Dept. of Neuroscience and Psychology, University of Florida, Gainesville, Fla.32601.

Electrical spiking activity (LGN spikes) may be recorded from lateral geniculate nucleus of cats during late slow-wave and fast-wave sleep, following reserpine administration, and in some cases accompanying awake eye movements. In cases where it is possible to record LGN spikes during fast-wave sleep, it is always possible to record them as well during slow-wave sleep and following reserpine administration. It is not always possible to record LGN spikes from these same electrode sites in the awake cat; however, sites from which LGN spikes can be recorded in the awake cat will invariable produce LGN spikes in the sleeping or reserpine-treated cat. The first of these sites we call Type SR (sleeping-reserpine); the second we call Type ASR (awake-sleeping-reserpine). Electrode placements in 20 LGN from 12 chronically implanted cats have been studied and classified according to the types of LGN spikes recorded from them. Type ASR sites are found reliably within LGN and optic tract terminals in stereotaxic planes A5 to A8 (Snider and Niemer). Type SR sites are found surrounding the Type ASR sites, in such structures as optic radiations, thalamocortical radiations, fimbria and optic tract. Sites of either type may be found within LGN posterior to plane A5. We consider the activity recorded from the Type SR sites to be volume conducted from active sites within LGN. The LGN spikes accompanying awake eye movements are smaller at their site of origin within LGN and are thus difficult to record at Type SR sites. (Research support derived from NSF Grant GB-7622 to JBM).

**16.2** EFFECTS ON ISOLATION INDUCED AGGRESSION IN MICE OF MONOAMINE PRECURSORS IN COMBINATION WITH A PERIPHERAL DECARBOXYLASE INHIBITOR. Gordon K. Hodge* and Larry L. Butcher. Department of Psychology, UCLA, Los Angeles, 90024

The monoamine precursors L-3,4-dihydroxyphenylalanine (L-DOPA) and DL-5-hydroxytryptophan (DL-5-HTP) have been shown to modify aggressive behavior in mice (cf., Garattini and Sigg, Eds., Aggressive Behaviour, New York: Academic, 1969). We have extended this work. To eliminate potentially toxic peripheral effects of the precursors, we used $N^1$-(DL-seryl)-$N^2$-(2,3,4-trihydroxybenzyl)hydrazine (Ro 4-4602; Courtesy Dr. W.E. Scott; Hoffman-La Roche; Nutley, N.J.) which in lower doses preferentially blocks extracerebral decarboxylase activity. Male albino mice of the Swiss-Webster strain were made aggressive by being isolated for at least 4 weeks prior to behavioral testing. The number of fights between pairs was recorded for 15 min every other day. On intervening days, the locomotor activity of each mouse was measured in stabilimeters for 15 min. This latter procedure was employed to assess the motor capabilities of the animals under both control and drug conditions. After establishing a baseline for both aggression and locomotor activity, drug procedures were instituted. Ro 4-4602, 50mg/kg, was injected 30 min prior to precursor administration. Behavioral testing commenced 60 min after L-DOPA or DL-5-HTP was given. All injections were i.p. At 200 mg/kg L-DOPA administration resulted in a decrease in both aggression and motility. In contrast to L-DOPA,DL-5-HTP at doses of 100, 200, and 400 mg/kg caused a dose-dependent decrease in fighting but had no significant effect on motor activity. We conclude that catecholamines may be essential for the expression of motor components of aggressive behavior but that 5-HT modulates motivational aspects. *(Supported by University of California Grant No. 2637)*

**16.3** Effects of L-Dopa and Reserpine on Evoked Responses from Basal Ganglia of Freely Behaving Rats. N. Dafny and S. Gilman, Dept. of Neurology, College of Physicians and Surgeons, Columbia University, New York, N.Y. 10032

In freely behaving, awake rats averaged potentials evoked by 32 click stimuli at 1/sec were recorded simultaneously with semi-microelectrodes implanted permanently in caudate nucleus (CN), globus pallidus (GP), and substantia nigra (SN). L-Dopa was given intraperitoneally (i.p.) as an aqueous suspension 100 mg/kg after control recording in one group of animals, and in the second group, one hour after administration of i.p. reserpine 1 mg/kg. The evoked potentials showed a small initial positive ($P_1$), negative ($N_1$) wave followed by a larger positive ($P_2$) negative ($N_2$), positive ($P_3$) wave. Only the last three components showed significant alterations; their amplitudes after treatment were expressed as a percentage of the amplitude before treatment in the same animal. In the first group, the mean amplitudes of the three components averaged together showed the following effects: 63, 33, 49% increase in CN, GP, and SN respectively; 12, 17, 28% decrease; and 25, 50, 23% no change. In the second group the effects of reserpine were: 19, 29, 52% increase; 48, 54, 29% decrease; 33, 17, 19% no response. Subsequent administrations of L-Dopa produced 71, 43, 66% increase; 5, 24, 19% decrease; and 24, 33, 25% no change, relative to the amplitudes after reserpine. These findings indicate that, in CN and SN, L-Dopa produces predominantly facilitatory effects which, in CN, are reciprocal to those of reserpine but in SN are similar to those of reserpine. In GP, L-Dopa is ineffective in a majority of animals, but produces effects similar to those in CN in the remaining animals. Thus, the effects of L-Dopa and reserpine differ in the three structures, suggesting marked physiological differences between these structures. (Supported by USPHS grants NS 2552 and NS 05184).

**16.4** CNS CATECHOLAMINE AND SEROTONIN INHIBITION OF MURICIDE: EVIDENCE FOR MONOAMINE INTERACTIONS. L.D. Grant, G.R. Breese and J.L. Howard. Child Development Inst., UNC Sch. of Med., Chapel Hill, N.C. 27514

Some reports suggest that CNS catecholamine (CA) and serotonin (5HT) systems inhibit muricide in rat. The present work adds support for this view and advances evidence for interactions between the monoamines in muricide control. Depletion of brain 5HT by p-chlorophenylalinine (PCPA) or midbrain raphe lesions have been shown to induce killing. Consistent with this, the present research found that intracisternal (I.C.) or direct injections into the raphe of 5,6-dihydroxytryptamine, which depletes brain 5HT, induced significantly more rats to kill than did sham saline injections. In another study, rats prescreened in five 48h tests with a mouse present in home cage were classed as killers if they killed at least once. Two I.C. injections of 200 μg 6-hydroxydopamine (6-OHDA), which depleted brain CA by over 75%, increased resistance to handling but not mouse killing. To test if brain CA depletion affects induction of killing by other manipulations, 6-OHDA and control Ss were tested after systemic PCPA injections. At doses ineffective for control Ss, PCPA evoked muricide in 6-OHDA Ss in a dosage dependent fashion. The highest dose (2 injections of 250 mg/kg 24h apart) caused 1 of 9 control Ss to kill, while 6 of 11 6-OHDA non-killers killed and with significantly shorter attack latencies. 10 μg 6-OHDA in 5 μl saline bilaterally in amygdala neither increased resistance to handling nor induced muricide. PCPA, however, induced some 6-OHDA amygdala Ss to kill (3 of 9 at maximum dose) but none of 6 sham operates. Fluorescence microscopy was used to assess location of CA depletion in killing and non-killing 6-OHDA amygdala Ss. Present results indicate that 5HT brain systems probably exert primary inhibitory influences on muricide responses, but some CA brain systems including components in amygdala may play a modulating role augmenting the 5HT inhibition.

**16.5** EFFECTS OF AMYGDALOID ADMINISTRATION OF TWO BETA-ADRENERGIC DRUGS ON THE TIMING BEHAVIOR (DRL-20) OF RATS. P. David Stacey, J. Steven Richardson, William R. Saxby*, and Richard E. Musty. Neuropsy. Lab., Dept. Psy., Univ. of Vt., Burlington, Vt., 05401

Rats with chronically placed cannulae in the basolateral amygdalae were directly injected with either propranolol, a beta-adrenergic antagonist, or isoproteranol, a beta-adrenergic agonist, to study the effects of these drugs on the performance of an appetitive operant conditioning schedule requiring the rats to respond based on the passage of time. Masuoka (E. Acta. pharmacol. 25: 447, 1970) has demonstrated that propranolol may quickly pass through the blood-brain barrier and remain in various limbic structures longer than in other areas of the brain. The recent observation of Richardson (Arch. Int. Pharmacodyn. 196: in press, 1972) showed that systemic administration of propranolol interfered with the inhibitory behavior of rats. These results closely paralleled findings by Pellegrino (JCPP 65: 483, 1968) in ablation studies of the basolateral amygdala of the rat. The present study showed that propranolol disrupted the performance of rats while isoproteranol improved the performance. Further, dependent upon dose level, these results suggested the differential presence of both specific beta-adrenergic effects and nonspecific quinidine-like effects.

**17.1** SELECTIVE DEPRESSION OF ORGANOTYPIC BIOELECTRIC DISCHARGES OF CNS EXPLANTS BY GLYCINE AND γ-AMINOBUTYRIC ACID.[1] Stanley M. Crain. Dept. Physiol. and Rose F. Kennedy Center, Albert Einstein Coll. Med., Bronx, N.Y. 10461

Explants of fetal mouse spinal cord and cerebral cortex can generate complex organotypic bioelectric discharges after development of synaptic networks *in vitro* (Crain, Intern. Rev. Neurobiol. 9, 1966). Strychnine or picrotoxin ($10^{-7}$ to $10^{-6}$M) greatly enhances the amplitude, duration, and complexity of the repetitive spike barrages and slow-waves (recorded extracellularly), whereas increasing the $Mg^{++}$ concentration of the medium from $10^{-3}$M to $10^{-2}$M, or removing $Ca^{++}$, blocks (reversibly) these synaptically mediated discharges. Increase of glycine or γ-aminobutyric acid (GABA) levels to $10^{-3}$M leads to rapid depression of most of the complex cord discharges, and only brief spike-bursts or simple monophasic slow-wave responses can be evoked, even with large electric stimuli. In cultures of cord-innervated skeletal muscle (Crain *et al*, J. Neurobiol. 1, 1970), coordinated muscle contractions can still be evoked by ventral-cord (or root) stimuli during this glycine blockade of internuncial CNS activity. The cord effects can be reversed after return to regular medium, and the glycine depression (unlike the high-$Mg^{++}$ or low-$Ca^{++}$ blockades) can be prevented by concomitant addition of a low concentration of strychnine ($10^{-7}$M). Cerebral explant activities appear to be more sensitive to depression by GABA, but less susceptible to glycine. These data suggest that strychnine and picrotoxin enhancement of bioelectric discharges of cord and cerebral explants may be due to selective interference with glycine- and GABA-sensitive receptors, possibly related to inhibitory synaptic membranes, as occurs *in situ* (e.g., Curtis *et al*, Brain Res. 32, 1971). These cultures provide a useful model system to supplement analyses of synaptic transmitters and receptors in mammalian CNS. ([1]Supported by NINDS grant NS-06545 and Kennedy Scholar Award.)

**17.2** UPTAKE OF γ-AMINOBUTYRATE, GLUTAMATE AND GLYCINE BY A CLONED LINE OF ASTROCYTOMA CELLS IN CULTURE. H. T. Hutchison* and B. Haber. Human Genetics and the Marine Biomedical Institute, UTMB, Galveston, Texas 77550

γ-Aminobutyric acid (GABA) and glycine (GLY) have been established as inhibitory transmitters in the mammalian cerebellum and spinal cord respectively, and glutamate (GLU) may be the excitatory transmitter at primary afferent synapses in spinal cord. Glial cells may function in the reuptake of some of these amino acids released by neuronal activity. In this connection we have examined the uptake of GABA, GLU and GLY in a cloned mouse astrocytoma cell line (2B15) in culture. These cells possess high affinity uptake systems for GABA and GLU which are temperature and concentration dependent. The Michaelis constants for GABA (Km=0.06 μM) and GLU (Km=6.7 μM) are similar to the values reported for glial fractions prepared by bulk isolation procedures (Henn & Hamberger, 1971). In contrast, the astrocytoma cell line exhibited a relatively low affinity for glycine (Km=374 μM) similar to that reported for tissue slices of cortex, cerebellum, and midbrain (Johnston and Iverson, 1971). Moreover, in astrocytoma, unlike slices we did not observe a high and low affinity component in the glycine uptake system. Aminoxyacetic acid (AOAA), a carbonyl trapping agent and inhibitor of GABA metabolism, reduced the uptake of GABA to background levels, reduced the uptake of GLU by about 50%, but had no effect on the uptake of GLY. The high affinity of astrocytoma cells for GLU and GABA, coupled with the relatively low maximum velocities observed, are consistent with a possible glial role in the removal of neuronally released neurotransmitters. Supported by the U.S.P.H.S. grant (5R01 MH19502 02) and the Moody Foundation of Galveston. Astrocytoma kindly supplied by Dr. J. de Vellis, UCLA.

17.3 UPTAKE OF $^3$H-GAMMA-AMINOBUTYRIC ACID BY NEURONS IN CULTURES OF DISSOCIATED POSTNATAL RAT CEREBELLUMS. Robert S. Lasher and S. Zagon*. Dept. Anat., Univ. Col. Med. Sch., Denver, Co. 80220

Uptake of $^3$H-gamma-aminobutyric acid ($^3$H-GABA) has permitted the identification of inhibitory stellate neurons in cultures of dissociated (dis) 2-day (d) postnatal (pn) rat cerebellums (CB)(R.S. Lasher and I.S. Zagon, Brain Res., in press). The aim of this study was to examine the specificity of this uptake, and factors controlling the differentiation of granule and stellate cells. 18 to 21-d cultures of dis 2-d pn rat CB were preincubated for 15 min in either 1 ml of Puck's saline G alone, containing 2mM L-2,4 diaminobutyric acid (DAB), or 10μM aminooxy acetic acid (AOAA); and then incubated in the same solutions containing 12 μCi $^3$H-GABA (1-6μM) for 45 min at 36°C. After thorough rinsing in saline G, the cultures were fixed in glutaraldehyde and processed for autoradiography. The DAB completely blocked the uptake of $^3$H-GABA; while little difference could be seen between untreated and AOAA treated cultures. Thus, the uptake of $^3$H-GABA is specific, and little degradation appears to occur during the incubation period. The ratio of small, unlabeled neurons to labeled stellate neurons was 5:1, which is about 20 fold lower than in vivo. To test whether the culture conditions might be selecting against granule cells or shifting the differentiation of the germinal cells towards stellate neurons, $^3$H-GABA uptake was determined in 21-d cultures of dis 10-d pn rat CB. The same ratio of unlabeled to labeled neurons was found. These results suggest that culture conditions or lack of mossy fiber afferents may be selecting against granule cells, and provide further evidence for GABA as an inhibitory transmitter. Supported by NIH grant NS-09641.

17.4 DISSOCIATED CELL CULTURES OF MOUSE SPINAL GANGLIA. Edward Tyszka, Charles Raiborn* and Silvio Varon. Dept. Biol., Sch. Med., Univ. Calif.-San Diego, La Jolla, 92037.

Spinal sensory ganglia (DRG's) from newborn mice were dissociated and cultured in a collagen-based, $CO_2$-equilibrated system. More than half of the neurons seeded were seen to attach and grow processes within the first 6-8 hrs, with an overall yield of about 3000 cultured neurons per ganglion. Less than 20% neuronal loss was observed over a period of three weeks in culture. Neuronal survival required Nerve Growth Factor (NGF) in the culture medium; without NGF, the number of neurons that attached and grew processes dropped by 10-fold with very few, if any, long-term survivors. The latter cultures were used as a source of non-neuronal cells to supplement fresh ganglionic dissociates at seeding time. In these supplemented cultures, neurons exhibited earlier attachment and onset of fiber growth, and for a limited period of time high culture yields were obtained even in the absence of NGF. Under all such culture conditions, surviving neurons were found to be electrically competent, with resting potentials of about -40 mV and evoked potentials (recorded intracellularly) of about 70 mV.

**18.1** SOMATOSENSORY CODING IN SINGLE CELLS OF CAT MESENCEPHALIC RETICULAR FORMATION. Karen B. Braden. Dept. Neurosurg., Schl. Med., CWRU, Cleveland, O.

Response patterns of single cells in cat mesencephalic reticular formation (MRF) to electronically controlled touch-pressure and noxious radiant heat stimulation were compared as a test of the cutaneous sensation theory of Wall and Melzak (Brain 85: 431, 1962). Four hypotheses were examined: MRF cells differentiate stimuli by means of excitatory vs. inhibitory cell inputs; MRF cells differentiate stimuli by means of adaptation rate; the somesthetic system is an integration of specialized components; and every discriminable cutaneous pattern is based on a unique pattern of MRF activity. Single cells were recorded from MRF of 29 acute decorticate cats in response to transient (1-2 sec.) and continuous (1 min.) somatic stimulation. Running averages were computed to reveal the response patterns to transient touch-pressure and heat, while both interspike interval histograms and running averages were plotted for the continuous stimuli. Analysis of 129 cells revealed that 66% responded to both stimuli, 30% only to noxious heat, and 14% only to touch-pressure. Both excitatory and inhibitory responses were found, with the majority (75%) excitatory. For the second hypothesis support was seen in the slowly adapting response of 93% of the heat responders, compared to rapid adaptation in 62% of the touch units. The third hypothesis gained support from the finding of both unimodal (specialized) and bimodal (integrated) responding cells. Finally a great variety of response patterns was seen in the 129 cells, in agreement with the last question. Of the 85 bimodal cells, only two showed interspike interval distributions whose characteristics for touch vs. heat did not differ significantly. The problem of interpreting responses of MRF cells is clearly one of accounting for the great variety of patterns observed to the same somatosensory stimulus mode in this nonspecific sensory area.

**18.2** CHARACTERISTIC PROPERTIES OF MAMMALIAN CUTANEOUS MECHANORECEPTORS. P. R. Burgess, M. C. Cornwall* and K. W. Horch*. Dept. Physiol., Col. Med., Univ. Utah, Salt Lake City, 84112.

Several physiological properties were studied in ten types of mechanoreceptors in cat hairy and glabrous skin. Each receptor type was found to be characterized by a particular cluster of properties which are functionally related. For example: a receptor responding only to abrupt stimuli (a) responds to velocity or higher derivatives of displacement and, hence, is most sensitive to higher frequencies of sinusoidal stimuli, (b) is insensitive to the direction of displacement, (c) has a short recovery cycle, (d) has a rapidly conducting axon, and (e) projects directly to the brain via the dorsal columns. Thus, these mechanoreceptors are uniquely characterized by functionally related properties. It is possible that this schema may be generally applied across taxonomic lines.

**18.3** CUTANEOUS MECHANORECEPTORS: PROBLEMS IN THE CLASSIFICATION OF UNITS ON THE BASIS OF TEMPORAL DISCHARGE PATTERNS. J. M. Gibson*, R. E. Beitel*, and W. I. Welker. Lab. of Neurophysiology, Univ. of Wis., Madison, Wis. 53706.

Anatomists have described several distinct mechanoreceptor types to which physiologists have assigned discrete types of stimulus-evoked firing patterns. We question the validity of polychotomous classification schemes based on temporal response patterns to specific features of a stimulus. We have investigated discharges in single first order mechanoreceptive afferents in response to quantitatively controlled indentation of glabrous forepaw skin of domestic kittens. Stimulus amplitude, velocity, acceleration, duration, and interstimulus interval were varied parametrically. With respect to any particular stimulus-response characteristic studied, all units were found to be members of a continuously distributed population. For example, adaptation rates were found to lie along a broad continuum ranging from very slow to very rapid. Although anatomically distinct receptor populations exist, the stimulus-response profiles for the sample of units studied gave little evidence for distinct populations of response patterns. It appears that the CNS receives a broad range, rather than a few distinct types, of information about stimulus features from the afferent population activated. Furthermore, a single unit, by itself, does not encode all features of a stimulus. In fact, it may fail to encode uniquely any single stimulus parameter. It follows that if feature extraction is to occur, it must be a function of central neural circuits. We conclude that polychotomous classification of units on the basis of either extremes or single features of temporal responses to a particular stimulus is premature, at least for glabrous mechanoreceptors in the kitten's forepaw. (Supported by USPHS grants 5326 and 6225).

**18.4** FIRST-ORDER TRIGEMINAL NEURONS RESPONDING TO MOVEMENT OF MYSTACIAL VIBRISSAE OF OPOSSUM. Benjamin H. Pubols, Jr., Peter J. Donovick and Lillian M. Pubols. Department of Anatomy, Hershey Medical Center, Pennsylvania State University, Hershey, Pennsylvania 17033.

Two hundred, thirty-eight single, first-order neurons innervating the mystacial vibrissae of the Virginia opossum were examined for their responses to mechanical stimulation of the vibrissae. Twenty were isolated by microdissection of infraorbital nerve fibers, the remainder by microelectrode recording from the trigeminal ganglion. Receptive fields of all but two units were confined to a single vibrissa. 47% of the units discharged only during vibrissa movement (rapidly adapting), while 53% continued to respond so long as the vibrissa remained deflected from its resting position (slowly adapting). 10% of the slowly adapting units displayed a resting discharge in the absence of mechanical stimulation. Different units were found to respond to movements in from 1 to 6 primary directions (anterior, dorsal, posterior, or ventral deflection, pushing, pulling), the modal unit responding to deflection in two adjacent primary directions, plus pushing. There were no systematic relationships between directional sensitivities and either adaptive properties, length of vibrissa, or location of the vibrissa on the mystacial pad. Each vibrissa is innervated by many units differing in their response properties. The discharge patterns of all the neurons innervating a given vibrissa are, in the aggregate, capable of providing much more precise information about stimulation of that vibrissa than could be provided by any one fiber alone. (Supported by USPHS grants NS-06371, NS-38,829, and MH-24906.)

**18.5** TACTILE DEFICITS RESULTING FROM DORSAL COLUMN LESIONS IN MONKEYS. Charles J. Vierck, Jr. Dept. of Neuroscience and Center for Neurobiological Sciences, Univ. of Fla. Col. of Med., Gainesville, Fla. 32601.

This study is one of a series of investigations designed to determine whether dorsal column section will produce primary sensory deficits that are not attributable to disruption of a motor component such as stimulus manipulation. One group of animals was trained to discriminate movement across a tactile field with a brush from stationary contact of the same field with the brush. Stimulation was delivered to the hairy skin of either leg or to the glabrous skin of either foot. Discriminative responses for food reward consisted of pressing one of two panels with either hand. Serial lesions of the right and left dorsal columns were made at thoracic levels and produced deficits that recovered over several months testing. A second group of animals was trained on a more difficult discrimination of direction of stimulus movement. The animals were trained to respond differentially to brush strokes directed with or against the grain of hair on the calf of either leg. Following dorsal column lesions, performance dropped to chance levels with stimulation of the ipsilateral leg, and these deficits persisted for months. Impairment of the ability to detect the direction of movement of tactile stimuli could clearly account for deficits from dorsal column section that other investigators have observed using tasks involving palpation of the stimulus objects.

**18.6** EVIDENCE FOR THE CONTRIBUTIONS OF DIFFERENT SPINAL PATHWAYS TO S-I. B. L. Whitsel, D. A. Dreyer and R. J. Schneider*. Dept. Physiol., Sch. Med., U. of N. C., Chapel Hill, N. C. 27514 and Dept. Pharm., Sch. Med., U. of Pgh., Pittsburgh, Pa., 15213.

Single unit analysis was employed to determine, in high resolution, the submodality composition and topographic organization of cortical cytoarchitectural fields 3a, 3, 1 and 2 of 50 unanesthetized macaques; 20 of these had undergone selective spinal tractotomies 30-60 days prior to the recording session. The results of these experiments support the hypothesis that spinal mechanoreceptive afferents are resorted to form multiple somatic afferent paths, each of which projects a unique spectrum of mechanoreceptive submodalities to a different region of the somatic sensory cortex. Specifically, lumbar dorsal column lesions were found to be non-selective in the sense that such lesions decreased the low-threshold mechanoreceptor representation in all 4 cytoarchitectural fields to the same degree. In contrast, cervical dorsal column lesions produced a selective deficit in the cortical map: i.e., the low-threshold cutaneous mechanoreceptor representation in area 3 and anterior area 1 was markedly reduced whereas the low-threshold representation in areas 3a, posterior area 1 and area 2 remained essentially intact. If, however, the cervical lesion was widened to include the dorsolateral funiculus the deficit in the cortical body representation could not be distinguished from the non-selective deficit which resulted from lumbar dorsal column transection. Accordingly, the S-I map is viewed as a composite of multiple and partially overlapping projection fields, each of which receives a distinct spinal afferent projection pathway.

**19.1** FUNCTIONAL CHAINING OF FREQUENCY-INDEPENDENT ELEMENTS IN SPONTANEOUS BRAIN ACTIVITY. Ahn, H.*and Fox, S. S. Dept. Psychol., Univ. of Iowa, Iowa City, 52240

Continuing studies from this laboratory have emphasized functional or behavioral coding or relevance of the sequential and momentary voltages of evoked potentials and spontaneous brain activity. (Fox, 1969) Based on the high correlations observed in our earlier studies of spike-wave relations in evoked potentials and spontaneous activity, (Fox & O'Brien 1965, Fox & Norman 1968) this laboratory has sought to develop operant conditioning techniques for functional validation of such sequential probabilities of firing in cell populations as indicated by wave voltage fluctuations. (Fox & Rudell 1968, Fox & Rudell 1970, Rosenfeld et al 1969.) Most recently (Ahn & Fox, 1971) we have successfully operantly conditioned a 20 msec. segment of spontaneous brain activity increasing its probability from 1/min to approx. 4/min. Such modification of "criterion event" occurrance was achieved with no concommittant systematic changes in background EEG frequency. Such frequency-independent modification of EEG elements, suggests new and alternative analyses for spontaneous activity of brain. New experiments to be emphasized in this discussion, involve operant conditioning of chains of elements in spontaneous brain activity, their independence, sequential relations and rules for order. Conditioned chains of spontaneously occurring elements up to 500 msec. long will be described, along with theoretical considerations for a general theory of EEG organization.

**19.2** DOPAMINE DEPLETION AND STRIATAL UNIT FIRING. N.A. Buchwald, M.S. Levine*, C.D. Hull and A. Heller. UCLA and Univ. of Chicago.

Experimental lesions in the area between the substantia nigra and the striatum results in a syndrome which has been compared with human Parkinsonism. Pharmacological, chemical and anatomical data indicate that such lesions produce depletion of dopamine in the ipsilateral caudate and interruption of the nigro-striatal tract. Missing from this data is careful study of the electrophysiological properties of the striatum. The facts that in intact subjects striatal neurons fire infrequently, are inhibited by iontophoretic application of dopamine and that nigral stimulation evokes brief EPSPs followed by long lasting hyperpolarizations suggested that lesions in the nigro-striatal pathway might increase striatal firing rates. In 3 monkeys, striatal unit firing was analyzed over a period of months. After production of unilateral lesions just dorsal to the nigra, slight increases in firing frequency occurred in the ipsilateral caudate while statistically significant slowing was produced contralaterally. Ipsilateral dopamine content fell 20 to 50% in these animals. To check this result, 5 cats were lesioned unilaterally in a more rostral locus of the nigro-striatal path, a lesion known to deplete caudate dopamine severely. Post-lesion recording again showed that contralateral striatal unit firing slowed significantly. Ipsilateral rates differed insignificantly from controls. Interval and frequency distribution measures supported these findings. Subsequent chemical analyses revealed >90% dopamine depletion in the ipsilateral caudates and normal concentrations contralaterally. The fact that dopamine depletion in one striatum is not accompanied by marked changes in unit activity and vice-versa, suggests that something in addition to interruption of dopaminergic fibers is necessary to account for the behavioral effects attributed to this lesion.
Supported by USPHS HD04612, MH07097, Dept. Mental Hygiene, State of Cal.

**19.3** SINGLE CELL DISCHARGE IN THE NUCLEUS MEDIALIS DORSALIS OF THE THALAMUS DURING DELAYED RESPONSE PERFORMANCE. Joaquin M. Fuster and Garrett E. Alexander*. Department of Psychiatry and Brain Research Institute, School of Medicine, University of California, Los Angeles, Calif. 90024.

Neuronal activity was recorded with microelectrodes from the nucleus medialis dorsalis (MD) in monkeys performing a delayed response (DR) task. Test trials consisted of the following sequence of events: the brief presentation of a visual cue, a delay period of about 18 sec and, following that, a motor response appropriate to the cue. Spontaneous unit activity in MD was often characterized by a tendency for spikes to occur in rhythmic groups. This tendency was accentuated in drowsiness and by cooling the dorsolateral prefrontal cortex by means of implanted thermodes. During DR trials the majority of MD units manifested: 1), dissolution of the rhythmic firing pattern, particularly in the period of cue presentation, and 2), changes of firing frequency, different in time course for each of several unit categories. The most prevalent type of change was an increase of firing frequency beginning with presentation of the cue and followed by sustained higher rate of discharge during the ensuing delay. Firing frequency returned to the intertrial baseline level after the animal's response. Cryogenic depression of the prefrontal cortex produced two correlated effects: a), deterioration of DR performance, measured by an increase in errors, and b), modification of the firing frequency changes normally exhibited by MD units during DR trials. Most characteristic of the latter effect was abbreviation of the activation during the delay in units that, prior to cooling, exhibited sustained elevations of firing during this period. The results are interpreted as experimental evidence for a role of MD, the prefrontal cortex, and their interconnections in short-term memory.

**19.4** OPERANTLY CONDITIONED SINGLE UNIT ACTIVITY OF RATS MAINTAINED DURING PARALYSIS. David E. Hiatt* (SPON: J. Olds). Biol. Div., Calif. Inst. of Tech., Pasadena, Calif. 91109.

The fact that many forms of brain and autonomic activity have been operantly conditioned leads to the impression that most of the brain is under some degree of direct operant control. Grounds for doubt are found in the possibility that any brain activity which appeared directly operant, might instead have been respondently activated by the overt behaviors which are commonly found to arise during operant conditioning of the brain activity of active animals. This study was undertaken to test this possibility. Rats were chronically implanted with microelectrodes for single unit recording and large electrodes for electrical stimulation of reinforcing brain areas. During periods signaled by a light, which itself produced no response, reinforcement was given contingent upon elevated unit rates. Consistent rate augmentation during these periods was taken as evidence of operant conditioning. The conditioned animal was removed from the experimental apparatus only long enough to be injected with Flaxedil, after which it became completely paralyzed and required artificial respiration while the experiment continued. Of the 18 units tested under paralysis, 12 were scattered in the cerebellum, hippocampus, midbrain, and superior colliculus and failed to maintain the conditioning, showing that a large percentage of the units had been activated by feedback from skeletal muscle movement. One of the remaining 6 was in the cerebellum; the rest of the "operant" units were in the dorsal medial brain stem in the region of the vestibular nuclei and were perhaps part of the extrapyramidal system. Except for this interesting exception, the brain seemed to be more respondent than operant.

**19.5** INHIBITION OF POLYSENSORY RESPONSES BY STRIATO-NIGRAL STIMULATION. George Krauthamer and Mario Dalsass*. Dept. Anat., Rutgers Med. Sch., CMDNJ, New Brunswick, N. J. 08903.

In cats anesthetized with chloralose and immoblized with Flaxedil, bipolar stimulating electrodes were introduced into substantia nigra (SN) and caudate nucleus (Cd). Polysensory unit responses and field potentials evoked by peripheral stimuli were recorded from posteromedial suprasylvian gyrus, centrum medianum (CM), SN and Cd. Single conditioning shocks of low intensity were applied to SN and the effect on polysensory test responses was observed. SN stimulation exerted a powerful blocking action of 70 - 80 msec on cortical and subcortical polysensory responses. Analysis of the time course of inhibition revealed a more prolonged effect on Cd responses than on cortical ones. More intense stimulation of SN produced additional excitatory effects in Cd and CM which appeared unrelated to the inhibitory action. Striatal (Cd) stimulation led to a similar but more prolonged (150 - 250 msec) inhibition of polysensory responses in SN, CM and cortex. SN responses to suprathreshold Cd stimulation were predominantly inhibitory whereas those of CM were mixed. The differences in the time course of inhibition, stimulus threshold parameters (duration and intensity) and responses to Cd and SN stimulation can be attributed to differences in the synaptic organization within the striato-nigral system. (Supported by NIH grant no. FR-05576.)

**19.6** PREFRONTAL CORTICAL UNIT ACTIVITY DURING DELAYED ALTERNATION (DA) IN MONKEYS. Hiroaki Niki* (Spon: E.V.Evarts). NIMH, Bethesda, Md. 20014

In a previous study on prefrontal unit activity during DA (J. Neurophysiol. 34: 337-347, 1971) it was found that related units were concentrated in the vicinity of s. principalis, but the exploratory nature of that study prevented an accurate assessment of the proportion of related units in this area. In the present study all units picked up in the vicinity of s. principalis (whether related or not) were studied during DA, with the aim of obtaining more reliable information on the proportion of related units and the nature of their relationship. During the delay period the monkey was required to press a centrally located lighted button. After a 5-second press, the central light went out and two laterally placed buttons became illuminated, and the animal was required to press one or the other of these on alternate trials. Thus, the starting position of the hand was controlled, and intradelay behavior was made relatively constant. Out of 340 units studied within the mid-principalis area of a single hemisphere in one monkey (A28-38, L10-18), 14% (50 units) showed an obvious relation to DA. Of these 50 related units, 20% showed directional specificity, i.e., a differential response depending on the direction (left or right) of the movement. In the remaining 80% of the related units there were a variety of changes. Most of them showed an increase in their discharge rate immediately before the response. Several units showed an increase as soon as the delay period began. Some units showed a decrease at the time of responding. The number of related units found makes analysis of the nature of the relationship feasible, and current studies are aimed at fractionating DA behavior so as to discover the aspects of DA to which unit discharges are related.

**20.1** PATTERN SENSITIVITY OF CRUSTACEAN NEUROMUSCULAR JUNCTIONS. George D. Bittner and José P. Segundo. Dept. Zool., Univ. of Texas, Austin, 78712, and Dept. Anat., UCLA, Los Angeles, 90024.

Intracellular recordings from opener muscle fibers of the crayfish Procambarus clarkii have shown that the amount of transmitter released by different terminals of the same motor neuron depends upon the frequency and pattern of stimulation. Some of these terminals show facilitation of facilitation and do not release quanta according to the model proposed for frog neuromuscular junctions by Mallart and Martin (J. Physiol., 193: 679, 1967). The net effect of different pattern sensitivity is that different muscle fibers produce variable amounts of tension by a mechanism analogous to the "resonance theory" originally proposed by Weiss (Biol. Zentralblatt, 50: 357, 1930).

**20.2** NEUROMUSCULAR JUNCTIONS IN THE LEECH. Richard E. Coggeshall. Department of Anatomy and Marine Biomedical Institute, University of Texas Medical Branch at Galveston, Galveston, Texas, 77550.

The leech body wall muscle is a preparation used for the bio-assay of both acetylcholine and 5-hydroxytryptamine (5-HT). However, the neuromuscular junctions on the body wall muscle of this animal have not been described. The present study is a fine structural analysis of the neuromuscular terminals on leech body wall muscle. Two types of neuromuscular junctions have been seen. The first contains small clear 400-500 A vesicles, as well as a few larger vesicles with electron-dense cores. These vesicles resemble those in known cholinergic junctions. The second type of neuromuscular junction on leech body wall muscle contains large granules, approximately 1200 A in diameter with irregular electron-dense cores. These granules 1) resemble the granules in identified 5-HT containing leech neurons, 2) become radioactive when tritiated 5-HT is administered to the animal, and 3) reduce dichromate salts. Thus the second type of terminal described here is presumably the neuromuscular junction which uses 5-HT to influence body wall muscle. Supported by the National Institutes of Health, Bethesda, Maryland.

**20.3** DEVELOPMENTAL CHANGES IN THE TIME COURSE OF SYNAPTIC POTENTIALS AT AN AMPHIBIAN NEUROMUSCULAR JUNCTION. M.W. Cohen and R.W. Kullberg*. Dept. Physiol., McGill University, Montreal, Canada.

Spontaneous post-synaptic potentials were recorded in the presence of tetrodotoxin with external micro-electrodes from myotomal neuromuscular junctions in embryos and tadpoles of Xenopus laevis. The duration and variability of these focal external potentials were found to decrease during development. At early stages the rise times of potentials recorded at single electrode positions had means of 2-3 msec and standard deviations of 0.6-1.5 msec. Corresponding values at later stages were 0.3-0.4 msec for the means, and 0.07-0.10 msec for the standard deviations. The means and standard deviations of the half-decay times also decreased by about ten-fold. Development of cholinesterase activity contributes to these changes but does not appear to be the only important factor since application of anticholinesterases (eserine, neostigmine, tensilon) at later stages produced less than a three-fold increase in the duration of the focal external potentials. A further observation at early stages of development was the tendency of the largest potentials to have the longest rise and half-decay times. This finding suggests the possibility that packets of transmitter cause saturation of receptors at the immature neuromuscular junction; larger packets saturate more distant receptors thereby prolonging the rising and falling phases of the conductance change produced by the transmitter.

Supported by M.R.C. (Canada).

**20.4** EFFECT OF LEAD ON THE ELECTROPHYSIOLOGY OF NEUROMUSCULAR TRANSMISSION IN THE FROG. R. S. Manalis and G. P. Cooper. Departments of Physiology and Environmental Health, University of Cincinnati, College of Medicine, Cincinnati, Ohio 45219.

Electrophysiological parameters were monitored using conventional microelectrode techniques to study the effect of lead on neuromuscular transmission in the isolated sciatic nerve-sartorius muscle preparation of the frog (Rana pipiens). Lead chloride was added to normal Ringer's that was buffered to a pH of 6.9 with tris maleate; experiments were performed at 15°C. Superficial endplates were located optically through a binocular microscope that has a magnification of 400 x. The following observations were made: 1) 0.1 mM Pb increased the frequency of the spontaneous release of transmitter (miniature endplate potentials); 2) 0.1 mM Pb reduced by fifty per cent the depolarization by acetylcholine when it was applied directly to the endplate receptors by iontophoresis from a micropipette; 3) 0.01 mM Pb completely blocked the endplate potential that was recorded from a curarized preparation; 4) lead had no effect on the input resistance of the muscle cell. All observed effects of lead were reversible. It is concluded that lead affects both presynaptic and postsynaptic events in neuromuscular transmission. (Supported by NIH Grant R01 ES00649-01.)

**20.5** SYMPATHETIC GANGLION: RELEASE OF ACETYLCHOLINE ELICITED BY BLACK WIDOW SPIDER VENOM. David W. Pumplin* and W. O. McClure. Department of Biochemistry, University of Illinois, Urbana, Illinois 61801.

When applied to the mammalian neuromuscular junction, black widow spider venom (BWSV) causes an initial increase, followed by a fall, in the frequency of miniature end-plate potentials. The venom also depletes the nerve endings of synaptic vesicles. We studied the venom-induced release of acetylcholine (ACh) from cholinergic endings in superior cervical ganglia of rats. The excised ganglia were incubated at 37°C in Ringer-Locke solution containing choline and neostigmine methyl sulfate. At intervals after the addition of venom, aliquots of the bathing solution were removed and assayed for ACh. The venom stimulates release of ACh in this system. Progress curves indicate that release follows first order kinetics. This fact, as well as other data, suggests that BWSV not only induces release, but also blocks replenishment of the pool of ACh which is available for release. The first-order rate constant for release is a linear function of the protein content of the venom. The rate constant for a given venom concentration is decreased by prior treatment of the ganglion with either botulinum toxin or cytochalasin B, or by using a modified Ringers solution containing a high concentration of $Mg^{2+}$. Since these conditions inhibit the release of ACh elicited by electrical stimulation of the ganglion, it is suggested that one action of BWSV is the stimulation of some step in the physiological mechanism for the release of neurotransmitter. The venom, or one of its component proteins, may be a useful tool for the further investigation of this mechanism. Supported by the National Institutes of Health and the State of Illinois Department of Mental Health.

**20.6** EPR MEASUREMENTS OF MUSCLE INTRACELLULAR VISCOSITY. Fred Sachs* and Ramon Latorre* (SPON: W.J. Adelman, Jr.). Laboratory of Biophysics, IR, NINDS, NIH, Bethesda, Md. 20014

The state of cell water is of intrinsic interest to biologists since water constitutes approximately 80% of a cell's volume. The terms "free" and "bound" have been loosely applied to cell water. However, different measuring techniques yield different answers since the measurements may cover different time scales. Water may be moving rapidly on a scale of minutes, but slowly on a scale of nanoseconds. We have used the tumbling time of a water soluble nitroxide free radical as a measure of intracellular microviscosity on a time scale of nanoseconds. The radical was introduced into single barnacle muscle fibers either by direct microinjection or by diffusion. The EPR spectrum of the radical was then measured in VARIAN E3 EPR spectrometer. Equilibrium experiments indicated that the probe was distributed throughout a minimum of 82% of the intracellular water. The intracellular microviscosity of the muscle fibers was 5 cp when fully hydrated. As water was removed from the fibers by low humidity $N_2$ or hypertonic solutions, the viscosity gradually increased. We expected that if some well structured water did exist then as the water content was reduced, the EPR spectrum of the radical would show a sudden change corresponding to the probe's interaction with a rigid matrix. In fact, a solid type spectrum did appear at about 25% total water, and increased in amplitude with further dehydration. On the basis of these and other data we suggest that the cell water consists of about 75% slightly viscous solution with normal solvation properties, and 25% which has reduced mobility and solvation properties. These findings have important implications for electrophysiological measurements.

**21.1** ORGANIZATION OF VESTIBULAR NYSTAGMUS IN THE OBLIQUE OCULOMOTOR SYSTEM. R. Baker and A. Berthoz*. Div. of Neurobiology, Dept. of Physiology and Biophysics, Univ. of Iowa, Iowa City 52240, and Laboratoire de Physiologie du Travail, 41 Rue Gay Lussac, Paris 5, France.

In encéphale isolé cats, acute lesions of the vestibular nerve produce a spontaneous nystagmus in which the slow and fast phases can be recorded as synchronous, but reciprocal, events in the inferior oblique (IO) and superior oblique (SO) nerves of the same eye. The temporal sequence of membrane potential changes recorded intracellularly from antidromically identified trochlear motoneurons (TMns) and inferior oblique motoneurons (IOMns) was closely correlated with the activity found in the IO and SO nerves. Cessation of activity in Mns producing the slow phase was signaled by an abrupt membrane hyperpolarization (disfacilitation and IPSP) which preceded the pause in nerve activity by 10-20 msec. In Mns generating the fast phase a synchronous depolarization (EPSP and disinhibition) preceded the nerve activity by 10-20 msec. These findings show that the appropriate synaptic information arrives at the agonist and antagonist Mns simultaneously, although the decrease in agonist nerve activity precedes that in the antagonist by 0-15 msec. Activity of inhibitory and excitatory vestibular neurons, identified by monosynaptic activation from vestibular nerve stimulation, was recorded from their axons (intracellularly) within the trochlear nucleus. The firing of both types of vestibular neurons was modulated during slow and fast phases and changes in their activity preceded those in the nerves by up to 20 msec. It is concluded that the reciprocally organized vestibular projection to IOMns and TMns via the MLF is utilized as the immediate supranuclear pathway providing rhythmic influences to the oblique oculomotor system during nystagmus. (Supported by C.N.R.S. and C.N.A.M. in Paris and U.S.P.H.S. Grant No. NS-09916 from NINDS)

**21.2** OPTOKINETIC NYSTAGMUS IN GOLDFISH. S. S. Easter, Jr., Department of Zoology, University of Michigan, Ann Arbor, Michigan 48104.

Horizontal eye movements made by restrained alert goldfish have been measured with an optical technique. The fish were surrounded by a cylindrical striped drum. When it was still, the eyes moved spontaneously over a wide range (30-40 degrees). But when the drum rotated about the vertical axis, and the animal responded with optokinetic nystagmus, this range was contracted to 5-10 degrees. In addition, the operating points of the eyes were shifted toward the origin of the movement. If, for example, the drum rotated clockwise, the eyes shifted counterclockwise nearly as far as they could go. From this extreme position, they smoothly pursued the drum for a few degrees and then reset to the extreme position. The range of positions assumed during nystagmus was independent of where in the field the movement occurred; it depended only on the direction of the movement.

Both eyes responded, but unequally, if only one of them saw the moving stripes. If the seeing eye was immobilized, so that the angular velocity of the retinal image equalled that of the target, the blind eye moved faster than when the seeing eye was free to move. The blind eye responded equally well to movement of the contralateral retinal image caused by motion of the drum past the immobilized eye or by (imposed) movement of the sighted eye past a stationary drum. These data are consistent with the hypothesis that ocular pursuit velocity depends only on retinal image movement. Proprioception and stationary landmarks play a minor role if indeed they play any at all.

This work was supported by a grant (EY-00168) from the United States Public Health Service.

**21.3** EXAMINATION OF THE NORMAL AND DEAFFERENTATED LATERAL VESTIBULAR NUCLEUS IN THE RAT BY ELECTRON MICROSCOPY. John E. Johnson, Jr. and Terence H. Williams. Dept. Anat., Sch. Med., Tulane Univ., New Orleans, Louisiana 70112

These experiments are designed to obtain information about morphological adaptability of neurons, with a view to obtaining clues about the mechanisms that underlie plastic responses in the CNS. The lateral vestibular nucleus is a suitable model because afferents can be lesioned selectively, and there is a substantial background of information about its general organization. Sotelo and Palay (Lab. Invest. 25, 653, 1971) have shown examples of altered axons and terminals in the normal rat, particularly in the central portion of the nucleus where projections from cerebellum and vestibule overlap. The examples included parallel arrays of tubules, whorls of endoplasmic reticulum and giant mitochondria. Dendritic expansions packed with mitochondria and glycogen are also a feature of the nucleus. The functions of these complex structures remain an open question. Experiments have been undertaken to determine which inputs are associated with the axonal variants, and what plastic changes follow partial deafferentation. This was carried out in 36 male rats by destroying the vestibular ganglia or removing the cerebellar vermis unilaterally by suction. The animals were sacrificed 24 hours to 6 months later, and the lateral vestibular nuclei compared with those of unoperated rats.

**21.4** NEURAL ACTIVITY IN THE VESTIBULAR NUCLEI. Jai H. Ryu and Brian F. McCabe*. Dept. of Otolaryngology and Maxillofacial Surg., Coll. of Med., Univ. of Iowa, Iowa City, Iowa 52240.

Activity of 600 single neurons in the vestibular nuclei in the cat was recorded stereotaxically through the intact cerebellum with a tungsten microelectrode. The resting activity, response to semicircular canal stimulation, firing pattern, and relationship between spike discharge and nystagmus were the parameters of interest with special attention to the relationship between anatomy and neurophysiology of the vestibular system. Animals were anesthetized. Neurons were stimulated by either 10 cc. cold water stimulation or a constant horizontal angular acceleration of $4°/sec^2$ for 25 seconds and followed by equal and opposite deceleration. Neurons were classified according to their responses to ampullopetal and ampullofugal flow of endolymph. The superior and medial nuclei contains a relatively larger number of type I and II neurons (related to semicircular canal) and the lateral and inferior nuclei contains a relatively larger number of type V neurons (related to otolith organ, spinal cord, etc.) which is in good agreement with the anatomical findings. However, histologic mapping did not show a clear topographical arrangement according to their response type. The results indicate that there is considerable crossed inhibitory arc between the two sides of the vestibular nuclei, and type I and II neurons have direct connections to bipolar hair-cells in the ampulla and reflect the highly damped cupula-endolymph system. The average resting frequency was about 30 spikes per sec. The majority of neurons discharge pattern was random, and the neuron firing was geared with the slow component of nystagmus.

**21.5** VISUAL-VESTIBULAR INTERACTION: EFFECTS OF VISION IN SUPPRESSING VESTIBULAR NYSTAGMUS. Setsuko Takemori* and Bernard Cohen. Dept. of Neurology, Mt. Sinai School of Medicine, New York, N.Y. 10029.

The vestibular system influences visual perception of space and motion and its dysfunction causes illusions of movement or tilting. Conversely, the visual system influences the vestibular system. Spontaneous nystagmus is better provoked with eyes closed or in darkness than in light. Patients without labyrinths lose balance more easily in darkness. The purpose of this note is to clarify the extent to which vision suppresses nystagmus which originates in the vestibular system.

Eye movements of 11 normal monkeys were recorded using electrooculography (EOG) in light and in darkness. The EOG was differentiated and rectified to obtain the velocity of the slow phases. Slow phase velocity and total deviation of the eyes were used as indices of the intensity of the response. Nystagmus was induced by caloric stimulation and by administration of alcohol. The latter causes subjects to have positional alcohol nystagmus (PAN). Caloric nystagmus reaches maximum intensity 5-10 sec after the end of stimulation and maintains this level for 20-25 mseq. Visual suppression was tested by turning on the lights for 10 sec during the maximum response. PAN was also recorded in light and in darkness.

In 11 animals there was a mean reduction of slow phase velocity of caloric nystagmus of 50.9% in light. In one animal the mean reduction in 6 tests was 50.2%. Mean values for visual suppression of nystagmus induced by water whose temperature ranged from 7°C to 47°C was 51.4%. Mean suppression of PAN was 49.1%. It would appear that the visual system can compensate for "inappropriate" vestibular nystagmus in a fixed, lighted environment by reducing the intensity of the response by about half. Supported by NINDS Grants NS-00294 and 1K3-34,987.

**22.1** DIFFERENCES IN THE VISUAL CORTICAL PROJECTION AREA IN ALBINO AND PIGMENTED GUINEA PIGS. Donnell J. Creel and Roland A. Giolli. Psychol. Res. Lab., V.A. Hospital and Arizona State Univ., Phoenix, 85012; and Human Morph., Sch. Med., Univ. of Calif., Irvine, 92664

The geniculocortical projections of albino and pigmented guinea pigs were studied by mapping the distribution of the visually evoked responses on the cortex. One eye was removed from each of six albino and six pigmented guinea pigs. Six to eight days after the operation, each animal was anesthetized and the dorsal cortex, including the extent of the visual projection area, was mapped. Visually evoked responses appeared almost entirely on the contralateral cortex of both strains indicating a greater proportion of decussating optic fibers in the guinea pig than in the rat, rabbit, or squirrel. Input to the striate cortex via nondecussating fibers was found only in the pigmented strain. A basic pattern of input to the contralateral striate cortex was observed in the pigmented strain, but was variable in the albinos. Combinations of abnormalities in pigmentation, vision, and audition occur in hereditary syndromes of several species of mammal, including man. The anomalous structure of the dorsal lateral geniculate nucleus as well as the reduced numbers of nondecussating optic fibers of albinic mammals appears to be a highly general transspecies phenomenon.

**22.2** ANATOMICAL ORGANIZATION OF THE PRIMARY OPTIC PROJECTIONS IN PIGMENTED AND ALBINO GUINEA PIGS. Roland A. Giolli and Donnell J. Creel. Human Morph., Sch. Med., Univ. of Calif., Irvine, Calif. 92664 and Psychology Research Lab, V.A. Hospital, Phoenix, Ariz. 85012.

An eye was enucleated in each of six pigmented and six albino guinea pigs. Six to eight days postoperatively the animals were killed and their brains were prepared by the Nauta and Nissl methods in order to study the projection and the terminal distribution of the degenerating optic fibers. An organized input to the dorsal lateral geniculate nucleus from the ipsilateral retina was always present in the pigmented, but was not seen in the albino guinea pigs. This input in the pigmented animals was represented by a single lamina located in the medial region of the geniculate nucleus. There was a distinct pattern to the geniculate input from the contralateral retina in the pigmented, but not in the albino guinea pigs. As with the optic projection to the dorsal lateral geniculate nucleus, the optic projections to the ventral lateral geniculate nucleus, the pretectal nuclei and the superior colliculus differed in the pigmented as compared with the albino guinea pigs. Thus, organized ipsilateral optic inputs to the ventral lateral geniculate nucleus, pretectal nuclei and superior colliculus were found in the pigmented but not the albino animals; and distinct differences in the patterns of the contralateral projections were noted between the two groups of animals. It has not yet been possible to demonstrate differences in the organization of the accessory optic fiber system in the two groups of animals.

**22.3** ABNORMAL RETINOGENICULATE AND GENICULOCORTICAL PROJECTIONS IN THE ALBINO ALLELOMORPHIC SERIES OF MAMMALS. K. J. Sanderson*, J. H. Kaas and R. W. Guillery. Dept. of Anat. and Lab. of Neurophysiol., Univ. of Wis., Madison, Wisconsin 53706.

Using fiber degeneration methods, we have compared the retinogeniculate projections of pigmented and albino rabbits, rats, ferrets and mink. In the albinos, some parts of the dorsal lateral geniculate nucleus (LGNd) which are normally innervated by the ipsilateral retina are innervated instead by the contralateral retina. A similar abnormality in the LGNd is also found in other mutants in the albino series, the Siamese cat and the Himalayan rabbit. More detailed studies on the LGNd of Siamese cats revealed that most of the nucleus has a normal representation of the contralateral half of the visual field. However, parts of layers A1 and C1, which normally receive terminations from the ipsilateral retina, represent a central 20° strip of the ipsilateral hemifield via projections from the contralateral retina. Within these abnormal parts of A1 and C1, the horizontal dimension of the visual field is represented as a mirror image of the normal representation. Microelectrode mapping of the striate cortex and thalamic retrograde degeneration after striate cortex lesions indicate that the retinotopic organization seen in the LGNd is maintained in the projections to the striate cortex in some Siamese cats. Thus, a "normal" representation of the contralateral hemifield is coextensive with striate cortex, while the abnormal input from the contralateral eye with a reversed retinotopic organization is superimposed on part of the "normal" representation. Separate groups of cells in the cortex appear to be devoted to each type of input. Relatively few cortical neurons were activated by the abnormal input suggesting that geniculate layers with normal retinal connections are more likely to establish successful contacts with cortical cells. (Supported by Grants 1 PO1 HD 03352, 5 PO1 NS 06225 and RO1 NS 06662 from USPHS.)

**22.4** THE STRUCTURE OF ALBINO VISUAL SYSTEMS IN RELATION TO BEHAVIOR. Charles L. Sheridan. Dept. Psych., Univ. Missouri and V.A. Hosp., Kansas City, 64110

A theory will be presented which relates visually-guided behavior of albinos to current information about the anatomy and physiology of their retino-geniculate projections. If it is assumed that: 1. discrimination learning can be represented as a sampling of subsets from a set of potentially connectable stimulus elements and 2. the size of the subset sampled is directly related to the density of optic fiber projections, then one can account for much current available data. For example, one can simulate the failure of albino rats to acquire pattern discriminations via optic uncrossed fibers as well as the success of similar animals in retaining such discriminations, once acquired via the more dense crossed pathways. To account for rapid acquisition under conditions of reversal and nonreversal shift, it is useful to extend the model to include a second probability, that of sampling a given cue dimension in general. The resulting model predicts unexpected behavioral phenomena, and accounts for most of the available data on monocular acquisition and interocular transfer in albino and pigmented rodents. It is easily generalizable to the nervous systems of other species. However, limitations of the model will be discussed, viz. that it fails to predict enhanced rates of learning after unilateral striate ablation in albino rats and that its predictions tend to be accurate only for learning done at asymptotic latencies.

**23.1** SYNAPTIC ORGANIZATION OF SOMATOSENSORY AFFERENT PROJECTIONS TO THE SQUIRREL MONKEY THALAMUS. Donna J. Forbes. Dept. Anat., University of Wisconsin Medical School, Madison, Wis., 53706.

Light and electron microscopic methods have been used to study the normal synaptic population in ventrobasal (VB) thalamus and the synaptic terminals which degenerate following unilateral ablation of dorsal column nuclei (DCN) or unilateral section of the anterolateral (AL) spinal cord. After appropriate survival periods and perfusion, tissue samples were taken from each animal for both light and electron microscopy. With the Nauta method of staining degeneration it was observed that the DCN projected in a somatotopic array to the contralateral ventral postero-lateral (VPL) portion of VB thalamus. The projections from the AL cord distributed for the most part ipsilaterally to the VPL portion of VB and to the intralaminar nuclei, primarily centralis lateralis (CL). The normal synaptic population in VB consisted of: large and small knobs with round vesicles and making asymmetrical contacts; knobs with flat or mixtures of flat and round vesicles and making symmetrical contacts; and a few axosomatic knobs. As early as 2 days after a DCN lesion the large knobs with round vesicles were seen to undergo neurofilamentous degeneration. By 5 days these knobs were very electron dense and surrounded by phagocytic glial elements. The material from the AL lesioned animals is presently under study with the electron microscope.

(Supported by NIH Grant NSI - EP 1 FO2 NS 46,583 - 01)

**23.2** QUANTITATIVE STRUCTURAL ORGANIZATION IN BRAIN STEM NUCLEI. Francis J. Fry. Indianapolis Center for Advanced Research, Indiana University-Purdue University at Indianapolis, Indianapolis, Indiana 46207

Dominant dependency type relationships among nuclear neuron populations in the mammillary bodies of the adult cat reveal a precise quantification of structural organization in these nuclei. The dominant dependency relationships are elicited by axonal transections in either the efferent and/or afferent system of a given nucleus. These transections, leading to either cell loss or atrophy, when precisely duplicated in position and severity from animal to animal in the adult cat, show that the residual neuron subpopulation numbers have a precise ratio with respect to the contralateral control nucleus in each animal. Precise ratios of this type stand in sharp contrast to the wide range of ratios of the total nuclear neuron populations of the same nuclear groups when compared from animal to animal in the normals (variations of from 20% to 40% in ratios of these neuron populations are typical). The medial and lateral mammillary bodies have been quantitatively described in terms of these characteristic dependency subpopulations, and as such provide a model for structural organization derived from the biological system. It is suggested that these precise connectivity dependency relationships may play a significant role in establishing the limits of function and behavior in the neural network.

**23.3** A GOLGI STUDY OF THE NUCLEUS GRACILIS IN THE RAT. Robert L. Gulley* (SPON: S. L. Palay). Harvard Medical School, Boston, Mass. 02115

The nucleus gracilis of the rat has been examined in Golgi-Kopsch and rapid Golgi material. Five different neuronal types can be distinguished in the nucleus on the basis of differences in cell size and dendritic branching patterns. Caudal to the obex the cell bodies are arranged in small groups with the dendrites entwined in narrow conical and vertical columns. Rostrally the cells are not organized into groups. The dendrites, however, have a distinct horizontal orientation. Golgi II neurons occur in both regions. The fibers in the dorsal white columns present a similar rostral caudal organization. The fibers course longitudinally through the nucleus, giving off collaterals that descend vertically and divide into several fine terminal branches within the territory of the vertical dendritic trees. At the level of the obex these fibers bend sharply to course transversely through the nucleus, emitting several fine terminal collaterals. Corticospinal fibers course throughout the nucleus but are more common rostral to the obex. The distinct pattern of dendritic arborizations and the distribution of the sensory afferents in the rostral and caudal regions correlate well with the somatotopic organization and receptive field data obtained from physiological studies on the nucleus gracilis. However, the heterogeneity of the neuronal population suggests a complexity which has not been anticipated by physiological data but which may account for the localization of specific modalities within the nucleus.

**23.4** PROJECTIONS OF THE SUBNUCLEAR AREAS OF THE PERIAQUEDUCTAL GRAY MATTER IN THE CAT. Betty L. Hamilton. Dept. Anat., Sch. Med.-Dent., Georgetown U., Washington D.C. 20007

Lesions were stereotaxically placed in each of three projected subnuclei in the periaqueductal gray matter (PAG) in the cat and the resulting degenerating axons were stained using silver impregnation techniques. The fibers of degeneration were tracked to determine if the three areas have different efferent connections. The pars medialis of the PAG is the relatively acellular innermost ring and is populated by small elongated neurons. A lesion here gives a small number of degenerating fibers radiating ventrally toward the tegmentum while the bulk of the fibers project rostrally in a bundle within the PAG. At rostral midbrain levels this tract turns ventrally and divides into two parts; one goes to the Field of Forel, and the other to the ventral tegmental area. The pars lateralis is the outermost ring of the PAG and is densely populated by medium sized, spherical neurons. Efferent connections from this area radiate laterally to the tegmentum, superior colliculus and inferior colliculus. In addition a bundle can be traced rostrally to the periventricular gray, the posterior hypothalamus and several thalamic nuclei including the paraventricular, parafascicular, reunions and ventral nuclei. The third subnucleus, the pars dorsalis, appears densely cellular due to the large number of glial cells plus the intermediate sized spherical neurons. There are few if any radial projections from a lesion in this area. The degenerating fibers run rostrally to reach the pretectal area and the lateral habenula.

**23.5** MATURATIVE PROCESSES IN DENDRITES OF SPINAL CORD AND BRAIN STEM IN THE CAT. Madge E. Scheibel*, Arnold B. Scheibel, and Thomas L. Davies* Dept. of Anat., Sch. Med. UCLA, Los Angeles, 90024

Golgi analysis of maturing dendrite systems in cat spinal cord and brain stem reveals several interesting structural changes. At birth, the vast majority of neuron somata and dendrites are covered by shaggy, polymorphic protospines. These structures begin to disappear at the 10th to 14th day of life and are essentially gone by the end of the second month, leaving dendrites that are smooth except for very small numbers of long, spine-like appendages. Starting with the second or third week of life, dendrites of many neuraxial systems including motoneurons of spinal ventral horn, medullo-pontine reticular neurons, and cells of the lateral portion of nucleus reticularis thalami are progressively reorganized into bundles. Considerable numbers (4-10) of dendrite shafts from cells often remote from each other, and in the case of spinal motoneurons, frequently supplying muscles of antagonistic function, run in close proximity or in contact, often for several hundred micra. Temporal correlations between development of dendrite bundling and onset of certain types of behavior have been noted. We suggest that early synaptic systems terminating on protospines informationally load the neuronal membrane to handle the majority of stereotyped or reflex response patterns. Subsequent bundling of these dendrites provides the actual loci where membrane-to-membrane interactions forge the central programs essential to reciprocal or repetitive activities. Subsequently established synaptic systems provide over-ride control from later-maturing, hierarchically higher centers.

**26.1** ELECTROPHYSIOLOGY OF HIPPOCAMPAL INPUT TO THE SEPTUM OF THE CAT. J.F.DeFrance*, C.Christensen*, K.Hatada*, S.T.Kitai. Morin Memorial Laboratory, Depts. Anat. and Psychol., Wayne State University,Detroit48207.

An attempt was made to determine if regional differences exist, within the septum, with respect to effects of hippocampal input. Field potentials were recorded with microelectrodes following stimulation of the ipsilateral fimbria (IFim).Antidromic ($N_1$) and monosynaptic ($N_{2-3}$) responses could be recorded in the septum following IFim stimulation. Both consisted of a small positivity followed by a relatively large negative potential. The monosynaptic negativity could be fractionated by power and double-shock testing into synaptic currents ($N_2$) and action currents ($N_3$). A small positivity ($P_1$) followed by $N_{2-3}$ complex. Intracellular recordings show $P_1$ to correspond to IPSPs (mediated via inhibitory interneurons) while $N_{2-3}$ corresponds to EPSPs and spikes. On the basis of differences in waveform and behavior of field responses to single and double shocks, three principal zones could be distinguished lying, more or less, in horizontal planes. In the upper zone, responses are characterized by having no $N_1$ and with $N_3$ components which are suppressed for long periods (300-600 msec) during double-shock testing. Furthermore, the $P_1$ component is only partially suppressed in the absence of $N_3$. The intermediate zone presents responses which include the $N_1$ component and whose $N_3$ component is suppressed for long periods; the $P_1$ component is suppressed with $N_3$. The responses in the deepest zone include $N_1$, but $N_3$ is suppressed only for relatively short periods (30-100 msec). The $P_1$ component in this region recovers only after the full recovery of $N_3$.

(Supported by UPSHS Grants NB 00405 and RR 5384)

**26.2** PERIRHINAL AFFERENTS TO THE DENTATE FASCIA. L.E. White, Jr. and R. B. Chronister*. Department of Neuroscience and Division of Neurological Surgery, College of Medicine, U. of Florida, Gainesville, 32601.

Access for isocortical information to the hippocampal formation and limbic structures have been demonstrated physiologically, but the anatomic pathways are poorly understood. Using rodents, lesions were placed in perirhinal cortex sparing the entorhinal area. The resultant degeneration was studied for terminal degeneration with several reduced silver techniques. A discrete pathway to the dentate fascia was revealed. These observations suggest that through such projections diffuse projections from isocortex can gain specific access to the limbic structures and hippocampal formation via transitional para-limbic zones. This study demonstrates one of these paths from area 35 to the dentate fascia.

**26.3** CONTRASTS IN MAMMILLARY BODY FLUORESCENCE FOLLOWING SEPTAL OR HIPPOCAMPAL LESIONS. Ervin W. Powell, Charles G. Winter*, Margaret E. Kirby*, and Barbara Austin*. Dept. Anat., Sch. Med., Univ. of Arkansas, Little Rock, 72201.

A recent study of limbic projections to the mammillary body revealed a 1:1 septum: hippocampal input to the medial nucleus. The present fluorescence study was undertaken to determine whether or not a qualitative differential projection exists in the mammillary body from these two limbic structures. The amount of fluorescence remaining in the mammillary body smears following transection of the fornix was about one-half of the fluorescence observed in smears from unlesioned animals. The amount of fluorescence remaining in the mammillary body samples subjected to lesions of the septum was about one-fourth of the fluorescence observed in controls. Furthermore, tissue smears following septal lesions primarily displayed green fluorescence while orange and yellow fluorescence was obvious in samples following fornix transection. Yellow fluorescence predominated in control animal smears. The authors interpret this as neurochemical evidence of the diverse structure-functional character of the septum. Color differences suggest that three (3) different neurotransmitters are present in the mammillary body. Furthermore, their relative concentration appears to depend upon the integrity of the structures of origin of the mammillary body afferents.

**26.4** RELEASE OF NOREPINEPHRINE AND SEROTONIN FROM THE AMYGDALA DURING REWARDING MEDIAN FOREBRAIN BUNDLE STIMULATION. Joan A. Holloway* (SPON: F. A. Holloway) Univ. Okla. Health Sciences Center, Oklahoma City, Okla. 73190.

Psychopharmacological and neurochemical research has strongly implicated norepinephrine (NE) as a mediator of the reward system. Some evidence also indicates that serotonin (5-HT) is importantly involved in this system. A push-pull cannula technique was used to determine the degree of specificity of release of NE and 5-HT during either rewarding or non-rewarding electrical stimulation of the brain (ESB). Auditory and visual stimulation (AVS) was employed to examine stimulation specificity. Release of urea (U) was examined to determine chemical specificity. Rats with stereotaxically implanted electrodes in the median forebrain bundle, injecter cannulae in the lateral ventricle, and push-pull cannulae in the amygdala were injected with isotopically labeled NE, 5-HT, or U. After 45 minutes the amygdala was perfused for 5-7 hours. During the perfusion 2 ESB and 1 AVS periods were interspersed with control periods of no stimulation. Samples of perfusate were collected every 15 minutes and counted in a liquid scintillation counter. There was a release of NE and 5-HT, but not U, during rewarding ESB and an inhibition of release of NE and 5-HT, but not U, during non-rewarding ESB. There was no release during AVS. During rewarding ESB near threshold levels there was an inhibition of release of 5-HT but not NE or U. Both NE and 5-HT appear to be mediators of the reward system. The argument is further strengthened by the inhibition of release during non-rewarding stimulation. The non-release of U in conjunction with non-release of NE and 5-HT during AVS indicate that the release is not an artifact of the technique and the push-pull method is a valid and valuable tool for the neurosciences.

**26.5** CORRELATION OF LATENCY TO DRINK AND UNIT ACTIVITY FOLLOWING CHOLINERGIC STIMULATION OF MEDIAL SEPTAL NUCLEUS IN RATS.
James Buggy*, Zaven Khachaturian†, Alan E. Fisher*, Psychology Department University of Pittsburgh, †Division Child Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, Pa. 15213

Cholinergic stimulation of several limbic sites induces water drinking in satiated rats after a characteristic latency period. To investigate further the neural events mediating this phenomenon microelectrodes were fastened to a cannulae and chronically implanted in medial septal nucleus of adult male rats. Recording electrodes were also implanted in various other limbic sites within the cholinergic thirst circuit. Under dial-urethane anesthesia, 1μg/μl carbachol solution was injected into the medial septum and multiple unit activity was recorded from the site of injection as well as from distal loci. The data was recorded on a magnetic tape recorder and subsequently analyzed with the aid of a PDP-12 computer. Different size units were discriminated and a baseline was obtained by observing the firing pattern of a selected unit population for 15 minutes before the administration of the drug. In most cases, a depression of baseline firing rate was initially observed, which was followed within 10-20 minutes by an increase in firing rate well above the baseline. The same rats were stimulated with carbachol while awake. The latency of the drinking response under these conditions was found to correlate well with the latency of the increased firing rate observed under anesthesia.

**26.6** THE ROLE OF THE SEPTUM IN THE REGULATION OF CONSUMMATORY RESPONDING IN RATS. Leonard W. Hamilton. Dept. Psychol., Rutgers Univ., New Brunswick, N.J. 08903

Several experiments have been conducted to determine the effects of septal lesions upon responsivity to taste and postingestive stimuli. In the first series of experiments, rats with septal lesions were compared to normal rats in terms of responsivity to absolute and relative taste factors associated with sucrose solutions. In the second series of experiments, septal rats were compared to controls on responsivity to the suppressant effects of saccharin and sucrose upon food intake. In the third series of experiments, a conditioned aversion paradigm (using lithium chloride and sodium chloride) was used to determine the role of taste and postingestive factors in conditioned aversion. The results of all of these experiments are consistent with the hypothesis that septal lesions enhance reactivity to taste factors and impair reactivity to postingestive factors.

**26.7** **EFFECT OF SEX REVERSAL ON SEX DIFFERENCES IN EMOTIONALITY FOLLOWING SEPTAL LESIONS IN RATS.** Anthony G. Phillips. Dept. Psychol., UBC, Vancouver 8, B.C.

When tested at 26 days of age, female rats displayed a hyperemotional reaction to capture and tactile stimulation after ablation of the septal nuclei. Male littermates receiving comparable lesions showed no change in emotional reactivity. Sexual differentiation of hypothalamic structure is subserved by the presence or absence of androgen during the perinatal period and these changes are thought to be responsible for sex differences in many forms of behavior. In an attempt to determine whether a similar process of differentiation is involved in the observed sex differences in emotionality, male rats were castrated on day 1 and female littermates exposed to 1.25 mg of testosterone propionate. Following sex reversal, castrated males became hyperemotional after septal lesions at 25 days, while androgenized females showed no change. As in the previous study, control females were hyperemotional while males were unaffected. The hyperemotionality produced by septal lesions may be due to the functional disruption of structures whose neuronal development depends on the presence or absence of androgen at critical periods.

**26.8** EFFECT OF LIMBIC INJURY ON TONIC IMMOBILITY IN CHICKENS. Jack D. Maser, Joan W. Klara, and Gordon G. Gallup, Jr.* Dept. of Psychology, Tulane University, New Orleans, La. 70118.

Hyperreactivity following septal region damage is well documented in rats, while that of non-mammalian species is not. The tonic immobility response in the chicken was selected for study since evidence indicates that this response is related to predation-induced fear. It was hypothesized that septal lesions would enhance immobility because of heightened fear of a natural predator, man. Bilateral archistriatal lesions were expected to produce low durations of tonic immobility. Separate groups of chickens sustaining either bilateral septal, archistriatal or sham operational damage were observed for the number of inductions necessary to elicit tonic immobility and the duration of self-paced immobility. The data were interpreted in terms of predation-induced fear interacting with neural mechanisms which mediate the incentive value of stimuli.

**26.9** STIMULUS-INDUCED MATING: PERIPHERAL vs. INTRACRANIAL STIMULATION. Jack H. McLean* and Molly Kenney* (SPON: James G. May). Dept. of Psychology, LSUNO, New Orleans, La. 70122 and National Center for Primate Biology, Davis, Calif. 95616.

The purpose of the present study was to compare the vigor of male copulatory behavior during 3 test sessions: one with intracranial stimulation (ICS); one with shock to the back of the neck (NS); and a control session without experimenter-produced stimulation (C). Twelve male hooded rats had intracranial electrodes implanted in the lateral hypothalamus-medial forebrain bundle (LH-MFB) as well as peripheral electrodes 'implanted' in the skin of the dorsal neck. Each S served in an ICS, a NS and a C session. In the ICS and NS sessions, Ss received the appropriate stimulation on an average of once every 60 sec. The order in which the 3 treatment sessions was administered to a S was determined by randomly assigning 2 Ss to each of the 6 possible permutations of treatments. The number of mounts, intromissions, and ejaculations was recorded in each 30-min. session. Separate analyses were run on each dependent variable although primary emphasis is placed on the analysis of a composite sex score made up of the total number of copulatory responses. Statistically significant differences were found between treatments, with both the NS and ICS conditions producing significantly more copulatory responses than the C condition (means were 33.25, 28.33 and 18.92 respectively). There was, however, no statistically significant difference between the 2 modes of stimulation, NS and ICS. Thus, electrical stimulation of the dorsal neck was just as effective in inducing copulation as was ICS of the LH-MFB. This is taken as an argument against the view that discrete hypothalamic areas are responsible for specific drive states.

**26.10** ANOSMIA AND MOUSE KILLING BY RATS: A NON-SENSORY, LIMBIC ROLE FOR THE OLFACTORY BULBS. Elaine M. Hull, Harvey D. Homan* and Stephen A. Spector*. Dept. Psychol. State Univ. of N. Y. at Buffalo, 14226

Olfactory bulbectomy facilitates mouse killing in previously non-killing rats. This has often been assumed to result from the anosmia produced by bulbectomy. In the present study two kinds of anosmia were compared for their effects on mouse killing: that produced by surgical removal of the nasal mucosa and afferents (bulbs intact) and that produced by removal of the olfactory bulbs. 20 rats which had not killed a mouse during a 6-week pretest sustained receptor ablations; 22 non-killing rats sustained olfactory bulbectomies. Of the 20 de-afferented rats, none killed a mouse during a 6-week test period. Of the 22 bulbectomized ones, 16 have killed mice and only 6 have failed to do so. Furthermore, many of the bulbectomized animals were more irritable when handled than were de-afferented ones. Since the presence of the bulbs in the de-afferented animals was sufficient to exert the normal inhibition on aggression and irritability, and since anosmia did not diminish the inhibitory control, the olfactory bulbs are shown to have a non-sensory, limbic function.

**27.1** EFFECTS OF INACTIVITY AND PROGRAMMED STIMULATION ON FELINE SKELETAL MUSCLE FIBERS. Dan A. Riley* (SPON: Margaret Wong-Riley) NIH,Bethesda, Md. 200014.

The role of impulse pattern in determining histochemical characteristics of muscle fibers was investigated in the intertransverse muscles of the cat's tail. Motor neuron activity was eliminated by transecting the spinal cord at $S_{2-3}$ and cutting all dorsal rootlets caudal to this level. In some of these cats, caudal nerves were stimulated for 1 mo in patterns approximating the output of either phasic or tonic motor neurons. Red, white, and intermediate fibers have a specific arrangement within muscle fasciculi, allowing their identification in experimental muscles. As seen in the table, normal differences in the diaphorase and phosphorylase activities of fibers were minimized by the experimental regimens, and each regimen produced a distinctive histochemical picture.

| FIBER TYPE | CONTROL | NO STIM. | TONIC STIM. | PHASIC STIM. |
|---|---|---|---|---|
| red | 1 1 3 W | 1 2 1 W | 1 1 2 W | 1 2 2 W |
| white | 3 3 1 N | 3 1 1 N | 3 2 3 N | 3 3 1 N |
| | | 2 1 1 M | 2 1 3 M | 2 2 2 M |
| intermediate | 3 2 2 M | 3 1 1 M | 3 1 3 M | 3 2 2 M |

Profile sequence (left to right): myofibrillar ATPase activity, phosphorylase activity, diaphorase activity, and fibril pattern (N=narrow, M=medium, W=wide). Highest enzymatic activity is scored 3. Tonic stim.= 10 Hz, in 40 sec bursts every 200 sec and phasic stim.=50 Hz, in 0.8 sec bursts every 200 sec. Both programs were given 6 hr/day for 1 mo.

Since phosphorylase and diaphorase are clearly modulated by impulse pattern, the variations in these enzymatic activities among fibers in control muscles probably reflect adaptation to different modes of use. However, since ATPase activity and fibril pattern remain relatively unaltered, these characteristics may be controlled by some mechanism other than impulse transmission.

**27.2** ACCOMMODATION VERSUS ADAPTATION IN MOTONEURON RHYTHMIC FIRING MECHANISMS. *William H. Calvin.* University of Washington, Departments of Neurological Surgery and of Physiology/Biophysics, Seattle, Washington 98195.

The spike *origination* regions of neurons (initial segment, soma, dendrites) typically differ from the spike *replication* regions (axon, dorsal root ganglion) in that they exhibit little accommodation to linearly rising depolarizations. They will also exhibit repetitive firing to a maintained depolarization much more readily. Cat spinal motoneurons were studied using injected currents. Following a step, the firing rate increases and then declines to a new steady rate. This lengthening of the interspike interval is called *adaptation*. The membrane potential sequence between spikes can be separated into a scoop-like repolarization following a spike and a subsequent ramp-like rise in the membrane potential towards the firing level for the next spike. It has been shown by Schwindt & Calvin (*J. Neurophysiol.*, May 1972) that changes in the interspike interval are primarily accomplished via alterations in the depth of the early scoop, with the subsequent ramp-like section remaining superposeable between different firing rates. The time course of the threshold between the spikes of a rhythmic train has now been examined, using EPSPs to probe for the firing level at various times. The firing level sequence also exhibits a scoop/ramp subdivision: the firing level curves downwards following the refractory period, but then rises linearly, finally intersecting the membrane potential sequence. This increase in threshold (*accommodation*) between spikes is not, however, the cause of the adaptation. The lengthening interspike intervals correlate with the increasing depth of the scoop with sucessive spikes. Another class of spinal neurons has been seen; they do not have the scoop-ramp membrane potential sequence between rhythmic spikes, and their threshold sequence is often flat between spikes following the refractory period. [NIH grant]

**27.3** BEHAVIOR AND HISTOCHEMISTRY OF FUNCTIONALLY ISOLATED ANKLE EXTENSORS IN THE CHRONIC CAT. Mary C. Wetzel, Rebecca L. Gerlach* and Lawrence Z. Stern. Dept. of Psychol., U. of A., Tucson, Az. 85721; Dept. of Physiol. and Division of Neurol., U. of Ariz. Med. Center, Tucson, 85724.

A synthesis of presumed ankle extensor action in posture and locomotion based on known neural, mechanical, and histochemical differences was formulated for cat gastrocnemius and soleus by Henneman and Olson (J. Neurophysiol. 28: 581, 1965) and extended to include plantaris by Goslow, Stauffer, Nemeth and Stuart (J. Morphol., in press, 1972). The latter study initiated a new approach to the problem: observation of plantaris in the chronic cat when all other ankle extensors were denervated. The present study extended behavioral observations to include a variety of tests of sitting, standing, walking, running and jumping in gastrocnemius and soleus as well as plantaris. It also tested for histochemical changes over time. The results showed that: 1) there were steady state performance differences among the three muscles, although all operated cats could run and jump readily, 2) the gastrocnemius cat's performance did not differ appreciably from that of a normal cat, 3) soleus and especially plantaris sustained long term deficits which were most apparent in ankle extension, 4) there were some performance changes over time as well as individual differences among subjects, and 5) isolated mixed muscles showed a greater than normal percentage of Type I fibers after six weeks. Adaptability of the muscles when the demand was altered by surgery was discussed in relation to action and usage. (Supported by USPHS grant NB 07888).

**27.4** BILATERAL EFFECTS OF VIIIth NERVE STIMULATION ON THE LUMBAR CORD. Arnold H. Hassen and Charles D. Barnes. Dept. of Life Sciences, Indiana State University, Terre Haute, IN. 47809.

Experiments were performed on unanesthetized cats, made decerebrate at the precollicular or midpontine-pretrigeminal level. Preliminary surgery was performed under ether anesthesia. The VIIIth nerve was stimulated with a bipolar electrode placed on the intradural portion of the nerve under visual control. Recordings were made from the ascending or descending medial longitudinal fasciculus, inferior colliculus and dorsal root of $L_6$. The test reflex used in all experiments was the lumbar monosynaptic reflex elicited bilaterally either by stimulation of the dorsal roots of $L_7$ and recording from the peripheral nerves or by H reflexes. A single stimulus or train of stimuli 100 msec in length to the VIIIth nerve produced a pattern of facilitation followed by inhibition in both flexor and extensor monosynaptic reflexes bilaterally. Negative dorsal root potentials were also produced when stimulus trains were used. At stimulus strengths which produced evoked potentials in the contralateral inferior colliculus, the lumbar cord pattern was altered but not removed by extirpation of the inferior colliculi. The pattern remains following lesions of the medial longitudinal fasciculus just below the obex, lateral portions of the medulla just below the obex, or the middle third of the brain stem just below the inferior colliculi. Sequences of lesions did alter and finally eliminate the pattern. Cholinergic agents have been found to have an effect on this pattern.

(This study was aided by a grant from the American Medical Association Education and Research Foundation.)

**27.5** ACTIVATION OF THE GAMMA MOTOR SYSTEM IN THE CAT FOLLOWING SELECTIVE STIMULATION OF THE MOTOR CORTEX AND THE PYRAMIDAL TRACT. James Forbes* and Alfred J. Szumski. Dept. Physiol., Med. Coll. Va., Va. Commonwealth Univ., Rich., Va. 23219

The motor cortex of adult cats lightly anesthetized with Nembutal (30 mg/kg) was stimulated with a constant current and through bipolar silver electrodes. The influence on the gamma motor system at varying stimulus parameters was monitored over teased dorsal root Ia filament from the Anterior Tibial muscle. The EMG from the muscle was also simultaneously recorded. These results were compared to results obtained by stimulating the pyramids exposed via a ventral surgical approach. Stimulation of the motor cortex resulted in an increase in the discharge rate of Ia fibers when no EMG activity was recorded. The Ia facilitation lasted throughout the stimulating period. At higher stimulus strengths, an initial EMG response was followed by a period of increased Ia discharge which preceeded a volley of EMG activity. With maintained stimulation, the Ia discharge continued, even when the EMG activity ceased. This pattern of increased dorsal root discharge and EMG activity has not been seen with pyramidal tract stimulation, suggesting an extra-pyramidal component being activated with stimulation of the motor cortex. These early results suggest a wider range and distribution of influence on the gamma system with stimulation of the motor cortex, and a more restricted, synchronous influence with stimulation of the pyramidal tract.

**27.6** EVALUATION OF SPINAL CORD INJURY USING CORTICAL EVOKED RESPONSES. Stephen H. Martin* and James R. Bloedel. Dept. Neurosurg. and Lab. Neurophysiol., Univ. of Minn. Sch. Med., Minneapolis, 55455.

Experiments were performed on cats anesthetized with halothane in order to determine if changes in cortical evoked responses could be used to predict the extent of the neurological deficits following spinal cord injury. The injury was produced by the epidural passage of a small Fogarty catheter several segments above a posterior laminectomy made at L2. The Fogarty balloon was suddenly inflated with water, and the extent of the lesion was varied by using different volumes (0.2cc-0.6cc). The cortical responses to stimulation of the posterior tibial nerve were recorded over the sigmoid gyrus at various times following the lesion and compared with the control response. Results have shown that severe, irreversible neurological deficits occurred only in cats in which there was an immediate post-injury loss of the evoked cortical response with no sustained return over the next 24 hours. At the end of six weeks following injury, these animals were paraplegic and had lost voluntary bowel and bladder function. Pathologically there was severe cystic degeneration in all but the anterolateral columns of their spinal cords. In those animals in which no complete loss of the evoked responses occurred, only minor paretic changes and minor spinal cord atrophy were observed after six weeks following surgery. It is concluded that this technique may be useful in ascertaining the severity and irreversibility of spinal cord lesions produced by trauma. Because this method is technically very simple, it may prove helpful in the clinical management of patients with spinal cord injury. This research was supported by NIH Grant NS09447 and the L.A. French Fund for Neurosurgical Research.

**27.7** RECOVERY OF FUNCTION AFTER PARTIAL DENERVATION OF THE SPINAL CORD: A BEHAVIORAL AND ANATOMICAL STUDY. Michael E. Goldberger and Marion Murray. Dept. Anat., Sch. Med., Univ. Chicago, Chicago, Ill. 60637

Recovery of motor function following CNS lesions has been observed by many workers and, in recent years, collateral sprouting by CNS axons following partial denervation of post-synaptic cells has been demonstrated. The relationship between the two phenomena in the adult CNS, however, remains unclear. A combination of behavioral, electromyographic, axon degeneration and radioautographic methods was used to study functional and anatomical changes following spinal lesions in cats. Following sub-total hemisection (sparing the dorsal funiculus), ipsilateral intrinsic spinal reflexes become hyperactive. After unilateral dorsal rhizotomy, on the other hand, some brainstem-spinal reflexes become extremely hyperactive in the deafferented limb, in particular the scratch reflex from the ipsilateral ear, and the vestibular drop reflex. Crossed reflexes from the intact limb are not exaggerated. Hyperactive supraspinal reflexes are abolished by ipsilateral section of the lateral and ventral funiculi which does not alter the status of the crossed reflexes. Spinal transection provokes a marked hyperactivity of reflex response of the deafferented limb to contralateral pinch (crossed extensor reflex) or joint rotation (Phillipson's reflex) after the first week. Anatomical changes consistent with axonal sprouting were observed, e.g. increased density and area of terminal fields of descending systems on the previously deafferented side in animals exhibiting unilaterally hyperactive brainstem-spinal reflexes. Following partial denervation, the several remaining systems are not equipotential in increasing control over the limb; the selective increased control may be related to selective increase in terminal fields. (Supported by NSF GB 27614 and USPHS NS-09311).

**27.8** RELATIONSHIP OF TWITCH AND METABOLIC PROPERTIES OF MUSCLE FIBERS TO RECRUITMENT PATTERNS IN VARIOUS KINDS OF MOVEMENTS IN ANIMALS. V. Reggie Edgerton and Hank Hewitt*. Neuromuscular Research Lab, UCLA, Los Angeles, 90024

Although the existence of skeletal muscle fiber types has been recognized for some time, information concerning the selective use of different fiber types during normal movements is not understood. EMG activity from chronic electrode implantations and biochemical (homogenates and frozen sections) properties of guinea pigs and the Prosimian, Galago senegalensis have been used to assess the relative activity of fast-twitch oxidative-glycolytic, fast-twitch glycolytic and slow-twitch oxidative muscle fiber while at rest, walking, running at slow and fast speeds, jumping and weight-lifting. Assessment of these three populations of fibers was based on myosin adenosine triphosphatase, reduced nicotinamide adenine dinucleotide diaphorase and α-glycerophosphate dehydrogenase activity. During slow, continuous movements fast-twitch glycolytic fibers are recruited with the least frequency but during forceful movements such as jumping fast-twitch glycolytic fibers are preferentially recruited. Slow-twitch oxidative fibers show much less bursting of EMG activity than either type of fast-twitch fiber. All fiber types appear to be recruited in most movements although there is a clear selective recruitment pattern of muscle fiber types that is predictable by the nature of the movements performed by the animal.

**27.9** DIFFERENTIAL RECRUITMENT PATTERNS OF SOLEUS AND GASTROCNEMIUS MOTOR UNITS. Judith L. Smith* and Nancy L. Herndon* (SPON: V. R. Edgerton). Neuromuscular Research Lab, UCLA, Los Angeles, 90024.

Biopsied and autopsied tissue from human gastrocnemius and soleus muscles assayed for myosin adenosine triphosphatase activity, glycolytic and oxidative capacities revealed a higher percentage of slow twitch oxidative fibers in soleus. Electromyograms (EMG) recorded with implanted fine-wire electrodes demonstrated motor units of gastrocnemius were recruited rapidly creating EMG bursts during walking, running and jumping, while soleus units were recruited slowly and seldom exhibited bursts. During slower movements and a sustained positions of toe raises and squats, soleus units displayed a constant level of activity, while gastrocnemius units were active phasically and fatigued at a faster rate. Recruitment patterns were not appreciably different during stretching exercises requiring extreme and rapid dorsiflexion of the ankle joint; however, soleus units were recruited more frequently during eccentric (lengthening) contraction. It is evident that the CNS selectively recruits muscle fibers of different metabolic profiles depending on the movement demands.

**27.10** THE FREQUENCY RESPONSE OF EXTRAOCULAR MOTONEURONS TO INTRACELLULAR STIMULATION. N. H. Barmack, Laboratory of Neurophysiology, Good Samaritan Hospital & Medical Center, Portland, Oregon 97210

Saccadic eye movements are preceded by a stereotyped neural command from the participating extraocular motoneurons. Depending on the size of the saccade, motoneurons which innervate the agonist muscle transiently increase their rate of discharge to 200-800 spikes/sec for periods of 10-50 msec. This burst is proportional to saccadic velocity and is followed by a maintained increment in steady state discharge which is proportional to commanded eye position. This "pulse-step" increment in frequency causes a "pulse-step" increment in force which overcomes the viscous drag of the orbit and produces the "step" change in eye position.

We have attempted to decipher the pre-motoneuronal command signal by recording intracellularly the activity of antidromically identified abducens motoneurons in anesthetized cats in response to intracellular stimulation. By applying depolarizing current steps of varying magnitude (0.5-10.0 nA), and duration (50-400 msec), discharges are evoked in abducens motoneurons which are similar to those seen during saccadic eye movements. A step increase in depolarizing current evokes a "pulse-step" increase in the frequency of cell discharge. Conversely, a step decrease in depolarizing current transiently silences cell discharge.

There is qualitative agreement between the behavior of extraocular motoneurons evoked under the present experimental conditions, and the behavior of extraocular motoneurons in unanesthetized animals; suggesting that the pre-motoneuronal command signal need convey information only concerned with eye position. Given this command, the adaptive properties of the motoneuron membrane could account for the "pulse-step" frequency response of motoneurons and for the linear relationship between saccadic amplitude and velocity. (Supported by NIH Grant EY00848)

**28.1** CONTROL OF GLYCOGEN METABOLISM IN BRAIN. J. V. Passonneau*, H. Watanabe*, and D. A. Rottenberg*. (SPON: I. Klatzo). NIH, Bethesda, Md. 20014.

The incorporation of $^{14}C$-glucose into cerebral glycogen of mice has been studied in normal animals and animals given anesthesia or hydrocortisone. The activities of glycogen synthetase and glycogen phosphorylase have been examined in the same animals. $^{14}C$-glucose (10μCi) was given intravenously and the animals sacrificed at intervals thereafter. One-half of the brain was used to measure enzyme activities; the other half was used to measure the amount of glycogen and radioactivity. The peak of radioactivity occurred 1 hr after glucose administration in all cases, in total glycogen as well as in limit dextrin. The half-time for disappearance of the label from glycogen was 2.9 hr and 3.6 hr for limit dextrin. Phenobarbital (125 mg/kg) increased the half-times to 4.1 and 8.3 hr for total glycogen and limit dextrin respectively. The concentration of glycogen in the brain was increased 2.5-fold. Glycogen synthetase activity was not altered by anesthesia, nor was the ratio of I (independent of glucose-6-P) and D (dependent on glucose-6-P) forms. Glycogen phosphorylase total activity was not affected, but the ratio of the a form to total activity was diminished, which accounts in part for glycogen accumulation. The administration of hydrocortisone (25 mg/kg i.p.) resulted in 164% greater incorporation of label into glycogen over control values. The half-time for disappearance of label for total glycogen was decreased to 2.0 hr, while that for limit dextrin remained near control values, 3.3 hr. Glycogen synthetase and phosphorylase activities and the ratios of the various forms showed no change. The increased rate of glycogen synthesis in the hydrocortisone treated animals was attributed to the increased concentration of cerebral glucose-6-P which stimulates synthetase activity. The control of cerebral glycogen levels is clearly due to a complex interaction of two enzymes, each of which exists in 2 forms with different activities and modifiers.

**28.2** ISOLATION AND PROPERTIES OF AN INHIBITOR OF TETRAZOLIUM REDUCTASE FROM MAMMALIAN BRAIN AND RELATED PROTEINS. Rainer Fried* (spon: D. Weidler) Dept. Biochem. Creighton Univ. Med. Sch., Omaha, Nebr. 68131

A protein (TRI) has been isolated from beef brain by acid precipitation, fractionation by ammonium sulfate and chloroform, and heat treatment, which inhibits enzymic reduction of tetrazolium, using cream xanthine oxidase and xanthine as assay system. This reductase inhibitor is similar to another enzyme obtained from mammalian liver (1). The activity is not shown by untreated brain homogenate, and cannot be released by preincubation with butanol or snake venom (CMV, Cottonmouth Moccasin Venom). The activity of cream xanthine oxidase is enhanced by incubation withbrain homogenate pretreated with CMV, but not by either component alone. Pre-incubation of TRI with CMV increased the reductase inhibition. Low levels of xanthine dehydrogenase activity were found in different brain fractions and were released by CMV treatment. TRI may be related to cerebrocuprein and to superoxide dismutase (2-4). The intracellular distribution and regional distribution in brain of this enzyme will be discussed.

1) FRIED R, FRIED LW, BABIN D, Eur J Biochem 16: 399, 1970
FRIED R, Am Chem Soc, 162nd meeting, Washington DC, Sept. 1971, #100
2) PORTER H, FOLCH J, J Neurochem 1: 260, 1957
3) CARRICO RJ, DEUTSCH HF, J biol chem 244: 6087, 1969
4) MCCORD JM, FRIDOVICH I, J biol chem 244: 6049, 1969

**28.3** THE RELATIONSHIP OF FOLATE METABOLISM AND THE ANTICONVULSANT EFFICACY OF PHENOBARBITAL. Dennis B. Smith* and Lorraine C. Racusen* (SPON: G. A. Schumacher). Dept. of Neuro., UVM Col. of Med. Burlington, 05401

Low serum and CSF folate levels have consistently been found in patients treated with anticonvulsant drugs. In addition to the known hematologic complications of folate deficiency, folate deficiency has been implicated in the development of mental deterioration in some epileptics. However, there have been scattered reports of exacerbation of seizures in epileptics who have received therapeutic administration of folate to correct these presumed complications of folate deficiency. The purpose of this study was to examine the effects of long-term phenobarbital (Ø) administration on plasma folate levels in rats, and to study the relationship between plasma folate levels and the anticonvulsant efficacy of Ø in these animals. The relationship of chronic Ø administration and vit B-12 metabolism was also studied because of the known interaction between folate and vit B-12.

Chronic administration of Ø was associated with relative reduction of plasma folate levels. Vit B-12 levels were unaffected. Seizure threshold (ST) was determined by measuring the time in secs from the onset of infusion of the volatile convulsant hexafluordiethyl ether to the first appearance of a myoclonic jerk (MJ), then to the beginning of a full tonic-clonic (TC) seizure. Under these experimental conditions low plasma folate levels were associated with an enhanced anticonvulsant effectiveness of Ø when ST was measured to the beginning of a TC seizure. Dietary supplementation with folate reduced the effectiveness of Ø in raising this measure of the ST. The degree of elevation of the MJ threshold produced by Ø was not affected by plasma levels of folate. Plasma vit B-12 levels did not affect the ST elevation produced by Ø. The importance of the method used in the determination of ST is emphasized. It is postulated that a block in the folate reductase system in brain may be responsible for the effects observed.

**28.4** INTRACELLULAR ELECTRICAL EVENTS AND NICOTINAMIDE ADENINE DINUCLEOTIDE LEVELS OF DORSAL ROOT GANGLION NEURONS. C. Rodriguez-Estrada* (SPON: G. P. Cooper). Catedra de Fisiologia, I.M.E. Facultad de Medicina, Univ. Central de Venezuela, Caracas, Venezuela.

Previous reports have shown that short-term nerve stimulation of dorsal root ganglia produces a change in the level of reduced Nicotinamide Adenine Dinucleotide (NADH) on the surface of this tissue. In this study fluorometric determinations were made of the level of NADH following several short periods of peripheral nerve stimulation of a 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 every 50 sec were used (square pulses, 0.1 msec duration, 20/sec, twice threshold). Recordings of intracellular action potentials were made with 3M KCl glass micropipettes. The first stimulation period produced a decrease of NADH (oxidation) followed by an increase of NADH content (reduction). The second and subsequent periods of stimulation always produce a decrease of NADH level. But the increase of NADH level progressively diminished until further stimulation had no effect. The results suggest that depolarization of a neuron soma starts a metabolic change in which two events can be separated, one, an increase of metabolic activity from the hydrogen carrier towards the oxygen and, second, an increase of activity from the substrate towards the hydrogen carrier.

**28.5** DISORDERED MITOCHONDRIAL RESPIRATION IN A HUMAN NEURO-DEGENERATIVE DISORDER. J.H. French, D. Holtzman*, & C.L. Moore*. Montefiore Hospital.

Ultrastructural abnormalities of mitochondria (Ghatak, N.R. et al: Arch. Neurol. 26: 60-72, 1972) and deficient mitochondrial cytochrome oxidase (French, J.H. et al: Arch.Neurol. 26: 229-44, 1972) are reported in Trichopoliodystrophy (TPD), a sex-linked recessive neurodegenerative disease (Menkes, J.J. et al: Pediatrics 29: 764-79, 1962). Four additional observations of isolated muscle mitochondria in three patients confirm the cytochrome oxidase deficiency in TPD. Observations on muscle mitochondria in an additional patient with TPD confirms the absence of coupled oxidative phosphorylation with NAD-linked substrates and succinate (French, J.H. & Moore, C.L.: Prog. & Abs. A.N.A., June, 1972). Continued observation of two patients treated with methylene blue, a terminal electron acceptor, documents normal head growth and suggests the efficacy of this agent in preventing the usual microcephaly. Tissue copper in cortical gray matter and blood is deficient in TPD even though dietary intake is normal. This finding is consistent with the cytochrome oxidase deficiency.

**28.6** THE ACTIVITY OF MONOAMINE OXIDASE IN PURIFIED BRAIN MITOCHONDRIA. F. M. Achee*, G. Togulga* and S. Gabay* (SPON: J. Harris). Biochem. Res. Lab., VA Hospital, Brockton, Ma. 02401

Monoamine oxidase (MAO) is known to be tightly bound to the outer membrane of the mitochondrion. As such, it may be inferred that attachment of the protein to the membrane is of some significance and it seemed desirable to study the enzyme in a state which would be more reflective of its activity in its physiological environment. Some properties of MAO in intact mitochondria of brain tissue have been investigated with regard to understanding the biochemical determinants in affective disorders and the possible targets of MAO. Highly purified brain mitochondria have been prepared using a procedure described by Basford (Meth. Enz. 10, 96, 1967) and the purity of such preparations assessed by the use of enzyme markers and by electron microscopy. By studying the influence of such parameters as pH, $O_2$ tension, ions and ionic strength, it appears that a differentiation may be made among the various substrates of MAO. Kynuramine, a non-physiologic substrate, has a higher pH optimum (9.1) than the biogenic amines as serotonin and tryptamine (8.4) which are indolyl-derivatives, or tyramine and dopamine (7.5), the phenyl-derived amines. This same order of pH-sensitivity is observed in the sensitivity to monovalent ions, particularly $Cl^-$. A reverse order is noted when the $O_2$ tension of the assay mixture is increased to 100%. All substrates have diminished activity with increasing ionic strength. These subtle differences would seem to have some bearing on the prevalent question of multiple enzymes vs a single enzyme for amine oxidation.
(Supported by VA Research Program: 01/3012.1/69-05).

**28.7** REGIONAL VARIATIONS IN BRAIN TISSUE GAS TENSIONS. Barry Burns. Dept. of Environmental Medicine, Johns Hopkins Univ., Baltimore, Maryland 21205.

Partial pressures of $O_2$ and $CO_2$ were measured simultaneously with a 300 u-diameter, membrane tipped probe connected to a mass spectrometer. The sampling probe was part of the inlet system of the mass spectrometer which operates at a high vacuum ($< 10^{-4}$ Torr). Gas diffuses from the tissue through the polypropylene membrane at the probe tip (Area = 900 microns$^2$) in amounts proportional to the partial pressure at the membrane-tissue interface. Calibration gases were saturated and temperature equilibrated. Cats, rats and monkeys (M. mulatta, S. sciureus) were anesthetized with pentobarbital sodium and the probe inserted through a 3 mm-dia. craniotomy hole following stereotaxic coordinates. Gross histology verified probe position. In all animals $PCO_2$ was highest in thalamus; lower in cortex and sub-cortical white matter. $PO_2$ was highest in cortex and lower in thalamus and sub-cortical white matter, respectively. Gas tensions in the caudate nucleus were similar to those observed in thalamic regions. In all instances tissue $CO_2$ tensions were higher than either CSF or cerebral venous blood $PCO_2$. Tissue $O_2$ tensions were lower than those in CSF or cerebral venous blood. Areas with high blood flow and metabolic rates generally had a higher $PO_2$ or $PCO_2$ than areas with lower blood flow or metabolic rates. In the normocapnic animals, the brain tissue $PCO_2$ varied from 65-125 mm Hg while $PO_2$ varied from 6-40 mm Hg. These findings suggest that the $CO_2$ tension of the neuronal environment is higher than previously suspected and that a reversible $CO_2$ gradient between tissue and cerebral venous blood may play a role in regulation of extracellular pH.

**28.8** METABOLIC AND ELECTROENCEPHALOGRAPHIC EFFECTS OF ACUTE ISCHEMIA IN GERBIL BRAIN. D. C. Howse* and T. E. Duffy* (SPON: F. Plum). Dept. of Neurology, Cornell Univ. Med. Col., New York, N.Y. 10021.

Measurement of changes in cerebral energy reserves following decapitation has been used to estimate in vivo cerebral metabolic rates (Lowry et al., JBC 239: 18, 1964). The relation between EEG activity and concentrations of brain ATP, P-creatine and lactate were studied in the quick-frozen brains of 25-30 gm gerbils following acute cerebral ischemia induced by decapitation or bilateral interruption of carotid blood flow, a procedure which in this species invariably renders the fore-brain ischemic (Levine & Payan, Exp. Neurol. 16: 255, 1966). Both treatments produced identical decreases of P-creatine (-30%) as compared with intact controls (brain frozen without decapitation). Therefore, forebrain stimulation secondary to decapitation (Maker & Lehrer, 1971) appears not to play a role. Calculated energy use rates [$\Delta$P=2 $\Delta$ATP + $\Delta$ P-creatine + $\Delta$ lactate] varied depending upon whether a) intact (19.3 mM/kg/min), b) decapitated (14.5) or c) carotid severed (12.9) animals were taken as zero time. The lower rates in the latter two groups reflect the lower energy state in the acutely ischemic brain. EEG records after decapitation or carotid interruption showed loss of recognizable cerebral activity within 8 sec in controls and after 3-13 sec in animals with seizures (150 mg/kg Metrazol I.P.). Thus, acute ischemia induces rapid changes in neural function in both the normal and pathologic (seizure) state, and would appear to render energy use data obtained at this time an unreliable index of the in vivo situation.

(Supported in part by the McLaughlin Foundation and USPHS, NIH Grant NS 0-2498-07).

**28.9** POSTISCHEMIC METABOLIC ACTIVITY OF NEURONS AND GLIA. D. H. Hinzen* and U.Müller* (SPON: Alfred Pope ). Institute of Normal and Pathological Physiology, University of Cologne, Germany.

Isolated dog heads were subjected to complete cerebral ischemia of 30 or 60 min.Following ischemia the isolated heads were reperfused with blood from a donor dog for 1,3 or 8 hrs.Intact neuronal and glial cells were separated in bulk from the temporal cortex of controls and at the end of each recovery period.The separation procedure depended on gentle tissue disruption by sieving through different layers of small pore size meshes and discontinuous density-gradient centrifugation.Identification and purity of the cell fractions were determined both by light and electron microscopy and by enzyme activities.The cells were incubated in Krebs-Henseleit medium with 0.01 M glucose.Uptake of oxygen was measured.Initial $O_2$-consumption showed nearly similar results in neurons and glia.Respiration was about 75% of that of cerebral cortex slices.After 8 hrs recovery consequent to 30 min ischemia respiratory rate both of neurons and glia was found at a constant level which did not differ from the initial values.Following 60 min ischemia there was an impairment in neurons and glia with respect to respiration. After 8 hrs recovery $O_2$-uptake in neurons was 71% and in glia 87% of that of controls.The results indicate high metabolic activity of neuroglia.Complete ischemia up to 30 min is apparently survived by neurons and glia without damage to cell respiration.After 60 min ischemia metabolic recovery is incomplete and a greater damage to neurons than to glia becomes apparent.

**28.10** EFFECT OF X-IRRADIATION AND VITAMIN A ALCOHOL ON FOUR LYSOSOMAL ENZYMES IN NORMAL RAT BRAIN AND EXPERIMENTAL BRAIN TUMORS: AN IN VIVO STUDY. Nancy R. Clendenon, Hiroshi Abe*, Norman Allen and Wanda Gordon*. College of Medicine, Ohio State University, Columbus, Ohio 43210.

Neuroectodermal tumors were induced in rats by intravenous and transplacental administration of methyl- and ethyl-nitrosourea. Control and tumor bearing animals were given vitamin A alcohol (ip) in a dose of 100 mg/kg for 3 days; another series received X-ray (1500-3000 rads); and a third received combined vitamin A and X-ray treatments. Total, free and soluble activities were determined for N-acetyl-β-D-glucosaminidase (GAD), β-glucuronidase (β-Glu), acid phosphatase (AcP), and arylsulfatase (AS) in 2-5% (w/v) brain or tumor suspensions, 24-72 hrs following treatment. In control brain, X-ray, vitamin A, and the combination resulted in a 20% decrease in total activity for GAD and AS. Vitamin A alone caused a 20% decrease in total β-Glu and a 12% decline in total AcP activities. Increases in free activities were found only for β-Glu after vitamin A or combined vitamin A and X-ray, and were relatively small (from 27% to 42%). No effect on soluble enzyme activity was detected. Among the gliomas, a marked decline in total activity over non-treated tumor values was found for β-Glu (55%) and AcP (75%) after X-ray or combined treatment, while vitamin A alone caused similar but smaller decreases. Free activities were increased for all four enzymes after X-ray or combined treatment, the greatest being with β-Glu (from 54% to 86% after the combined treatment). The neurinomas displayed similar effects on free β-Glu, GAD and AS activities. Soluble activities of gliomas and neurinomas were not altered by these in vivo labilization studies. Total activities of neurinomas were markedly elevated in GAD and β-Glu and moderately increased in AcP activities after vitamin A or combined treatments, while X-ray alone raised AS total activity 57%. A difference in labilizing response has been shown between control brain and neuroectodermal tumors.

**28.11** ORIGIN OF CEREBRAL TEMPERATURE CHANGES EVOKED BY SENSORY STIMULATION.
M.A. Baker, F. Mc.Frye* and V.E. Millet*. Dept. of Physiology, School of Medicine, University of Southern California, Los Angeles, Calif. 90033.

It is known that the large (1-2C) temperature changes which occur throughout the brain in behaving animals are produced by temp. changes in cerebral arterial blood (Hayward & Baker, Am.J.Physiol.1968; Baker & Hayward, Science,1967; Baker, J.Physiol.(Lond.)1972. Small cerebral temp. changes (0.001-0.01C) evoked by sensory stimulation were attributed to altered neuronal heat production or local blood flow (Melzack & Casey, Exptl. Neurol.,1967; McElligott & Melzack, ibid.). The present study demonstrates that small thermal changes which occur in the brain following visual, auditory or somatic stimuli are produced by blood temp. changes. In cats and monkeys, thermocouples were chronically implanted in lateral geniculate, inferior colliculus, ventrobasal thalamus and at the circle of Willis outside the brain at the middle cerebral or posterior cerebral artery. Experiments were conducted in animals awake or under pentobarbital anaesthesia. (Pentobarbital causes pronounced peripheral vasodilatation and a 2-2.5C drop in blood and brain temps., and abolishes the large spontaneous temp. shifts which occur in normal animals). Cerebral arterial blood temp. was monitored simultaneously with brain temp. Light flashes, sounds and somatic stimuli all elicit thermal responses in cerebral arterial blood in awake and lightly-anaesthetized animals; responses are rare in deeply-anaesthetized animals. When the blood temp. change is great enough, a subsequent change in brain temp. occurs. Changes in brain temp. never occur without a previous change in blood temp. The most common thermal response to sensory stimulation was a rise in blood temp.(0.008-0.133C) followed by a brain temp. rise (0.004-0.06C). Peripheral vasoconstriction often preceded the blood temp. rise, suggesting that the initial thermal response to sensory stimulation is peripheral autonomic activity.
(Supported in part by NIH Grant NS 09599-02)

**29.1** EFFECT OF TEMPERATURE ON PATTERN FIRING IN LIMULUS OPTIC NERVE.
G. David Lange and John F. McCleary*. Dept. Neurosciences, Sch. Med. and Dept. Biol., UCSD, La Jolla, California 92037

There is a very large literature on the repetitive firing of the eccentric cells in the lateral eye of Limulus. This has included statistical analyses of nonuniform firing (Ratliff, Hartline, Lange PNAS 60:464-469, 1968; Shapley, Nature 221:437-440, 1969). These statistical treatments did not deal with patterned firing per se. We have found that by raising the temperature of the sea water bath surrounding an excised Limulus eye to 20°C or above we can cause a single eccentric cell to fire in pairs, triplets or higher order multiplets. [These results are contrary to those found by Biederman (Thesis UCLA, 1965) in crayfish caudal photoreceptor]. The presence and duration of the bursts are a function of light intensity and light adaptation as well as temperature. They cannot be predicted from mean firing frequency and temperature alone. This rules out models which explain bursting by properties of the spike generating system alone; it necessitates consideration of a role by the phototransducing system as well. These findings are consistent with the sources of noise discussed in the references above. The implications of this work are threefold: 1) A mechanism (whether actually used or not) for coding temperature information in nerve spike pattern is apparent. 2) Variation of temperature may be an important tool for study of other burst generating systems. 3) The Limulus eye gets more complicated every day.

This investigation supported by grants from the Academic Senate UCSD and PHS (NS09342).

**29.2** TEMPERATURE COEFICIENT FOR SPONTANEOUS AND LIGHT INDUCED DISCRETE WAVES IN THE LIMULUS PHOTORECEPTOR. Richard Srebro and Mahmood Behbehani,* State Univ. of N. Y. Buffalo, N. Y. 14214.

Discrete depolarizations of the photoreceptor cell membrane (discrete waves) occur spontaneously and in response to illumination. Each light induced discrete wave is the response to a single photon absorption. The duration of a discrete wave is from approximately 100 msecs (at 25°C) to 400 msecs (at 5°C). They also vary in amplitude (at a fixed temperature). Temporal overlap and amplitude variation make it difficult to count discrete waves by simple visual inspection. We have developed a new method of counting discrete waves based on the theory of paralyzable counters (type II particle counters) which avoids errors due to temporal overlap and amplitude variation and have applied the method to study the temperature coeficient for discrete waves. The frequency of spontaneous discrete waves follows Arrhenius kinetics over the range 0°C to 25°C with an activation energy of 49 kcal. The $Q_{10}$ in the range 10°C to 20°C is 19. Light induced discrete waves have no significant temperature coeficient in the temperature range 0°C to 25°C. The extraordinarily high activation energy of spontaneous discrete waves is comparable to the mole quantum energy of a photon at the wavelength of maximal sensitivity (520 nm), approximately 55 kcal. This suggests that spontaneous discrete waves are due to the thermal bleaching of visual pigment.

**29.3** LIGHT ADAPATION OF DISCRETE WAVES IN THE LIMULUS. Mahmood Behbehani* and Richard Srebro, Neurosensory Laboratory S. U. N. Y. Buffalo, New York 14214.

The photoreceptor of the Limulus lateral eye responds to a low energy flash of light with a variable depolarization made up of one or more discrete waves (discrete depolarization). Each light induced discrete wave is caused by the absorption of a single photon. We studied the affect of light adaptation on the response to a low energy flash of light in the following experiment. First, a 20 msec light flash (test flash) was choosen with sufficient energy, $E_t$, to produce (on the average) on discrete wave per trial. A second flash of light with energy, $E_a$, was used as an adapting flash. A sequence of several hundred flashes consisting of an adapting flash followed after 5 seconds by a test flash (or occasionally by no light) constituted a run. The ratio of $E_a/E_t$ was changed from 0 to 125 in separate runs. The value of $E_t$ was kept constant throughout an experiment which consisted of 9 runs. Our results indicated that the light adaptation had the following affects on the properties of discrete waves. 1) The size of discrete waves decreased. The reduction in size was very sensitive to light adaptation. For example an adapting flash that delivered only 10 photons to the cell significantly decreased the sizes of the discrete waves. 2) The quantum efficiency, defined as the probability that a photon incident at the cornea produces a discrete wave, decreased. 3) There was no significant affect of light adaptation on the average latency to the first discrete wave. 4) The frequency of spontaneous discrete waves was also decreased.

**29.4** RETINAL SENSITIVITY IN THE MUDPUPPY (NECTURUS MACULOSUS). Luis M. Proenza. Vision Research Laboratory, Dept. of Psychol., Univ. of Ga., Athens, Ga. 30601

Although the mudpuppy (Necturus maculosus) has recently facilitated intracellular electrophysiological investigations of all major types of retinal neurons, little is yet known about vision in this light-shunning, neotenic amphibian. To study some aspects of visual sensitivity in the mudpuppy, we have used the Proximal Negative Response (PNR)--a localized and tractable extracellular potential recorded with microelectrodes from the proximal retina and thought to be primarily related to the activity of amacrine cells. An integrated series of experiments measured spatial and temporal summation, spectral sensitivity, and absolute sensitivity by determining stimulus intensities necessary to produce equal amplitudes or latencies of the PNR. The results of this work indicate that clear parallels exist between the mudpuppy and other vertebrate species. Thus, Ricco's and Bloch's Laws respectively describe the rise in sensitivity for stimulus diameters up to 250 μm and for stimulus durations up to 500 msec; Spectral sensitivity functions of the dark- and light-adapted retina correspond closely to the absorption spectra of the rod and cone pigments respectively; And in the well dark-adapted retina, the PNR is reliably detected when on the average less than one quantum is absorbed per rod.

**29.5** IONIC BASIS OF HYPERPOLARIZING RECEPTOR POTENTIAL IN AN INVERTEBRATE PHOTORECEPTOR. John S. McReynolds and Anthony L.F. Gorman, N.I.H., Bethesda, Md. 20014.

Not only vertebrate rods and cones, but also some types of invertebrate photoreceptors respond to light with a hyperpolarizing receptor potential. Although the vertebrate photoreceptor response, like other receptor potentials, appears to be due mainly to a change in $Na^+$ conductance, nothing is known about the ions involved in the hyperpolarizing responses of these invertebrate photoreceptors. We have previously shown that the hyperpolarizing receptor potential of the distal photoreceptor cells of the mollusc Pecten irradians is associated with an increase in membrane conductance, with a reversal potential near -80 mV. We have now developed a technique for changing the ionic composition of the fluid surrounding these small cells during continuous intracellular recording of the changes in membrane potential and response to light. Complete replacement of extracellular $Cl^-$ ions with impermeant anions had negligible effect on either the resting potential or the response to light. However, the potential reached by the response to light varied inversely with log external $K^+$ concentration over a wide range. The resting, or dark, potential also varied inversely with log external $K^+$ concentration, but the slope of this relationship was much less steep. Replacement of external $Na^+$ with impermeant cations resulted in hyperpolarization of the resting potential, thereby reducing the size of the response to light. Our tentative interpretation is that the membrane potential is kept at a low value in the dark by a relatively high sodium conductance, while the receptor potential is due primarily to an increase in conductance to potassium ions.

**29.6** CIRCADIAN RHYTHM IN APLYSIA OPTIC NERVE ACTIVITY: EFFECT OF CALCIUM AND CHLORIDE SUBSTITUTION. Jon W. Jacklet. Dept. Biol. Sci., SUNYA, 12222

Continuous recording from the whole optic nerve with tubing electrodes for up to 10 days from the isolated eye-optic nerve in culture medium at 15°C in darkness shows that the compound action potentials exhibit a circadian rhythm with a period of 26-27 hours. This preparation also will run for 2-3 days in artificial sea water under the same conditions but the period is shorter, 22-24 hours. If the calcium, 10 mM, in the artificial sea water is removed the circadian rhythm is still expressed and has a period of 24 hours. If the calcium in the culture medium is reduced to 2.6 mM, the rhythm is likewise expressed and the period is slightly longer. Substituting 15% of the chloride in the culture medium with acetate or proprionate but not nitrate abolishes the circadian rhythm although the preparation remains active at a substantial level for up to 10 days. Substituting 50% of the chloride with acetate abolishes the rhythm but the preparation only remains active about 36 hours. Substituting all the chloride abolishes the compound action potentials in the optic nerve. Since low calcium does not abolish the circadian rhythm, the oscillators do not drive the optic nerve potentials via a chemical synapse. Since very low chloride abolishes the compound action potentials by desynchronization, they are thought to be dependent on electrotonic coupling in the population. Substitution of 15% of the chloride partially disrupts coupling in the population and leads to abolition of the circadian rhythm. (Supported by NINDS 08443.)

**29.7** FOURIER ANALYSIS OF THE CAT'S ELECTRORETINOGRAMS. R. Frank Quick*, Wlodzimierz M. Kozak and Thomas W. Calvert*. Biotechnology Program, Carnegie-Mellon Univ., Pittsburgh, Pa. 15213

Oscillatory components of the electroretinograms (ERG's) elicited by the onset or the cessation of light were analyzed in Urethan-anaesthetized cats using Fourier transforms. ERG's were recorded with corneal electrodes, AC preamplifiers, band-pass filters and a 9-bit input digitizer. The flashes were applied at 0.1-1 Hz and each ERG was digitized at 0.4-1.0 msec intervals and repeated 8-128 times for averaging in time domain. The time series thus obtained was windowed to avoid a step function at the end of the data file and thus prevent any spurious spectral peaks. These data were run on an IBM 360 computer for a cepstral analysis and autocorrelation, in order to determine the fundamental oscillatory harmonics (modes of oscillation) in the ERG's. It was found that at least two non-harmonically related modes of oscillation were always present, the one in the 25-50 Hz band and the other in the 80-120 Hz band. The first one corresponds to the retinal resonance frequency band as revealed by flickering light. The second one corresponds to the ERG wavelets, or oscillatory potentials, which are superimposed on the b-wave. Possible mechanisms for the oscillatory processes in the retinal nerve network are discussed, as well as their relationship to the oscillatory visually evoked potentials in the brain.

**29.8** VISUAL FUNCTION IN RATS WITHOUT PHOTORECEPTORS. W. Keith O'Steen and Kenneth V. Anderson. Dept. Anat., Emory Univ., Atlanta, GA 30322.

When albino rats are exposed to continuous, low intensity (18 ft-c) fluorescent or incandescent light, the photoreceptors completely degenerate after 30 days of exposure. Ganglion cells and bipolar neurons are unaffected. Electron microscopic studies of retinas exposed for prolonged periods (4-6 months) indicate that only the photoreceptors are destroyed and that the other neurons and pigment epithelium are intact. Photically evoked potentials recorded from the optic tract, lateral geniculate nucleus, and visual cortex are of reduced amplitude and have longer latencies of onset after only 4 days of exposure, and although some responses occasionally are recorded after 30 days of exposure, they are typically absent. ERGs decreased in amplitude during the first 4 days of exposure; A waves were reduced after 24 hours and absent after 48 hours of exposure. B waves were absent after 4 days of exposure. ERG recovery occurred if rats exposed to light for less than 4 days were returned to darkness. Spontaneous, rhythmic potentials were recorded from the visual system of normal, albino rats anesthetized with barbiturates, but they were not found in enucleated rats or in rats after severe photoreceptor damage, indicating that these potentials originate within the retina. Female rats with complete photoreceptor destruction developed a persistent estrous syndrome during continuous light exposure, but these animals responded to cyclic photoperiods by reestablishing cyclic estrus, mating, and bearing young. Rats without receptor cells performed at high levels on visual discrimination tests involving both black-white and pattern tasks and had the ability to learn the tests prior to and after photoreceptor destruction. These results indicate that rats without "classical" photoreceptors retain the ability to respond to visual stimuli.

**29.9** VISUAL DISCRIMINATION PERFORMANCE IN RATS WITHOUT PHOTORECEPTORS OR PIGMENT EPITHELIAL CELLS. Kenneth V. Anderson and W. Keith O'Steen. Dept. Anat., Emory Univ., Atlanta, Ga., 30322.

The discrimination performance of albino rats whose retinas lacked receptor cells or receptor cells and pigment epithelial cells was compared with the performance of normal, control rats. Retinal degeneration was produced by exposing animals to constant, fluorescent light for varying periods of time up to 30 days. Both control rats and those with retinal degeneration were trained and tested in a T-maze on a black-white discrimination and two pattern discriminations. One of the pattern tasks was designed to test discrimination performance near the rat's limit of visual acuity. Each animal received 20 trials a day and was trained until it reached a criterion of 90% correct responding per day for three consecutive days. Olfactory, taste, auditory, and thermal cues were rigorously controlled. The general finding was that rats without receptor cells and pigment epithelial cells were not impaired on any of the discrimination tests used in this experiment, but could readily perform at high levels on both black-white and pattern tasks. They could not only retain a visual habit learned prior to the degeneration, but could learn new discriminations at rates indistinguishable from control animals. These results strongly suggest that reginal elements other than the classical receptor cells are sensitive to light and that the pigment epithelial cells do not play a role in the mediation of visually guided behavior in animals without receptor cells.

**30.1** ELECTROPHYSIOLOGICAL CORRELATES OF PATTERN PREFERENCES IN HUMAN INFANTS. Bernard Z. Karmel*, Robert F. Hoffmann* and Martin J. Fegy*. (SPON: S. C. Maxson). Dept. Psychol., Univ. of Connecticut, Storrs, Conn. 06268.

Visual preferences in human infants are constrained by properties related to contour density information contained in the visual stimulus. This report evidences such contour processing mechanisms in infants by contrasting behaviorally derived preference functions (using the total time spent looking at a pattern) with contour-dependent visually evoked potential (VEP) functions elicited by patterns used in preference studies. Analysis of P(≃130)-N(≃200) differences or of the P(≃130) amplitude alone elicited by flashes viewed through pattern transparencies indicated an inverted U-shaped function of amplitude differences peaking at a 1° check size in 9 and 12 week-old Ss. Sine light modulation (4.5 cps; 100% depth) through both redundant (checkerboard) and random matrix grain stimuli revealed that preferred patterns show the greatest amplitude differences between P(≃180° out of phase) and P(≃360° out of phase). Shifts toward smaller check sizes in the maximum P-P differences reflected increasing age and dark adaptation. Sine light modulation proved superior to flashes 1. in maintaining behavioral attention by S to the task, 2. in producing individual psychophysical functions, and 3. in objective scoring of meaningful brain information in infants. Finally, use of patterned light as a stimulus for developmental studies is suggested if active, awake and attending states are desired. The importance of the superior colliculus (SC) for these developing visual responses is implicated if contour dependent receptive field characteristics can be shown to correlate with responses measured. Cells in SC dominate eye movements and behavioral orientation. Further, these cells contain receptive fields which depend on size and not on shape information.

**30.2** *AVERAGED EVOKED POTENTIAL CORRELATES OF INFORMATION PROCESSING IN SCHIZO*PHRENICS, PSYCHOTIC DEPRESSIVES AND NORMALS. Robert A. Levit*, Samuel Sutton and Joseph Zubin. Biometrics Research, New York State Dept. of Ment. Hyg., New York, N.Y., 10032

Visual and auditory evoked potentials were recorded from scalp under conditions of stimulus uncertainty, stimulus modality shift and right and wrong pretrial guesses. Schizophrenic patients, psychotic depressive patients and normal controls were matched for age, sex, race and socio-economic background. In addition, the two patient groups were matched for type of medication (chlorpromazine), daily medication dosage and total medication intake since hospitalization. Under all conditions normals exhibited the largest $N_1$-$P_3$ evoked potential amplitudes while depressives exhibited the next largest and schizophrenics the smallest. All three groups had larger $N_1$-$P_3$ amplitudes in the uncertain condition than in the certain condition. However, the effect of uncertainty was greatest in the normal group and least in the schizophrenic group. The three groups also differed significantly on the degree to which they were affected by modality shift (for normals, $N_1$-$P_3$ is larger when the stimulus in the previous trial was in a different modality), and in the degree to which they were affected by the correctness of the guess (for normals, $N_1$-$P_3$ is larger for stimuli associated with a correct guess). The evoked potential amplitudes of the schizophrenic patients were least affected by modality shift and correctness of guess while the depressive patients' amplitudes were closer to those of the normal controls.

**30.3** HEMISPHERIC SHARING BETWEEN VERBAL AND MANUAL PERFORMANCE AFTER CALLOSAL SECTION. Marcel Kinsbourne*[1] (SPON: M. L. Wolbarsht). Department of Pediatrics, Duke University Medical Center, Durham, N. C., 27710.

Humans are generally able to do two things at the same time. However, when right handers repeated sentences while balancing a dowel rod, right index finger balancing was impaired, while left was not (Kinsbourne and Cook, 1971)[2]. Thus, when programs for speech and limb movement share a cerebral hemisphere, one program may interfere with the other. Maximum rate of tapping with right and left index fingers was studied in four callosally sectioned patients. The patients were able to tap at a normal rate with each hand in isolation but synchronous and alternate tapping was inaccurate and slow. We studied "hemispheric sharing" in one patient who recited alternate alphabet letters and mental arithmetic while tapping. While in 100 normal subjects we found diminished efficiency of tapping while speaking, there was no interaction between speaking and relative efficiency of tapping on the two sides, the patient's right index tapping stopped while she spoke; the left did not. When she made an error, both stopped. Callosal section impairs the accuracy of synchronization of bilateral movements. Further, it amplifies the effect of hemispheric sharing. This suggests that the intact corpus callosum equilibrates excitation between the hemispheres, thus obviating gross lateral bias in performance during cerebrally lateralized cognitive activity. When performance reached its ceiling (and errors result) then capacity was fully engaged by the task and concurrent tapping stopped. Thus the callosally sectioned patient still draws upon a unitary reserve of capacity.

[1] In collaboration with Charles Kreuter and C. W. Trevarthen.

[2] Kinsbourne, M. and Cook, J. Quarterly Journal of Experimental Psychology, 1971, 32, 341-345.

**30.4** HEMISPHERIC ASYMMETRY IN SLOW CORTICAL POTENTIALS AS A FUNCTION OF VERBAL OR NONVERBAL SET. Gail R. Marsh and Larry W. Thompson* Department of Psychiatry and Center for the Study of Aging and Human Development, Duke University Medical Center, Durham, N. C. 27710.

Subjects warned that they were about to receive a brief verbal stimulus shifted the electrocortical potential of the right temporal lobe to a more negative level than the left. When warned of an impending nonverbal stimulus the left parietal area shifted to a more negative potential than the right. These differences arose due to changes in the activity of the right hemisphere in both cases. These potentials seem to reflect a brain process underlying the preparation to receive verbal or nonverbal stimuli and suggest a reciprocal inhibitory relationship between these two brain states.

**30.5** CARDIO-RESPIRATORY MECHANISM IN PLATEAU WAVES AMONG HEAD-INJURED PATIENTS. C. P. McGraw, G. T. Tindall*, K. Iwata*, and R. W. Vanderveer*, University of Texas Medical Branch, Galveston, Texas, 77550

Consistent cardiovascular and respiratory changes were found to have a role in the initiation and termination of intracranial pressure (plateau) waves. These relationships were noted during the continuous monitoring of subdural intracranial pressure (ICP) in 27 head-injured patients by means of an absolute pressure transducer placed in a trephine opening. It was found that with higher baseline levels of ICP there was an increase in the length and magnitude of the ICP waves and a progression toward the formation of plateau waves. The sequence of events during a plateau wave were determined. First, there was a transient increase in expired $CO_2$, usually the result of irregular respiration. The ICP gradually increased and was accompanied by a simultaneous decrease in heart rate, respiratory rate and depth. When the ICP reached a peak there was an abrupt increase in heart rate, respiratory rate and depth above the pre-wave levels. This series of responses effected a transient decrease in the expired $CO_2$ and the ICP returned to baseline level. When the ICP had returned to the pre-wave level, the heart rate and respiration also returned to the pre-wave levels. Transient increases in arterial $pCO_2$ and subsequent cerebral vasodilatation were responsible for the initiation of the ICP waves. The length of the wave was due to high baseline ICP which caused vascular engorgement by collapsing small cerebral veins. The terminal heart rate increase was a release mechanism which terminated the ICP wave.

**30.6** COCAINE: CLINICAL EFFECTS IN DEPRESSED PATIENTS. Robert M. Post*, Joel Kotin*, and Frederick K. Goodwin. Section on Psychiatry, Lab. of Clin. Science, National Institute of Mental Health, Bethesda, Maryland 20014

Since cocaine has a long history of reported mood elevating properties and more recently its brain amine potentiating effects have been documented, an experimental trial in depression is of theoretical importance. Eleven depressed patients in this study were hospitalized on a metabolic research ward at NIMH and followed with double-blind behavioral ratings of mood and monitored for vital sign & EEG changes. Oral cocaine was administered during 14 trials at slowly increasing doses to a maximum of 30 mg Q.D. to 100 mg B.I.D. Seven patients received intravenous cocaine (2-16 mg) over 1 to 3 minutes. After oral cocaine, no unequivocal antidepressant responses were observed and vital signs did not change; however, rapid eye movement sleep showed a significant decrease and withdrawal rebound. Given intravenously, cocaine caused an initial feeling of sleepiness or calmness followed by dramatic episodes of affective release and tearfulness (4 of 7 patients) associated with marked increases in pulse and blood pressure. Two patients showed no vital sign or mood changes at the doses employed. One profoundly depressed patient became more anxious. The lack of antidepressant effect after oral cocaine must be viewed with reservation because of questions of absorption and storage. Intravenous cocaine, however, caused marked vital sign changes and a profound mobilization of affect and tearfulness. Although some of these episodes were accompanied by positive subjective reports and appeared to have therapeutic consequences, they could not be viewed simply as mood elevating or antidepressant responses.

**30.7** A COMPARATIVE STUDY OF MENTAL STATUS. Iver F. Small, Victor Milstein and Joyce G. Small. Larue D. Carter Memorial Hospital, 1315 W. 10th Street, Indianapolis, Indiana, 46202

Aside from the longitudinal psychiatric and medical history, the mental status examination is the most commonly employed method of psychiatric assessment. In some ways it is the psychiatric counterpart of the physical examination in general medicine and employs interview techniques to assess mental functioning in a variety of areas. The nature of the questions is such that they are rarely posed to persons considered to be mentally healthy. The present study concerned itself with the mental status characteristics of 50 acutely ill adult admissions to a psychiatric hospital, each of whom had a healthy sibling who had never been treated or hospitalized for mental disorder. Mental status examinations of both patients and sibs were conducted with identical questions designed to probe process and content of thought, with specific inquiries about hallucinatory phenomena, delusional and supernatural concerns and personal opinions, as well as assessments of intellectual and cognitive abilities.

Comparisons of patient and sibling verbal responses revealed surprisingly few differences even in areas supposedly typical of psychosis. Differences that were found were more quantitative than qualitative, as for example the patients were more disturbed by their strange experiences and erratic thinking and noted such things more often than did the relatives. This was most strikingly demonstrated when correlations between the responses of the patient and his own sibling versus the responses of the patient and randomly chosen siblings were examined. There were 28 significant ($P<.05$) positive correlations between the answers of patients and their own sibs, versus only 4 with the other sibling group. Interpretation of these surprising findings will be discussed, including questions about the reliability and sensitivity of the mental status examination and its limitations as a diagnostic instrument.

**30.8** ELECTRON-TRANSFER FACTORS IN PSYCHOSIS AND DYSKINESIA. Peter H. Proctor, Physics Dept., M. D. Anderson Hospital, UTGSBS, Houston, Texas, 77025

In man, chronic systemic exposure to elevated levels of compounds having electron-transfer properties -- e.g., uric acid (Lesch-Nyhan Syndrome), L-dopa, phenothiazines, copper (hepatolenticular degeneration), iron (hemochromatosis), manganese, bromide, iodide, thyroid hormones, or sulfur-containing amino acids (homocystinuria) -- is typically associated with one or more of three characteristic signs. These are psychosis, dyskinesia, and pigmentary abnormalities. For example, all three signs are found in hepatolenticular degeneration and in thyrotoxicosis, psychosis and dyskinesia in the Lesch-Nyhan Syndrome, psychosis and hyperpigmentation in bromism, dyskinesia and hyperpigmentation in phenothiazine treatment, and psychosis alone in homocystinuria. A partial listing of relevant common in vivo interactions of such electron-transfer agents includes interactions with biological semiconductors such as brain melanin (Cotzias et al, Fedn. Proc., 23, 713 [1964]), nucleic acids, or lipid membranes, activation of molecular oxygen and cofactor properties (Ingraham, Comprehensive Biochem., 14, 424 [1966]), generation of psychoactive free radicals (Polis et al, PNAS, 64, 755 [1969]), activation of psychoactive plasma protein components (Bergen, Res. Comm. Chem. Path. Pharmacol., 1, 403 [1970]), or disruption of lysosomal function (Edgar, Nature, 227, 24 [1970]). It is suggested that similar electron-transfer factors may be relevant to the increased incidence of both hyperpigmentation (Greinor and Nicholson, Lancet, ii, 1165 [1965]) and dyskinesia (Goldman, Dis. Nerv. Sys. (sup.) 24, 33 [1968]) reported in schizophrenic populations prior to the use of the phenothiazines.

**30.9** THE SCHIZEXPERIENCE: A LEARNING AND FEEDBACK MODEL FOR SCHIZOPHRENIA AND SCHIZOID PROCESS. Virginia Johnson. 1516 Westwood Boulevard, Los Angeles, California 90024.

The hypothesis is presented that a specific premorbid schizexperience is necessary (but not sufficient) to initiate schizophrenic process, and that conditional feedback from such an experience can be traced clinically in retrospect. Schizexperiences are characterized by dissociative states, during which the cortex is minimally involved. This neurological dysfunction and its accompanying altered state of consciousness (ASC) are necessary aspects of the schizexperience. The suggested model is based on an analysis of over 25,000 hours of interviews with subjects representing a wide range of psychopathological syndromes, including acute schizophrenic episodes and schizoid process. The findings indicate that the necessary factor in the schizexperience is a dissociative state (e.g., drugs, fever, anoxia, concussion, etc.), which state is information processed as such, and continues to function as a feedback system reflecting state dependent learning which finally emerges as the "schizophrenic process." There is some evidence that schizophrenia follows only when the necessary schizexperience occurs very early in development, probably pre- or perinatally. Clinical symptom patterns relate specifically to the individual schizexperience, while the schizoid process is a "common behavioral end product." This model may be applicable to other functional disorders characterized by behavior patterns reflecting stimulus and response modalities of a prior ASC conditional experience.

**30.10** A CLINICAL SERVICES SYSTEM REPLICATING THE "TOTE" MODEL. Mark N. Ozer. Dept. Child Health Devel., G.W. Univ. Med. Sch., Child. Nat. Med. Center, Washington, D.C., 20009

A clinical system has been designed in relation to children with learning problems. Diagnosis in this system is an interactive process in which the examiner and child explore a limited number of problem solving strategies on a set of prototype tasks. The effective communication of such strategies from the diagnostic consultant to the primary participants (child, parents and teachers) has been considered as a problem in information transfer. The activities of the participants under the auspices of the clinical system are a short term model of the longer term activities of these participants outside the boundaries of the clinical setting. The procedures followed to enhance information transfer are viewed as a model of an adaptive system. A limited number of strategies is used at any one time in a series of interactions between the consultants and primary participants. These strategies are incorporated in a preliminary Report Form and then demonstrated during a clinical session on prototype tasks. The selective perception of the observer during the clinical session determines which of the strategies are to be illustrated by suggestions specific to context in which the child actually functions. The Evaluation-Planning Form at the end of every session clarifies what had occurred as well as aiding future planning. Particularly emphasized will be the implications of exemplifying in a large scale the feed-forward as well as feed-back principles of the TOTE model of Pribram. Theoretical implications also relate to the process by which these new models of brain function relate to making changes in large scale systems such as that of education.

**31.1** AMPHETAMINE: DIRECT EVIDENCE FOR AN ACTION ON DOPAMINERGIC NEURONS. B.S. Bunney*, G.K. Aghajanian, R.H. Roth & J.R. Walters*, Depts. Psychiat. & Pharmacol. Yale Univ. Sch. Med. & Conn. Ment. Hlth. Ctr. New Haven, Conn.

Amphetamine produces a paranoid psychosis in man and "stereotyped" behavior in man, rats and various other animals. These effects have been attributed to an excess of dopamine present at postsynaptic receptor sites, resulting from an increased release and block of reuptake of dopamine by amphetamine. Pretreatment of animals with α-methyl-p-tyrosine (AMPT), a tyrosine hydroxylase inhibitor, leads to decreased amounts of newly synthesized dopamine available for release and prevents the development of stereotyped behavior induced by amphetamine. Subsequent administration of L-DOPA, the immediate precursor of dopamine, elicits the typical stereotyped behavior. Antipsychotic phenothiazines and the butyrophenone, haloperidol, have also been shown to block amphetamine induced stereotypy, possibly through a blockade of dopamine receptor sites. In an effort to correlate the behavioral interaction of these various drugs with their interactions at a neuronal level, extracellular recordings were made to determine the effect of amphetamine, various antipsychotic drugs, L-DOPA and AMPT on the firing rate of dopamine-containing cells in the substantia nigra and ventral tegmental area of the rat midbrain. Both anesthetized and gallamine paralyzed rats were used. D-Amphetamine was extremely potent in decreasing the spontaneous activity of dopaminergic neurons. The antipsychotic drugs as well as AMPT reversed the d-amphetamine depression. Pretreatment with AMPT prevented the amphetamine-induced decrease in firing rate. Subsequent administration of L-DOPA produced a marked slowing of unit activity. Thus, the interaction of these drugs with amphetamine in producing an effect on dopamine cell activity directly parallels their ability to block or potentiate amphetamine-induced stereotyped or other behaviors.

**31.2** PREDICTORS OF RESPONSE TO STIMULANT DRUG TREATMENT IN MBD CHILDREN. James H. Satterfield, Grigor E. Atoian*, and Ronald E. Saul*. Gateways Hospital, 1891 Effie Street, Los Angeles, 90026

Minimal Brain Dysfunction (MBD) children ages 6 through 9 were evaluated in a double blind methylphenidate-placebo study. Clinical evaluation included a structured interview with parents, teacher rating scales, psychiatric examination by two child psychiatrists, neurological examination by a neurologist, clinical electroencephalograms, and a battery of psychological tests, including Wechsler Intelligence Scale for Children (WISC), Wide Range Achievement Test (WRAT), Illinois Test of Psycholinguistic Abilities (ITPA), Bender-Gestalt, and Porteus Maze. Laboratory tests included power spectral analysis of the EEG, auditory evoked cortical responses and skin conductance measures. All before treatment measures were examined to see which predicted response to treatment. Classification by the psychiatrists into an organic or psychogenic group did not predict response to treatment. The presence of an abnormal EEG and/or neurological soft signs did predict a good response to treatment. The behavioral rating scales and some of the laboratory measures were also predictive of response to treatment. These data suggest that there is a pathophysiological basis for the behavioral disturbance of the MBD child.

**31.3** RECENT ADVANCES IN THE BIOCHEMICAL PHARMACOLOGY OF AMPHETAMINE AND ITS CHLORINATED DERIVATIVES. F. Sulser and E. Sanders-Bush. Dept. of Pharmacol., Vanderbilt Univ. Sch. of Med., Nashville, TN 37232

p-Chlorinated amphetamine derivatives (PCA) elicit a number of changes in cerebral biochemistry which are not produced by amphetamine. Among these are marked alterations in the metabolism and release of serotonin (5HT) and 5-hydroxyindole acetic acid. Recently, we have found that the administration of PCA to rats causes a pronounced reduction in cerebral tryptophan hydroxylase with no change in the activity of 5-hydroxytryptophan decarboxylase. Since these drugs do not inhibit tryptophan hydroxylase when added in vitro, experiments were designed to study the mechanism of the decrease in enzyme activity which follows their in vivo administration. The in vivo formation of a metabolite of PCA which inhibits tryptophan hydroxylase, does not appear to occur. Our results suggest that PCA may reduce the amount of the active enzyme without altering its properties. Following the administration of PCA to rats, the uptake of 5HT-$H^3$ into a crude suspension of synaptosomes and mitochrondria is reduced. Both the enzyme inhibition and the blockade of uptake are extremely long-lasting. Two weeks following the administration of PCA (10 mg/kg, i.p.), the concentration of 5HT and the activity of tryptophan hydroxylase are significantly reduced in all regions of the brain and the spinal cord. In contrast to amphetamine, PCA lowers the endogenous level of cyclic AMP in brain. The significance of this change in relation to other effects of PCA as well as the role of p- and B-hydroxylation in the action of amphetamine will be discussed. (Supported by USPHS-Grant MH-11468).

**31.4** PROVOCATION OF PSYCHOTIC SYMPTOMS IN SCHIZOPHRENICS BY METHYLPHENIDATE. J.M. Davis*, D.S. Janowsky*, M.K. El-Yousef* and H.J. Sekerke* (SPON: D.X. Freedman). Depts. of Psychiat. and Pharmacol., Vanderbilt Univ. Sch. Med., and the Tenn. Neuropsychiatric Institute, Nashville, Tenn. 37232.

The purpose of this investigation is to evaluate whether the amphetamine-like psychostimulant, methylphenidate (Ritalin) provokes an exacerbation of schizophrenia symptoms in predisposed subjects. Eight manic, four depressed and sixteen schizophrenic patients were studied when acutely ill and when recovered. Eight psychoneurotics were also studied. All subjects received methylphenidate 0.5 mg/Kg or a saline placebo injection I.V. on a double blind basis, and were evaluated on a quantative rating scale. Injection of methylphenidate in actively psychotic schizophrenic patients produced a marked worsening of their symptoms, lasting from thirty minutes to three hours, and consisting of an emergence of florid symptomatology. When the patients later recovered, either spontaneously or following psychotropic drug administration, methylphenidate failed to produce, or only minimally produced, schizophrenic symptoms. Although methylphenidate produced a mild euphoria, increased interactions and increased talkativeness in psychoneurotics, it failed to produce any schizophrenic symptoms. It did not significantly produce schizophrenic symptoms in manic or depressed patients. Placebo did not produce any behavioral changes. Increasing central cholinergic activity with physostigmine antagonised methylphenidate's effects. Serum cyclic AMP and Tryptophan were not altered by methylphenidate in the patients. (Supported in part by NIH grant GM 15431 and NIMH grant 11468.)

**32.1** HISTOFLUORESCENT AND ELECTRON MICROSCOPIC STUDIES OF THE DEVELOPING SUBSTANTIA NIGRA IN THE RABBIT. Virginia M. Tennyson, Catherine Mytilineou*, and Robert Barrett*. Dept. of Pathology (Division of Neuropathology) and Neurology. Columbia Univ., College of Physicians & Surgeons, New York, N.Y. 10032

Neurons of the substantia nigra of the adult rabbit are multipolar cells with centrally placed indented nuclei. The cell body has an intense fluorescence, which extends into the proximal processes. Numerous fluorescent beaded axons and dots course in the neuropil intervening between the neurons. The neurons have small zones of parallel cisternae of endoplasmic reticulum. Multiple foci of the Golgi complex associated with 1000Å dense core vesicles surround the nuclei. Although synaptic terminals typically encircle large dendrites, terminals on small dendrites and axosomatic junctions are common. Dopamine-containing neurons are present at day 19 of gestation. They are less differentiated rostrally. The neuropil contains sparse immature synaptic junctions with few axonal vesicles. The synapses are preferentially associated with large dendrites. Varicosities of growing axons are common throughout the neuropil. By day 26 of gestation, large numbers of fluorescent neurons of small to large size are present, which have short, but branching dendrites. Synaptic terminals are relatively mature, and have masses of agranular vesicles and some large granular vesicles. Only a few establish axosomatic contacts. By the 9th postnatal day, the fluorescent neurons are larger and have broader and longer dendrites. Some exhibit a greenish fluorescence, others have a yellow fluorescence. Synaptic profiles encircle large dendrites and frequently make axosomatic junctions. The fluorescent profiles and fine structure of the substantia nigra after the 3rd postnatal week closely resemble that of the adult. Supported by NS 05184.

**32.2** PROLIFERATION RATE AND LATENCY BETWEEN FINAL CELL DIVISION AND ONSET OF DIFFERENTIATION OF CEREBELLAR STELLATE AND BASKET NEURONS. Pasko Rakic. Dept. of Neuropath., Harvard Med. Sch., Boston, Mass. 02115.

Thymidine-$H^3$ autoradiographic, Golgi, and electronmicroscopic methods are combined to analyze proliferation kinetics and to determine the interval from final division to initial dendritic outgrowth and synaptogenesis of interneurons of the cerebellar molecular layer (stellate and basket cells) in rhesus monkeys. Labeling index measurements in autoradiograms of adult animals injected at different developmental ages indicate that interneurons are generated at a steady rate of about 1% per day from the 80th embryonic day to just after birth. The precursor pool is about 250,000 cells,each yielding on the average one differentiating and one proliferating daughter cell. The rate of interneuron proliferation parallels neither the exponential production of granule cells nor the 40-fold expansion of cerebellar surface. Adult position of interneurons correlates with time of cell origin; the deep cells are generated first, the more superficial ones progressively later. By comparison of autoradiographic maps with Golgi impregnations and electronmicrographs at developmental stages,the interval from mitosis to dendritic outgrowth and onset of synaptogenesis was found to increase systematically,reaching a maximum of two months for the last-forming interneurons.Postmitotic interneurons, as yet without dendrites,accumulate at the interface between the external granular layer and the thickening molecular layer before becoming enveloped by newly-formed neighboring processes of other cells. Identified among these were mainly parallel fibers and some climbing fibers,axons of previously generated interneurons and Purkinje dendrites.It is speculated that any or all of these may induce interneuron differentiation,since proliferation of any given interneuron is completed relatively early while it differentiates only later when its local milieu has developed.

**32.3** EFFECT OF OLFACTORY BULBECTOMY ON NURSING BEHAVIOR IN THE WISTAR (DAB) RAT PUP. Pauline J. Singh* and Ethel Tobach. Dept. Animal Behavior, The American Museum of Natural History, New York, 10024

Previous work showed that bilateral olfactory bulbectomy in the Wistar (DAB) rat pup resulted in the death of the pup. To determine whether the bulbectomy led to a change in the nursing behavior of the pup, which then resulted in death, 17 litters (7 pups each) were observed from day 2 through day 16 after birth. Bilateral olfactory bulbectomies were performed on pups aged 2, 7 and 11 days. Three litters were handled only. All other litters consisted of 3 bulbectomized pups (BX), 2 surgical control pups and 2 handled only pups. Using survival to day 16 as a criterion, no differences among the litters were found. However, a greater number of surgical control pups and pups that were handled only survived to day 16 than BX pups. The differences in actual number of days of survival were also statistically reliable. Observations of the female and litter were made in a special cage two times a day when the pups were 4, 7, 10, 13 and 16 days old. Each of the two daily observations included a complete nursing sequence. BX pups spent less time nursing, more time away from the female and other pups, and more time locomoting while in the observation cage. The mammary glands of the females were functional, but, the BX pups had little or no milk in their stomachs. Partially bulbectomized pups survived longer than BX pups, and of those that survived (12 out of 15) all except one pup were lighter than their litter mates.

**32.4** DEVELOPMENT OF SPECIES-SPECIFIC AUDITORY PERCEPTION IN DUCK EMBRYOS: BEHAVIORAL ANALYSIS. GILBERT GOTTLIEB AND MARIETA B. HEATON. DIV. OF RESEARCH, DEPT. MENTAL HEALTH, RALEIGH 27611.

The newly hatched duckling (Anas platyrhynchos) is selectively responsive to the maternal assembly call of its species in advance of exposure to that call. The ontogeny of the duckling's ability to respond discriminatively to the species maternal call has been studied in the embryo. Such study indicates that behavioral responsiveness to the maternal call is evident as early as 5 days before hatching in the duck embryo. This early response is not a fully differentiated one with respect to the distinctive features of the maternal call, however. For example, the young embryo's response is restricted to the low frequency component of the call (<825 Hz), it is capable of responding to the call at only one pulse rate (4/sec), and it also responds to white noise pulsed at 4/sec. Several days later, after pulmonary respiration has started and the embryo itself becomes capable of vocalizing, the embryo's response to the parameters of the maternal call broadens to include the high frequency components (825-2300 Hz), it becomes capable of responding to the call at various pulse rates (1/sec., 2.5/sec., 4/sec., 6/sec.), and it will no longer respond to white noise pulsed at 4/sec. Manipulative studies of the embryo's auditory experience show that (1) premature exposure of the embryo to embryonic vocalizations accelerates these progressive behavioral changes, (2) diminished exposure to embryonic vocalizations decelerates these changes, and (3) the complete absence of embryonic exposure to self or sib vocalizations leads to imperfections in the selectivity of the duckling's response to the maternal assembly call after hatching. Thus, normally occurring auditory stimulation plays a role in expanding the functional capabilities of the developing auditory system in the embryo and in the hatchling.

**33.1** NUTRITIONAL RESEARCH AND MENTAL RETARDATION. Myron Winick* Institute of Human Nutrition, Columbia Univ., New York, N.Y. 10032

Normal brain development is a process involving sequential changes in the number and size of cells, the amount of myelin, the quality of the lipid constituents, the quantity and localization of certain enzymes and a number of other cellular and chemical changes. Concomittant with these, a series of functional changes occur as the organism matures. Malnutrition during this period will induce profound changes, some of which are permanent. RNA, DNA and protein synthesis are curtailed, myelin is deposited more slowly and enzyme activities do not reach expected levels. It would appear that neonatal undernutrition induces these changes by increasing RNA degradation more than synthesis. This is accompanied by an increase in the activity of alkaline RNase and a reduction in overall protein synthesis. The latter is reflected in a decrease in a number of enzymes involved in DNA synthesis, i.e., DNA polymerase and a slowing of cell division. Thus malnutrition during early life will retard brain growth by curtailing the synthesis of protein and DNA and increasing the breakdown of RNA.

**33.3** PSYCHOPHARMACOLOGICAL CONTRIBUTIONS TO PATIENT CARE IN PSYCHIATRY. Solomon H. Snyder. Dept. Pharmacology and Dept. of Psychiatry, Johns Hopkins Univ. Sch. Med., Baltimore, Md. 21205

It is somewhat embarrassing, but nonetheless somewhat true that psychotropic drug use in patients has contributed more to basic neuroscience than vice versa. For instance, monoamine oxidase inhibitors and the tricyclic antidepressants were discovered to be efficacious in the treatment of depression prior to any awareness of the nature of or even the fact of their interactions with the biogenic amines. Similarly, chlorpromazine was administered to schizophrenic patients for no rigorously scientific rationale. Only subsequently was it apparent that the phenothiazines had specific antischizophrenic activity. And it is just quite recently that the interaction of phenothiazines with catecholamine receptors has been worked out in a way suggesting a relationship to the mode of action of these drugs. The important features of neurotransmitter disposition in the brain which have been elucidated with the aid of psychotropic drugs will be reviewed. Knowing some of the effects upon transmitter systems which are related to therapeutic action, it is possible to address the issue of new drug development in a scientific way. Examples of the design of agents with selective effects upon specific transmitter systems will be presented to illustrate how such investigations may both further our understanding of synaptic transmission in the central nervous system and hopefully result in new therapeutic modalities for psychiatric illness. (Supported by USPHS Grants MH-18501, NS-07275 and RSDA MH-33128).

**34.1** INHIBITION IN THE FUNCTION OF THE STOMATOGASTRIC GANGLION. Donald M. Maynard and Kerry Walton*. Dept. Biol., Univ. Oregon, Eugene, 97403

At least 22 of the 28-30 nonsensory neurons of the stomatogastric ganglion in the lobster, Panulirus argus, are motor, sending axons to stomach muscles where they produce excitatory junction potentials. Within the ganglion neuropil many of the same identified cells synapse with one another, but elicit inhibitory post-synaptic potentials. Such inhibitory interaction is one mechanism whereby integrated output patterns are carved from ongoing activity in individual neurons. Reversal potentials of IPSP of three different synaptic pairs, ci-gm, lp-pd, and pd-py were measured with varying external $K^+$ and $Cl^-$ concentrations. In all three, variation of $K^+$ produced major changes in reversal potential. Reduction of external $Cl^-$ also shifted the IPSP reversal potential, particularly in the lp-pd synapse. It is likely that conductance changes of both $K^+$ and $Cl^-$ are involved in the IPSP. Possible transmitters, glutamate, GABA, dopamine, serotonin, Ach, and octopamine were applied iontophoretically and/or to the bath. Only glutamate hyperpolarized postsynaptic elements of all three synapses; GABA also hyperpolarized the GM and PD cells to a lesser extent, but depolarized the PY neuron. Picrotoxin blocked all glutamate and GABA effects and also IPSP of the ci-gm and lp-pd synapses. Picrotoxin did not affect the third synapse, pd-py. The transmitter at the pd-py synapse is probably neither glutamate nor GABA. Transmitter identities at the ci-gm and lp-pd synapses remain uncertain, glutamate cannot be excluded. (supported by NIH grants NS 06017, NS 09474 and HSAA 5-S04FROGO27)

**34.2** INHIBITORY EFFECTS OF IMIDAZOLE AND SOME DERIVATIVES ON CORTICAL NEURONES. K. Krnjević, J.M. Godfraind* and R. Pumain*. Dept. of Anaesthesia Research, McGill Univ., Montreal 110, Canada

In view of previous observations of an inhibitory action of imidazole acetic acid (Krnjević & Phillis, 1963, Br. J. Pharmac. 20, 471) the effects of some related compounds were tested by microiontophoresis in cats under Dial. They all depressed glutamate-evoked unit firing, the order of potency being: imidazole propionic acid > imidazole acetic acid > imidazole > 4-imidazole carboxylic acid. Their effect was relatively quick in onset and rapidly reversible, not unlike that of the inhibitory omega amino-acids. Judging by the equipotent iontophoretic currents, these compounds were between 1/2 and 1/10 as active as GABA. If they are released in the central nervous system they could have a significant inhibitory role.

Supported by the Medical Research Council of Canada

**34.3** SYNAPTIC PROPERTIES OF STRIATAL AND PALLIDAL NEURONS. C. D. Hull, M. S. Levine* and N. A. Buchwald. Depts. of Anatomy & Psychiatry, UCLA, Los Angeles, 90024.

We have attempted to integrate data from a series of intracellular studies of postsynaptic responses of striatal and pallidal neurons with recently published data concerning fine structure of these neurons (Kemp & Powell, 1971). The result of this integration is a provisional model concerning the function of striatal afferents, striatal interneurons and striopallidal connections which is generally consistent with available data. The assumptions are: (1) all inputs to the striatum are excitatory; (2) the morphologically most common cell (96% of all caudate neurons according to Kemp & Powell) is inhibitory to its neighbors via a relatively short branched axon; (3) axons of many different neurons from structures afferent to the striatum synapse with this most common cell; (4) cortical and most thalamic neurons have synaptic connections with many common cells. [An exception may be neurons in the central median-parafascicular region of the intralaminar thalamus.] Nigral and other mesencephalic inputs contact fewer common cells; (5) striatal output axons are mainly inhibitory with respect to pallidal neurons with a fewer number excitatory; (6) interneurons other than the most common are presumed to be excitatory. The model accounts for the facts that: (1) spontaneous rates of unit firing in the striatum are low; (2) the predominant response to striatal input stimulation is an EPSP-IPSP sequence; (3) cortical stimulation will inhibit striatal responses to nigral and some thalamic inputs, although the converse is not true; (4) responses of pallidal neurons indicate that a predominant effect of striatal output is to inhibit pallidal firing.

Supported by USPHS HD04612, MH07097, Dept. of Mental Hygiene, State of California.

**34.4** DISINHIBITION OF FROG TECTAL UNITS AFTER PRETECTAL LESIONS. David Ingle, McLean Hospital and Harvard Medical School, Belmont, Mass. 02178.

In frogs and toads appropriate pretectal damage produces a dramatic release of prey-catching behavior from normal restraints. Such animals attempt to feed on large objects that they would normally avoid, and show negligible habituation of this response. Since the optic tectum is thought to mediate prey-catching responses toward visual objects (i.e. orienting and snapping), the question arises whether tectal neurons would alter their normal response properties after pretectal lesions. In normal frogs tectal neurons recorded at the Class 3 fiber level had mainly receptive fields of 15-20$^{o}$ and showed strong habituation. The equivalent population of neurons in each of 7 frogs, that had shown behavioral disinhibition following pretectal lesions, was in fact much altered. Receptive fields now ranged around 30$^{o}$ in size, and these units showed no more adaptation on repeated stimulation than the Class 2 retinal fibers that are presumed to be afferent to these particular neurons. The study confirms the hypotheses that pretectal neurons exert a tonic inhibitory influence upon at least one class of cells within the optic tectum.

**35.1** MORPHOLOGICAL TRANSFORMATION OF DISSOCIATED EMBRYONIC BRAIN CELLS IN THE PRESENCE OF BRAIN EXTRACTS. Ramon Lim, William K.P. Li* and Katsusuke Mitsunobu*. Div. of Neurosurgery and Dept. of Biochemistry, Univ. of Chicago, Chicago, Illinois 60637

Brain cells were dissociated from 17-day rat embryos by trypsinization in calcium-magnesium-free Tyrode solution. The cells were grown to confluency in a monolayer in the F10 medium supplemented with 17% fetal calf serum. The cells were then subcultured under similar conditions for 2 more days before exposure to various test media. Testing was conducted by replacing the original medium with one of the following: (A) 4 parts F10 plus 1 part fetal calf serum, (B) 4 parts F10 plus 1 part Tyrode solution, (C) 4 parts F10 plus 1 part rat brain extract. The brain extract was prepared from a 20% homogenate in Tyrode solution; the 100,000xg supernatant was exhaustively dialyzed against several changes of Tyrode solution before use. Cells grown in media A and B were ameboid in shape, while cells grown in medium C were characterized by an extensive outgrowth of cell processes. Under phase contrast microscopy most of the cells in medium C resembled astrocytes; others looked like oligodendroglia. The presence of neurons could not be ruled out. Heat treatment of the rat brain extract abolished the transforming activity. Rat liver and kidney extracts gave dubious results whereas pig brain extract was as active as rat brain extract. Like fetal calf serum, no transforming activity was observed with horse serum, bovine serum and rat serum. The results suggest the presence of a heat labile macromolecular component in the brain capable of inducing morphological transformation in dissociated brain cells. (Supported by U.S. Public Health Service grants No. NS-09228 and NB-07376).

**35.2** BIOCHEMICAL CORRELATES OF INHIBITION OF OLIGODENDROCYTES DIFFERENTIATION IN TISSUE CULTURE. Gerard M. Lehrer, June M. Fry*, and Murray B. Bornstein, Dept. of Neurol., Mt. Sinai Sch. Med., CUNY, New York, 10029 and A. Einstein Coll. Med., Bx., New York 10463.

It was previously reported that myelination in cultures of mouse spinal cord is inhibited in presence of small concentrations of serum from animals with experimental allergic encephalomyelitis (EAE) accompanied by failure of differentiation of oligodendrocytes. Replacement of cultures in normal medium produces appearance of oligodendrocytes as well as myelin within two days.

It is now demonstrated that $^{35}SO_4$ incorporation into cerebroside $SO_4$ is markedly inhibited not only when cultures are grown in presence of 3% EAE serum, but also within 8 hours of placing normal cultures into 3% EAE serum from days 6 through 21 in vitro. This inhibition is reversed within 24 hours of replacement of the culture in normal feeding solution.

When specific enzyme activities were assayed under conditions of inhibition and disinhibition, no specific differences from controls were found for glucose-6-phosphate dehydrogenase, β-D-galactosidase, β-glucoronidase, acid phosphatase, or isocitrate dehydrogenase. However 2'-3'-cyclic adenosine monophosphate phosphohydrolase, an enzyme which has been specifically associated with mature oligodendrocytes, showed identical patterns of inhibition and disinhibition as were observed for sulfatide synthesis. The methods described should provide a precise tool for the investigation of the molecular events involved in the differentiation of of the oligodendrocyte. Such information is crucial to the understanding of normal myelination as well as defects in myelination.

**35.3** DIFFERENTIAL EFFECTS OF INHIBITORS OF RNA SYNTHESIS ON THE CATECHOLAMINE AND CORTISOL INDUCTIONS OF ENZYMES IN A RAT GLIAL CELL LINE. Jean de Vellis and Diane Inglish* Laboratory of Nuclear Medicine and Radiation Biology and Dept. of Anatomy, UCLA, Los Angeles, 90024.

The rat brain astrocytoma cell line, $RGC_6$, is characterized by several specialized functions of glial cells, including the cortisol induction of glycerol phosphate dehydrogenase (EC 1.1.1.8) (GPDH) and the induction of lactate dehydrogenase (LDH) by norepinephrine (NE). Cyclic AMP appears to be the mediator for the action of NE but not for cortisol (J. Neurochem. 15, 1061, 1968; Cellular Aspects of Neural Growth and Differentiation, D. Pease, Ed., pp 23-32, Univ. Calif. Press, 1971; de Vellis and Brooker, Fed. Proc. 31 (2), 573, 1972). In the present study, the effect of inhibitors of RNA synthesis on GPDH and LDH inductions was investigated. Cells were grown for 9 days to a density-inhibited confluent monolayer, using Ham's $F_{10}$ medium supplemented with 10% fetal calf serum. Alpha-Amanitin ($10^{-5}$M), a specific inhibitor of RNA polymerase (RP'ase) II (Science 170, 447, 1970), blocked the induction of GPDH but not LDH. Actinomycin D (AMD), which at 0.05 μg/ml inhibits only rRNA synthesis, blocked the induction of GPDH but not LDH. AMD which at 1 μg/ml inhibits all RNA synthesis, and cordycepin, an inhibitor of mRNA (PNAS 67, 1878, 1970), blocked GPDH and LDH inductions. Ethidium bromide, an inhibitor of mitochondrial RNA synthesis blocked neither GPDH nor LDH. The data suggest that both enzyme inductions require de novo synthesis of mRNA but that their mRNAs are transcribed by different nucleoplasmic RP'ases. The GPDH mRNA is synthesized by RP'ase II and therefore the LDH mRNA is probably produced by RP'ase III. The effect of low level of AMD suggests that the synthesis of rRNA is also required for GPDH induction unless the synthesis of GPDH mRNA is as sensitive as rRNA to AMD. Supported by USAEC contract AT(04-1) GEN-12 and grant HD-05615 from NICHHD.

**35.4** RESPONSES OF SYMPATHETIC CHAIN-GANGLIA ISOLATED IN LONG-TERM CULTURE, TO AGENTS AFFECTING ADRENERGIC NEURONS. Helena H. Benitez and Margaret R. Murray. Dept. Surg., P and S, Columbia Univ., New York City, 10032.

Right and left sympathetic chains from 13-14 da chick embryos were explanted on collagen-coated coverslips and carried in the Maximow culture assembly for ca. 3 wk in biological media. During this period they become morphologically mature and manifest accumulation of catecholamine, as assayed by fluorescence histochemistry (Falk and Thorp method).

Administration of exogenous co-factor (biopterin) increases the rate and amount of norepinephrine (NE) production during the first 6 hr of exposure. α-methyl-tyrosine (inhibitor of tyrosine hydroxylase) reduces NE biosynthesis and nearly obliterates fluorescence within a similar period.

Monoamine oxidase inhibitors (Pargyline, Parnate, Katron) bring about an increase in numbers of fluorescing neurons (20-40 %) within the 6 hr period; but simultaneous administration of Pargyline and biopterin produces a sharp decrease in numbers and intensity of NE-fluorescing neurons. Reasons for this anomalous finding are not yet clear.

Direct exposure to Reserpine results in virtual extinction of NE fluorescence within 24 hr. Colchicine induces loss of fluorescence in neurites only, during a 10-hr period; later, recovery occurs. 6-OH-dopamine over 48 hr increases intensity and numbers of fluorescent somas with concomitant reduction of neuritic fluorescence, first discernible within 4hr.

In this entirely post-ganglionic living model, serial observations of catechol fluorescence, taken as indication of NE synthesis or metabolism, demonstrate that no preganglionic connection is necessary to activate any of the above responses. They further confirm the prevalent belief that synthesis takes place in the soma and that synthetic products pass rapidly distad, - in these neurites proceeding 1-2 mm/hr; outward-bound materials are dammed up by chemical injury to axons. [H.E.W., 2 RO1 NS00858].

**35.5** Effects of Maple Syrup Urine Disease Metabolites on L-Strain Mouse Fibroblasts. Michael G. Bissell*, Klaus G. Bensch*, and Mary M. Herman, Dept. Pathology, Stanford University, School Medicine, Stanford, Calif. 94305.

Alpha-ketoisocaproic acid (AKICA), the major toxic metabolite in Maple Syrup Urine Disease (MSUD), was added to mouse strain L fibroblasts in monolayer and suspension cultures. Treated cells were studied by light and electron microscopy and analyzed for their content of neutral and phospholipids. Suspension cultures grown at several concentrations of cold AKICA were treated with UL-($^{14}$C-) AKICA and $^{3}$H-L-isoleucine to determine uptake. The unused hot cell pellets from these studies were then subjected to Folch-Lees extraction for lipid and the extractable radioactivity determined. In addition, growth curves and electron microscopic surveys were carried out on suspension cultures treated with L-leucine, L-isoleucine, L-valine and alpha-ketoisovaleric acid (AKIVA).

At concentrations 10 to 30 times the levels of AKICA found in MSUD, the fibroblasts showed a decreased growth rate. Similar growth curves were seen with leucine and AKIVA, while isoleucine and valine at the same concentrations showed no effects. In AKICA-treated cells lipid droplets were increased, and numerous annulate lamellae were observed. Cells treated with the other compounds did not show annulate lamellae. Chemical analysis revealed elevated concentrations per cell of free fatty acids, triglycerides, sterols and some classes of phospholipids. $^{14}$C from labelled AKICA was not incorporated into these compounds. Uptake studies showed that AKICA is actively taken up by fibroblasts and that it inhibits the uptake of isoleucine at AKICA concentrations comparable to those seen in the serum of MSUD patients.
(Supported by USPHS Grants GM-1922-03, GM-16445 and NS-08276).

**35.6** INTRACELLULAR CHANGES RESULTING FROM EXPOSURE TO MORPHINE SULFATE. PHASE CONTRAST AND ELECTRON MICROSCOPIC STUDY OF TISSUE CULTURE LINE DERIVED FROM GLIOBLASTOMA MULTIFORME. Leopold Liss. Div. Neuropath., Dept. Path. OSU, Col. Med., Columbus, Ohio 43210

The cells derived from human Glioblastoma Multiforme have been subjected to various concentrations of Morphine Sulfate (MS). Some of the cells have been maintained in concentrations of 5mg% and 10mg% for a period exceeding two years. These cells have developed tolerance to MS and exhibit delayed and reduced alterations when exposed to higher concentrations if compared with cells not previously exposed to MS. The changes were observed in glial and mesenchymal cells, the multinucleated being the most susceptible. The observed changes were mainly occurring in the cytoplasm and, when observed with living phase contrast, were characterized by peripheral vacuoles, juxtanuclear vacuoles, crystalline inclusions, and dark granules. The nuclei showed damage to the membrane which indicated severe cell injury resulting either in cell death or inability of the cell to survive a transfer. The electron microscopic examination disclosed dilatation of the cisterns of the endoplasmic reticulum. Crystalline structures were scattered in the cytoplasm and frequently congregated as membrane-bound bodies occupying large portions of the cytoplasm. In addition small, light bodies and also small and giant dark bodies were encountered. These changes are a quantitative indicator of the ability of the cells to survive exposure to MS.

This investigation was supported in part by General Support Grant #5409 from the National Institutes of Health.

**35.7** DEVELOPMENTAL AND BIOSYNTHETIC STUDIES ON THE GUINEA PIG HYPOTHALAMO-NEUROHYPOPHYSIAL COMPLEX; IN VIVO AND IN ORGAN CULTURE. Rosanne Goodman*, Joseph Osinchak* and Howard Sachs* (SPON: C.Z. Neurath). Roche Institute of Molecular Biology, Nutley, New Jersey 07110.

The perikarya of nerve cells of the supraoptic nuclei are the main sites for the synthesis of the octapeptide hormone, vasopressin, and its binding protein, neurophysin. The hormone-protein complex is subsequently packaged within neurosecretory granules (NSG) and transported to the nerve terminals in the posterior pituitary where storage and release occur. Morphological studies on the developing guinea pig hypothalamo-neurohypophysial complex (HNC) showed that NSG first appear at the 39th and 40th day of gestation (Donev, S., Z. Zellforsch. 104, 517, 1970). Consistent with these observations is the finding that vasopressin is not demonstraable (by radioimmunoassay) until the 39th and 40th day in utero. Thereafter, the hormone content rises from less than one milliunit at 39 days to 600 milliunits by the 52nd day. In order to study directly hormone and binding protein biosynthesis, organ cultures of the HNC were developed initially utilizing adult tissues. Supraoptic neurons of the HNC in culture remain viable for periods up to 15 days, and retain the ability to synthesize vasopressin, neurophysin and RNA. Under similar in vitro conditions biosynthetic studies with embryonic tissues have confirmed the analytic results in that hormone biosynthesis is measurable only with the HNC of embryos beyond the 40th day. This organ culture system should prove useful in studies concerned with regulation of gene expression in nerve cells.

**36.1** TRIGEMINAL PAIN PROJECTIONS TO THE BULBAR LATERAL RETICULAR FORMATION. Samuel G. Nord and Gilbert S. Ross*. Dept. Neurol., Upstate Med. Cntr., S.U.N.Y., Syracuse, N. Y. 13210

Functional properties of mechanoreceptive cells in the lateral reticular formation (LRF) of the rhesus monkey were studied and were compared to those of cells in the immediately adjacent pars caudalis (NVcaud) of the spinal trigeminal complex. Neurons in NVcaud commonly displayed the detailed somatotopy, small peripheral fields and low thresholds reported for this structure in other macaques. In contrast, the somatosensory cells in LRF or in the transition zone between LRF and NVcaud exhibited marked differences in threshold, response patterns and functional organization. Ultimately, four general types of units emerged: (1) High threshold (nocioceptive) cells responding exclusively to empirically determined painful stimuli; (2) "medium threshold" units which responded to non-painful crude stimuli; (3) cells with low thresholds; (4) relatively high frequency "spontaneously active" neurons which were inhibited by gentle, repetitive, mechanical stimulation of restricted facial areas. The excitatory LRF cells had no apparent somatotopic organization and the size of their peripheral fields varied considerably, with the nocioceptive units generally having smaller fields than those with lower thresholds. The data support the proposals of Nord and Kyler (J.Comp. Neur., 134:485-494, 1968) that (1) LRF operates in facial pain sensibility and that (2) it does so by modulating nocioceptive neuronal activity flowing centripetally along classically described pathways from trigeminal structures of the medulla.

**36.2** SENSORY ORGANIZATION OF THE MESENCEPHALIC PONTINE RETICULAR FORMATION IN RATS. S. Walden Miller* and Philip M. Groves. Dept. Psych., Univ. Colo., Boulder, 80302

Sensory responsiveness of neurons in the reticular formation of the albino rat, extending from the level of the anterior border of the superior colliculus posteriorly to the level of entrance of the eighth nerve, was determined using extracellular tungsten microelectrode recording. Peripheral stimuli in three modalities (light flash, auditory click, tactile stimulation) were used to determine response properties. Electrolytic lesions at the base of electrode tracks were used to localize cells in a given animal. Distributions of cells responsive to one or more of these peripheral stimuli were mapped along the length of the reticular core. Neurons responsive to visual stimulation were located anteriorly in the reticular formation subjacent to the superior colliculus. Those responsive to auditory stimulation were located most extensively where the inferior colliculus and nucleus of the lateral lemniscus merge with the reticular formation. Tactile responsive elements were evenly distributed throughout the reticular core although some evidence of "somatotopic" organization was found for cells having small receptive fields. Those with receptive fields restricted to the posterior third of the body were most commonly in the posterior portion of the reticular formation, those responding to the middle third of the body were in the middle portions of the reticular formation, and those responding to the anterior third of the body were located anteriorly, or posteriorly near the sensory nucleus of the trigeminal nerve. These distributions are consistent with the known anatomical inputs to the reticular formation of the brain stem.

Supported by Grant MH 19515 from NIMH.

**36.3** DYNAMIC TRANSFER CHARACTERISTICS OF THALAMIC SENSORY NEURONS. T.C.T. Yin* and W.J. Williams. Bioelectrical Sciences Lab., Dept. Elect. and Computer Engineering, University of Michigan, Ann Arbor, Michigan 48105.

The dynamic transfer characteristics of sensory cells in the nucleus ventralis posterolateralis (VPL) of the thalamus were studied in lightly anesthetized and unanesthetized cats. Standard techniques for recording extracellular single unit activity were employed. The unanesthetized preparations were held in the standard Horsley-Clarke plane by an acrylic chamber mounted on the skull several days preceding the recording session. The response of rapidly-adapting neurons in the knee joint proprioceptive system were studied. The input parameter was movement of knee angle, i.e. rotation of the tibia with respect to the femur. Discrete and logarithmically swept sinusoidal inputs from .1 to 7.0 Hz were applied to the knee joint. The describing function of the neural output was found by correlation and spectral analysis techniques on a minicomputer. The frequency response for VPL phasic responses showed a high-pass, acceleration-sensitive characteristic. When this was compared with dorsal column nuclei cells of the same modality and with a similar response (Williams, et al., Soc. Neurosciences, 1: 10.8, 1971), it was found that the thalamic neurons contributed a low-pass filtering effect. In addition there is less harmonic distortion at the VPL level than at lower levels. The evidence indicates that the thalamic synapses may integrate the afferent pulse trains temporally by low-pass filtering and spatially by reciprocal inhibition. The results for the anesthetized cats were quite similar to the unanesthetized results for these phasic responses. Our results suggest that angular acceleration information may project, via the dorsal columns, to the dorsal column nuclei, the VPL, and the cortex. (Supported by USPHS Grant NS 08470).

**36.4** THE IMPORTANCE OF CEREBRAL CORTEX FOR THE CENTRAL PROCESSING OF TEMPORALLY ORDERED SOMESTHETIC AFFERENT INPUT. R.H. LaMotte and V. B. Mountcastle. The Johns Hopkins University School of Medicine, Baltimore, Maryland 21205.

Rhesus monkeys were trained to detect the presence of mechanical sine wave stimuli delivered to the palmar skin, and detection thresholds measured at a number of frequencies. In another task, they were trained to make a successive discrimination between two such stimuli of different frequency. Detection thresholds and the frequency-difference limen were measured for both monkeys and humans; they were identical for the two, i.e., the frequency limen is 2 - 3 Hz at 40 Hz. Monkeys were then subjected to removal of cortical areas 3, 1, 2, 5, and the second somatic, and tested for detection and frequency discrimination capacity over long postoperative periods. There was a temporary elevation of thresholds for detection on the contralateral hand, especially for lower frequencies followed by a return to normal. The cortical removal resulted in a complete and permanent incapacity to discriminate between mechanical stimuli delivered to the contralateral hand, at least for the frequency differences up to 30 x normal limen tested. (Supported by USPHS Grant NB-06828)

**36.5** LONG DURATION SEQUENCE OF RESPONSES IN SENSORIMOTOR CORTEX N.R. Kreisman and I.D. Zimmerman, Depts. of Physiology, Tulane U. Sch. Med., New Orleans, La. 70112 and Med. Coll. Penna., Phila., Pa. 19129.

Single cortical neurons have been reported to yield a short high-frequency burst of action potentials in response to stimulation of the contralateral body surface. In contrast, we found in squirrel monkeys anesthetized with chloralose that electrical or tactile stimulation of the contralateral forepaw produced a discharge sequence lasting 140-2000 msec. This response was observed in 80% of the 123 neurons tested and was found to be composed of as many as four distinct phases in an excitation-inhibition-excitation-inhibition sequence. In many cases, however, only portions of this sequence were present. All phases of the response were graded with intensity of stimulation with each of the phases becoming more distinct as intensity increased. The number of action potentials evoked at different intensities was not always a good indicator of the strength of stimulation. The later phases of the sequential response appeared to be independent of the presence of the earlier phases since later phases often occurred in the absence of the earlier ones. These findings indicate that the potential for representation of cutaneous tactile information in the discharge of single neurons in sensorimotor cortex may be greater than previously expected.

**36.6** REGULATORY INFLUENCES ON THE LARYNGEAL INPUT TO THE SOLITARY TRACT NUCLEUS. Barry J. Sessle, University of Toronto, Toronto, Canada.

Previous studies indicate that the solitary tract nucleus (NST) is the site for the first synaptic relay of laryngeal sensory information passing to higher centers or to other brain stem areas involved in reflex activity such as swallowing and coughing. Studies have been undertaken to examine central mechanisms underlying laryngeal function, and in the present investigation, extra-cellular recordings were made from single NST neurons with a laryngeal input. Neuronal discharges evoked from the larynx could be inhibited for up to 300 msec by conditioning stimuli applied to cranial nerves V, IX, or X (its superior laryngeal branch, SLN). A possible presynaptic contribution to this inhibition was investigated by recording in the nodose ganglion from single primary neurons which innervated the larynx and which could be antidromically activated from NST. A presynaptic effect on the NST endings of a laryngeal unit was determined by noting any change in the excitability of its endings produced by conditioning stimuli applied to various cranial nerves and central structures. Conditioning stimulation of V, IX and SLN produced an increase in excitability (presynaptic depolarization) with an onset, peak and duration similar to the time course of the inhibition noted in NST neurons. These findings indicate that the laryngeal input to NST neurons is modulated by inputs from other orofacial regions and that presynaptic inhibition contributes to this regulation.

Supported by Canadian Medical Research Council Grant D.G.-73.

**36.7** Modification of unit activity in hypothalamus and reticular formation by sensory and central stimulation. G. Dauth, N. Dafny, L. Marco, M. Glusman, and S. Gilman
Depts. of Neurology and Psychiatry, College of P&S, Columbia Univ., N. Y. 10032

Spontaneous activity and effects of click and amygdala stimulation on single units in anterior hypothalamus (AH), ventromedial hypothalamus (VMH) and mesencephalic reticular formation (MRF) were recorded extracellularly in rats and evaluated with a PDP-12 Computer, providing post-stimulus (PST) and time interval (TI) histograms, mean intervals, standard deviation, and total number of spikes. The Critical Ratio Test was used to evaluate the responsiveness. 50, 60 and 73% of neurons responded to clicks in AH, VMH, and MRF, respectively, while 80, 70 and 75%, respectively, responded to amygdala. In AH and also in VMH, 64% of the units responsive to clicks increased in firing rate but in MRF only 35% increased. In AH 47% of the units responsive to amygdala increased in firing rate, in MRF 45%, but in VMH, 62% increased. In AH, 66% of units responded to both stimuli (convergence cells); the remaining 34% responded only to amygdala. 50% of convergence cells responded by increase, 50% by mixed responses (increase to one modality, decrease to the other). In VMH 69% of units were convergence cells, 19% responded only to click, and 12% only to amygdala. 65% of convergence cells responded by increase, 23% by decrease and 12% by mixed responses. In MRF, 80% of units were covergence cells, 10% responded only to click, and 10% only to amygdala. 32% of convergence cells responded by increase, 55% by decrease and 13% by mixed responses. The PST and TI histograms showed four patterns of inhibition and four of facilitation. These results indicate that the two stimuli utilized produce different patterns of responses in the three sites of recording, indicating that these three structures have significantly different properties.

Supported by USPHS Grants NS 2552, NS 05184 and NH 10315.

**36.8** DYNAMIC RESPONSES OF PRIMATE WARM FIBERS. Carole Lamotte*, Kenneth Johnson, Ian Darian-Smith, Martin Goswell*, and Randall Long*. Dept. Physiol., Johns Hopkins Med. Sch., Baltimore, Md. 21205

Single "warm" fibers were dissected from the median nerve of the Rhesus. Warm fibers were common; 133 were isolated in 45 experiments. Fibers had spot-like receptive fields 1 mm. or less in diameter; mean conduction velocity for 40 fibers was 1.31 $\pm$ 0.57. The responses to near-rectangular warming pulses were examined at 3 adaptation temperatures (29, 34, 39C). The temporal profiles of these responses contrasted with those seen in "cold" fibers; "warm" fibers rarely responded with the onset transient characteristic of "cold" fibers. The responses to warming pulses, measured as the cumulative impulse count, was dependent on three factors. A. The response increased with stimulus amplitudes from 0 to 8C. B. The response to a warming pulse of fixed intensity increased as the adaptation temperature was increased from 29 to 39C. C. The response was suppressed by preceding stimuli; the greater the intensity and the closer the occurrence of the preceding stimuli, the greater the suppression. When the intensities and interstimulus intervals of warming pulses occurring in the 20 sec. previous to the test stimulus were defined, the response to the test stimulus was accurately predictable.

**37.1** MECHANICAL MECHANISMS OF TRANSDUCTION IN THE GOLGI TENDON ORGAN. John E. Swett and Ture W. Schoultz*. Dept. of Anatomy, Univ. of Colorado Medical Center, Denver, Colorado 80220

Golgi Tendon Organs (GTO) from Ext. Carpi Ulnaris of the cat were prepared using standard electron microscopic techniques. Reconstructions were made from serial sections through areas in the receptor where axon terminals surround bundles of collagen. From the relationships observed, mechanical events within the GTO are proposed which are consistent with known discharge characteristics of Ib axons. Evidence indicates that the mechanical component of the transducer process probably involves physical distortion of the axonal membrane during an increase in tensile forces along the collagen strands. In considering the different ways in which this could be achieved we found evidence to suggest there could be four different mechanical mechanisms: 1. Hydrostatic pressure changes within the GTO capsule, 2. Direct termination of collagen on axons or their coverings, 3. Shearing forces on the axonal membrane, 4. Collagen bundles squeeze the axons. The last is the most plausible explanation for the mechanical event. Contraction or passive muscle stretch would tighten the braided strands of collagen, reduce the size of the spaces, and pinch the nerves laced between them. A collagen bundle which splits to envelop an axon over a short distance can perform the same function. A weak contractile force can theoretically cause a powerful, and maintained, compression of large portions of the Ib terminals' surface area.

Supported by USPHS grants NB 07949, NS 08453 and GM 01981.

**37.2** SIGNIFICANCE OF THE SILENT PERIOD DURING MUSCULAR CONTRACTION. Anthony M. Iannone and Lee T. Andrews*. Dept. Neurosciences, Medical College of Ohio, Toledo, 43614

The pause in firing of muscle spindles during extrafusal isotonic and isometric contraction was studied under varied conditions of load. Shortening was induced by single supramaximal shock to the muscle nerve. Under these conditions a constant force was generated by the muscle for each shock. The duration of the pause in spindle firing was then correlated with different sizes of load on the muscle. Increase of load resulted in decrease of velocity of shortening. This in turn was related to a decrease in duration of the silent period to an irreducible minimum of 60 msecs. The silent period could not be abolished by increase in load until the load was increased beyond the physiologic limits of the muscle. In the isometric situation the same results were obtained. It was concluded that under these conditions (single shock, rapid contraction) the silent period was a constant phenomenon that would exert important central effects, e.g., decrease afferent bombardment of agonist motorneurones, and release from inhibition the motorneurones of antagonist muscles.

**37.3** NEURAL CONTROL OF THE CAT STEP CYCLE: NATURE AND ROLE OF LENGTHENING CONTRACTIONS. George E. Goslow, Jr. and Douglas G. Stuart. Dept. Biol. Sci., NAU, Flagstaff 86001 and Dept. Physiol. Univ. of Arizona, Tucson, 85724.

In studies on the neural control of stepping it is conventional to divide the cat step cycle into swing (foot off ground) and stance (foot on ground) phases, the swing involving F and $E^1$ stages and the stance $E^2$ and $E^3$ stages (cf Engberg and Lundberg, Acta Physiol. Scand. 75: 614, 1969). During $E^2$ (the yield) we have evidence that hip extensors undergo near isometric contractions while knee, ankle and toe extensors undergo lengthening contractions. During $E^3$ all hind limb extensors undergo shortening contractions that culminate in the leg being thrust off the ground. By relating our cinematographic analysis of cat hind limb joint angles and muscle lengths during stepping, jumping and landing to EMG analyses of cat stepping (Engberg and Lundberg, 1969) and human hopping (Melvill Jones and Watt, J. Physiol. 219: 709, 1971) it is possible to emphasize 3 fundamental biomechanical aspects of the step cycle: 1) "elastic bounce" (cf Cavagna, J. Appl. Physiol. 29: 279, 1970) developed when limb extensors become active before rather than after the foot hits the ground; 2) pronounced rates and extents of lengthening contraction during high speed locomotion and landing; and, 3) the stance ($E^2$ and $E^3$) phase as a single mechanical event for extensors: an active stretch-shorten cycle for those operating on knee and ankle and an active isometric-shorten cycle for those operating on the hip. In no way should it be construed that the muscle apparatus operates independent to the nervous system during any phase of stepping. Rather the nervous system can program or even preprogram appropriate mechanical changes for the smooth execution of stepping. (Supported by USPHS grant NB 07888).

**37.4** SLOWLY DEVELOPING HYPERREFLEXIA IN THE CRAYFISH ABDOMEN FOLLOWING NERVE CORD TRANSECTION. Jeffrey J. Wine, Dept. Psychology, Stanford University, Stanford, California 94305.

Long term plastic changes of central neurons could most easily be analyzed if they occurred in restricted neural systems where most of the constituent neurons could be identified. The fast flexor (FF) system of the crayfish abdomen consists of a small number (c. 20) of identified motoneurons in each abdominal ganglion; these motoneurons are activated by two pairs of identified giant command interneurons and by other, as yet unidentified, elements. Prior work established that a reflex mediated by one pair of command interneurons showed a marked increase in excitability immediately after the abdominal cord was isolated from the rostral nervous system. This immediate increase was interpreted as disinhibition (Wine & Krasne, 1969, Proc. Ann. Conv. APA, 237-238).Several days after nerve cord transection, there are further signs of increased central excitability: (1) The electromyogram (EMG) from the FF muscle increases in duration in response to single, threshold shocks to the nerve cord; (2) prolonged discharges can be recorded from the FF motoneuron axons; (3) previously ineffective stimuli, such as pinching the tail, become increasingly effective in eliciting motoneuron discharges. These changes peak about 3 weeks postoperatively, at which time the EMG duration may be 50 times normal. All of these effects can be further characterized by their extreme lability: EMG duration can be reduced to 40% of its initial amplitude by 5 stimuli at 5 min. intervals, and recovery takes longer than 24 hrs. The time course, magnitude and lability of these changes are characteristic features of disuse or denervation supersensitivity. Previous reports of central supersensitivity have been entirely restricted to vertebrates. Supported by USPHS Fellowship, 5-TI-MH-6666, and USPHS Grant (1-R01-NB-8108) to F. B. Krasne.

**37.5** PARADOXICAL CHANGES IN A MOTOR REFLEX RESPONSE TO RETICULAR FORMATION STIMULATION DURING ACTIVE SLEEP. Michael H. Chase and Margaret Babb*, Depts. Anat., Physiol., Sch. Med., UCLA, Los Angeles, 90024.

It is essential in any comprehensive description of physiological phenomena to evaluate state-dependent variations since the activity of practically all neural and hormonal systems changes during sleep and wakefulness. The present research was designed to clarify some of the basic neurophysiological mechanisms underlying the state-dependent central neural control of motor activity. This approach is relatively new, since most studies of the interaction between the central nervous system and somatic activity have involved permanent alteration of the nervous system by lesions, or stimulation in unanesthetized or immobilized animals. Six adult cats were implanted with electrodes in order to record EEG, EOG and EMG activity from a freely moving, unanesthetized animal. Other electrodes were placed to induce and record the brain stem monosynaptic masseteric reflex (jaw closing reflex). Bipolar strut electrodes were positioned in the mesencephalic reticular formation. After recovery from the effects of surgery the animals were stimulated unilaterally (4 pulses - 400 cps - to the reticular formation followed by reflex induction at conditioning latencies of 5-50 msec). Reticular excitation resulted in masseteric reflex facilitation during wakefulness. During quiet sleep reflex facilitation was also present, although its degree was reduced compared with wakefulness. However, as soon as the animal passed into active sleep the response reversed and reflex suppression (inhibition) occurred where there had previously been facilitation. Thus, the direction of response was completely dependent upon the state of the animal. Supported by MH10083 and 1R01 NS09999-01.

**37.6** AVERSIVE CONDITIONING OF CONTACT PLACING IN CATS AND ITS DEVELOPMENTAL ASPECTS. Christian T. Wertenbaker*, Richard J. Ross* and Vahe E. Amassian. Dept. Physiol., Albert Einstein Coll. Med., New York, 10461.

Contact placing is usually modified if a compartment filled with water is substituted for the solid surface upon which the forepaw has previously landed. One-half the cats that placed consistently onto solid stopped placing after 1-15 water trials. The pattern of inhibition varies from no movement upon initial contact to flexion to the paw hanging over the water. Resting the affected paw on a solid for a few seconds usually restores placing; immediate retesting of the same paw into water usually requires fewer trials for inhibition. However, no savings were demonstrated when the contralateral paw was tested. Cats could be trained to inhibit placing selectively to stimulation of either the radial or ulnar aspect of the paw.

Although young kittens exhibit an aversive response to immersion of the forepaw in water, at ages 1-6 weeks they usually continue to place onto water. Inhibition by water is clearly present at 10 weeks, ie several weeks after the sensorimotor cortex is required for contact placing (Fed. Proc. (1971) 30, 434). During the development of inhibition, the initial withdrawal component is affected less than the subsequent landing phase.

In adult cats, unilateral lesions of Forel's fields $H_1$ and $H_2$ resulted in impaired water inhibition of the contralateral forepaw even when lowering the paw into water resulted in withdrawal. Massive lesions of nucleus interpositus or fastigius did not impair water inhibition, nor did lesions of globus pallidus. (Supported in part by USPHS, NIH Grants NS-01603 and NS-5304.)

**38.1** ALTERATIONS IN THE PATTERN OF RNA SYNTHESIS IN GOLDFISH BRAIN DURING TRAINING. Victor E. Shashoua. Department of Biological Chemistry, Harvard Medical School, Boston, MA 02115 and McLean Hospital Research Laboratory, Belmont, MA 02178

The search for biochemical correlates of the information recording and storage process of the nervous system has implicated a role for RNA and protein synthesis. We have developed a sensitive method for detecting changes in the pattern of RNA synthesis during training. The method depends on separating the RNA associated with the brain synaptosomal fraction from its nuclear and cytoplasmic components. In single labelling studies with uridine as the RNA precursor, 16% of the incorporated label was associated with the synaptosomes. This represents the membrane bound RNA fraction. The time course of synthesis and sedimentation patterns of this RNA was determined. In double labelling experiments, groups of goldfish were trained in a new swimming skill and labelled with uridine $H^3$; control groups received uridine $C^{14}$ label. The pooled brains from the two groups were homogenized and fractionated into their cytoplasmic, nuclear and synaptosomal components. The RNA from the synaptosomal fraction showed the largest changes. Increased ratios of $H^3/C^{14}$ were observed in the 4 to 18s regions of the sucrose density gradient patterns of the RNA. These RNA changes were not observed in a variety of non-learning situations. The results suggest that there is a more rapid turnover of specific classes of RNA molecules, corresponding to 2% of the total synthesized, during training. The possibility that this represents an increased demand level for specific classes of proteins is being investigated. (Supported by NIH grant NS09407 and the Grant Foundation).

**38.2** CHANGES IN RADIOACTIVITY IN BRAIN URIDINE NUCLEOTIDE POOLS DURING ACTIVE AVOIDANCE LEARNING. Dan Entingh, Terri Entingh*, Edward Glassman and John E. Wilson. Dept. Biochem., Sch. Med., U. North Carolina, Chapel Hill, 27514

After either subcutaneous or intracerebral injections of uridine-5-$^{3}H$, naive C57Bl/6J male mice were trained for 15 min on a footshock-avoidance task. Training reduced the net amount of radioactivity in brain uridine monophosphate by 20%, while raising the net radioactivity in brain uridine diphosphate sugars by 60%. The same training produced no detectable changes in the incorporation of uridine into total brain RNA. The chemical response was largest in the subcortical forebrain of trained mice, and did not occur in the brains of yoked control subjects. This phenomenon suggests that training may alter the metabolism of brain sugars or polysaccharides. This phenomenon also has important implications for the interpretation of some aspects of previous experiments (E. Glassman & J. Wilson, Brain Research, 21, 157, 1970) which employed the amount of radioactivity in uridine monophosphate as the normalization factor in studying the effects of avoidance training upon the incorporation of uridine into brain RNA. The limited magnitude of the changes in uridine monophosphate substantiates reports of larger increases in the incorporation of uridine into brain polysomes during avoidance training.

**38.3** GRADIENT AND PERMANENCE OF AMNESIA OF A PASSIVE AVOIDANCE TASK IN CYCLOHEXIMIDE TREATED MICE AS A FUNCTION OF THE NUMBER OF TRAINING TRIALS. Elton E. Quinton. Dept. of Psych., Univ. of Louisville, Louisville, 40208

Cycloheximide (cyc) or saline (sal) injected mice were given two (2T) or three (3T) training trials in a passive avoidance (PA) task and tested 1,1.5,3,5,24, or 72 hrs. later (T1). They were tested again (T2) 72 hrs. after the first test. All cyc groups except the 1 hr. groups were inferior to saline controls on T1, but there was no difference in performance on T1 or T2 between any of the 1.5,3,5, or 24 hr. cyc groups. However, the 3T 72 hr. T1 cyc group was superior to the 2T 72 hr. T1, and the 3T 24 hr. T1 cyc groups on both T1 and T2. On T2 all cyc groups were inferior to sal groups except the 3T 72 hr. T1 cyc group, which was also superior to all other cyc groups. The data suggest that 2 or 3 PA training trials do not prevent amnesia during intermediate test intervals, but do abolish the amnesia gradient usually observed at these intervals after 1 training trial; and that recovery from amnesia is a function of the number of PA training trials, partial recovery occuring at 72 hrs. after training in mice given 3 training trials in this study.

**38.4** EVIDENCE THAT MEMORY DEPENDS ON PROTEIN SYNTHESIS WITHIN MINUTES AFTER THE BEGINNING OF TRAINING. Larry R. Squire, Gary A. Smith *, and Samuel H. Barondes. Dept. Psychiatry, Sch. Med., UCSD, La Jolla, 92037.

When mice are trained in a discrimination task (10 sec intertrial interval) 30 min after subcutaneous injection of cycloheximide, they exhibit normal learning for the first 20-30 trials. With continued training, however, performance of cycloheximide-treated mice does not improve as rapidly as that of control mice. When the intertrial interval is lengthened from 10 sec to 45 sec, the deficit is detectable after 10-20 trials. A number of control experiments indicate that this impairment of acquisition cannot be explained by sickness or by known side effects of cycloheximide on locomotor activity. Cerebral protein synthesized during or shortly after training has been presumed to be required some time later for normal expression of memory. In previous studies a requirement was detectable only hours after training. It now appears that in some circumstances proteins synthesized during training may be required within minutes after the beginning of training for normal expression of memory.

**38.5** POTENTIATING EFFECT OF ADRENOCORTICOTROPHIC HORMONE ON CYCLOHEXIMIDE-INDUCED AMNESIA IN MICE. Arnold M. Golub and Robert H. McCluer. Eunice Kennedy Shriver Center, Waltham, Massachusetts, 02154.

The purpose of these experiments was to study the effect of adrenocorticotrophic hormone (ACTH) on cycloheximide (CXM) induced amnesia. Mice (C57BL/6J) were injected with 90 mg/kg of CXM and trained 30 min. later in a passive avoidance task. These animals learned normally and had normal "short-term" memory; however, they were amnesic when tested 24 hrs. after training. Amino acid incorporation studies indicated that cerebral $^{14}$C-leucine uptake was inhibited 90-95 percent within 30-60 min. after CXM injection and that recovery of normal cerebral amino acid incorporation was complete within 24 hrs. Mice injected with 12 I.U. of ACTH and subsequently (30 min.) injected with 90 mg/kg CXM died within 12-30 hrs. Mice given ACTH alone behaved normally. Of animals injected with a lower dose (40 mg/kg) of CXM, which inhibited cerebral $^{14}$C-leucine incorporation 80-85 percent at 30-60 min. after injection but which was without effect after 6 hrs., about half had memory deficits. An injection of 12 I.U. of ACTH preceding the 40 mg/kg CXM dose produced amnesia 24 hrs. later in virtually 100 percent of the animals, a result not seen with ACTH or CXM alone at the doses used. The ACTH pre-injection did not appear to potentiate (affect) the CXM-induced inhibition of cerebral $^{14}$C-leucine incorporation. These results suggest that the potentiation of the CXM induced amnesia by ACTH is not related to cerebral protein synthesis inhibition.

**38.6** THE LEARNING-ENHANCING DRUG UCB 6215: EFFECTS IN GOLDFISH. Gary Barnett, Rodney C. Bryant, Frederick Petty, Larry A. Kepner, and William L. Byrne. Brain Research Institute, Univ. of Tenn. Med. Units, Memphis 38103.

The report that the experimental drug UCB 6215 (2-oxo-1-pyrrolidine acetamide) considerably enhances learning in the rat (Wolthuis, Eur. J. Pharmacol. 16:283-297, 1971), raises the question of how a drug that is practically non-toxic (LD50> 8 g/kg) exerts its effect on learning, and poses the additional question of its activity in lower vertebrates. Common goldfish (Carrasius auratus) were given a single training session of active dark-avoidance, a relatively difficult task for fish and one which minimizes the problems of pseudo-conditioning and sensitization characteristic of light-avoidance training. When incubated in a solution of the drug before and after training (UU), or before only (UW), fish displayed enhanced learning when tested in extinction. By contrast, fish not exposed to the drug (WW), or fish incubated only after training (WU), showed similar, lower, levels of dark avoidance responding in extinction. When fish trained to dark avoid were tested for spontaneous light-avoidance in addition to dark avoidance testing, WU fish made more light-avoidance responses than WW fish, while UU and UW fish made fewer. Analysis of general shuttling activity showed that fish tested under the influence of the drug (WU and UU) were less active during testing than WW and UW fish. Results indicate the effects of UCB 6215 are not state dependent in the goldfish.

**38.7** THE EFFECTS OF MAGNESIUM PEMOLINE ON THE HABITUATION OF AN IMMOBILITY RESPONSE IN CARASSIUS AURATUS. Richard D. Olson*, S. Thomas Elder* and James G. May. Dept. of Psychology, LSUNO, Lakefront, New Orleans, Louisiana 70122.

After an initial adaption period in a tall, narrow tank, fish typically swim up and down at a fairly constant rate. If a loud buzzer is sounded during the ascent, a fish will often become immobile and remain near the bottom of the tank. Upon repeated experience with the buzzer, this immobility response habituates and the rate of ascent and descent gradually approaches the normal rate. The immobility response was facilitated by a 10 mg/Kg IP injection of magnesium pemoline. Rate of habituation was greater in the experimental drug group than either the drug or buzzer control. General activity among the three groups was not found to differ significantly although testing time did. It was concluded that the observed experimental drug effect resulted from an increased reactivity to novel stimuli due possibly to the facilitation of adrenergic transmission.

**38.8** EFFECTS OF CARBON DIOXIDE AND FLUROTHYL UPON RETENTION OF ONE-TRIAL LEARNING 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.

Goldfish were trained in a single trial with electric shock (15 V) to avoid swimming upstream into a quiet well. The measure of memory retention was their median avoidance time during a 30-sec test trial. Independent groups were tested at graded intervals after shock (1, 4, 16, 64, or 256 hr); experiments were run at 15°, 20°, and 25°C. Under these conditions, avoidance decreases biphasically, with a minimum 1 min after training [Science 172: 966, 1971]. In the present experiment, trained fish (N=76) were immersed for 3 min in water saturated with 80% $CO_2$: 20% $O_2$, starting 1 min post-training. The $CO_2$-treated fish showed no avoidance in subsequent tests, indicating retrograde amnesia. Trained fish (N=130) were also immersed for 15 min in aerated water containing 566 mg/l of a convulsant ether (flurothyl, $CF_3CH_2OCH_2CF_3$), starting 1 min after training; 90% recovered within 10 min after transfer to fresh water. Flurothyl-treated fish showed little avoidance 1 or 4 hr after training but their avoidance increased at the 16-, 64-, and 256-hr intervals and exceeded significantly that of untrained, flurothyl-treated controls and of trained, untreated fish ($p < 0.01$, Mann-Whitney U tests), indicating an apparent enhancement of retention. The avoidance of trained fish, with or without flurothyl treatment, was an inverted-U function of temperature. The enhancing effect of flurothyl upon memory in goldfish differs from the amnesic effect reported for rodents and chicks.

**39.1** A MATHEMATICAL DESCRIPTION OF THRESHOLDS FOR ELECTRICAL STIMULATION OF SUBCORTICAL AUDITORY STRUCTURES. George M. Gerken. Callier Hearing and Speech Center, Dallas TX 75235

A mathematical formulation has been developed to describe behaviorally measured detection-thresholds obtained with various parameters of electrical stimulation. The formulation is derived from the work of L. Lapicque, B. Katz, and J. Zwislocki. It is assumed that: (1) only the portion of a current pulse, $I$, greater than a constant, $R$, is effective in activating the neural elements; (2) the effectiveness of the pulse increases as $1-e^{-d/\delta}$ where $d$ is the pulse duration and $\delta$ is the duration time-constant; (3) the effectiveness of a pulse decays exponentially with time and that the effects of several pulses summate according to the present value of the exponential sum, $\sum_n e^{-t/\tau}$, where $t$ is time of pulse presentation re the present time, $\tau$ is the repetition-rate time constant, and $n$ is the number of pulses presented. The neural excitation is detected behaviorally when it reaches a value $L=(I-R)(1-e^{-d/\delta})\cdot\sum_n e^{-t/\tau}$. An empirical procedure is used in conjunction with the behaviorally measured thresholds to evaluate $R$, $\delta$ and $\tau$. The formulation can be used to predict detection thresholds for a wide range of electrical-stimulation parameters, and provides a parameter-free index, $L$, of regional brain-sensitivity. This work supported in part by a grant from the National Institute of Neurological Diseases and Stroke.

**39.2** BULLFROG INNER EAR RECEPTORS: STRUCTURAL DIFFERENCES RELATED TO FUNCTION. E. R. Lewis. Electr. Engrg. Dept., Univ. of Calif., Berkeley, 94720.

Scanning electron microscopy of frog labyrinthine sensory areas reveals marked differences in the arrays of stereocilia and true cilia (kinocilia). Some differences appear related to the accessory structures associated with each area. The length and shape of the kinocilium appears also to be related to the specific sensory task of the area. All four pars-superior areas (three cristae and the utricular macula) show tonic or slowly adapting responses [Precht et al.,Exp. Brain Res.13:378,1971; Ross,J.Physiol. 86:117,1936]; the hair cells of all four have kinocilia of uniform diameter and considerably longer than the longest stereocilia. Among the four pars-inferior areas, the lagenar macula alone seems to respond tonically, while the saccular macula (with its otolithic superstructure similar to those of the utricular and lagenar maculae) is a phasic, vibration sensor [Ross, ibid.]. The basilar and amphibian papillae also are phasic, responding primarily to acoustic stimuli [Frishkopf et al.,Proc. IEEE 56:969, 1968]. On the surface, lagenar hair cells are nearly indistinguishable from utricular hair cells; the kinocilium is uniform and several times as long as the longest stereocilia. On the other hand, each hair cell of the saccular macula has a short kinocilium expanded at its distal end to form a large bulb which connects to the tips of the several longest stereocilia and to the membrane supporting the otolith [Hillman, Brain Res.13:407, 1969]. In the two papillar maculae, which are associated with tectorial membranes rather than otoliths, the hair cells are nearly indistinguishable from those of the saccular macula; here the bulb of the kinocilium apparently connects to the tectorium as well as to the tips of the longest stereocilia. Thus, in the frog, tonic or nearly tonic receptors have long kinocilia without bulbs; phasic receptors (both otolithic and tectorial) have short kinocilia with distal bulbs. We suspect that therein lies a significant clue to the mechanisms of transduction.

**39.3** A NEURAL MODEL OF THE LATERALITY EFFECT IN DICHOTIC LISTENING. Karl E. Achenbach. Dept. Psychology, Univ. of South Florida, Tampa, Fla. 33620

When different verbal materials with the same meaning value or saliency, e.g., digits, are presented simultaneously to the two ears in the paradigm developed by Broadbent (JEP 47:191, 1954), right-handed subjects with speech controlled by the left hemisphere show a superiority of the right ear by a variety of criteria. This right-ear dominance for verbal material has been reported by a number of investigators. Bryden (JEP 65: 103, 1963) concluded that the auditory system is better organized for the perception of verbal materials to the right ear. The following model is an attempt to specify the nature of this organization. Although both ears project, ipsilaterally and contralaterally, to both hemispheres, the contralateral pathway seems to be stronger, i.e., more numerous or more efficient fibers. This model predicts that all ipsilateral projections, at some point, synapse on a population of neurons which also receive converging contralateral input. Not all contralateral fibers, however, impinge on neurons receiving ipsilateral input as well. When different material is presented to both ears, the neurons receiving converging input cannot process the confounded information. Consequently, only the unconfounded contralateral paths carry ungarbled information to the language decoding areas. The pathway from the ear contralateral to the speech hemisphere is direct, whereas the information from the ipsilateral ear must be relayed from the non-speech hemisphere via callosal pathways. This model accounts for the results obtained by Milner, et al. (Science 161:184, 1968) and Sparks and Geschwind (Cortex 4:3, 1968) on patients with section of the neocortical commissures who showed complete suppression of ipsilateral inputs in the dichotic task with no suppression of monaural ipsilateral input. The model does not specify, at this time, the locus of the convergence.

**39.4** ANATOMICAL CONNECTIONS OF THE INFERIOR COLLICULUS OF THE TREE SHREW (TUPAIA GLIS). J. H. Casseday and J. K. Harting*. Departs. of Anat. and Psychol., Duke Univ., Durham, N. C. 27706.

As one in a series of experiments on the evolution of the mammalian auditory system, we are investigating the afferent and efferent connections of the inferior colliculus of the tree shrew utilizing anterograde degeneration techniques. Following large lesions in the inferior colliculus, degenerating fibers pass rostrally exclusively within the brachium of the inferior colliculus and terminate within the medial geniculate nucleus, the posterior nuclear group and to a lesser extent within the ventral posterior nucleus. Little if any terminal degeneration was observed within the superior colliculus. These findings suggest (1) that whatever auditory input there is to the superior colliculus does not arise from the inferior colliculus and (2) that degeneration previously observed in the posterior nuclear group after lesions of the superior colliculus was not the result of the interruption of fibers en passage from the inferior colliculus. In addition to the ascending pathway, a major portion of the efferents descended and terminated in auditory structures within the lower brainstem. A division of the inferior colliculus of Tupaia can be made on the basis of its afferent supply. The capsule receives fibers primarily from the cortex while the central nucleus receives fibers primarily from the lateral lemniscus. We have not yet determined whether this division of the inferior colliculus is reflected in its efferent projections. (Supported by NINDS Grant NS-09623 to W. C. Hall and NIMH Grant MH-4849 to I. T. Diamond)

**39.5** THE EFFECTS OF UNILATERAL AND BILATERAL ABLATIONS OF AUDITORY CORTEX IN THE CAT ON BINAURAL MASKING AND UNMASKING. Jerry L. Cranford. Center for Neural Sciences, Indiana Univ., Bloomington, Ind. 47401.

Cats with earphones were trained in a grill box to respond to the occurrence of intermittent 1k tone pips at one ear while continuous white noise bursts were presented to the opposite ear. Normal cats exhibited a contralateral masking effect at both ears as evidenced by a 5-6 db rise in threshold for the detection of the tone. For cats with large unilateral auditory cortex lesions there was an asymmetry between the ears in the size of the masking effect. When the tone was presented to the ear contralateral to the lesion there was a 10-12 db rise in threshold whereas the threshold shift at the ipsilateral ear was 3-4 db. With both operated and normal cats these masking effects were only observed if the tone and noise occurred simultaneously in time. No masking occurred if a silent interval separated the tone and noise. Preliminary evidence indicates that subsequent ablation of the remaining auditory cortex results in a cancellation of the unilateral lesion effect in that bilateral cats exhibit the smaller symmetrical masking effect characteristic of normals. In addition to presenting tones and noise to opposite ears we also investigated the effects of presenting the tone to only one ear but with noise of similar or dissimilar intensity levels being simultaneously presented to both ears. This resulted in evidence for an additional asymmetry, this time with respect to the degree of "unmasking" observed at ears ipsilateral or contralateral to the cortical lesion.

**39.6** RESPONSES OF NEURONS IN THE AUDITORY CORTEX OF SQUIRREL MONKEYS TO ACOUSTICALLY SIMILAR VOCALIZATIONS. John D. Newman and Zvi Wollberg, NIH, NICHD, Bethesda, Maryland 20014

Single neurons in the auditory cortex of squirrel monkeys were tested for their ability to discriminate between pairs of acoustically similar vocalizations. Tape recordings of four natural vocalizations, representing acoustically different call groups, were each paired with another similar vocalization. The members of each pair of vocalizations differed in one or more aspects of acoustic structure, but were within the normal range of acoustic variation for that call-type. More than half of the 46 neurons tested responded to only one member of one or more call pairs. In addition, a significant number of neurons responded with distinctly different discharge patterns to each member of a call-pair. Single neurons in this brain region were also tested with nine natural variants of a single call-type (Isolation Peep). Seven of these variants were judged to be typical of this call type. The responses of 21 units tested with all nine variants were analyzed. A majority (57%) responded to all nine Isolation Peeps. Another 19% responded to all seven typical Isolation Peeps, but not to one or the other atypical call. In only one case did a cell fail to give a clear response to one of the seven typical Isolation Peeps while responding to the rest. The remaining 21% of the units showed selective responsiveness to different sub-groups of typical Isolation Peeps. This selective behavior of neurons was not readily attributable to any clear-cut acoustic differences in Isolation Peep variations.

**39.7** MOTIVATIONAL FACTORS INFLUENCING AUDITORY CORTICAL EVOKED POTENTIALS IN THE CAT. George Karmos* (Spon: K.R. Unna). Dept. of Pharmacol., Univ. of Ill. Med. Center, Chicago, Ill. 60680 and Inst. of Physiol., Univ. Med. School, Pécs, Hungary

Changes in auditory cortical evoked potential (AEP) waveforms were studied in different behavioral situations in chronically implanted cats. To maintain the constancy of the auditory input the click stimuli were delivered through a bone conductor (Electroenceph. clin. Neurophysiol. 1970, 28:637). After a long term habituation three AEP patterns could be recorded from the different parts of the primary auditory area in the waking animal. The early components showed only minor changes. The changes in the late components were closely related to the alterations in the animal's arousal level. A negative component of 40-60 msec peak latency appeared in the highly alert animal. In drowsiness and slow wave sleep it was gradually replaced by a positive component. During the rapid eye movement periods in paradoxical sleep AEP patterns were obtained which were similar to those appearing in highly alert animals. Similar changes were recorded when the AEPs, elicited by clicks of no signal meaning, were studied during the acquisition and performance of a conditioned avoidance response. It is concluded that the changes in the animal's motivational level are sensitively reflected by the changes of the AEP waveforms.

**39.8** "MIRROR-IMAGES" IN HEARING. Marilyn L. Pinheiro and Lee Thomas Andrews*. Dept. Neurosciences, Medical College of Ohio, Toledo, 43614

The perception of auditory patterns involving an intensity difference was tested by using triads of temporally spaced noise bursts. A PDP-12 computer randomly selected patterns and presented them binaurally to normal-hearing subjects. Digital-to-analog converters controlled the intensity and duration of the noise bursts and interstimulus intervals. Pattern stimulus and response were stored in pairs, and results were analyzed by the computer. Reversals, similar to mirror-images in vision, made up a significant percentage of error responses. Three types of pattern reversals occurred: (1) reversal of the acoustic image of the pattern, (2) reversal of the temporal sequence of the pattern, and (3) a reversal made up of a combination of the first two. Other investigators have found that pigeons and optic chiasm-sectioned monkeys, monocularly trained to discriminate visual patterns, showed preference for reversed responses when the other eye was tested. Results of the present study also support the hypothesis that interhemispheric interaction is involved in pattern discrimination and reversals. The physiology of auditory pattern discrimination may parallel that of visual pattern discrimination, since both primary sensory systems demonstrate similar perceptual phenomena.

**41.1** VISUAL-VESTIBULAR INTERACTION: EFFECT OF VISION ON PER- AND POST-ROTATORY NYSTAGMUS. Bernard Cohen. Dept. of Neurology, Mt. Sinai School of Medicine, New York, N.Y. 10029.

Optokinetic nystagmus (OKN) is followed in the monkey by 60 to 70 sec of after-nystagmus (OKAN) in the same direction if the animal is placed in total darkness. OKAN does not occur in light. We have previously shown (Neuroscience, 1971) that OKAN is abolished if the labyrinths are destroyed. The purpose of this note is to further ellucidate the interaction between nystagmus induced by the visual and vestibular systems. (The work was done with S. Takemori.)

Eye movements of normal monkeys were recorded using electrooculography (EOG). Animals were rotated on a rotating platform and/or watched a moving drum which surrounded them and filled their field of vision. Both drum and platform could be moved independently. Rotation in darkness induced per-rotatory nystagmus which disappeared after 20-30 sec of continuous rotation. Rotation in light induced nystagmus whose slow phase velocity was maintained throughout the period of rotation. At the end of rotation OKAN and post-rotatory nystagmus summated precisely in darkness. Thus animals could have post-rotatory nystagmus, OKAN or neither depending on the intensity of the optokinetic and rotating stimuli which were used. Post-rotatory nystagmus was consistently shorter if animals were rotated in light rather than in darkness.

Under most circumstances movement of the whole visual field implies that the head is moving in space rather than vice versa. Thus it seems appropriate that OKN and OKAN act to enhance nystagmus during rotation and reduce it after rotation. The suggestion that an important function of OKAN is to reduce post-rotatory nystagmus is consistent with the fact that OKAN appears to arise from activity generated in the peripheral labyrinths during OKN. Supported by Grants NS-00294 and 1K3-34,987.

41.2 RESPONSES OF INTERPOSITUS CELLS TO STIMULATION OF CUTANEOUS MECHANORECEPTORS. John C. Eccles, Ingmar Rosén*, Peter Scheid* and Helena Táboříková. Dept. of Physiology, State Univ. of N.Y. at Buffalo, N. Y. 14226.

The Pacinian corpuscles (PC), the rapidly adapting mechanoreceptors (RA) and the slowly adapting mechanoreceptors (SA) of the cat forefoot and hindfoot as well as the hair follicle receptors of the adjacent hairy skin were stimulated by precisely controlled and timed brief mechanical stimuli. Cutaneous or mixed nerves in each of the four limbs were stimulated in continuity. The unitary action potentials in the interpositus nucleus were recorded by extracellular technique, using averaging procedures. Strong excitatory and inhibitory effects were produced by inputs from the PC and RA receptors in the footpads of both forelimb and hindlimb, often with thresholds as low as to activate PC selectively. Similarly, strong effects were evoked from hair follicle receptors. In contrast, SA receptors were much less effective. Typically the cells showed a wide convergence of receptors of different types with large receptive fields often comprising more than one limb. The latency distributions reveal only weak input from the direct spino-cerebellar or cuneo-cerebellar pathways. As with the fastigial nucleus (Eccles et al., Brain Research 35 (1971) 523-527) the interpositus nucleus was demonstrated to have direct afferent connections from the lateral reticular nucleus; similar connections presumably exist also from the inferior olive. These inputs exert both excitatory and inhibitory effects by facilitation and disfacilitation respectively. The Purkyně cells exert a direct inhibitory action in the interpositus cells, but also excite by disinhibition.

41.3 THE ACTIVITY OF DENTATE NEURONES DURING THE PERFORMANCE OF A PATTERN MOVEMENT. R. J. Grimm, D. S. Rushmer, Robert Wear*, Ronalds Newton*. Laboratory of Neurophysiology, Good Samaritan Medical Center, Portland, Oregon, 97210.

Discharge properties of dentate neurones were studied in squirrel monkeys taught to touch on command a sequence of buttons to obtain a hypothalamic stimulus reward. The object of this work was to determine if single units in this nucleus are involved in the performance of complex, but stereotyped motor patterns utilizing repeating sequences of many muscles, or instead, are more concerned with the activity of single muscles. Thach J. Neurophysiol., 31:359-367, 1968) has shown that dentate cells alter their discharge rates prior to the onset of simple wrist movements against active resistance. Older clinical literature (Holmes, G., Brain, 62:1-30, 1939) has suggested that the cerebellar hemispheres were involved with the initiation of movement. In our experiments, pre- and post-event (button touches) histograms correlating spike event times with specific epochs within the performance reveal that specific subpopulations of dentate cells alter their discharge characteristics after the onset of movement; that such alterations are invariably associated with a portion of the complex pattern; that different areas of the nucleus appear to deal with different parts of the complex movement pattern; and, that unit correlations are grossly stable in location as seen in recordings from subsequent days in the same animals. Conclusions from these studies are that (1) dentate neurones discharge at specific times in a pattern performance and that different subsets of neurones within the nucleus are concerned with different parts of the performance, and (2) the cerebellar hemispheral system appears more interested in sequences of multiple muscles involved in the strategy of performance rather than the performance or control of specific parameters of single muscle activity.

**41.4** SINGLE CELL RESPONSES FROM THE CEREBELLUM OF RHESUS PRECEDING VOLUNTARY, VESTIBULAR AND OPTOKINETIC SACCADIC EYE MOVEMENTS. R. Llinás and J. W. Wolfe*. Div. Neurobiology, Dept. Physiology & Biophysics, Univ. Iowa, Iowa City 52240, and Vestibular Lab., USAF School Aerospace Medicine, San Antonio, Texas 78235.

Purkinje and granule cell responses were recorded extracellularly from vermal folium VIIa in unanesthetized rhesus monkeys (Macacca mulatta). Their heads were restrained with a special device while the animals were sitting, free to move their limbs. Ocular movements were monitored in the horizontal plane by means of electro-oculogram (EOG) with electrodes placed bilaterally at the outer canthi. Special computer facilities were utilized to indicate the exact onset of saccadic eye movement induced by either voluntary, vestibular (responding to angular acceleration in the dark) or optokinetic stimulus. Purkinje cells recorded with NaCl-filled micropipettes were seen to fire 15 to 20 msec prior to the beginning of the saccade, regardless of stimulus utilized, and to continue firing for a period of about 30 msec from the initiation of the spike train. Granule cell activation had a similar temporal distribution. This response, which is slightly directional, was especially clear during small saccades. The relation between size of the saccade and the duration and frequency of the Purkinje cell spike train seems to be inversely related to the amplitude of the saccade (in fact to the duration of the twitch in the extraocular muscles). These findings suggest that the cerebellum is involved in the control of duration of the saccade in a ballistic sense and thus the final position which the eye is to reach at the end of the movement. These findings are also consistent with the view that the same pathways are utilized for reflex and voluntary saccades. (The research was conducted at the USAF School of Aerospace Medicine and supported in part by USPHS grant No. NS-09916 from NINDS)

**42.1** ALTERATION IN CATECHOLAMINE FLUORESCENCE AFTER LOCAL FREEZE LESIONS IN CEREBRAL CORTEX OF RABBITS= Florry P. Bowen*,(Spon: D. H. Harter). Dept. Neurol.,Columbia College Phys. & Surgeons.New York 10032

Previous studies have described the accummulation of intra-axonal catecholamines as a consequence of injury to peripheral nerve and to subcortical pathways. This investigation was begun in order to study in situ the distribution of biogenic amines under neuropathological conditions of the rabbit cerebral cortex using the histofluorescent technique of Falck et al.(1962). Freeze lesions were made in rabbit motor cortex and animals were sacrificed at 3 hours, 24 hours, 1, 2, 4 and 12 weeks after surgery. At three hours there is an increase in the visible fine network of adrenergic nerve terminals as well as an increase of noradrenaline within individual varicosities. By one day, many of the terminals around the lesion appear very swollen and distorted because of excessive accummulation of noradrenaline. The swollen terminals are still present after 4 weeks within the edge of the lesion together with short thin green fluorescent fibers. At 12 weeks there is still an increase in the adrenergic network. Reserpine injection 18 hours prior to removal of brain abolished fluorescence in terminals and vessels. In addition to the catecholamine fluorescence, green autofluorescent motor cortex cells become visible one week after freezing. When the freeze lesions are contrasted with stab wound lesions, it is found that autofluorescent cells are present inboth, but the very swollen terminals are not seen in the stab wound lesion. Sham operated controls do not have abnormal fluorescence. Since freeze lesions have a marked effect on the noradrenaline in the terminals, it is postulated that this may contribute to the development of epileptogenic foci as a consequence of freezing.

(This work is supported by NSO 5184)

**42.2** EFFECTS OF MONOAMINE PRECURSORS ON ENHANCEMENT OF THE SPINAL MONOSYNAPTIC REFLEX BY PARA-METHOXYPHENYLETHYLAMINE (PMPEA). J. D. Coulter, A. M. Bird*, J. C. Willis* and W. D. Willis. Marine Biomedical Institute, University of Texas Medical Branch, Galveston, Texas, 77550

In spinal cats anesthetized with chloralose and paralyzed with gallamine triethiodide, intraveneous injections of PMPEA produce a consistently repeatable enhancement of the monosynaptic reflex recorded from hindlimb muscle nerves in response to stimulation of dorsal roots. Since alpha-adrenergic and tryptominergic blocking agents anatagonize this effect (Walker, Willis & Willis, Br. J. Pharm 38:106, 1970), the action of PMPEA on monosynaptic reflex transmission may be mediated indirectly via monoamine synapses in the spinal cord. Therefore, the present experiments sought to determine whether alterations of monoamine stores by administration of 5-hydroxytryptophan (5-HTP) or 3, 4-dihydroxyphenylalanine (DOPA), precursors of serotonin and norepinephrine respectively, might also affect the ability of PMPEA to enhance monosynaptic reflexes. Compared to baseline, a single 2.5 mg/kg dose of PMPEA typically produces a 100 to 200 percent increase in size of the monosynaptic reflex, an effect which persists for 10 to 15 minutes. However, an identical injection of PMPEA, when given 30 to 60 minutes following a single 50 mg/kg dose of 5-HTP, produces an increase in reflex size which is 4 to 5 times greater than that obtained without the 5-HTP pretreatment. Although less consistently, a 50 mg/kg dose of DOPA also produces a potentiation of the action of PMPEA on the monosynaptic reflex. 5-HTP and DOPA alone may increase the baseline reflex size, but the magnitude of this effect is comparatively slight. These findings are consistent with the suggestion that the enhancement of monosynaptic reflex transmission by PMPEA may be mediated by release of monoamines within the spinal cord. (Supported by grants from the U.S.P.H.S. (NS09743) and the Moody Foundation.)

**42.3** RADIOAUTOGRAPHIC STUDIES ON NORADRENERGIC AXON TERMINALS OF RAT FRONTAL CORTEX. Laurent Descarries and Yves Lapierre*. Centre de recherche en sciences neurologiques, Université de Montréal, Montréal, Québec, Canada.

Noradrenergic axons, which take up and retain exogenous labeled catecholamines, have been visualized in the frontal cortex of adult rats, using high resolution radioautography following topical application of tritiated DL-norepinephrine (NA-$^3$H). The specificity of the labeling was evidenced by its complete absence in the cortex of rats pretreated, 4 wk earlier, with a single intraventricular injection of 6-hydroxydopamine (300 µg) resulting in the selective destruction of central catecholaminergic neurons. Three hr after a 30 min application of NA-$^3$H (330-340 µCi) in the presence of monoamine oxidase inhibitor, the tracer was highly concentrated within axonal enlargements exhibiting synaptic vesicles. In electron microscope radioautographs, typical junctional zones of synaptic contact were frequently observed between reactive bulbs and dendritic profiles. After optimal labeling, the total number of reactive nerve endings in the frontal cortex was estimated at $13 \times 10^4$ per mm$^3$, representing a mean incidence of 1 noradrenergic terminal per $2.3\text{-}6.9 \times 10^3$ cortical synapses. These reactive bulbs were most numerous in the molecular layer (40%), where their incidence rose to 1 per $.85\text{-}2.6 \times 10^3$ synapses. In layers II-IV, the labeled axon terminals appeared somewhat equally distributed, whereas only few were visible in the upper portion of layer V. Assuming that all noradrenergic endings had been detected, the mean content of endogenous norepinephrine per terminal was roughly estimated at $1.7 \times 10^{-3}$ pg.
(Supported by MRC grant MA-3544).

**42.4** DYNAMIC CHANGES IN DOPAMINE-β-HYDROXYLASE ACTIVITY IN CORTEX, BRAINSTEM, AND CEREBELLUM AFTER HYPOTHALAMIC LESIONS IN RAT. Robert A. Ross* and Donald J. Reis, Laboratory of Neurobiology, Department of Neurology, Cornell University Medical College, New York, New York 10021

The activity of the enzyme dopamine-β-hydroxylase (DBH) was measured in cerebral cortex, brainstem and cerebellum of rat after a unilateral lesion of the lateral hypothalamus. This lesion interrupts ascending axons of noradrenergic (NE) neurons whose cell bodies lie in brainstem. Ipsilaterally, cortical DBH fell to 30% by day 14. DBH in brainstem rose to 135% (day 1-2), fell to 50% (day 5-14) and increased to 116% after day 21. A 50% fall was also observed in locus coeruleus (day 12). Cerebellar DBH fell in parallel with the brainstem. Contralaterally, cortical DBH fell and then increased by day 21 to 120% of control. DBH in brainstem fell to 60% (day 14) and then rose to 120% of control by day 21. The results suggest: (a) that during anterograde degeneration DBH slowly disappears in lesioned axon terminals; (b) after an initial pile-up, DBH activity is reversibly reduced in NE cell bodies during the time of retrograde (chromatolytic) cell reaction, probably reflecting altered synthesis; (c) the impairment of DBH activity is reflected in unlesioned collaterals of NE-neurons in cerebellum; (d) the overshoot is consistent with the time-course of collateral sprouting from unlesioned NE-axons; (e) during chromatolysis there may be a selective decrease in production of proteins subserving neurotransmitter synthesis. (Supported by NIH grants.)

**42.5** DISRUPTION OF PHYSIOLOGIC FUNCTION BY 6-HYDROXYDOPAMINE. R.D. Smith*, R.A. Mueller* and G.R. Breese. UNC Sch. of Med., Chapel Hill, N.C., 27514

Although brain norepinephrine and dopamine have been proposed to be of functional significance in homeostatic systems controlling blood pressure and water consumption, possible effects of centrally sympathectomy with 6-OHDA on these important control functions have not been examined. Measurement of tail blood pressure (B.P.) by a cuff method revealed that the 6-OHDA treated animals had significantly lower B.P. values than controls. Since adrenal and sympathetic ganglia tyrosine hydroxylase were not significantly altered by 6-OHDA treatment, a mechanism other than decreased efferent sympathetic activity was suggested. To explore the magnitude of altered B.P. regulation, the ability of these rats to develop hypertension after DOCA-NaCl treatment was explored. Despite marked depletion of central amines by 6-OHDA, production of hypertension was not changed although the initial and final blood pressures were lower than controls. In a search for other mechanisms to explain the lower B.P., it was observed that there was a dramatic difference in both the onset and volume of salt consumption following DOCA. This unexpected finding prompted further examination of intake of various solutions by 6-OHDA treated rats. When exposed to 5% sucrose, 6-OHDA rats increased fluid intake 50% while the controls increased intake by 300%. In response to a quinine solution both 6-OHDA and control animals decreased their fluid intake by 50%. These results emphasize that 6-OHDA treatment markedly affects consummatory behavior; this may subsequently produce changes in cardiovascular function. (Supported by grants from N.C. Heart Association and USPHS).

**43.1** FIXATION OF INHIBITION OF A SPINAL REFLEX BY ELECTRICAL STIMULATION OF THE MEDULLA. Vivian C. Abrahams and Jenny Daynes*. Cerebral Functions Group, University College, London, and Dept. of Physiol., Queen's Univ., Kingston, Ontario, Canada.

Most descending spinal effects are brief, enduring for a few milliseconds, or a few seconds at most. We now report on a descending inhibition of the plantar reflex which may persist for hours following its initiation. This prolonged inhibition resembles the phenomenon of fixation, since once established it will persist after cord section. The plantar reflex was recorded bilaterally from the ventral roots of Dial anaesthetised cats. The spinal cord was partially sectioned at the mid-thoracic level leaving only one dorso-lateral quadrant intact. A stimulating micro-electrode was then inserted into the medulla to a site whose excitation produced inhibition of the ipsilateral plantar reflex. Stimulation through the electrode with brief trains every 3 seconds for one hour either abolished the ipsilateral plantar reflex or reduced it to below 40% of its control value. The contralateral reflex was largely unaffected. Despite the loss of the ipsilateral plantar reflex, other reflexes from that spinal root were normal. When the residual dorsolateral cord was sectioned the reduced ipsilateral plantar reflex continued unchanged in 5 experiments, but there was a transient return of the reflex in 2 experiments. The "fixation" of inhibition of the ipsilateral plantar reflex persisted for the remaining 2-4 hours of the experiment, whilst the contralateral reflex was still normal.

Supported by the M.R.C. of Canada.

**43.2** FACILITATION OF A FLEXION REFLEX IN THE SPINAL CAT USING CLASSICAL CONDITIONING TECHNIQUES. R. G. Durkovic* (SPON: J. B. Preston) Dept. Physiology, Upstate Med. Ctr., Syracuse, N. Y. 13210.

In acute decerebrate cats the spinal cord was transected at a low thoracic level. The tendon of the tibialis anterior muscle of the rigidly fixed hind limb was attached to a force-displacement transducer. Electrical stimulation of the cutaneous saphenous nerve (SN) of this leg at an intensity which evoked activity in $A_\beta$ and $A_\delta$ afferent fibers served as the conditioned stimulus (10 impulses/sec. for 1.5 seconds). This train of stimuli which evoked a flexion reflex in the muscle was repeated once each minute in both the conditioning group and in sensitization control animals. Conditioning animals also received, during the last 0.5 seconds of each conditioned stimulus presentation, electrical stimulation of the cutaneous superficial peroneal nerve (SPN) of this leg. This served as the unconditioned stimulus (40 impulses/sec. for .05 seconds) and evoked $A_\beta$ and $A_\delta$ afferent fiber activity in the SPN. Over a thirty-minute conditioning period the flexion reflex evoked in the muscle during the first second of SN stimulation increased in magnitude in the conditioning group of animals. In sensitization control animals the SN and SPN stimulations were alternated every 30 seconds. Over a thirty-minute stimulation period the magnitude of the flexion reflex evoked by SN stimulation did not increase in these sensitization control animals. For the conditioning group the overall change in the flexion reflex magnitude was significantly greater than that of sensitization controls. Results obtained thus far suggest that the isolated spinal cord is capable of exhibiting activity characteristic of conditioned responses. The importance of this simplified preparation is that it is amenable to neurophysiological analysis at the cellular level and could provide information pertaining to neural mechanisms which are involved in learning.

**43.3** OPERANTLY CONDITIONED PATTERNS OF EPILEPTIC CELL ACTIVITY. Eberhard E. Fetz, Allen R. Wyler* and Arthur A. Ward, Jr., Depts. of Neurol. Surg., Physiol. & Biophys., and Primate Center, U. of Wash., School of Med., Seattle, Wash. 98195

In an awake Rhesus monkey we recorded activity of single precentral pyramidal tract cells near a chronic alumina-induced epileptic focus. Units chosen for conditioning fired predominantly in stereotyped high-frequency long-first-interval (LFI) bursts (Calvin, Sypert & Ward, Exptl. Neurol. 21: 535, 1968). Most units also exhibited brief periods of tonic "regular" firing, typical of normal precentral cells. The proportion of spikes occurring as LFI bursts was determined on the basis of interspike intervals and defined as the "epileptic index" (EI). Operantly reinforcing transient increases in unit activity with applesauce produced increases in average rates in all 9 cells, with no consistent change in the mean EI. Reinforcing transient decreases in rate produced no sustained rate changes in 6 cells, a clear decrease in 2, and an increase in 1; the average EI did not change consistently, although transient pauses in cell activity were invariably preceded and followed by LFI bursts. Reinforcing decreases in the EI (1 cell) produced a sustained drop in the number of LFI bursts per minute and a concomitant increase in both regular firing and total rate. Reinforcing an increase in EI (3 cells) produced no consistent changes. These results suggest that firing patterns of epileptic cells may be synaptically modified in awake animals.

**43.4** CONCEPTUAL IMPEDIMENTS IN THE STUDY OF BIOCHEMICAL CORRELATES OF NEURAL PLASTICITY. Louis Irwin. Col. Pharm. Sci., Columbia U., New York, N.Y. 10023

Several prevailing trends are hampering the progress of research on physiological, and especially biochemical, correlates of neural plasticity. First is the misconception that plasticity at the molecular or cellular level in the brain constitutes a physical basis for "learning". This is false by definition because learning is an emergent property of supramolecular and supracellular systems. Second is the failure to identify what represents information in the brain. While impulse frequencies, labelled-line pathways, and a small number of neurotransmitters clearly convey some information, the high degree of structural differentiation and the richness of chemical variety within the brain provide the basis for the representation of information in modes more complex than is usually appreciated. Third is the disproportionate emphasis on the neocortex, on nucleic acids, and on the synapse. While the importance of these components cannot be doubted, other regions, molecules, and subcellular elements are surely more important than the attention which they currently receive would indicate. At our present state of knowledge, insights into the biochemical basis of brain plasticity are more likely to arise from systematic and comprehensive study of many biochemical processes and the way in which they relate to the overall morphological, chemical, and cybernetic organization of the brain.

**43.5** CNS inhibitory and facilitatory effects on peripherally mediated habituation of gill withdrawal in Aplysia. B. Peretz and D. Black* University of Kentucky, Medical Center, Lexington, Kentucky 40506.

The Aplysia gill habituates to repetitively applied water drops after removal of the CNS; the neural plexus in the gill presumably accounts for habituation (Peretz, 1970). With the CNS (parieto-visceral ganglion, PVG) intact the response amplitude (RA) in the gill was lower and the rate of habituation (HR) was faster than after PVG removal. Habituation was observed in the same animal with and without the PVG connected to the gill and other peripheral structures. Sessions were separated by 3 hrs. rest to minimize carry-over effects. RA with PVG intact was only 26% (N=16, P<.005) of that after PVG removal. HR was significantly faster, 33%, (N=16, P<.005) with than without PVG. When the PVG was intact and the gill withdrawal response observed in 3 sessions separated by rest, no difference in habituation among sessions was seen indicating no deterioration of and no surgical trauma to the preparation. Retention of habituation effects, with or without the PVG, lasted about 3 hrs. Electrical activity recorded in the pinnule and ctenidial nerve decreased, paralleling the withdrawal decrement, with repeated stimulation. With the PVG intact, electrical stimulation of gill lobe and ctenidial nerve (CNS to gill) dishabituated the gill response. Dishabituated RA's, to water drops, exceeded initial responses, sometimes by 2 to 8 times. Cutting only the branchial nerve significantly increased RA and slowed HR compared to that with intact PVG but results were not different after PVG removal. Habituation, cutting only the ctenidial nerve, was not significantly different from that with intact PVG. These studies show that the CNS modulates gill habituation with each effect probably subserved by a nerve trunk and possibly by a subset of central neurons. During habituation the greater and faster response decrement could be due to an increase of centrally initiated inhibitory activity which is peripherally mediated. (NIMH)

**43.6** MECHANISMS OF CONDITIONING IN THE LIMBIC TELENCEPHALIC SYSTEM OF THE RAT. M. Segal*. (SPON: J. Olds) Div. of Biology, Cal Tech, Pasadena, CA 91109.

The behavior of units in the components of the hippocampus and in areas afferent to the hippocampus of the rat was monitored during a conditioning experiment. Rats were trained that a tone, out of two, presented in random order, is correlated with a food pellet. The responses to the tone were recorded during pseudoconditioning, conditioning, and extinction sessions. The results indicate that medial septal units had unconditioned short (15-20 ms.) latency phasic responses to the tone. These responses were prolonged during conditioning. CA3 and CA1 units had short latency conditioned responses to the tone. Entorhinal units had a long latency conditioned response; the same was true for dentate units. Posterior cingulate units had relatively short latency conditioned responses. It is suggested that sensory unconditioned input enters the hippocampus from the septal side and it is able to trigger the CA3 units effectively only during conditioning. The entorhinal area feeds into the hippocampus via the perforant path and the dentate, reinforcing information which helps to set the hippocampal units to respond to septal and perhaps cingulate inputs during conditioning, with short latency and long duration.

**43.7** THE ROLE OF CALCIUM IN POTENTIATION AT THE NEUROMUSCULAR JUNCTION OF FROG SARTORIUS. Steven G. Younkin* (Spon: S.D. Erulkar). Dept. Pharm., Sch. Med., U. of Pa., Phila., Pa. 19104.

Miledi and Thies (J. Physiol. 212: 245, 1971) have proposed that both the facilitation and the post-tetanic potentiation (PTP) which occur on repetitive stimulation of the frog NMJ are due to Ca which remains on active sites following tetanization. Our experiments were performed to determine: 1) if the second component of facilitation depends on the presence of calcium during tetanization as required by this residual active Ca hypothesis; 2) if the quantitative behavior of the potentiation occurring during and after tetanization is consistent with this hypothesis. Recording was by intracellular KCL filled microelectrodes. For the experiments on facilitation the Ringer's solution bathing the sartorius contained 10.0 mM Mg and 1.0 mM Ca. For those on PTP it contained 4.0 mM Mg and 0.4 mM Ca. The facilitation present 200 msec after a 100/sec tetanus lasting 300 msec is virtually all second component facilitation. By placing an iontophoretic pulse of Ca just prior to a testing impulse at this time it was possible to vary the Ca present during tetanization and that present at the time of the test impulse independently. In each experiment substantial reduction in the Ca present during tetanization caused a significant reduction in the second component of facilitation. The facilitation following tetani of 50, 100, and 130/sec lasting 300 msec and 150/sec lasting 50 msec was examined quantitatively and found to be consistent with the residual CaX hypothesis given several assumptions concerning the decay of CaX. The PTP occurring during and after 2000 impulse trains at 10, 20, and 50/sec was also examined quantitatively. The slow continual development of PTP during tetanization together with its relatively rapid decay in the post-tetanic period suggests that PTP cannot be accounted for by a simple residual CaX hypothesis.

**44.1** EFFECTIVENESS OF CAT MOTONEURON DENDRITIC SYNAPSES. John N. Barrett* and W.E. Crill. Dept. Physiology and Biophysics, Univ. Wash. Seattle, 98195

The relative effectiveness of dendritic synapses, S(X), may be expressed as the product of two normalized factors, J(X), giving the relative amount of charge injected at the dendritic site and T(X), the fraction of injected charge that reaches the soma. These factors were calculated using anatomical reconstructions from procion dye injected motoneurons and quantal synaptic conductance changes approximated by $g(T) = a^2Te^{-aT}$ (Jack and Redman, 1971, Rall, 1967). Even quantal conductance changes predicted voltage changes of up to 20 mV (in agreement with Kuno 1969) on the distal dendritic branches, giving rise to significant nonlinear summation (1-J). J(X) values for single quanta ranged from 0.86 near the dendritic tips to approximately 0.99 on the soma. Synchronous release of multiple quanta reduces the normalized J values substantially at the more distal dendritic sites. T(X) values at the dendritic tips averaged 0.44 yielding S(X) equal to 0.38. Calculations of S(X) for various dendritic locations show that synapses located on 76% of the dendritic membrane surface will be at least 50% as effective as somatic synapses.

Supported by USPHS Grants NS 07987, GM 00739, FR00374

**44.2** EFFECTS OF HYPERVENTILATION ON THE PLANTAR CUSHION REFLEX IN CATS. M. David Egger, John W. Bishop*, Elizabeth W. Clark* and Constance H. Cone*. Dept. Anat., Sch. Med., Yale Univ., New Haven, Conn. 06510

The neuronal circuitry of the plantar cushion (PC) reflex in cats has been described recently by Egger and Wall (J. Physiol., Lond., 216: 483, 1971). Tactile or electrical stimulation of PC produces a reflex discharge in the first sacral ventral root (S1). This reflex is mediated by interneurons located near the medial border of the dorsal horn in Rexed's laminae IV and V at the seventh lumbar level. Marked increases in the PC reflex occur during forced hyperventilation in cats anesthetized with Dial or Nembutal and paralyzed with Flaxedil. Measurements of arterial pH and $pCO_2$ were made on blood samples taken from a femoral cannula during reflex testing, using an IL 113-S1 blood analysis system. Between pH 7.44 (upper limit of normal) and pH 7.60, there was typically about an 100% increase in reflex magnitude, linearly related to pH. Correlation coefficients ranged from 0.88 to 0.97 in five cats. There was a similar, though negative, correlation between response magnitude and $pCO_2$. The monosynaptic reflex recorded in ventral root S1 in response to stimulation of dorsal root S1 also increased with hyperventilation, but the magnitude of the increase in the polysynaptic response was consistently less than that for the PC reflex. To determine the effects of increasing pH without decreasing $pCO_2$, alkalosis was induced by slow I.V. infusion of 0.3 M $NaHCO_3$. Increases in the magnitude of the PC reflex and of the monosynaptic reflex occurred, linearly related to increases in pH. Our results indicate that there is an effect of pH on reflex transmission through the spinal cord, independent of a possible effect of $pCO_2$.

Supported by grants NB-06297 from NINDS, 5-K2-MH-11,952 from NIMH, and NGR-07-004-090 from NASA.

**44.3** MEMBRANE EFFECTS-ANALYSIS OF CEREBRAL 5HT, LSD, AND CPZ INTERACTION Chuong C. Huang* and Amedeo S. Marrazzi, University of Missouri Institute of Psychiatry, St. Louis, Missouri 63139.

Monitoring of cerebral synaptic transmission by means of evoked potentials has led Marrazzi et al to the conclusions that serotonin (5HT) is the most powerful natural synaptic inhibitor in mammalian brain and that it is probably an inhibitory neurohumor. LSD has a similar but weaker inhibitory action, while chlorpromazine (CPZ) also has a similar, but so much weaker action, that ordinarily it becomes apparent only in large doses; while small doses serve to reduce the action of 5HT and LSD especially when given shortly prior to them. Direct recording of cerebral neuronal membrane changes by intracellular electrode shows, indeed, that each of the three produces the changes that indicate it is a synaptic inhibitor, viz. hyperpolarization, increased transmembrane resistance and IPSPs preceeding and accompanying a reduction in spike discharge. This accounts for both the additive and competitive effects among the three. In the case of the relatively, quite weak CPZ this results in a competitive inhibition for 5HT and LSD, confirming the explanation we have previously offered for the blocking action of CPZ. The data are consistent with the view that a major component of the action of all three is exerted on the same membrane mechanism, presumably on the same receptors triggering postsynaptic inhibition.

Aided by Psychiatric Research Foundation of Missouri.

**44.4** EFFECT OF MICROELECTROPHORETICALLY APPLIED PARA-METHOXYPHENYL-ETHYLAMINE ON CAT SPINAL CORD NEURONS. Larry M. Jordan* (Spon: J. W. Phillis). Department of Physiology, Faculty of Medicine, U. Manitoba, Winnipeg, Manitoba R3E OW3, Canada.

Para-methoxyphenylethylamine (PMPEA) is a substance capable of producing a catatonic syndrome in cats. When administered intravenously into spinal cats anaesthetized with alpha-chloralose, it causes enhancement of monosynaptic reflexes (Walker, et. al., Brit. J. Pharmacol., 38: 106-116, 1970). It also produces depolarization of motoneurons in the lumbar spinal cord and depresses polysynaptic excitatory and inhibitory postsynaptic potentials (Jordan, et. al., Pharm. Exp. Ther., in press). In an effort to illucidate the mechanism whereby PMPEA causes these changes, interneuronsand motoneurons of the lumbar spinal cord of spinal cats anaesthetized with alpha-chloralose have been studied using the technique of microelectrophoresis. The actions of noradrenaline (NA) and 5-hydroxytryptamine (5-HT) were also observed. PMPEA consistently mimiced the depressant actions of NA and 5-HT on interneurons. Preliminary studies on motoneurons reveal that PMPEA, as well as NA, can block invasion of motoneurons by antidromically conducted action potentials produced by ventral root stimulation. This indicates that PMPEA applied microelectrophoretically decreases the excitability of the motoneurons. These results suggest that intravenously administered PMPEA does not directly depolarize motoneurons but may cause enhanced monosynaptic reflexes and depolarization of motoneurons by an indirect action, possibly through depression of inhibitory interneurons.

**44.5** CONVERGENCE OF PAIRS OF GROUP Ia FIBERS TO SPINAL MOTONEURONS IN THE CAT. Lorne Mendell and Richard Weiner*. Dept. of Physiology, Duke University Medical Center. 27710

To assess the relation between location of Ia terminals on the soma-dendritic membrane of motoneurons and the amplitude of the associated (somatic) EPSP, individual EPSP's have been recorded from medial gastrocnemius motoneurons in response to separate activation of 2 Ia afferent fibers from this muscle. The method of Mendell and Henneman (J. Neurophysiol. 31 )1971) ) was used to obtain the individual EPSP's. These measurements allow a direct comparison of EPSP's from 2 identified afferents in the same motoneuron. The largest EPSP amplitude ratio which has been observed in any motoneuron is 5.34 but generally it is less than 3.0. The ratio of rise times has varied from 0.16 to 1.0 (measured 0-100%). For pairs of EPSP's in the same motoneuron a tendency is observed for EPSP's with brief rise times to be larger than ones with long rise times. No such relation between rise time and amplitude is observed in the EPSP's produced by a single Ia afferent fiber in several different motoneurons presumably due to variability introduced by motoneuron input impedance, membrane potential, etc. The largest amplitude differences tend to occur between EPSP's which have the greatest disparity in rise times, although the data suggest that other unanalyzed factors contribute to the differences in EPSP amplitudes. It is suggested that EPSP amplitude at the recording electrode (the soma) is smaller for distal homonymous Ia synaptic inputs (slow rise times) than for proximal ones (fast rise times). (Supported by NIH NS-08411 and NS-34608)

**44.6** ACETYLCHOLINE-INDUCED RESPONSES MEASURED UNDER VOLTAGE CLAMP AND THEIR DEPENDENCE ON MEMBRANE POTENTIALS. Makoto Sato and Juro Maruhashi*. Neuroscience Lab., Div. of Neurosurgery, University of Oregon Medical School, Portland, Oregon, 97201

Membrane potentials of Aplysia ganglion cells were clamped at various levels during the application of acetylcholine (ACh). The increase in variational conductance ($\Delta G$) during the ACh-induced response was plotted against the membrane potentials. Results were compared between the excitatory (D) and the inhibitory (H) type of postsynaptic membranes. The $\Delta G$ of the D-type membrane was not altered over the wide range of hyperpolarization but linearly depressed when depolarization was increased. $\Delta G$ became nearly zero at 50 mV depolarization. The $\Delta G$ of the H-type membrane was linearly depressed when hyperpolarization was increased. $\Delta G$ became nearly zero at 90 mV hyperpolarization. On the other hand, it was only slightly depressed over the wide range of depolarization. In both types of membranes, the resting variational conductance ($G_o$) sharply increased when the membrane was abruptly depolarized but it exponentially decayed during sustained depolarization, practically reaching a plateau around 30 sec. In all experiments, ACh was applied after $G_o$ reached the practical plateau. However, $G_o$ did not always decay but remained considerably high when repetitive firing proceeded, as the result of sustained depolarization. In such cases, $\Delta G$ of the H-type membrane was markedly depressed, as much as that of the D-type membrane. It is suggested that the D-type receptor loses its activity more readily than the H-type receptor when the potassium conductance of the electrogenic component increases, whereas the H-type receptor becomes less active when the chloride conductance of the electrogenic component increases. (Supported by USPHS grant 5 Rol NS 01687-14)

**44.7** A MOLECULAR MECHANISM OF DEPOLARIZATION GENERATED BY ACETYLCHOLINE. Clara Torda. Mount Sinai School of Med.,New York,N.Y.,10029.

Triphosphoinositide phosphomonoesterase ( TPIPM ) was isolated from various types of brains. It was fractionated by means of repeated chromatography on various types of Sephadex columns, incl.Sephadex LH-20. An enzymatically active (C) and one inactive (R) fraction was obtained. Biochemical experiments revealed that minute amounts of acetylcholine (ACH) can activate TPIPM in fractions of 0.2 msec both in vitro and in vivo. The activated TPIPM dephosphorylates triphosphoinositide to diphosphoinositide. This dephosphorylation reaction initiates a molecular chain reaction that leads to membrane depolarization. The details of this chain reaction were identified. The validity of these results and assumptions was tested in vivo experiments. The bioelectric processes generated in the postsynaptic neuron were recorded by means of intracellular microelectrodes. The effects of presynaptic stimulation with rectangular pulses were compared with the effects of intra-(or near-) synaptic microinjections of the active fraction of TPIPM (C). Furthermore, the effects of similar microinjections of the second fraction obtained from TPIPM on the effects of both the presynaptic stimulation and the synaptic microinjections were also ascertained. Comparable results were obtained by either the presynaptically applied rectangular pulses or the synaptic microinjections of the active fraction of TPIPM. The effects of weak stimuli and low concentrations of C fraction were additive. Intra-(or near-) synaptic microinjections of the R fraction inhibited the postsynaptic response to either the presynaptic stimuli or the synaptic microinjections of the C fraction in a comparable manner.The results suggest that both acetylcholine and electrical stimulation of the presynaptic neuron may induce postsynaptic activation through activation of TPIPM to dephosphorylate triphosphoinositide.The results suggest that the activation of TPIPM is the coupling mechanism for depolarization.

**45.1** MOTOR CORTEX ACTIVITY IN ASSOCIATION WITH QUICK REFLEX MOVEMENTS.
E. V. Evarts, NIMH, Bethesda, Maryland 20014

Hammond's finding (J. Physiol. 132: 17P-18P, 1956) that prior instruction can modify motor responses to kinesthetic inputs when the latency from kinesthetic input to muscle response is as short as 50 msec led him to propose that spinal stretch reflex mechanisms can be preset by nervous activity from the brain. In Hammond's experiments on man the very short latency of the muscle response seemed to rule out the cerebral cortex as a link between input and output. Studies on motor cortex pyramidal tract neuron (PTN) activity in monkeys in association with quick responses to visual stimuli have supported this view: the interval from visual stimulus to PTN response is 100 msec. For kinesthetic stimuli, however, it would seem that results might be quite different. Kinesthetic inputs have a much more direct path to motor cortex than do visual inputs. To compare PTN output triggered by these two modalities, some monkeys were trained to push or pull a handle in response to a visual stimulus and other monkeys were trained to perform a similar movement in response to a perturbation of the handle. In both cases neuronal activity in hand area of sensorimotor cortex was studied in relation to the learned movement. In contrast to the 100 msec PTN latency for the visual modality, a kinesthetic stimulus delivered via the responding hand initiated a PTN response at latencies as short as 20 msec. It thus appears that for kinesthetic inputs, PTN activity may be initiated with sufficiently short latency to allow it a role in reflex movements which depend on the volitional set of the subject.

**45.2** SENSORY ALTERATION OF WALKING IN LAND CRABS. William H. Evoy and Charles R. Fourtner * Lab. for Quantitative Biol., Univ. Miami, Coral Gables, Fla. 33124.

As part of an investigation of the neural basis of motor control movements of the mero-carpopodite (M-C) and propo-dactylopodite (P-D) joints of walking legs in the land crab, Cardisoma guanhumi, have been analyzed from motion pictures and in some cases correlated with electrical recordings of neuromuscular activity. Modifications of the normal stepping pattern have been obtained by disturbance of the proprioceptive input as follows: 1) removal of the meropodite muscle receptor (Cohen, 1963; Evoy & Cohen, 1969) causes hyperflexion of the M-C joint, resulting in a "rocking" gait; 2) addition of resistive load causes an increased output to the powerstroke muscles; 3) the operation described in 1) has no effect on the load response; 4) binding of the walking leg joints causes changes in the output to that leg as well as phase changes in the stepping pattern. Attempts are being made to utilize these findings to test an earlier hypothesis that the fine control of posture and locomotion is derived from an interaction of motor commands with proprioceptive inputs (Barnes et al., 1972). Supported by NSF GB 30605 and USPHS Training Grant HD00187.

**45.3** A NEURONAL BASIS FOR INTERAPPENDAGE PHASE DELAY DURING LOCOMOTION. Paul S. G. Stein. Dept. Biol., Washington Univ., St. Louis, Mo. 63130

During rhythmic locomotion there is a regulated temporal delay between homologous movements in neighboring swimmeret appendages of crayfish. The temporal delay may be influenced by excitability gradients of segmental oscillators. Such gradients are not necessary, however, to produce the interappendage delays (Stein, P.S.G., J. Neurophysiol. 34: 310, 1971). The present study demonstrates that the delays may be understood by examining the contingent responses of one swimmeret oscillator to coordinating neuron input from another oscillator. A single burst of coordinating neuron input during the returnstroke portion of an oscillator cycle will advance the onset of the next powerstroke discharge, i.e. it will shorten the current cycle. A single burst of coordinating neuron input during the powerstroke portion of the cycle will cause a more vigorous powerstroke and will delay the onset of the subsequent powerstroke discharge, i.e. it will lengthen the current cycle. During rhythmic beating of the swimmerets, the coordinating neuron burst begins late in the returnstroke and ends late in the powerstroke portion of the cycle. Thus each coordinating neuron burst will cause a shortening of the current cycle and a lengthening of the subsequent cycle. Interappendage delay is a consequence of the interplay between the lengthening effect of the prior coordinating neuron burst and the shortening effect of the current coordinating neuron burst.

**45.4** NEURAL CONTROL OF THE CAT STEP CYCLE: NATURE AND ROLE OF PROPRIOCEPTIVE INPUT. Douglas G. Stuart and George E. Goslow, Jr. Dept. Physiol., U. of Ariz., Tucson 85724 and Dept. Biol. Sci., NAU, Flagstaff 86001.

A quantitative estimation of the relative input to the spinal cord during stepping from the Ia, Ib and group II afferents of cat hind limb extensor muscles can now be made by consideration of: 1) our cinematographic analysis of the step cycle during the conversion from low to high speed locomotion; 2) our recordings of Ia, Ib and group II afferent discharge from soleus and medial gastrocnemius during passive stretches within the locomotor range; 3) an EMG analysis of stepping by Engberg and Lundberg (Acta Physiol. Scand. 75: 614, 1969); and, 4) recordings of stretch receptor discharge from ankle extensors during "controlled" walking of the mesencephalic cat by Severin et al (Biophysics 12: 575, 1967). This estimation reveals substantial Ia, Ib and group II input throughout the stance ($E^2$ and $E^3$) phase of stepping and a small but potentially significant Ia input during the F part of the swing phase. It is also possible to quantitate the delays built into short latency segmental reflex systems, including the time for: receptor activation; impulse conduction to cord; segmental delay to change in motoneuronal firing pattern; impulse conduction to muscle; neuromuscular transmission; excitation-contraction coupling; and, changes in muscle tension resulting from the asynchronous activation or de-activation of motor unit discharge. Taking all these factors into account, it would appear that many reflex changes in muscle tension attributable to proprioceptive input occur in a subsequent phase of the same step cycle to that in which the input is initiated. There is also indication that some proprioceptive input is needed for the control of succeeding cycles in the same limb and in the other 3 limbs. These calculations emphasize the value of long rather than short loop proprioceptive reflexes for assisting the central program that controls the stepping sequence. (Supported by USPHS grant NB 07888).

**45.5** UTILITY OF A LIMB FOLLOWING UNILATERAL DEAFFERENTATION IN MONKEYS. Edward Taub, Gilbert Barro*, Bruce Parker* and Teresa Gorska*. Inst. Behavioral Research, Silver Spring, Md. 20910

Following deafferentation of both forelimbs by dorsal rhizotomy, monkeys are able to make extensive use of the affected extremities. In contrast, deafferentation of only one forelimb results in an effectively useless extremity in the free situation. However, it proved possible to induce use of a single deafferented limb when the intact limb was immobilized in a straitjacket and in a conditioned response situation where, again, the intact limb was restrained. Use of the deafferented limb did not generalize to the free situation. The unilateral results could be accounted for by the existence of an interlimb inhibitory mechanism, released by unilateral dorsal rhizotomy, and functioning so that movements of the intact limb inhibit movements of the deafferented limb. A strong form of this hypothesis was disconfirmed in two conditioned response experiments where (1) the deafferented limb was used when the intact limb was unrestrained, and (2) the deafferented and intact limbs were used simultaneously. An alternate explanation was evaluated in a third experiment. Monkeys were placed in a straitjacket which immobilized the intact limb for 3 days, a longer period than employed previously. The animals exhibited extensive purposive movement with the deafferented forelimb when wearing the straitjacket and--in contrast to our earlier work--continued to do so permanently following removal of the device. The data support the notion that monkeys learn nonuse of a single deafferented limb in the immediate postoperative period, when the limb is truly useless. Later, when restitutive processes have progressed, use of the limb is exhibited when motivation is increased sufficiently; but unless extensive experience is given (e.g., 3 full days in the straitjacket), the new habit does not gain enough strength to successfully compete with and overcome the well-learned habit of non-use in the free situation. (Supported by NIH grant MH16954)

**46.1** THE IMPREGNABLE OLFACTORY TRANSDUCTION CODE AND ITS SOLVABILITY. Richard G. Davis* (SPON: R. Fox). Dept. Psychol., Univ. of Northern Iowa, Cedar Falls, Iowa 50613.

The basic issue examined by a large segment of studies of vertebrate olfaction is the nature of the odor transduction mechanism. Electrophysiologists attack the "olfactory code" with the encouragement of successes met by similar efforts in other sensory systems; however, such studies have not exposed the olfactory code. Current interpretations of electrophysiological (EP) results express optimism for ultimate success. One basic assumption of EP technique of sensor transducer study is valid for many types of biological transducers; but it may not be true for the chemically sensitive transducers of olfaction. The assumption is that each stimulus applied to the transducer is an instance of a "point source" in a 2-dimensional Euclidian space. If this assumption is not true for olfaction, then classical EP technique will not yield interpretable data. Existing EP studies have produced vague results; but, if this assumption is rejected, these same results become expected. Further, if the "point source" assumption is invalid for olfactory experiments, then an alternative experimental strategy is required. This paper proposes a behaviorally oriented technique which aims at defining a set of odor recognition/confusion zones in the olfactory perceptual space which are mutually exclusive. These behaviorally derived zones can be shown to possess properties which justify the assumption of "point source" under certain restricted conditions. Knowledge of these zones will guide the reanalysis of existing EP data and the conduct of future EP studies as well. The outcome of such a combined approach should produce a rapid revelation of the elusive olfactory code.

**46.2** ROLE OF THE HABENULAR NUCLEI IN SIMPLE VS. COMPLEX OLFACTORY DISCRIMINATION LEARNING. Lyle J. Rausch*, Rebecca Rausch* and Charles J. Long. Dept. Psych., Memphis State Univ., Memphis, TN 38111

Forty rats were divided into two groups--habenular lesions and sham-operated controls--and given olfactory discrimination training in a T-maze for water reward. The odor stimulus was a 10% concentration of Linalool, provided by the Givaudan Co. Ten animals from each group were trained on the discrimination task prior to surgery and tested for retention 1 week post-operatively; the remaining 20 rats received acquisition training post-surgically. Habenular lesions impaired both acquisition and retention of the discrimination. These findings, taken in conjunction with other data from our laboratory, suggest that the habenula is differentially involved in integrating olfactory information with complex motor sequences. Previous studies have shown that habenulectomy does not disrupt the learning of olfactory discriminations in simple tasks (bar-press or nose-press manipulanda), but does impair locomotor responding to odor cues in instrumental situations. Thus the habenula apparently plays an important role in the rat's learning to utilize odor cues in instrumental tasks such as the T-maze and Grice apparatus, but becomes progressively less important as the motor requirements of a task decline. This hypothesis is essentially in agreement with Herrick's notion of the habenula as an olfacto-somatic correlation center. Alternative explanations for performance deficits following habenular lesions include: (1) possible changes in the arousal or activating properties of odors or other situational cues; (2) elevation of sensory threshold as a function of increased background "noise" during locomotor activities; and (3) likely changes in hormonal levels which might interfere with chemoreceptive abilities.

**46.3** A CORTICOMEDIAL AMYGDALOBULBAR CENTRIFUGAL SYSTEM IN OLFACTION IN THE MALE RAT. G.K. Rieke* and M.H. Bennett* (SPON: B.M. Wenzel). Dept. Physiology, Sch. Med., UCLA, Los Angeles, 90024 and Div. Neurological Surgery, Univ. Pitts., 15213

Centripetal responses evoked in centers of distribution of the lateral olfactory tract (LOT) by bulb stimulation, and responses in the bulb to tract stimulation are affected by this centrifugal system with ipsilateral and contralateral components, which respectively suppress or enhance the responses. Concurrent stimulation of centers of the ipsilateral component [corticomedial amygdala (CAN), horizontal portion of the bed nucleus of the diagonal band, prepiriform cortex pyramidal cell lamina (PPC), anterior olfactory nucleus pars medialis] suppresses the bulbar response to tract stimulation (-16 to -32% pretest amplitude, 4 min (PBSP) postburst suppression period) and the centripetal response in the PPC (-13 to -100% pretest amplitude). The contralateral component [CAN, both bed nuclei of the stria terminalis] enhances these responses (+0 to 40%, LOT, +0 to 20% PPC, postburst enhancement period of 1-3 min). Bursts (200 Hz, 20 msec duration) to contralateral centers paired repetitively with single pulses (1 Hz, 1 msec duration) to centers of the opposing ipsilateral component consistently suppress ipsilateral centrifugal responses evoked in the granule cell core of the olfactory bulb. Suppression ranges from -3 to -47% of the pretest amplitude with a PBSP of 1-5 min. The contralateral component suppresses the ipsilateral centrifugal responses evoked in the three extra-bulbar centers by CAN stimulation (-4 to -40% pretest amplitude, 1-5 min PBSP). Enhancement of centripetal and antidromically evoked responses results from suppression by the contralateral component of the suppressive influence of the opposing ipsilateral component.

**46.4** ODOR DETECTION AND DISCRIMINATION IN RATS FOLLOWING SECTION OF LATERAL OLFACTORY TRACT. Burton M. Slotnick. Laboratory of Brain Evolution and Behavior, NIMH, Bethesda, Md. 20014

Rats were trained in a wind-tunnel olfactometer to detect the presence of a 1 sec odor sample of dilute amyl acetate (circa $10^{-4}$). Following extensive overtraining and determination of detection threshold, the lateral olfactory tract was exposed bilaterally and sectioned in six rats at the level of the olfactory peduncle. A small segment of cortex dorsal to the olfactory tract was ablated bilaterally in 3 controls. Postoperatively controls showed perfect or near-perfect retention, no change in detection threshold, and rapid acquisition of two-odor discrimination problems. Experimental rats had no retention of the detection problem but were able to acquire the discrimination after extensive retraining. There was little or no change in detection threshold. In subsequent two-odor acquisition tasks the tract-sectioned animals failed or showed marked retardation in learning. The results demonstrate that section of the lateral olfactory tract does not produce anosmia but that remaining olfactory function is severely limited.

**49.1** TEMPORAL CHANGES IN ENZYME ACTIVITIES AFTER BRAIN HEMISECTION OR 6-HYDROXYDOPAMINE ADMINISTRATION. E.G. McGeer and H.C. Fibiger. Kinsmen Laboratory of Neurological Research, University of British Columbia, Vancouver, Canada.

Time course studies were done of the rate of loss of enzyme activities in the caudate and substantia nigra following either subcortical hemisections or intraventricular injection of 6-hydroxydopamine. These studies showed: (a) Degeneration of tyrosine hydroxylase activity in the nigral cell bodies as well as in caudate nerve endings after 6-hydroxydopamine or surgical lesions. (b) A more rapid deterioration of tyrosine hydroxylase in nerve endings as compared with cell bodies. (c) A rapid decrease in substantia nigra glutamic acid decarboxylase following brain hemisection suggestive of nerve ending deterioration with no change in neostriatal glutamic acid decarboxylase. (d) No change in caudate choline acetylase following brain hemisection. The data provide additional evidence for an ascending nigro-striatal dopaminergic tract and a descending gabaminergic tract to the substantia nigra. No evidence for a major cholinergic tract ascending to the caudate or descending from it could be found. This work was supported by Medical Research Council of Canada Grant No. MA-3633 and a Medical Research Council Scholarship.

**49.2** ELECTRON MICROSCOPIC AND ENZYME MARKER STUDIES IN AREAS OF BOVINE BRAIN WITH SPECIAL EMPHASIS ON MAO. Elizabeth Koch*, Boris Tabakoff, Frieda Ungar*, Laurence Meyerson*, Robert Anderson*, and Spyridon G.A. Alivisatos. Department of Biochemistry, The Chicago Medical School, Chicago, Ill.60612

Considering that MAO must play a determinant role in the mechanism of action and catabolism of biogenic amines, especially the indoleamines, we have studied its subcellular and regional distribution in various areas of bovine brain. Electron microscopy and marker enzyme studies, including succinic dehydrogenase, acetylcholinesterase, sodium, potassium dependent ATPase and rotenone-insensitive NADH-cytochrome c reductase, were studied in fractions obtained from various areas of bovine brain. The substrate specificity of MAO derived from the various brain areas was ascertained by measurement of kinetic parameters both in intact mitochondria and solubilized preparations. Both the mitochondrial composition and $K_m$ values for norepinephrine and serotonin with MAO were found to differ between the areas tested. In addition, we demonstrated that the subsequent fate of biogenic aldehydes produced by the action of MAO depends on their chemical structure. Oxidation of various aldehydes by $NAD^+$-dependent aldehyde dehydrogenases derived from both the mitochondria and the cytosol or reduction by a NADPH dependent reductase (J. Biol. Chem. 245, 3263, 1970) or binding onto membrane constituents, was found to depend on the substituents (hydroxy or methoxy) on both the aromatic nucleus and the aliphatic side chain of the biogenic amines. (Supported by NIMH Grants 15410 and 20758, Illinois Dept. Ment. Health 101-13-RD, Am. Canc. Soc. P-424B, NSF GB-30295 and W.S. Deree.)

**49.3** METABOLISM OF $H^3$-NORMETANEPHRINE AND $C^{14}$-NOREPINEPHRINE IN BRAIN AND PERIPHERAL TISSUE HOMOGENATES. Haroutune Dekirmenjian and James W. Maas. Illinois State Psychiatric Institute, 1601 W. Taylor St., Chicago, Ill.

In homogenates of whole rat brain $C^{14}$-Norepinephrine (NE) was metabolized to 3-methoxy-4-hydroxyphenylethylene glycol (MHPG), 3-methoxy-4-hydroxymandelic acid (VMA). 3,4-dihydroxyphenylethylene glycol (DHPG), 3,4-dihydroxymandelic acid (DHMA) and normetanephrine (NM). In contrast, in the same system, $H^3$-NM was metabolized only to MHPG, and no VMA could be detected. In homogenates of cat, pig, dog and sheep brain the only metabolite of $H^3$-NM was found to be MHPG. This specific metabolism of $H^3$-NM to MHPG was not due to a difference in the oxidation-reduction potential required for the oxidation of the NE and NM aldehydes produced by Monoamine Oxidase, enzyme, since variation of NADP-$NADPH_2$ or NAD-$NADH_2$ ratios over a wide range in the incubation system did not alter the $H^3$-NM metabolism to MHPG. This difference in the metabolism of $C^{14}$-NE and $H^3$-NM might be explained by a difference in the substrate specificity of the aldehyde dehydrogenase-reductase enzyme system. This conclusion is supported by the fact that the addition of horse heart alcohol dehydrogenase and/or the addition of NAD and NADP did not result in the formation of any other product than MHPG. Similarly the addition of barbituric acid (inhibitor of aldehyde-reductase) was found to inhibit the $H^3$-NM metabolism to MHPG by 50% although no other metabolite was formed. The primary metabolite of $H^3$-NM in the heart, liver, kidney, and adrenals of the cat and in the heart, liver and kidney of the rat was MHPG. Studies are underway involving the addition of enzymes, enzyme inhibitors and the manipulation of cofactors in various tissue homogenates. These results will be discussed in terms of the mechanisms that are responsible for different metabolism of $C^{14}$-NE compared to $H^3$-NM.

**49.4** BEHAVIORAL CORRELATES OF BRAIN HISTAMINE LEVELS AND LEVELS AND UPTAKE OF BRAIN CATECHOLAMINES. D. Aures, M.K. Menon* and W.G. Clark. Psychopharmacology Research Lab., V.A. Hospital, Sepulveda, California, 91343; Dept. Medical Pharmacol. & Therap., College of Med., Univ. of California, Irvine.

Histamine (Hm) recently has been invoked in CNS neuronal function. High i.p. doses of histidine (Hd) elevated Hm only in the hypothalamus, but had little effect on the remainder of the brain. Chronic injections of Hm caused a bizarre stereotyped rearing behavior in rats when grouped, similar to that described by Lammers and Van Rossom (Europ. J. Pharmacol. 5:103, 1968) after treatment with L-dopa and a peripheral dopa decarboxylase inhibitor, and by Murpurgo and Theobald (Int. J. Neuropharmacol. 5:375, 1966) after treating reserpinized rats with amphetamine. Brain Hm was not significantly affected by the chronic Hm treatment. There was an increase in active dopamine (DA) uptake by slices of caudate nucleus from brains of the chronically treated rats, which did not occur in slices from rats after a single injection of Hm. Norepinephrine uptake in hypothalamus was not affected. Brain DA levels were increased in the chronically treated rats. For these and other reasons we believe that brain neuronal catecholamine systems interact with the brain Hm neuronal system.

* Fellow of the FSVCPS Foundation.

**49.5** A NEW MECHANISM OF ACTION OF DIPHENYLHYDANTOIN: EFFECT ON NOREPINEPHRINE UPTAKE AND BINDING IN SYNAPTOSOMES. M.Gary Hadfield* and Michael E. Boykin*. (SPON: W.I. Rosenblum). Dept. Path., Div. Neuropathology and Dept. Med., Div. Neurology, Medical College of Virginia, Richmond, Va. 23219.

Widespread interest in the clinical anticonvulsant, diphenylhydantoin (Dilantin, DPH), has been generated by the ability of this agent to control seizure activity without causing neuronal depression. Therefore numerous investigations into the mechanisms by which DPH exerts its unusual pharmacological properties have been carried out. Heretofore these studies have frequently centered upon the effects of DPH on ionic transport across cell membranes or upon bioelectrical activity. However, work from this laboratory concerns the effect of DPH on putative neurotransmitters within nerve endings. Previously, *in vitro* work was carried out (Arch. Neurol. 26:78-84, 1972) in which an effect of DPH was reported on the uptake and binding of radioactively labelled norepinephrine (NE) in synaptosomes isolated from rat brain. When compared with controls, DPH stimulated the uptake and binding of NE when synaptosomes were incubated in unoxygenated isotonic sucrose. An effect at DPH concentration as low as $10^{-6}$ M was noted. This effect was reversed and inhibition of uptake of catecholamine occurred when the incubation medium consisted of oxygenated physiologic solution. In the present *in vivo* study, male Sprague-Dawley rats were orally treated with DPH or alkalinized water for six weeks prior to isolation of synaptosomes and incubation with $H^3$-l-NE. The *in vivo* results paralleled those of the *in vitro* studies. Namely, DPH stimulated uptake of labelled NE in unoxygenated isotonic sucrose and inhibited uptake of labelled NE in oxygenated physiologic media. The degree of uptake and binding appeared related to serum levels of DPH. The results indicate that DPH may mediate its anticonvulsant action through an effect on neurotransmitter kinetics at the synapse. (Supported by Dreyfus Medical Foundation).

**49.6** PHENYLETHYLAMINE-LIKE SUBSTANCE(S) IN MAMMALIAN BRAIN AND THEIR INCREASE BY REPEATED ELECTROSHOCK SEIZURES. A. D. Mosnaim*, E. E. Inwang* and H. C. Sabelli. Dept. Pharmacol., Chgo. Med. Sch., Chicago, 60612.

2-Phenylethylamine (PEA) is a monoamine oxidase-sensitive amphetamine-like stimulant with weak anticonvulsant effects. Phenylethylamine-like substances (PLS) were found in mammalian brain (Nakajima et al., 1964). By a combination of ultraviolet, thin layer and gas chromatography techniques we detected PEA and 2-phenylethanolamine in the brain of several species including man. PLS were quantitated by measuring the UV absorption at 287 nm of the product of their heterogeneous reaction with $Ce(SO_4)_2$. Although the method used for PEA determination is not specific for this substance, other brain amines, their metabolites and amino acid precursors do not interfere. Replacement of $Ce(SO_4)_2$ by equimolar amounts of $Ce^{\bullet}$, $CeF_2$ or $CeCl_2$ did not yield significant amounts of the product absorbing at 287 nm, whereas replacement by $Ce(NH_4)_2SO_4$ decreased the yield by 50%. Replacement of HCl by NaCl or KCl decreased the yield, whereas $CaCl_2$, $MgCl_2$, $MnCl_2$ did not give any reaction; n-hexane can be replaced by n-heptane. The product slowly decomposes at room temperature; this process does not seem affected by daylight. PLS brain levels were approximately doubled 24 hr after the last electroshock in mice shocked daily for 10 days (N = 60; 6 experiments) in comparison to control mice (N = 60; 2 experiments). Other antidepressive treatments (imipramine, pargyline) also increased brain levels of PLS (Mosnaim and Sabelli, Pharmacol. 13: 283, 1971), while PLS urinary excretion is reduced in depressed patients (Fischer et al., Arzneim.-Forsch. 18: 1486, 1968; Inwang et al., Biol. Psychiat., 1972). A deficit in PEA may play a physiopathological role in depression and its increase may contribute to the antidepressive effect of electroshock and drugs. Supported by USPHS grant MH-14110, State of Illinois grant 243-11-RD and the Epilepsy Foundation of America.

**49.7** DEPRESSION OF ACETYLCHOLINE RELEASE FROM CEREBRAL CORTICAL STRIPS BY CHOLINESTERASE INHIBITION. J.C. Szerb and G. Somogyi.*, Dept. Physiol. & Biophysics, Dalhousie U., Halifax, N.S., Canada.

Acetylcholine (ACh) release from rat cortical strips resulting from electrical stimulation was measured by following the efflux of radioactivity from strips that had been previously incubated with $5 \times 10^{-5}$M [$^3$H] choline. In the absence of a cholinesterase inhibitor, 75 pulses at 0.25 Hz evoked an increase of 534 ±76 pmole/g of [$^3$H] choline which was reduced to an equivalent of 207 ±55 pmole/g by $2 \times 10^{=4}$M eserine. Similarly eserine reduced evoked release of ACh due to 600 pulses at 4 Hz from 1412 ±110 to 482 ±60 pmole/g. Neostigmine ($10^{-5}$M) had a similar depressant effect. Atropine ($3 \times 10^{-7}$M) prevented the inhibition of ACh release due to cholinesterase inhibitors. Results indicate that unphysiologically high extracellular ACh levels resulting from cholinesterase inhibition reduce ACh release and that the potentiating effect of atropine on ACh release from slices reported by others (Bertels-Meeuws and Polak, Brit. J. Pharmacol. 1968, 33:368) is due to the fact that atropine overcomes this unphysiological depression.

**49.8** CHOLINE: HIGH AFFINITY UPTAKE INTO CHOLINERGIC NERVE TERMINALS IN THE BRAIN AND PERIPHERY. Henry I. Yamamura, Candace B. Pert*, Tommy L. Gardner* and Solomon H. Snyder. Dept. Pharmacol., Johns Hopkins Univ. Sch. of Med., Baltimore, Md. 21205.

We have examined the uptake of $^{3}$H-choline into synaptosomes of the rat corpus striatum and into the longitudinal muscle of the guinea pig ileum. In both tissues uptake kinetics best satisfy two transport components, a high affinity uptake with Km value of about 1 x $10^{-6}$ M and a low affinity system with Km of 1 x $10^{-4}$ M. The high affinity system has an absolute requirement for sodium, is inhibited markedly by metabolic inhibitors such as KCN and dinitrophenol, and is associated with a considerable formation of acetylcholine, while the low affinity system has little energy or sodium dependence, and choline accumulated by the low affinity system is not transformed into acetylcholine. Removal of the myenteric plexus of the guinea pig ileum results in a profound decrease in choline accumulation by the high affinity system, while the low affinity transport is relatively unaffected. Drugs such as atropine and acetylcholine affect the high and low affinity systems differently. Agents with selective actions on the high affinity choline transport may prove useful in elucidating cholinergic neuronal function. The high affinity transport may also facilitate the labeling of cholinergic nerve terminals. (Supported by USPHS grants NS-07275, GM-16492, MH-18501 and MH-33128).

**49.9** AN ENZYMATIC ASSAY FOR THE DETERMINATION OF PICOMOLE AMOUNTS OF ACETYLCHOLINE. A.M.Goldberg and R.E.McCaman,Johns Hopkins Univ.,Balto.,Md. 21205 and City of Hope,Duarte, Calif. 91010.

In any assay for the determination of acetylcholine based on the conversion of choline to a product, the immediate problem is the removal of endogenous choline. Other published enzymatic assays have taken advantage of electrophoresis to accomplish this goal. In the assay to be described, this is accomplished by the enzymatic phosphorylation of endogenous choline by choline kinase. Once this reaction is complete (less than 20 min), endogenous acetylcholine is simultaneously hydrolyzed and then phosphorylated with $^{32}$P-ATP. The labeled product (choline $^{32}$P-phosphate) is separated from the labeled substrate by precipatation of the ATP and further separation is accomplished on microcolumns of ion exchange resin. Using this methodology, picomole amounts of acetylcholine, derived from tissue, can be measured. Acetylcholine standards give linearity through at least 1000 pmoles. If the specific activity of the labeled ATP, during incubation, is 40mCi/mmole the calculated limit sensitivity is 4 pmoles. Thus, this assay will easily detect the acetylcholine content in 0.5 mg of brain tissue. Values obtained for whole mouse brain based on 0.5 to 2 mg of tissue, range between 20 and 25 nmoles/g wet. The major advantages of this assay are sensitivity, convenience, and reproducibility.

**49.10** ACETYLCHOLINESTERASE: RECOVERY IN BRAIN TISSUE, CEREBROSPINAL FLUID AND PLASMA FOLLOWING PINACOLYL METHYLPHOSPHONOFLUORIDATE. Tony L. Yaksh*, Louis A. Fedele*, Tommy L. Gardner* and Henry I. Yamamura. Medical Research Division, Biomedical Laboratory, Edgewood Arsenal, MD 21010, USA.

The reappearance of acetylcholinesterase (AChE) in the cerebrospinal fluid (CSF) and plasma of atropinized (1 mg/kg, im.) cats chronically implanted with cannulae in the cisterna magna was studied following administration of a dose of 27 ug/kg (0.9 LD50) of pinacolyl methylphosphonofluoridate (PMPF) given subcutaneously. Within the first hour following injection, AChE activity, as measured by the radiometric method, fell to approximately 10% of base line levels in both CSF and plasma. The apparent half-time of recovery for AChE activity in CSF was approx. 17 hrs. as opposed to 69 hrs. in plasma. To determine the relationship of enzyme recovery in CSF with that of brain, cats were sacrificed one hour, 1,2,3, 4,5 or 8 days after injection of PMPF. The brains were perfused in situ with saline, quickly removed, dissected, weighed and assayed for enzyme activity. The highest control concentration of enzyme activity was found in the caudate nucleus (176 umoles/gm/hr). Other brain structures, including the hypothalamus, cortex, cerebellum and pons, had in comparison to the caudate only 10-25% as much AChE activity. The half-time for recovery in these tissues varied from approx. 4-5 days. Parallel studies were also performed with guinea pig whole brain and an equivalent recovery time was observed. Further, studies with subcellular fractionation of guinea pig brain following treatment with PMPF showed that a rapid recovery of microsomal AChE occurred in contrast to the recovery of synaptosomal AChE which was more prolonged (4 vs 8 days). This is taken to indicate the role of protein turnover in the recovery of brain AChE. Studies are presently underway to determine the mechanism of AChE recovery in the brain as well as the source of this enzyme in the CSF.

**50.1** Effect Of Methylmercury On Performance Of Mice On A Multiple Schedule. John A. Hughes* (Spon. Z. Annau) Dept. Env. Med. The Johns Hopkins Univ. 615 N. Wolfe St., Baltimore, Md. 2120

Since it is a known intoxicant of the CNS, it is reasonable to suppose that chronic administration of low doses of methylmercury might produce measurable changes in performance in a complex operant paradigm. With this end in mind, adult male CFW mice were trained to lever press on a multiple schedule which consisted of two chains. Performance on chain FR 10 DRL 1 (5minutes) employed water as primary reinforcement and chain FR 10 VI 1 (5 minutes) used food. A complete session was comprised of 10 trials with each chain. Once reliable baseline information had been obtained, the animals were treated perorally with physiological saline or with 1.5 mg/kg methylmercury hydroxide once weekly for seven weeks. Administration of the saline solution produced no change in performance relative to the period before treatment. The mercury compound caused no apparent effect for the first five weeks of treatment. By the sixth week, however, four of the ten poisoned mice had begun to show a diminished performance in VI amounting to 50% of control values (lever presses per minute) and a 100% increase in the time taken to complete the FR component. By week seven eight of the mice showed deteriorated performance in VI and FR with no change in DRL. Six of the mice continued to decline after ten weeks and two began to improve. We feel that methylmercury intoxication is capable of being detected by behavioral means at dosage levels smaller than those producing gross neurological symptoms.

**50.2** CORTICOFUGAL FIBER DEGENERATION FOLLOWING LESIONS OF THE INSULAR CORTEX IN MACACA MULATTA. Juan Astruc. Department of Anatomy, Medical College of Virginia, Health Sciences Division, Virginia Commonwealth University, Richmond, Virginia 23219.

Unilateral partial ablation of the rostral region of the insular cortex was performed by suction in four rhesus monkeys. Special care was taken not to damage either the neighboring operculum nor the underlying extreme capsule. Damage to the operculum was avoided by dissecting away the leptomeninx that covers the lateral fissure and then by opening the fissure with the aid of saline under pressure. Shallow lesions were produced by gentle aspiration of the insular cortex. Five to ten days after surgery the animals were sacrificed and perfused transcardially with normal saline followed by 10% formalin. Fiber degeneration was identified using the Fink-Heimer or the Nauta silver impregnation techniques on frozen serial sections. In each case fiber degeneration could be traced from the lesion to the prefrontal cortex (granular cortical areas) and motor cortex (agranular cortical areas). The supracingulate, that is the dorsomedial frontal granular and agranular cortices, appeared to receive the heaviest projection of the frontal lobe. There is, in addition, a projection to the orbitofrontal cortex. The insula projects to the cingulate gyrus through the cingulum and through the uncinate fascicle to rostral areas of the temporal lobe. Fiber degeneration to the contralateral symmetrical insular area have been traced through the corpus callosum and anterior commissure. Fiber degeneration enters the dorsal region of the claustrum and the laterodorsal part of the putamen through the extreme and external capsules. Finally, degenerating fibers enter the dorsal and ventral thalamus via the internal capsule. (Supported by USPHS Research Grant NB 08418)

**50.3** PROJECTIONS FROM THE ORBITAL CORTEX IN THE MARMOSET (Saquinus oedipus). G. R. Leichnetz* and J. Astruc. Department of Anatomy, Medical College of Virginia, Health Sciences Division, Virginia Commonwealth University, Richmond, Virginia 23219.

Lesions were made by subpial suction in the orbitofrontal cortex of the marmoset. The animals were allowed to survive for four to twelve days, and then were sacrificed and perfused transcardially with normal saline followed by 10% formalin. Fiber degeneration was identified using the Nauta or Fink-Heimer silver impregnation techniques on frozen serial sections. The degeneration was observed to take four different courses after entering the subcortical white matter. Some fibers joined the cingulum to terminate in the cingulate cortex. Some entered the uncinate fascicle and terminated in the entorhinal cortex and rostral parts of the temporal lobe. Another bundle was observed coursing in the external capsule which terminated in the putamen and ventral region of the claustrum. Others, following a sublenticular approach to the internal capsule, terminated in the head of the caudate and in the putamen. Degeneration was followed into the reticular, magnocellular part of the dorsomedial and intralaminar nuclei and also into the lateral hypothalamic area. Fiber degeneration was not observed more caudal than that in the prerubral field (Field H of Forel) and the rostral midbrain tegmentum. These findings on a new world monkey will be compared with others made on rhesus, an old world primate. (Supported in part by USPHS Grant No. 8418)

**50.4** AGE-INDEPENDENT EFFECTS OF ORBITAL PREFRONTAL LESIONS IN INFANT MONKEYS. Epp A. Miller* and Patricia S. Goldman. Laboratory of Psychology, Section on Neuropsychology, National Institute of Mental Health, Bethesda, Maryland, 20014

Cortical injury in infancy is commonly followed by impressive recovery of function, whereas the same injury in the adult produces lasting impairments. A notable exception to this pattern of results occurs in the case of rhesus monkeys with orbital prefrontal lesions: monkeys operated at 2 months of age are just as impaired as monkeys given orbital lesions as adults. The question arises as to whether the functions of the orbital prefrontal cortex are inherently more vulnerable to early injury than are other cortical regions or whether these functions might also be spared if the lesions were made earlier than 2 months of age. Accordingly, monkeys given orbital lesions within the first week of life, at 4 weeks, or at 8 weeks were compared with each other and with age-matched unoperated controls on a number of tests designed to measure orbital functions. If the maturational status of the cortex when it is damaged is an important determinant of subsequent recovery, as the findings in the literature would imply, then there should be greater recovery the earlier the lesion. Contrary to this expectation, we found severe and selective impairments in behavior, irrespective of the age at surgery. These findings suggest that factors other than the maturational status of the damaged cortex determine whether or not recovery occurs following brain injury in infancy.

**50.5** SPATIAL LEARNING IN MONKEYS WITH DORSOLATERAL PREFRONTAL LESIONS. Roger W. Buddington*, Patricia S. Goldman and H. Enger Rosvold*. Section on Neuropsychology, Laboratory of Psychology, National Institute of Mental Health, Bethesda, Maryland 20014

The classical delayed-response task typically lacks salient exteroceptive cues to guide spatial orientation during the delay. This fact has led many investigators to conclude that proprioceptive cues are relied upon in solving such tasks and that proprioception is disrupted in some way by dorsolateral prefrontal lesions in the monkey. In order to test this hypothesis monkeys with dorsolateral prefrontal lesions and normal controls were trained to run to one of the two goal boxes in a locomotor T-Maze under conditions which forced them to rely primarily upon either proprioception, or upon vision, in distinguishing left from right. Prefrontal monkeys performed as well as normals when learning of the runway habit was based upon proprioception, but were impaired when learning involved primarily visual cues. These results strongly indicate that spatial learning impairments in monkeys with dorsolateral prefrontal lesions are not due simply to a defect in proprioceptive sensation.

**50.6** SOME CONSEQUENCES OF ONE AND TWO STAGE LESIONS OF THE VENTROBASAL COMPLEX. Renato Reyes*, Stanley Finger and John Frye*. Dept. Psychol., Washington Univ., St. Louis, 63130.

Rats with one-stage bilateral lesions of the ventrobasal homologue, sequential unilateral lesions of Vb with a three week interoperative period, and one and two-stage control operations were compared for (1) survival from surgery, (2) performance on neurological tests, and (3) the ability to make two ridge-smooth tactile discriminations in a T-maze. Many rats with one-stage Vb lesions were adipsic, aphagic, and even comatose after surgery, and 18 or 35 of these Ss died 1-14 days later in spite of intensive efforts to keep them alive. Rats with two-stage lesions did not show these effects (only 1 of 12 animals was lost prior to tactile testing), and these animals performed better than the surviving one-stage rats on many of the neurological tests. Both lesion groups did very poorly on the ridge-smooth tactile discriminations and there was no evidence for seriatim sparing on this measure. (Supported by Public Health Service Grant MH-21419)

**50.7** IMPAIRED ACQUISITION OF CLASSICALLY CONDITIONED EYE BLINK TO CLICK-CS AFTER ABLATION OF CORTICAL MOTOR AREAS IN CATS. C.D. Woody, P. Yarowsky* and J. Owens*. Laboratory of Neurophysiology, Mental Retardation Center, UCLA, Los Angeles, Calif. 90024

Five cats were unable to learn a blink CR to pairing glabella tap with click after bilateral ablation of cortical motor and associated somatosensory areas. Auditory cortex was spared, and startle responses to auditory stimuli were present in the animals. Training was begun 9-10 days post operatively and continued for as many as 3000 pairings over a period of more than 3 months. Normal animals learned to perform the CR after several hundred pairings. The force required to elicit an unconditioned blink by tapping the glabella and rates of spontaneous eye blink were no different in lesioned animals than in normals. Less force was required to elicit a blink in normal cats conditioned to blink to a click. These animals also had higher rates of spontaneous blinking. Previous electrophysiologic evidence (Fed. Proc. 30: 265, 1971) suggests that the motor cortex of the cat is a possible locus for some plastic changes required for classical conditioning. Present ablational evidence indicates that intactness of the motor cortex is required for establishment of a classically conditioned blink to an auditory CS. Lesions of the motor cortex do not appear to impair conditioning by indirectly impairing the function of the facial nucleus since our tests of this nucleus were normal in the lesioned animals and were sensitive enough to detect functional facilitation of trigeminal input to the facial nucleus in conditioned animals. (Supported by USPHS HD04612 and California Dept. of Mental Hygiene.)

**50.8** SOMATOSENSORY AND AUDITORY BEHAVIORAL FUNCTION OF CATS' ORBITAL, ANTERIOR SYLVIAN AND ANTERIOR ECTOSYLVIAN CORTEX. Robert B. Glassman. Dept. Psychol. Lake Forest College, Lake Forest, Illinois 60045

Massive or restricted ablation of the cat's posterior sigmoid gyrus, containing the SI representation of trunk and limbs, causes a deficit in motor control but not in cutaneous sensation (Glassman, Physiol. Behav. 5:1009, 1970 & Exp. Neurol. 33:16, 1971). Massive ablation of the anterior ectosylvian gyrus (AEG), containing SII, is followed by a cutaneous deficit in orientation-localization of points on the body and in learned discriminations (Glassman, 1970; cf. also Norrsell, Experientia 27:1284, 1971) but superficial AEG ablations have led either to no cutaneous deficit or to a very small one. Experiments involving unilateral ablations of neighboring areas are in progress in an attempt to determine whether there is some small area crucial and specific to cutaneous sensation or whether it is rather a question of removing a sufficient mass of relevant tissue. Each cat is being trained in several tasks, involving orientation-localization or else learned discrimination of tactile and auditory stimuli, as well as a task requiring fine control of movement. Reexamination of histological material from earlier studies in addition to new results from 6 animals thus far suggest participation of anterior sylvian and orbital gyri in auditory and tactile behaviors as well as in visual orientation. Careful observations of the tactile orientation response of 2 animals with extensive ablations and severe deficits showed that they not only failed to turn toward the deficient side (say the right) but they also had difficulty turning right to the left forepaw if first induced to bend the body into an acute orientation to the left hindlimb. In free locomotion, though there was a tendency to circle ipsiversively, they often turned contraversively.

**50.9** THE TRIGEMINAL SYSTEM AND HUNGER IN THE PIGEON:DIFFERENTIAL ROLE OF CENTRAL AND PERIPHERAL TRIGEMINAL STRUCTURES IN THE CONTROL OF APPETITIVE AND CONSUMMATORY BEHAVIOR. H. Philip Zeigler. Dept.Psychol.,Hunter College, CUNY:N.Y.10021

The role of peripheral and central trigeminal structures in the neural control of hunger and thirst was explored in test situations permitting independent assessment of food or water reinforced key-pecking responses and of ad-lib eating or drinking. The effects upon such behaviors of trigeminal deafferentation were compared with those of lesions of nucleus basalis--a telencephalic component of the avian trigeminal system. Both groups exhibited deficits in the sensory control of feeding as indicated by significant increases in the number of feeding responses required to obtain a unit quantity of grain. Trigeminal deafferentation did not directly effect food reinforced key-pecking but produced gradual extinction of the behavior by abolishing the bird's response to food presented as reinforcement in the Skinner box. Lesions of nucleus basalis abolished food reinforced key-pecking for periods of up to several weeks but did not effect ad-lib eating. Neither trigeminal deafferentation nor nucleus basalis lesions effected water reinforced key-pecking or ad-lib drinking. Surgical or lesion controls had no effect upon any of the measures. The results extend our previous finding that trigeminal structures constitute an afferent limb of a "feeding-behavior system" in the pigeon and indicate that these structures are involved not only in the neurosensory but also in the motivational control of feeding behavior in this species.

**50.10** TERMINAL DEGENERATION AND BEHAVIORAL CHANGE DUE TO THALAMIC LESIONS IN ANURANS. Michael C. Trachtenberg. Neuropsychology Laboratory, McLean Hospital, Belmont, Mass. 02178.

The Anuran optic tectum receives inputs from the contralateral retina into the superficial laminae, layers 8 and 9 and from the contralateral tectum to the major pyramidal cell lamina, layer 6. Neither ipsilateral retinal nor telencephalic inputs have been demonstrated. However, the diencephalon and midbrain tegmentum serve as end stations for telencephalic, retinal, and tectal neurons. As the tectum responds physiologically to stimulation of the ipsilateral retina and serves as a major motor coordinating center it would not be unreasonable to expect connections from the diencephalon and tegmentum to the optic tectum. In the tectum ipsilateral to the lesion degeneration is most prominent in the deep fiber and cell laminae, layers 3, 5 and 2, 4 although some degenerating material is seen in other laminae. Contralateral to the lesion the amount of degeneration seen in the tectum is less than is the case on the ipsilateral side. However, some degenerating material is seen in layers 3, 5; still less is seen in superficial laminae. Depending on the site of the lesion and the state of the animal these lesions may result in hyperavoidance or hyperaggressivity. In the former case the animals now retreat from or become defensive towards small objects which are pursued by the normal Anuran. In the latter, they now orient and snap at large objects toward which the normal animal acts defensively.

**51.1** IN-VITRO REVERSAL BY DIPHENYLHYDANTOIN OF THE ELECTROPHYSIOLOGICAL EFFECTS OF STEROID-INDUCED MYOPATHY. Raphael Gruener and Lawrence Z. Stern. Dept. Physiol. and Div. Neurol., Univ. of Arizona Sch. of Medicine, Tucson, 85724.

Experimental steroid myopathy was induced in rats by daily administration of cortisone (50 mg/kg) for 24 weeks. We have previously shown that such chronically elevated levels of corticosteroids result in muscle membrane depolarization and a shift in the hyperpolarized direction of membrane excitability (Arch. Neurol. 26:181:72). These changes are reversed after in-vivo administration of diphenylhydantoin (DPH). We postulated (Nature 235:54:72) that DPH acts by stimulating a decelerated Na/K pump. While this hypothesis agrees with the presumed action of DPH, the route of drug administration (intraperitoneally, in-vivo) did not permit us to conclude a direct action on the sarcolemma. We have therefore measured resting potentials (RP) of the extensor digitorum muscle fibers at 30°C, from steroid-treated rats, before and at various intervals after in-vitro incubation with $3.95 \times 10^{-4}$M DPH. We also monitored the RP of individual fibers before and during DPH incubation. The RP of fibers from four treated rats hyperpolarized from 4-12 mV. The RP reached a steady-state after about 20 minutes incubation. The RP of fibers from three controls either did not change or depolarized after exposure to DPH. We conclude that DPH has a direct effect on the membrane, and that this effect is most likely mediated via the Na/K pump.

Resting Potentials* After In-Vitro Incubation with Diphenylhydantoin

| | Control | DPH 15' | DPH 30' | Number of Fibers |
|---|---|---|---|---|
| Myopathic | 70.9±0.9 | 74.5±1.8 | 76.3±0.8 | 80 |
| Normal | 75.3±0.8 | 71.7±1.3 | 71.8±1.2 | 60 |

* Absolute values in mV. Mean ± S.E.

Supported by NIH grant NS-08184 and the Dreyfus Medical Foundation.

**51.2** INHIBITION OF RADIOACTIVITY UPTAKE IN BRAIN AND PERIPHERAL TISSUES AFTER THE INJECTION OF 1,2 $^{3}H$ TESTOSTERONE BY CYPROTERONE ACETATE OR PROGESTERONE. Madhabananda Sar* and Walter E. Stumpf. Laboratories for Reproductive Biology, Departments of Anatomy and Pharmacology, Univ. of North Carolina, Chapel Hill, N.C. 27514.

Twenty five 35-day old male Sprague-Dawley rats were castrated, divided into 3 groups, and injected subcutaneously with the following substances daily for 5 days: group 1, controls, sesame oil; group 2 cyproterone acetate 10 mg.; and group 3, progesterone 4 mg. On the 6th day the rats were injected with .5 µg, per 100 gm. body weight, of 1,2 $^{3}H$ testosterone, specific activity 45 Ci/mM, and killed after 1 hour. Samples of the preoptic region, central hypothalamus, posterior hypothalamus, midbrain, amygdala, hippocampus, septum, cerebellum, neocortex, pituitary, prostate, seminal vesicles, adrenal and muscle were dissected, weighed, individually oxidized in a Packard Tri-Carb Sample oxidizer, and the radioactivity determined in a scintillation counter. Cyproterone acetate significantly reduced the accumulation of radioactivity in the hypothalamus, preoptic region, hippocampus, septum, pituitary, prostate, and seminal vesicles, but not in other brain tissues and muscle. These results suggest that cyproterone acetate selectively inhibits the uptake and retention of androgen in central nervous as well as in peripheral target tissues. The tissues that show competition after cyproterone acetate are in agreement with the androgen target tissues as demonstrated by dry autoradiography (Sar, M. and Stumpf, W.E., 1971. Fed. Proc. 30, 363; Stumpf, W.E. and Sar, M., 1971. Exc. Med., 184, 503-507.) Progesterone reduced the accumulation of radioactivity significantly in the pituitary but to a lesser extent in the central hypothalamus and preoptic region.

**51.3** EFFECT OF ADRENAL SECRETION ON MIDBRAIN TRYPTOPHAN HYDROXYLASE ACTIVITY IN RATS. Efrain C. Azmitia, Jr. and Bruce S. McEwen. Rockefeller University, New York, N. Y. 10021.

The involvement of adrenal steroids in influencing the tryptophan hydroxylase activity (THA) in rats was studied by subjecting normal and adrenalectomized animals to various treatments known to cause an increase in plasma corticosterone levels. THA in midbrain whole homogenate was measured by a modification of the $CO_2$ trapping method of Ichiyama et al. (Adv. Pharmacol.6A, 5, 1968). Plasma corticosterone levels were determined by the well-known sulfuric acid fluorescence method. Normal rats were stressed by electric foot shock (EFS), ether, and cold temperature (4°C). It was found that EFS and ether led to approximately 20% increases in THA and a corresponding 100% increase in plasma corticosterone level measured at time of sacrifice. Cold stress led to changes in THA and plasma corticosterone levels of 70% and 100%, respectively, after 5 hours; and of 22% and 50%, respectively, after 8 hours; after 48 hours there was no significant change. Parachlorophenylalanine ($10^{-3}$ M), a specific inhibitor of THA, inhibited control, EFS, and 5-hour cold stress THA by more than 90%. That this elevation in THA was due to adrenal secretion is supported by the following two experiments: (1) No increase in THA was found in adrenalectomized animals subjected to 5-hour cold stress and EFS. (2) Intraperitoneal injection of 5 mg of corticosterone in 0.1 ml of ethanol in normal animals led within 4 hours to a 20% increase of THA compared to ethanol-injected controls. (Supported by NIH grants MH 13189, NS 07080, and GM 01789.)

**51.4** THE ORGANIZATION OF TUBERO-HYPOPHYSIAL AND RETICULO-INFUNDIBULAR CATECHOLAMINE NEURON SYSTEMS IN THE RAT BRAIN. Anders Björklund*, Robert Y. Moore, Anders Nobin*, and Ulf Stenevi*. Dept. Histology, U. Lund, Lund, Sweden and U. Chicago, Chicago 60637.

Central catecholamine (CA) neuron systems are believed to play an important role in hypothalamo-pituitary function. The distribution of CA terminals in the median eminence and pituitary region has been described in detail (cf. Fuxe and Hökfelt, 1969; Björklund et al., 1970). However, the origin, course and exact topography of the components of this innervation has not yet been established and was the subject of the present study. In this lesions were placed in selected areas of the basal telencephalon, thalamus, hypothalamus (particularly the ventral periventricular zone) and brainstem of 13 groups of female rats. The brains, including the median eminence-pituitary region, were prepared using the Falck-Hillarp method for histochemical localization of cellular monoamines. The results can be summarized as follows. There are reticulo-infundibular noradrenaline neurons with cell-bodies located in the caudal medulla and axons traversing the medial forebrain bundle to innervate the internal and subependymal layers of the medial eminence. This projection is partially crossed and partially uncrossed. The remaining terminals in the median eminence-pituitary region all arise from dopamine-containing cell-bodies in the arcuate nucleus and adjacent periventricular zone. These constitute a tubero-hypophysial system which can be separated into three components. One arises from the most rostral zone of the arcuate nucleus and innervates the entire pars intermedia. A second group originates in a small group of cells immediately caudal to the first and innervates the neural lobe. The third group is an arcuato-infundibular system innervating the external layer of the median eminence and, probably, the internal and subependymal layers as well.

**51.5** EFFECT OF ACUTE STARVATION ON THE SLEEP-GROWTH HORMONE RESPONSE. Ismet Karacan and Robert L. Williams*. Dept. Psychiatry, Univ. of Florida, Gainesville, Florida 32601

To determine whether acute starvation potentiates the release of human growth hormone (GH) during sleep, as would be expected if the sleep-GH response serves metabolic needs, all-night EEG's and electro-oculograms were recorded from 11 previously adapted healthy male medical students during two three-night periods. During the first period subjects (Ss) fasted from after dinner on the first night to the morning following the third night. GH was sampled every 20 minutes throughout the first and third nights, and was analyzed with radioimmunoassay methods. During the second period 6 months later, Ss fasted and slept in an identical manner, but GH was not sampled. There was a significant increase in peak GH concentration and in area under the GH curves on the third night of the first period. Sleep was significantly disturbed on the GH sampling nights, as reflected by the shorter total sleep times, longer sleep latencies, greater number of awakenings, and greater amount of wakefulness during the night. This disturbed sleep was due to the GH sampling, and not to the starvation, since sleep was not significantly disturbed on either of the starvation nights of the second study period. There were no significant increases in slow-wave sleep during acute starvation. These results indicate that phenomenological sleep is differentially reflected by the EEG and the sleep-GH response, and that the two types of response do not always respond in a parallel fashion to manipulation.

**51.6** RELEASE OF RAT PITUITARY PROLACTIN AND LH FOLLOWING APPLICATION OF KCL TO THE CEREBRAL CORTEX. Jorge A. Colombo*, Charles A. Blake and Charles H. Sawyer, Dept. Anat., and Brain Res. Inst., UCLA, Los Angeles, 90024.

Application of hypertonic KCl to the cortex causes spreading depression. The EEG was monitored while 25% KCl, 25% NaCl or Ringer's solution was applied to the frontal cortex, and heart blood was withdrawn from an indwelling cannula for radioimmunoassay of prolactin and LH. Under ether, in rats made "pseudopregnant" with PMS and HCG by the method of McCann and Taleisnik (Am. J. Physiol. 199: 847, 1960), there was a 2-6 fold rise in plasma prolactin starting about 1 hr after KCl. Hypertonic NaCl, but not Ringer's, also caused a rise which was of lower magnitude and shorter duration. None of the treatments elevated plasma LH in these rats. In ovariectomized (OVX) rats under urethane, plasma LH rose 2-4 fold starting about 1 hr after cortical application of KCl. A more rapid ( 20 min) onset of LH release after KCl was seen in OVX estrogen-progesterone primed rats under ether. In none of the OVX groups did KCl elevate plasma prolactin. Under urethane, cortical spreading depression was accompanied within 2-3 min by decreases in multiple unit activity in the preoptic area, amygdala, and dorsal hippocampus; they returned to baseline in about 15-20 min. The results suggest that the influences of cortical activity on release of prolactin or LH depend on the hormonal condition of the animal. (Supported by NIH and The Ford Foundation.)

**51.7** EFFECT OF AN ANTIPSYCHOTIC TRANQUILIZER ON THE SECRETION OF PROLACTIN IN VIVO AND IN VITRO. Richard Blackwell*, Wylie Vale*, Catherine Rivier*, and Roger Guillemin. The Salk Institute, La Jolla, California 92037.

Injection (i.v.) of perphenazine, an antipsychotic tranquilizer, into rats produces a 10-fold increase in plasma prolactin levels as measured by radioimmunoassay; a similar response is seen when using adult male or female rats; plasma prolactin levels are increased significantly by 10 min. post-injection and a maximal response occurs after 30 min. 10 $\mu$g of perphenazine is the minimal active dose that will cause an elevation in plasma prolactin levels. Simultaneous administration of 7 fragment equivalents of ovine hypothalamic extract produces a marginal inhibition of the release of prolactin. Administration of 50 $\mu$g of either TRF, LRF, norepinephrine, epinephrine, dopamine, L-dopa, or 8-lysine vasopressin does not inhibit or potentiate the response 30 min. post-injection. Addition of up to 10 $\mu$g/ml media of perphenazine to in vitro cultures of enzymatically dispersed rat pituitary cells does not stimulate secretion of prolactin. Also, (i.p.) injection of 1 mg perphenazine into rats bearing 2 pituitary transplants under the kidney capsule, does not significantly alter prolactin secretion. These data indicate that perphenazine releases prolactin by acting on brain centers above the level of the pituitary and that the acute release of prolactin is unaffected by various hypothalamic neurohumors, which thus do not appear to correspond to prolactin (release) inhibiting factor (PIF) or prolactin releasing factor (PRF) activity.

Research supported by AID Contract (No. AID/csd 2785), Ford Foundation and Rockefeller Foundation.

**51.8** INCREASED SENSITIVITY OF THE CYCLIC 3',5'-AMP SYSTEM OF RAT PINEAL GLAND INDUCED BY DECREASED SYMPATHETIC NERVE ACTIVITY. Samuel J. Strada and Benjamin Weiss* Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, D.C. 20032.

The rat pineal gland serves as a useful model for studying short and long term influences of sympathetic nerve activity on the adrenergic receptor since the sympathetic input to the gland can be modified by a variety of surgical, chemical and environmental procedures. The acute addition of norepinephrine (NE) to pineal homogenates or to pineals in organ culture increases the formation of cyclic-AMP. These effects of NE are inhibited by β- but not by α-adrenergic blocking agents. Several conditions that chronically decrease sympathetic input to the pineal, such as superior cervical ganglionectomy, decentralization of these ganglia, chemical sympathectomy with 6-hydroxydopamine or exposing rats to continuous light increased by several fold the NE (50μM)-induced elevation in the levels of cyclic-AMP in cultured pineals in vitro as well as the isoproterenol (3 μmoles/kg, i.p.)-induced elevation of cyclic-AMP in pineals in vivo. Chronic administration of NE (6.25 μmoles/kg, in oil s.c.; 14 days) during this period of reduced sympathetic activity prevented the enhanced response to the in vitro addition of NE. Moreover, increasing sympathetic input to the pineal by blinding the rats decreased the responsiveness of the pineal cyclic-AMP system to the stimulatory effects of NE. These results suggest that NE released from sympathetic nerve endings has two opposing effects on adenylate cyclase: firstly, it activates the enzyme, increasing the rate of formation of cyclic-AMP, and secondly, perhaps through another mechanism it inhibits the NE-sensitive adenylate cyclase system rendering the enzyme less sensitive to the stimulatory effects of the adrenergic neurotransmitter.

**51.9** ELECTROPHYSIOLOGICAL CORRELATES OF EXPERIMENTAL HYPERTHYROIDISM. Lawrence Z. Stern and Raphael Gruener. Dept. Physiol. and Div. Neurol., Univ. of Arizona Sch. Medicine, Tucson, Arizona 85724.

Chronic hyperthyroidism is associated with proximal muscle weakness and atrophy. Clinical and morphologic findings suggest a direct effect on muscle. Routine electromyography, while indicative of a myopathic process, provides little information on specific site(s) of membrane dysfunction. Such specific information may, however, be obtained from in-vitro intracellular electrophysiological studies. We have administered levothyroxine intraperitoneally to rats at a daily dose of 2 mg/kg for 6 weeks. Extensor digitorum longus (EDL) and soleus (SOL) muscles were isolated, mounted in a chamber and continuously perfused with oxygenated Tyrode solution at 30°C. Membrane potentials were measured using a 3M KCl microelectrode; another microelectrode was used for intracellular current injections. Mean resting potentials (RP) of EDL and SOL fibers showed a marked reduction from -72±1.9 mV (n=80) for controls to -61±0.9 mV (n=240) for treated rats. Membrane resistance was also significantly reduced in the EDL fibers from thyroxine-treated rats. Action potentials (AP) could usually not be elicited by intracellular injection without concomitant hyperpolarization by a DC current. When elicited, the action potential overshoot was normal but its duration was prolonged. This prolongation was due to a marked decrease in the dV/dt of the repolarization phase. In addition, a large hyperpolarization was very often seen at the termination of the evoked AP. The return to the controlled RP from such a hyperpolarization occasionally resulted in a rebound causing multiple spiking and prolonged potential oscillations in response to a single short depolarizing pulse.

Supported by NIH grant NS-08184 and the GRS Fund of the School of Medicine.

**51.10** INTENSE LORDOSIS IN THE ABSENCE OF OVARIAN HORMONES AFTER SEPTAL ABLATION IN RATS. B.R. Komisaruk, K. Larsson*, and R. Cooper*. Rutgers - The State University, Institute of Animal Behavior, Newark, New Jersey 07102

The lordosis reflex intensity (L) was quantified photographically by adding the elevations (in mm) of the top of the nose and the rump above a horizontal line drawn through the lowest point of the back. Lordosis was induced by flank-perineum palpation in conjunction with probing the vaginal cervix. 3+ weeks after ovariectomy, L was measured and each of 27 rats was then assigned to one of three treatment groups; (1) suction ablation of the septum and overlying cortex (S); (2) control ablation of overlying cortex (CC); (3) sham operation (C). Median L of S increased from a pre-op level of 12 mm to 60 mm ($p<.05$, Wilcoxon test) 10 days post-op. In contrast, the median pre- and post-op L's in CC were 13 and 22, resp. ($p>.05$), and those in C were 24 and 27 mm, resp. ($p>.05$). Subsequent administration of estradiol benzoate (EB) (10 µg/kg/day x 4 days) followed by progesterone (P) (.5 mg) on day 4 brought the median L's to 64, 61, and 70 mm in S, CC, and C, resp., with no significant differences among the groups.

Despite the intense L in S in the absence of ovarian hormones, these rats failed to mate with vigorous males. However, S showed a greater response to EB than did CC or C ($p<.05$), and by day 4 of EB, 87.5% of S mated (Lordosis Quotient [LQ]:60.0) while only 30% (LQ:18.0) of CC and 22.2% (LQ:13.3) of C mated. 4 hr post P 90-100% of the rats in each group mated, indicating their ability to show lordosis in response to male mounting.

We suggest that the septum or related systems suppress the lordosis response, and ovarian hormones disinhibit this mechanism.

Research Support: PHS-MH 13279-04, MH 14711-02 (B.K.); National Bank of Sweden (K.L.); PHS-1-F01-MH 47269-1 (R.C.).

**52.1** BASIS OF ELECTRICALLY EVOKED POTENTIALS FROM THE GOLDFISH OPTIC TECTUM. George C. Offutt. Dept. Biol. City College, CUNY, New York, 10031

Evoked potentials were recorded and averaged from the optic tectum of goldfish with electrical stimulation of the tectum and the contralateral optic nerve. The wave form of the potentials was influenced by several factors including the site of stimulation and the resistance of the recording electrodes. Low resistance electrodes apparently distorted the potential field. The double peaked negative surface potential and other observed phenomena were explained by hypothesizing the presence of source-sink potentials with similar wave shapes but a difference in onset time. An analog model was constructed from concentric screen cylinders. When integrated square pulses were applied to the cylinders with a small onset lag between them, potentials could be recorded from the model that were quite similar in wave form to those recorded in the tectum. The tectal positivity is apparently a source potential from the somas of cells located deep in the tectum. The onset of this potential is about 0.5 msec later than the superficial negative postsynaptic potential. This delay is probably due to the time necessary for the dendritic potentials to reach the somas. The amplitude of the deep positivity appeared to be relatively greater than the negativity and seemed to be a function of the tectum's geometric shape.

**52.2** FORMATION OF ANOMALOUS PROJECTIONS FROM THE RETINA TO THE PULVINAR FOLLOWING REMOVAL OF THE SUPERIOR COLLICULUS IN NEONATAL TREE SHREWS. V. A. Casagrande*, W. C. Hall, and I. T. Diamond, Departments of Anatomy and Psychology, Duke University, Durham, North Carolina 27706.

In the normal tree shrew the pulvinar nucleus receives a heavy visual projection from the superficial layers of the superior colliculus but no direct projections from the retina. In the present experiments the superior colliculus was ablated in three day old tree shrews; then in adulthood one eye was removed and optic tract degeneration was traced with the Fink-Heimer method. In all cases dense terminal degeneration was found in a restricted part of the pulvinar nucleus. Since similar results have been reported by Schneider in the hamster, this capacity for neural reorganization may be characteristic of all mammals. To account for these results the following question must be answered: Does the pulvinar receive the anomalous projections from the retina because it is the major target of the superior colliculus, or simply because it has been denervated by the lesion? Since tree shrews which receive superior colliculus ablations as neonates are as severely retarded on our visual discrimination tests as those which receive similar ablations as adults, it remains to be determined whether this type of neural reorganization is the structural basis for the recovery of function commonly observed following brain damage in infants. (Supported by NINDS Grant NS-09623 and NIMH Grant MH-4849 and Research Scientist Award 1 K02 MH-25734 from NIMH).

**52.3** ULTRASTRUCTURE OF THE ACCESSORY OPTIC TRACT NUCLEUS IN THE MONKEY. Tauba Pasik, Pedro Pasik, József Hámori* and János Szentágothai*. Dept. Neurol. Mount Sinai Sch. Med. CUNY, New York 10029, and Dept. Anat., Semmelweis Univ. Med. Sch., Budapest, Hungary.

In a series of studies, Pasik and Pasik have shown that the accessory optic system is critical for the visually guided behavior of monkeys with total destruction of the geniculostriate system. The present investigation attempted to describe the fine morphology and synaptic organization of the n. of the accessory optic tract. Electron microscopic examination of the normal nucleus revealed medium-large neurons of uniform type with relatively frequent occurrence of somatic spines. The dendritic profiles had a thick and smooth initial portion followed by the appearance of increasing numbers of spines. The dendrites bifurcated and finally ended in brush-like fashion. Axon terminals made synaptic contacts with the soma, dendrites (spines and trunk) and dendritic endings. The latter articulations appeared as "glomeruli" with abundant axo-axonic synapses and resembling those of the pulvinar in that the central element was always a dendritic profile. Following the enucleation of one eye, both the contralateral and ipsilateral nuclei showed terminal boutons in different stages of degeneration, dependent on the survival time. The mode of termination of these optic terminals was predominantly axosomatic. Axodendritic contacts were also observed, particularly at the bifurcation of the dendrites. There were no optic terminals participating in the "glomeruli". Findings confirmed the fact that this nucleus receives direct retinal fibers; the system is both crossed and uncrossed; the presence of axosomatic contacts of optic terminals suggests a very different functional mechanism than that of the geniculate pathway; the nucleus receives many more afferents of unknown origin. (Aided by U.S.P.H.S. Grants # MH-02261 and K3-EY-16,865).

**52.4** IDENTIFICATION OF GOLGI TYPE II INTERNEURON PROFILES IN LATERAL GENICULATE NUCLEUS OF MONKEYS. Pedro Pasik, Tauba Pasik, József Hámori* and János Szentágothai*. Dept. Neurol., Mount Sinai Sch. Med., CUNY, New York 10029 and Semmelweis Univ. Med. Sch., Budapest, Hungary.

Total excision of areas 17-18-19 in the monkey leads to disappearance of relay cells and corticogeniculate axon terminals in the LGN (lateral geniculate nucleus). The few remaining neurons, which are constantly present, can be safely considered as Golgi type II cells. Electron microscopic examination of such material revealed small ovoid neurons and synaptic clusters encapsulated by glia. Within the cluster there were the characteristic axon terminal of retinal origin, and a peculiar light and large profile with features of both axons (small, flattened synaptic vesicles) and dendrites (many microtubules, endoplasmic cisterns and free ribosomes) in varying proportions. These elements were also present within the heavily gliotic general neuropil and, in longitudinal section, showed segments with strongly dendritic features, and others with vesicles either scattered or grouped near synaptic specializations. Similar profiles were also seen in normal LGN. Light microscopic examination of Golgi series from adult normal monkeys revealed two types of interneurons in the LGN, both having extremely thin axons which could not correspond in size to the ambiguous profiles described above. The latter could well match the appendages so frequently shown by the dendrites of one of the interneuron types. These findings suggest that the synapses in the glomeruli of LGN previously defined as "axo-axonic" may in fact be between optic axon terminals and the dendritic profiles with synaptic vesicles delineated in this study. Thence, the role of the Golgi type II interneuron could be parsimoniously explained as lateral inhibition, without the need for the hitherto postulated mechanisms of presynaptic inhibition or disinhibition. (Aided by U.S.P.H.S. Grants # MH-02261 and K3-EY-16,865).

**52.5** EFFECTS OF SACCADIC IMAGE MOTION ON THE GENICULO-STRIATE SYSTEM OF CHRONIC CATS. Hiroharu Noda☆ and W. Ross Adey. Dept. Anat., Sch. Med., UCLA, Los Angeles, 90024.

Responses of lateral geniculate and visual cortex to electrical stimulation of optic chiasm were studied during spontaneous eye movements in chronically implanted cats. The head of the cat was fixed rigidly in the center of a half-cylinder screen, so that image motion of stationary objects on the retina was caused only when the eyes moved. The responses were tested from moment to moment during the course of saccades by triggering a stimulator from potential shifts in electrooculograms and altering delays of stimulus pulses. Amplitudes of pre- and post-synaptic components of lateral geniculate and visual cortical responses were examined in four different conditions: 1) When the eyes moved in the presence of visual patterns. 2) When the eyes moved in total darkness. 3) When the eyes were stationary in front of the visual patterns. 4) When the eyes were stationary in total darkness. The postsynaptic response of lateral geniculate ( $r_1$ ) and presynaptic response of visual cortex ( $C_1$ ) were inhibited when the eyes moved in the presence of the visual patterns. At the same time, the postsynaptic responses of visual cortex ( $C_4$, $C_5$ ) were greatly enhanced. These effects reached a peak at approximately 100 msec after initiation of each saccade and lasted as long as 200 msec. Because these effects 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 stationary objects moved over the retina.

**52.6** A RETINOTOPIC PROJECTION AREA IN THE HYPERSTRIATIUM OF THE BURROWING OWL. J. W. Gray * and A. M. Revzin. Dept. of Psychiatry, Sch. Med., Okla. Univ., Okla. City, Okla. 73104 and Civil Aeromedical Institute, Okla. City, Okla.

Response characteristics of units in a visual projection area in the hyperstriatum of the urethane anethesized burrowing owl (Speotyto Cuniculo) were investigated. Visual field, direction sensitivity and other characteristics were recorded with tungsten-glass microelectrodes. The bulk of the units recorded had receptive fields ranging from 1-3 degrees. Most units responded to diffuse light, movement of target and showed some degree of direction sensitivity. Retinotopic projections were mapped and it was found that the nasal retina projects entirely to the contralateral wulst. The projection is distorted such that the visual field midline area, presumably foveal, projects to a large extent to the lateral wulst. Angular magnitudes of the visual field as represented on the wulst measure in magnitude from the lateral wulst to the midline. The projection of the retina to the wulst in the owl appears to consist only of crossed components of the optic chiasm.

**52.7** PHARMACOLOGICAL PROPERTIES AND RECEPTIVE FIELDS OF NEURONS OF THE PRIMARY VISUAL CORTEX OF THE CAT. E. Wallingford,* R. Ostdahl,* P. Zarzecki,* R. Glendenning and G. Somjen. Dept. of Physiology and Pharmacology and Dept. of Psychology, Duke Univ., Durham, N.C. 27710

Neurons in the cerebral cortex which can be excited by the microiontophoretic release of acetylcholine (ACh) are a special class of cells, found only in the deeper layers, and forming 10 to 20% of the cortical neuron population. (Krnjevic and Phillis, J. Physiol. 166:296, 1963). Since the cells of the primary visual receiving area (V I) can be classified into several types according to their receptive field organization (Hubel and Wiesel, J. Physiol. 160:106, 1962; Pettigrew, Nikara and Bishop, Exp. Brain Res., 6:373, 1968), one could ask whether sensitivity to ACh, and receptive fields properties are in any way correlated. Exploration by five-barreled electrodes revealed that cholinoceptive cells in the cat can be found amongst the simple, complex, and hypercomplex cells of V l area, and therefore we conclude that these two sets of properties are not correlated. Another special class of neural units are those which are not preferentially excited by straight-edged optical stimuli of a specified angle of tilt. Whether such non-oriented units are cortical cells, or the terminations of optic radiation fibers, is a matter of controversy. We found such units to be excited by iontophoretically released glutamate, and to be inhibited by gamma-amino butyric acid. Such observations suggests that the non-oriented units we found were cortical cells and not axon terminals. (Supported by PHS Grant NS 05330, and by the United Health Services of N. C.)

**52.8** CORRELATION BETWEEN POTENTIALS PHOTICALLY EVOKED IN PRECRUCIATE CORTEX AND BEHAVIORAL RECOVERY FROM VISUAL DEPRIVATION. Jay Glass* (SPON: Robert W. Doty). Center for Brain Research, University of Rochester, Rochester, New York 14642.

One eye of kittens was kept closed from birth to 9-12 months of age. Responses evoked by stroboscopic flashes were then recorded from neocortex under chloralose anesthesia with extra-dural electrodes. For flashes to the deprived eye the response from precruciate gyrus was either absent or greatly reduced in comparison with responses evoked by stimulation of the normal eye. Similar comparisons showed the initial components from marginal and suprasylvian gyri to be minimally altered, but the late components from these areas were greatly reduced by the deprivation. At this time visually guided behavior was also absent when the deprived eye was used. Permanently reversing the eye closure effected a gradual acquisition of normal visual behavior using the previously deprived eye. Following such behavioral recovery for 12 months, photically evoked potentials in precruciate cortex were normal from either eye. The late components from the suprasylvian gyrus also became normal whereas the deficits in late components of the response in marginal gyrus persisted. Thus, the restitution of behavioral efficacy of vision through the deprived eye is reflected in development of photic responsiveness in the precruciate cortex. The deprivation of the previously normal eye did not alter its electrophysiological effects. (Supported by Grants NS 03606 and MH 08034.)

**52.9** AREA 17: LAYER I AS THE TERMINATION SITE OF A TOPOGRAPHICALLY ORGANIZED FIBER PROJECTION FROM AREA 18. J. Tigges, M. Tigges* and W. B. Spatz*. Yerkes Regional Primate Research Center and Dept. of Anatomy, Emory Univ., Atlanta, Ga., and Max Planck-Institut für Hirnforschung, Neurobiologische Abteilung, Frankfurt/M., Germany.

A massive fiber projection upon area 17 was detected by placing unilateral gray matter lesions (2 mm in diameter) in area 18 of squirrel monkeys (Saimiri) and tracing antegrade degenerating fibers with the Fink-Heimer method. Each lesion caused a circumscribed dense focus of terminal degeneration in area 17, almost exclusively in layer I. Therefore, during surgery great care was taken not to injure the cortical surface except for the site of the lesion which was made by thermocoagulation with the dura intact. Dorsal portions of area 18 project to dorsal portions of area 17, whereas ventral portions of area 18 project to ventral area 17; further, anterior parts of area 18 are connected with posterior parts of area 17 and posterior area 18 with anterior area 17. The correspondence between the sites of the lesions and the resulting degeneration foci indicated that this fiber projection is a mirror-imaged point-to-point connection. The present results combined with those in a previous study of the association of area 17 with area 18 (Spatz, Tigges and Tigges, J. comp. Neurol. 140, 155-174, '70) led to the conclusion that areas 17 and 18 are reciprocally connected. (Supported in part by NIH grants RR-00165 and RO1-00638-02).

**52.10** ELECTROPHYSIOLOGICAL EFFECTS OF A CHELATING ION EXCHANGE RESIN (CHELEX 100) INTRODUCED INTO THE LATERAL GENICULATE BODY OF THE CAT. Anatol Costin, Elizabeth M. Rovner* and Irene M. Sabbot*. Dept. of Anat. and Brain Res. Inst., UCLA, Los Angeles, 90024

Changes in impedance of cerebral cortex after topical application of calcium and magnesium solutions were previously reported (Adey et al., Exptl. Neurol., 23: 29-50, 1969).

In the present study, cats with chronically implanted electrodes and cannulae into the lateral geniculate body (LG) were used. Electrical impedance measures at 1.0 kHz with low current levels ($10^{-13}$ A per square micron of electrode surface) and flash evoked potentials were recorded from the electrodes.

1-2 $mm^3$ of a chelating ion exchange resin (Chelex 100) when introduced into the LG of the cat brain brings about decreases of tissue impedance and flash evoked potentials.

No electrophysiological changes were observed if the chelating capacity of the resin for Ca and Mg was reduced by prior (24 hr) equilibration with 1-2 mEq $CaCl_2$ or $MgCl_2$ per g of resin.

The results contribute further evidence to the physiological role of divalent ions Ca and Mg in the neuronal membrane environment.

(Supported by NSF Grant GB 27740X1).

**53.1** TASTE AS A MODEL FOR THE NEUROGENESIS OF RECEPTOR PROPERTIES AND SYNAPTIC CONNECTIONS. Bruce Oakley. Dept. Zool., Univ. of Michigan, Ann Arbor, Michigan, 48104

The mammalian taste system has three advantageous features: (1) the first synapse is conveniently located in the tongue; (2) the crucial developmental processes are present in the adult as evidenced by the ready reformation of denervated taste buds with reinnervation and the continuous normal replacement of receptor cells; and (3) the multiplicity of receptor types aids in the precision of experimental analysis of connectivity. The basic processes to be explained are: the formation of the molecular receptors for taste; the determination or labelling of taste receptor cell types; the labelling of fiber types; the process of differentiation and maintenance of taste receptor cells (trophic functions) and finally the rules governing connectivity. The possible modes of fiber-receptor cell interaction will be presented along with experiments ruling on their validity. The role of the receptor (periphery) in the control of primary afferent connections will be discussed. Three conclusions emerge: (1) some sensory fibers are labelled as taste fibers prior to receptor innervation (2) taste receptor cells must be labelled as to their type prior to innervation and (3) a process of cell-recognition or matching between labelled receptor and labelled taste fiber must occur at some stage, although it may not be the exclusive process governing connectivity.

Supported by NS-07072.

**53.2** CENTRAL GUSTATORY PATHWAYS. R.E. Norgren*, C.M. Leonard and Carl Pfaffmann. Rockefeller Univ., New York, N.Y. 10021.

Gustatory information reaches the brain through the VIIth, IXth, and Xth cranial nerves which terminate in the nucleus of the solitary tract (NST) in the medulla. The rostral course and distribution of fibers carrying gustatory information has been determined in rats using multiunit recording, evoked potential, and axonal degeneration techniques. When a small lesion is placed in the rostral NST at a point which responds to taste stimuli applied to the tongue, terminal degeneration can be located in a cellular area surrounding the ipsilateral brachium conjunctivum (BC) as it enters the pons from the cerebellum (Norgren and Leonard, Science 173: 1136, 1971). Recordings from this pontine taste area (PTA) while independently stimulating the anterior or posterior tongue with sapid solutions indicate that both the chorda tympani (VII) and glossopharyngeal (IX) receptive fields project to the pons. Lesions in the PTA result in bilateral degeneration of axons in the dorsomedial tegmentum, and terminal fields in the medial tip of the thalamic ventrobasal complex. Units in this area respond to taste stimuli. Bipolar stimulating electrodes located in either NST or PTA produce short latency evoked potentials in the thalamic taste area (TTA), but those produced by NST stimulation follow poorly at 15 per sec., while the thalamic evoked potentials elicited by PTA stimulation follow at rates above 100 per sec. Although stimulation of the TTA produces no evoked potentials in the solitary nucleus, large amplitude, short latency potentials occur in the PTA, and follow stimulation rates above 150 per sec. More extensive anatomical studies have revealed that the pontine taste area projects not only to the thalamus, but also ventrally through the subthalamus into the far lateral hypothalamus, the entopeduncular nucleus, and rostrally into the ventral forebrain.

Supported by NIH NS10150-01, NSF GB2500X

**53.3** SYNAPTIC ORGANIZATION IN THE OLFACTORY PATHWAY OF MAMMALS. Gordon M. Shepherd. Dept. Physiol., Yale Univ. Sch. Med., New Haven, 06510.

Recent results from electronmicroscopy and electrophysiology provide a new basis for analysing neuronal mechanisms in the olfactory pathway. The organization of the glomerular layer of the olfactory bulb relates particularly to mechanisms for olfactory discrimination. There is EM evidence for dendrodendritic as well as axodendritic synaptic interconnections in the glomerular layer. The functional interpretations of these synaptic patterns are supported by preliminary evidence from physiological experiments on glomerular unit responses to olfactory nerve volleys. The organization of the granule layer of the olfactory bulb, on the other hand, relates particularly to mechanisms underlying olfactory-related behavior. Basal telencephalic regions receive direct inputs from the olfactory bulb; these regions in turn project to the granule cells, which, through dendrodendritic synapses on the mitral cells, exert inhibitory control over the bulbar output. A separate centrifugal pathway from the basal telencephalon to both the granule cells and the glomerular layer has also been described. Theories of olfactory discrimination and olfactory-related behavior need now to be reassessed in the light of this new information on the synaptic organization of the olfactory bulb.

**54.1** PROTEOLIPIDS FROM MEMBRANE SYSTEMS by J. Folch-Pi, M.D., Harvard Medical School and McLean Hospital, Belmont, Mass. 02178.

Proteolipids (PL) are $H_2O$ insol., $CHCl_3$:$CH_3OH$ soluble lipoproteins which constitute <50% of myelin proteins, and are also found in most vegetable and animal tissues, usually associated with membranous structures. PL are resistant to most proteolytic enzymes, and their amino acid (AA) composition is low in acidic and basic AA, and high in non-polar AA, S-AA and tryptophan. By dialysis in CM containing HCl PL yield proteolipid apoprotein (PLA), free of TLC demonstrable lipids. Brain white matter (WM) PLA thus prepared is soluble in both water and organic solvents. It is homogeneous by ultracentrifugation and moving boundary electrophoresis, and shows one single or one main band on different polyacrylamide gels on which molecular sizes of 34-36,000 and 22-23,000 have been reported. PLA minimal computed size (12,000) and its partial dialyzability suggest different states of aggregation. By ORD and CD, PL and PLA in CM show 66-70% α-helix. In water, PLA α-helix content is 32-42%; it becomes again 66-70% upon replacing PLA in CM. This reversible change in conformation of PLA is prevented by the presence of lipids which seem to stabilize PLA into the highly helical, water insol., conformation typical of PL. PL and PLA are equally resistant to proteolytic enzymes except pronase. Chemically, PLA exhibits the AA pattern typical of PL. It also contains 2.5-3.6% fatty acid residues (FA), (3/5 palmitic, 1/10 stearic and 3/10 oleic). Reaction with $CH_2N_2$ and $NaBH_4$ show FA to be combined in ester linkages. The absence in PLA of other known lipid moieties suggest that FA present are combined with the protein itself. PLA from gray matter (GM) is quite similar to WM PLA. PLA's from liver (L), kidney (K) and heart muscle (HM) differ from both WM and GM PLA's in the absence, or very low concentration of half cystine. L PLA shows combined fatty acids with a pattern different from WM PLA, HM and K PLA show little or no combined fatty acids. (Supported by USPHS Grant NS 00130).

**54.2** EVIDENCE FOR CONFORMATIONAL CHANGE IN AXONAL MEMBRANE DURING EXCITATION. I. Tasaki, M. Hallett* and E. Carbone*. Laboratory of Neurobiology, NIMH, Bethesda, Md. 20014

By using electrophysiological and optical methods, experimental results were obtained indicating that there is a drastic conformational change in the membrane macromolecules associated with the process of action potential production. When a squid giant axon capable of developing prolonged action potentials is exposed to a medium with a low Ca-Na ratio, an abrupt depolarization (Osterhout phenomenon) takes place. By lowering the temperature of such an axon, evidence for the existence of a first order phase-transition in the membrane macromolecules is obtained (experiments with Y. Kobatake and I. Inoue). When a giant axon is stained internally with the hydrophobic probe 2-p-toluidinyl-6-naphthalene sulfonate (2-6 TNS) a transient decrease in fluorescence is noted during the action potential. Analysis of the spectrum of this optical signal suggests that the dye molecules are probing a change in the polarity of their microenvironment with a change in Z-number so that the quantum yield falls from about 0.60 to 0.35. For depolarizing voltage clamp pulses, the amplitude of the optical signal measured at the peak of the inward current can be correlated with the total conductance change of the membrane. It is important to note that this information comes from a select class of the 2-6 TNS molecules which can be isolated with the use of a polarizer and analyzer arranged so that their polarizing axes are parallel to the longitudinal axis of the axon. The long axes of the molecules in this class are orderly and rigidly arranged parallel to the longitudinal axis of the axon. There is at least one more class of 2-6 TNS molecules which are arranged with their axes perpendicular to the longitudinal axis of the axon and which reflect different membrane phenomena. In order to obtain confirmatory evidence for these biophysical ideas, comparisons have been made with a variety of other derivatives of amino-naphthalene sulfonate.

**54.3** THE MEMBRANE ACTIONS OF THE EXCITABILITY-CONTROLLING DRUGS (or THE "HYDROPHOBIC EXPANSION THEORY OF ANESTHESIA").

P. Seeman, Pharmacology Department, Univ. of Toronto, Toronto 5, Canada.

1) Membrane electrical stabilization: The membrane action potential is blocked by many hydrophobic drugs (gases, alcohols, anesthetics, phenols, tranquilizers, morphine, methadone, barbiturates, diphenylhydantoin, and the active component of marijuana, delta-9-tetrahydrocannabinol).
2) Membrane occupation: Under conditions of general anesthesia by each of these drugs the membrane concentration of the drug is always about 3 milli-moles/Kg dry membrane (or 20,000 molecules/$\mu^2$ membrane), and the drug occupies a volume of about 0.02% in the membrane phase. Under conditions of local anesthesia the membrane concentration is about 40 milli--moles/Kg membrane (or 250,000 molecules/$\mu^2$ membrane), with an occupying volume of about 0.3% in the membrane phase.
3) Membrane expansion: The biomembranes expand or swell about 10 times more than the anesthetic volume of occupation in the membrane, 0.4% expansion occurring under conditions of general anesthesia, and 2-3% expansion occurring in local anesthesia. K.W. Miller et al. found that compression of anesthetized animals by 0.4% (at 100 Atm.) reversed anesthesia.
4) Membrane fluidization: The anesthetics fluidize and disorder the membrane; this may explain drug-enhanced neurosecretion by a mechanism of membrane-membrane melting or fusion. Membrane globules are rearranged.
5) Membrane enzymes: As a consequence of membrane expansion, membrane enzymes or proteins may be either stimulated or inhibited.
6) Membrane-$Ca^{++}$: The anesthetic amines displace membrane-bound $Ca^{++}$, reducing stimulus-response coupling; neutral drugs generally increase membrane-$Ca^{++}$ and may thus enhance contractions or neurosecretion.
7) Ion fluxes: Facilitated fluxes are invariably depressed, possibly as a result of membrane expansion; the $Na^{+}$ channel may be such a pathway.
(M.R.C. grant MT-2951; Ontario Mental Health; Addiction Research Found.)

**55.1** SYNAPTIC COMPLEX FORMATION AND AXONAL GROWTH ROSTRAL TO SITE OF HEMISECTION IN MONKEY SPINAL CORD. Jerald J. Bernstein and Mary E. Bernstein. Dept. of Neurosci. and Ophthal., University of Florida Col. of Med., Gainesville, Florida 32601.

Recent findings have shown regeneration of severed axons and sprouts of uninjured axons following lesion of rat spinal cord. The following study investigates the regenerative capacity of hemisected spinal cord in 14 Rhesus monkeys. Animals were utilized 7, 14, 21 days, and 1, 2, 3, and 4 months posthemisection. Tissue was prepared for Golgi impregnation, Protargol, cresyl violet, and eosin staining and electron microscopy. Dendrites of motor horn cells facing and close to the site of lesion were the first to develop terminal varicosities at about day 7. Varicosity formation progressed to primary dendrites by day 14-30 posthemisection. Motor neurons 0-5mm from lesion site possessed short, varicose dendrites by 30 days posthemisection. 5-9mm from the lesion site varicosities were found only on secondary and tertiary dendrites; however, dendrites facing degenerating tracts were often completely varicose. At 30 days posthemisection fascicles of neurites, often free of neuroglial cell processes were observed in enlarged extracellular spaces. Several types of synaptic combinations were observed. In addition to normal synapses, synapses were observed with large postsynaptic Nissl bodies contiguous with the postsynaptic membrane or with subsurface postsynaptic cisterns. The majority of synapses had multiple synaptic bars on the periphery of a cup-shaped bouton with a central core of enlarged extracellular space between pre- and postsynaptic elements. Postsynaptic membrane thickenings or subsurface cisterns were associated with these enlarged spaces. (Supported by Grant NS-06164, NINDS, NIH).

**55.2** ULTRASTRUCTURE OF INTENSELY STIMULATED PREGANGLIONIC NERVE ENDINGS WITH AND WITHOUT RECOVERY. J.J.Pysh and Ronald G. Wiley*. Depts. of Anatomy and Pharmacology, Northwestern University-McGaw Medical Center, Chicago, Illinois, 60611.

Previous studies (Pysh & Wiley, Science, 176(4031), 1972) have shown that prolonged, repetitive stimulation ($2\frac{1}{2}$-3 hrs) of the cervical sympathetic trunk in cats produced characteristic ultrastructural changes in some axon endings of the superior cervical ganglion. The normally bulbous profiles of axon endings became crescent-shaped, contained fewer synaptic vesicles, and had greater circumferences. In an effort to assess the rapidity of occurrence and reversibility of these changes, experiments were performed using shorter stimulation times with and without a subsequent recovery period prior to perfuse-fixation. Additionally, since previous experiments showed changes in only a portion of all axon endings, the stimulus strength was raised considerably. Stimuli consisting of continuous trains of monophasic rectangular pulses 1 msec in duration and 20 V (0.6-1.5 mA) at a frequency of 40 Hz were applied to one sympathetic trunk for 30 mins while the other side served as a nonstimulated control. Nictitating membrane contractions were monitored with force-displacement transducers at all times. Fixation was accomplished by intraaortic perfusion either with the stimulator on, or after the stimulator had been turned off for a period of time. Electron micrographs of ganglia perfused during stimulation showed the same changes as reported previously but in a greater percentage of endings. These changes showed partial recovery after turning the stimulator off for 30 mins. Thus, ultrastructural effects of stimulation can be observed within 30 mins and are, at least partially, reversible. These findings may relate to the role of synaptic vesicles in cholinergic neurotransmission.

**55.3** NEURONAL ADJUSTMENTS IN THE HIPPOCAMPUS FOLLOWING LESIONS OF THE ENTORHINAL CORTEX. Gary S. Lynch and Carl W. Cotman. Dept. Psychobiology, UCI, Irvine, California 92664.

We have investigated a series of anatomical, physiological, and chemical changes associated with the commissural and septal inputs to the hippocampus following lesions of the entorhinal cortex. Following entorhinal lesions, an intense band of acetylcholinesterase (AChE) developes in the molecular layer of the dentate gyrus exactly where the entorhinal fibers normally terminate. This layer develops over a period of 30 to 40 days and is eliminated by septal lesions, which causes the disappearance of the normal bands of AChE. In contrast to the change observed in adults, entorhinal lesions made in neonatal animals induces a more rapid change in AChE which is confined to a thin zone in the top one-fifth of the molecular layer of the dentate gyrus. The histochemical change in AChE has been verified by micro-chemical assays which have also revealed a concommitant increase in choline acetyltransferase. Electron microscope histochemistry localizes the AChE changes to axons and terminals.

In other experiments, we have obtained evidence that entorhinal lesions also induce comparable changes in the commissural fibers, the second afferent system remaining to the dentate. Taken together, these data imply that the removal of a major afferent source catalyzes the competitive growth of the remaining fiber inputs to those zones vacated by the lesioned input. (Supported by research grants from NIMH #MH 19691 and NSF #GB 16973.)

**55.4** PHYSIOLOGICAL AND HISTOCHEMICAL PROPERTIES OF THE SOLEUS MUSCLE AFTER DENERVATION OF ITS ANTAGONISTS. Lloyd Guth and Jay B. Wells*. NIH, Bethesda, Md. 20014.

Muscle fibers undergo physiological and metabolic changes in response to altered functional demands. For example, muscles exhibit prolonged contraction time and decreased ATPase activity when their synergists are removed. The present experiment was performed to determine whether inactivation of a muscle's antagonists produces physiological and metabolic changes indicative of speeding. The common peroneal nerve was transected unilaterally in rats and the ipsilateral soleus muscle examined seven to eight months later. Evidence of physiological speeding was indicated by faster isotonic speed of shortening and isometric rate of tension development, decreased contraction time, and decreased tetanus: twitch tension ratio. Histological sections incubated for actomyosin ATPase activity revealed an increase in the proportion of dark, high-ATPase fibers. A quantitatively similar result was obtained when the central end of the transected nerve was implanted into the normally innervated soleus muscle. Under these conditions the implanted nerve did not form a transmissive neuromuscular connection. Thus, in contradistinction to previous assertions (Fex, Physiol. Bohemoslov., 1969) we found no "trophic" effect specific to the implanted, nonfunctional nerve. Since the physiological and metabolic properties of muscle can be altered without nerve crossing, we suggest that these properties are regulated by an interaction between neural and muscular factors. A specific trophic function cannot be attributed to the nerve until the regulatory role of all factors is more fully evaluated.

**56.1** AMINO ACIDS IN MAMMALIAN CNS: BIOCHEMICAL SYNAPTIC PROPERTIES. William J. Logan, Alberto Arregui*, James P. Bennett* and Solomon H. Snyder. Dept. Pharmacology, Johns Hopkins Univ., Sch. Med., Baltimore, Md. 21205.

Glutamic (Glu) and aspartic (Asp) acids and glycine (Gly) have been considered putative neurotransmitters in the mammalian CNS primarily from their neurophysiologic characteristics. We have obtained neurochemical support for this view by demonstrating distinct synaptic properties for these substances in comparison to other amino acids. The accumulation of low concentrations of Glu and Asp into rat cerebral cortex and spinal cord synaptosomes and of Gly into spinal cord but not cortex synaptosomes utilizes high affinity uptake systems not seen with other amino acids (Logan and Snyder, Nature 234: 297, 1971). The population of cortical synaptosomes accumulating Glu and Asp is distinct from that accumulating other amino acids on an inequilibrium sucrose density gradient centrifugation (Wofsey et al., PNAS 68: 1102, 1971). Since Gly physiologically resembles the natural inhibitory transmitter in the spinal cord but not cortex, we utilized this centrifugation technique in the separation of spinal cord synaptosomes. In both spinal cord and lower brainstem, the population of synaptosomes accumulating Gly sedimented in a less dense portion of the gradient than that accumulating other amino acids. An additional specific characteristic of the high affinity uptake systems for Glu, Asp and Gly is their marked sodium requirement. In contrast to other amino acids, the synaptosomal accumulation of Glu and Asp in the cortex and of Glu, Asp and Gly in the spinal cord was strikingly reduced in the absence of sodium. This demonstration of distinct synaptosomal biochemistry for Glu, Asp and Gly provides support for their unique synaptic role in the mammalian CNS.

**56.2** AMINO ACID INCORPORATION BY SYNAPTOSOMES ISOLATED FROM THE TELEOST (GALEICHTHYS FELIS). Phil Maxcy, Jr.* and Donald A. Rappoport, Div. Mol. Biol., Dept. Pediat., U. Texas Med. Branch, Galveston, Texas 77550.

Isolated synaptosomes from marine catfish brain were ruptured by suspension and vigorous homogenization in distilled deionized water. These preparations exhibited increased incorporation of $^{14}$C-L-leucine into the acid insoluble fraction when incubated with pH 5 fraction isolated from catfish liver. There was a partial requirement for guanosine triphosphate (GTP), but an adenosine triphosphate (ATP) generating system was slightly inhibitory. Known inhibitors of protein synthesis such as chloramphenicol, puromycin and cycloheximide, at concentrations of $10^{-4}$ M, had little or no effect on the incorporation of leucine, nor did RNase at 100 ug/ml.

The stimulatory activity of the pH 5 fraction on leucine uptake by the ruptured synaptosomes was heat stable. Heating the pH 5 fraction in boiling water for 0.5 to 1.0 minute precipitated approximately 75% of the protein, but did not markedly affect leucine incorporation. Yeast transfer RNA (tRNA) (100 ug/ml) did not stimulate leucine uptake when added to the incubation medium. The results suggest that amino acid incorporation in this preparation does not conform to the conventional protein biosynthetic mechanism.

This study was supported in part by a J.W. McLaughlin predoctoral fellowship, a National Institutes of Health grant, DHEW 5R01 NB07707, and a Robert A. Welch Foundation grant, H-180.

**56.3** INTRINSIC INHIBITOR OF GLUTAMIC ACID DECARBOXYLASE (GLUTAMIC CARBOXYL-LYASE) IN THE COCKROACH (Periplaneta americana). Claude F. Baxter, Gloria F. Torralba* and Janice L. Emge*. Neurochemistry Labs. V.A. Hospital, Sepulveda, Calif. 91343

The properties of glutamic acid decarboxylase (GAD) extracted from the ganglia and axons of cockroach differ somewhat from those described for the GAD in the nervous tissues of crustaceans or mammals. Average GAD activity in roach ganglia is 800 $\mu$moles $CO_2$/g. prot./hr. Stability of GAD is decreased by $O_2$ and enhanced by potassium phosphate. GAD activity is increased 3-fold by $1x10^{-4}$M pyridoxal phosphate and inhibited by carbonyl-trapping agents, $Cl^-$, GABA and by an intrinsic inhibitor (IH) found in the tissues surrounding axons and ganglia. The crude GAD enzyme from the cockroach has two pH optima (6.9 and 7.2). IH inhibits preferentially activity at the lower pH optimum. IH is not glycogen and cannot be extracted with chloroform-methanol. When tissues containing the inhibitor are homogenized, IH is particulate bound, stable to heat (100° for 5 min) and not appreciably affected by hydrolysis in 1 N. HCl for 24 hrs. at 100°. After boiling, some dialyzable IH is found in the supernatant. Dry or wet combustion abolished all IH activity. The action of IH is enhanced by EDTA and suppressed by reduced glutathione. IH is not significantly affected by pyridoxal phosphate ($1x10^{-3}$M). Further studies will define the inhibitor and its relationship to GAD activity in normal and regenerating nervous tissues. Supported in part by NIH Grant NS-03743.

**56.4** CHLORPROMAZINE INDUCED INHIBITION OF GLUTAMATE UPTAKE BY INSECT NERVE. I. R. Faeder* and M. M. Salpeter. Med. Sch., Duke, Durham, N. C. and Cornell University, Ithaca, N. Y.

Faeder and Salpeter (JCB 46:300, 1970; Prog. Brain Res. 34:103, 1971) demonstrated that after nerve stimulation glutamate uptake at the insect neuromuscular junction, especially in the sheath cells, is greatly enhanced. Subsequent nerve stimulation preferentially unloads this pool. The sheath may thus contain a glutamate pool available for nervous activity. Sheath cells have since been found to similarly bind other amino acids suspected of being transmitters in the nervous system (Orkand and Kravitz, JCB 49:75, 1971; Hokfelt and Ljungdahl, Br. Res. 32:189, 1971). The effect of chlorpromazine (CP) on glutamate uptake was investigated, since CP reversibly blocks insect nerve muscle transmission, (Faeder and O'Brien, J. Exp. Zool. 173:187, 1970) and also inhibits GABA uptake by nerve tissue (Iversen and Kravitz, J. Neurochem. 15:699, 1968; Iversen and Johnston, J. Neurochem. 18:1939, 1971). Paired neuromuscular preparations received nerve stimulation and were then incubated in $H^3$-L-glutamate ($2x10^{-6}$M) with and without CP ($5x10^{-4}$M). CP eliminated the stimulation-enhanced glutamate uptake. Since CP was not applied to the preparation until after nerve stimulation, its action cannot be ascribed to interference with nerve conduction, but must reside in the transport (or binding) mechanisms of the sheath cells themselves.
Supported by U.S. NIH NS-09315.

**56.5** POLYAMINES IN THE BRAIN: ENZYMATIC-ISOTOPIC ASSAY OF PUTRESCINE AND BLOCKADE OF ITS SYNTHESIS BY α-HYDRAZINO-ORNITHINE. Sami I. Harik, Gavril W. Pasternak* and Solomon H. Snyder. Dept. Pharmacol., Johns Hopkins Univ. Sch. of Med., Baltimore, Md. 21205.

Putrescine (1,4-diaminobutane), the precursor of the polyamines, spermidine and spermine, is formed by the decarboxylation of ornithine. Because ornithine decarboxylase is rate-limiting enzyme in polyamine synthesis and tissue levels of putrescine are low, we developed a sensitive assay for tissue putrescine. This micromethod for putrescine depends on its ability to stimulate the activities of mammalian and yeast S-adenosylmethionine decarboxylase. The evolution of $^{14}CO_2$ from carboxyl-labeled S-adenosylmethionine is related linearly to putrescine concentration, and detects as little as 10 picomoles of putrescine. Spermidine gives 1% the reaction of putrescine and is elimited in some spermidine-rich tissues by cellulose phosphate adsorption. Subcellular and regional distributions of putrescine have been elucidated as well as the effects of a variety of drugs. Knowledge of the biological functions of the polyamines would be greatly enhanced if a specific inhibitor of their synthesis were available. We have screened a large number of ornithine analogues and observed that α-hydrazino-ornithine inhibits ornithine decarboxylase with Ki values for prostatic and E. coli enzymes of $4 \times 10^{-6}$ M and $2 \times 10^{-7}$ M respectively. Effects of this drug on brain levels of putrescine will be reported. (Supported by USPHS grants NS-07275, GM-16492, MH-18501 and MH-33128.)

**56.6** N-ACETYLNEURAMINIC ACID IN THE DEVELOPING OPTIC TECTUM OF THE CHICK EMBRYO. Douglas B. Gray* (Spon: Louis Irwin). Col. Pharm. Sci., Columbia University., New York, N.Y. 10023.

To further resolve the role of cell surface heterosaccharides in the developing nervous system, N-acetylneuraminic acid (NANA), a negatively charged terminal amino sugar , was studied throughout periods of differentiation and synaptogenesis in the optic tectum of the chick embryo. The NANA content of (1) whole homogenate, (2) total particulate, and (3) lipid-insoluble (glycoprotein) particulate fractions was determined. Total NANA increased in proportion to total protein from 3 through 15 days incubation. Total particulate NANA increased from 5 µg/mg protein at 3 days to 26 µg/mg protein at 15 days incubation, with no further increase through one day post-hatching. The highest rate of increase in total particulate NANA occurred between 6 and 10 days of incubation. Glycoprotein NANA decreased from 69% of total particulate NANA at day 6 to 35% at day 14, remaining constant through one day post-hatching. These results suggest a proportionately greater increase in particulate glycolipid NANA than in particulate glycoprotein NANA during this period. These changes may reflect an increase in the ratio of glycolipids to glycoproteins, and/or an increase in the ratio of multisialo- to monosialo- glycolipids, in conjunction with retino-tectal synaptogenesis. (Supported by a grant from the Merck Company Foundation.)

**56.7** UPTAKE AND ACCUMULATION OF $H^3$-6,7-DIHYDROXYTETRAHYDROISOQUINOLINE BY SYMPATHETIC NERVES IN VIVO. Gerald Cohen* and Steven E. Locke* (SPON: James Lieberman). College of Physicians and Surgeons, Columbia University, New York, New York, 10032.

Tetrahydroisoquinoline (TIQ) alkaloids can be formed by condensation of catecholamines with acetaldehyde or formaldehyde. It has been suggested that TIQ's may form in man when acetaldehyde is generated during the metabolism of ethanol. In this study, we showed that 6,7-dihydroxy-TIQ (the condensation product of dopamine with formaldehyde) can be taken up and stored in vivo by sympathetic nerves. $H^3$-6,7-Dihydroxy-TIQ (11 Ci/mmole) was given intravenously (200 µCi/kg) to Swiss Webster mice. Fifteen minutes later, the animals were killed by cervical dislocation and the hearts were removed and extracted by homogenization in acidified ethanol. The $H^3$-TIQ was isolated by binding to and elution from aluminum hydroxide. Thin-layer chromatography showed that the isolated material was the expected $H^3$-TIQ. The uptake of $H^3$-6,7-dihydroxy-TIQ by mouse heart was diminished 50% ($p < 0.001$) when the sympathetic nerves to the heart were destroyed by 6-hydroxydopamine, administered several days earlier. When the animals were pretreated with cocaine (5 mg/kg) or desmethylimipramine (20 mg/kg), two well-known inhibitors of the axonal membrane pump, there was a 50-70% reduction in accumulation of the $H^3$-TIQ. Similar experiments with surgically sympathectomized rats showed uptake of the $H^3$-TIQ into sympathetic nerves of rat submaxillary glands and irides. Thus, 6,7-dihydroxy-TIQ is similar to the natural neurotransmitter, norepinephrine, in that it can be taken up and stored by sympathetic nerve endings. These results make it likely that endogenously synthesized TIQ's may be capable of acting as false transmitters. These findings may have relevance to changes in sympathetic nerve function in alcoholism. (Supported by PHS Grant MH-17071.)

**56.8** RELATIONSHIP BETWEEN NUCLEAR AND CYTOSOL BINDING OF $^{3}$H-CORTICOSTERONE IN THE RAT BRAIN. R. W. Rhees*, W. Stevens* and B. I. Grosser. Departments of Anatomy and Psychiatry, College of Medicine, University of Utah, Salt Lake City, Utah, 84112.

Recent studies have shown that both nuclei and cytosol from cells of rat brain possess protein molecules which bind labeled corticosterone. Nuclear binding of cortisol in the liver, of estradiol in the uterus, and of progesterone in the oviduct is dependent on an initial association of the steroid to cytosol proteins. Therefore, in the present study the interaction between nuclear and cytosol binding of corticosterone in the brain was investigated. Brain neuronal nuclei were isolated from adrenalectomized rats and incubated in the presence of a $^{3}$H-corticosterone-protein complex derived from brain cytosol. As controls, nuclei were incubated with $^{3}$H-corticosterone alone or with a $^{3}$H-corticosterone-protein complex derived from thymus cytosol. All three preparations contained an equal amount of labeled corticosterone. The nuclei were centrifuged, washed twice in Tris-EDTA sucrose buffer, and extracted with buffer containing 0.4 M NaCl. For three experiments the average amounts of labeled corticosterone (dpm/mg DNA) extracted from the nuclei were: nuclei with labeled brain cytosol--2541; nuclei with labeled thymus cytosol--829; nuclei with $^{3}$H-corticosterone alone--192. Thus, 13 times as much labeled corticosterone was extracted from the neuronal nuclei incubated with the labeled brain cytosol-protein complex than from the nuclei incubated with $^{3}$H-corticosterone alone. The binding pattern of astrocyte nuclei incubated with the three preparations was similar to that of the neuronal nuclei. These data and the results of other experiments indicate that the nuclear binding of $^{3}$H-corticosterone in rat brain is considerably enhanced by the presence of brain cytosol proteins. Supported by Grants NIH GM0958, NSF 19040, NIH 5 K02-MH 18270 and NS 07761.

**57.1** **BLOCKADE OF BRAIN DOPAMINE (DA) RELEASE BY GAMMA-HYDROXYBUTYRIC ACID (GHB) AND ITS USE AS A TOOL IN STUDYING MECHANISMS OF ACTION OF PSYCHOTROPIC DRUGS.** **W.G. Clark and M.K. Menon*. Psychopharmacology Research Lab., VA Hospital, Sepulveda, California 91343; Dept. of Biological Chemistry, University of California, Los Angeles, California.**

**GHB was found to cause marked akinesia and rigidity in mice (350 mg/kg). GHB caused a small, but significant increase in DA level of mouse brain and was ineffective in blocking the uptake of labeled DA, NE and 5HT by brain slices in vitro. In a dose of 200 mg/kg i.p., GHB completely blocked the chlorpromazine-induced increase in homovanillic acid levels of caudate nucleus of mice by blocking the release of DA from storage sites. This property makes GHB a useful tool in studying the mechanism of action of drugs affecting behavior. Of the drugs tested, d-amphetamine (10 mg/kg) was most effective in antagonizing the GHB-induced akinesia in mice. l-Amphetamine was about five times less potent than the d-isomer. Cocaine·HCl (60 mg/kg) was effective as an antagonist but LSD-25 (1 mg/kg), l-dopa (100 mg/kg) and apomorphine·HCl (12 mg/kg) were without effect. GHB antagonized the central stimulant effect of amantadine·HCl. From such studies it seems possible to differentiate between drugs which act by causing DA release from those which act by other mechanisms.**

*** Fellow of the FSVCPS Foundation**

**57.2** EFFECTS OF DEPRESSANT DRUGS ON DEPRIVATION-INDUCED FLUID CONSUMPTION IN RATS. Greg J. Maloney* and Roger P. Maickel, Dept. of Pharmacology, Med. Sci. Program, Indiana Univ., Bloomington, In. 47401.

The influence of various drugs on the consumption of fluids by water-deprived rats has been a subject of study in this laboratory for some time. Cholinergic drugs, both blocking agents and stimulants, have been shown to reduce the intake of water by rats on a 23 hour deprivation schedule. Antihistamines, phenothiazine tranquilizers, and amphetamines have been shown to have a similar effect. In all these cases, the drugs were effective at doses that had little or no effect on gross motor activity. More recently, we have begun to examine the effects of various sedative-hypnotic and antianxiety agents on the same deprivation-induced fluid consumption system. "Short-acting" barbiturates such as hexobarbital and methohexital were without effect, while longer-acting barbiturates such as barbital increased fluid consumption of deprived rats in a linear, dose-related manner. Antianxiety agents such as chlordiazepoxide also markedly increased fluid consumption under these conditions. The motor depressant and dipsogenic actions of barbital could easily be separated by time-response and dose-response studies. When barbital was given chronically, a moderate degree of tolerance was observed; withdrawal of the drug evoked a transient decrease in fluid consumption and body weight. The results obtained with water as the consummatory fluid, when compared with similar studies using sucrose, saccharin or tartaric acid, carry significant implications for the punishment attenuation hypothesis of drug action. (Supported by USPHS grants MH-18852 and KO2-MH-41083 to R.P. Maickel.)

**57.3** EFFECT OF ANTIDIURETIC HORMONE ON THE LEVEL OF PENTAZOCINE IN THE BRAIN OF RODENTS. William L. Dewey, Thanh-Thuy Chau* and Louis S. Harris, Dept. Pharmacol., Univ. North Carolina, Chapel Hill, N.C. 27514.

We have previously reported that antidiuretic hormone (ADH) potentiated the lethality of pentazocine (P) in rats but not in dogs or mice (Fed. Proc. 30: 502,1971). A spectrophotofluorometric method was used to quantitate pentazocine in brain and a direct relationship between dose of (P) given and the quantity in brain was observed. However, as the dose of (P) injected intramuscularly (i.m.) was doubled the concentration in brain went up 3 fold. The mean level of pentazocine in the brain of rats following an i.m. injection of 60 mg/kg pentazocine was $0.98 \pm 0.15$ μg/g. When an (i.m.) injection of 10 μ/kg ADH was given immediately after the injection of pentazocine the mean level of (P) in the brains was $2.85 \pm 0.43$ μg/g. Oxytocin a polypeptide structurally related to ADH which did not potentiate the lethality of (P) also did not cause an increase in the levels of (P) in the brain. In the mouse, where synergistic lethality between (P) and (ADH) was not observed, the levels of (P) in the brain were lower after an injection of ADH. (Supported by MH-19759, NAS-NRC D-71-4, and a grant from the Sterling-Winthrop Research Institute.)

**57.4** ASPECTS OF ALKALOID INVOLVEMENT IN ALCOHOLISM. Michael J. Walsh, Department of Pharmacology, Bowman Gray School of Medicine, Winston-Salem, N. C. 27103.

A possible role of alkaloids derived from biogenic amines for the effects of alcohol or in alcoholism is a relatively recent concept. The mechanism involves Schiff's base (imine) formation of the amine with an aldehyde and subsequent ring closure. This reaction results in the genesis of tetrahydro-β-carbolines in the case of indolethylamines or tetrahydroisoquinolines in the case of phenylethylamines. Acetaldehyde or formaldehyde can react with various amines including serotonin, tryptamine, norepinephrine (NE) and dopamine (DA). These result in simple condensation products. Similarly, complex alkaloid formation can occur by condensation of the amine with an aromatic aldehyde. This pathway is promoted by agents which inhibit the oxidative or reductive metabolism of biogenic aldehydes. Agents such as alcohol, methanol, paraldehyde and chloral hydrate have been shown to competitively inhibit aldehyde dehydrogenase and promote tetrahydropapaveroline (THP) formation from DA. The barbiturates and chloral hydrate are known to inhibit aldehyde reductase and form dihydroxy-THP from NE. Several of these alkaloids have been demonstrated in vivo. The simple and complex alkaloids are metabolized by O-Methylation as well as conjugation. All of the alkaloids are pharmacologically active and have been found to interact with neuroamine storage, release and re-uptake, as well as affect lipolysis, blood pressure and heart rate. These alkaloids and various amines, their aldehydes and alcohols can also induce sleep and potentiate alcohol hypnosis. (Supported in part by N. C. Mental Health.)

**57.5** EFFECTS OF ETHANOL AND ACETALDEHYDE IN BRAIN TISSUE: SEROTONERGIC CORRELATES. Boris Tabakoff, William O. Boggan , Frieda Ungar*, and S.G.A. Alivisatos. Dept. Biochem., The Chicago Medical School, and Dept. Psychiatry, Univ. of Chicago, Chicago, Ill. 60612

A significant reaction of indoleamines in the CNS is the binding of their deaminated products (indoleacetaldehydes,IAAld) to subcellular components. We have shown such binding to occur *in vitro* and *in vivo* in brain tissue from rats and mice in the presence of MAO activity. Such binding is reversible in the presence of other enzyme activities, i.e., dehydrogenases and reductases, responsible for the further metabolism of the indoleacetaldehydes. In rat brain homogenates, acetaldehyde was shown to increase the binding of indoleacetaldehyde to tissue. To investigate the *in vivo* interaction of acetaldehyde as a metabolic product of ethanol with serotonin metabolism, mice were either injected with sub-hypnotic doses of ethanol or exposed to ethanol vapor for various periods. Behavioral measures (audiogenic seizures) of CNS excitability after 72 hours of exposure to ethanol vapor followed by abrupt withdrawal, indicate an increase in seizure susceptibility as the blood levels of ethanol diminish. Mice chronically exposed to ethanol vapor also were shown to differ from controls in the amount of bound material (IAAld) in brain stem after withdrawal from ethanol. Since acetaldehyde has been shown to interact with catecholamines and promote the formation of tetrahydroisoquinolines (Science 167,1749, 1970; Science 167,1005,1970), such compounds and morphine were tested as displacing agents of 5HT at serotonergic receptors. Salsolinol was found to be a relatively good displacing agent, as was morphine, while the substituted phenylethylamines, i.e., dopamine and mescaline, were poor displacing agents. Such displacement might lead to an increase in release of indoleamines promoting deamination and binding. (Supported by NIMH Grants 20758 and 15410, Am. Canc. Soc. P-424B, Ill. Dept. Ment. Health 101-13-RD and NSF GB-30295.)

**57.6** MODIFICATION OF PHYSICAL DEPENDENCE TO MORPHINE BY AVERSIVE STIMULI IN RATS. S.N. Dutta*, Paul T. Bailey* and S.N. Pradhan, Department of Pharmacology, Howard University College of Medicine, Washington, D. C., 20001.

Attempts were made to alter the course of development and intensity of physical dependence to morphine by subjecting rats to aversive foot shocks before and after the administration of the drug. Male Wistar rats (80-150g) were injected subcutaneously with morphine sulfate twice daily. The dose of the drug was 10 mg/kg to begin with and increased by 10 mg/kg each day until it reached 150 mg/kg. Subjects were divided into two groups. While rats of one group were maintained as controls, those from the other group were subjected to electric foot shock in Skinner boxes. Shocks of 1 sec duration were delivered every 5 sec and their intensity was adjusted to slightly above their threshold limits for individual rats. Shock sessions lasted for 30 min before and 30 min after each morphine injection. Withdrawal manifestations were induced by intraperitoneal injection of nalorphine (10 mg/kg) usually at the end of every week. The rating of these manifestations were made by modification of the method of Watanabe (Japan. J. Pharmacol. 21, 383, 1971). The difference between the intensities of physical dependence found in the rats of the two groups was found to be significant by the third week, as indicated by the scoring of their withdrawal manifestations. It appeared that application of aversive stimuli concurrent to morphine injection increased the intensity of physical dependence in rats. (Supported by a U.S.P.H.S. Grant No. GM-17824).

**57.7** TOLERANCE EFFECTS OF DIRECT MORPHINE STIMULATION OF THE ANTERIOR THALAMUS AND VENTRAL MEDIAL NUCLEUS OF THE HYPOTHALAMUS OF THE RAT.
Joseph Masserano†, Gregg Little†, Pat D'Encarnacao* and Paul D'Encarnacao*
(SPON: W. L. Byrne) Dept. Psychol. Memphis State Univ. Memphis, Tn. 38111 and Veterans Administration Hospital, Memphis, TN. 38103

Male albino rats were bilaterally implanted with stainless steel cannulae in the anteriorthalamic nuclei (AT) ventral medial nucleus of the hypothalamus (VMN), the caudate nucleus (CN) and the lateral ventricles (LV). All subjects were then run under orientation, saline control or experimental conditions in automated photoelectric activity cages. Experimental sessions consisted of direct morphine injections into CNS structures in a volume of 1-2 ul. Each animal was run over a thirty day period. Hoyoya, Oguri and Akita (1963) have shown a biphasic effect on activity with morphine injections administered intraperitoneally. Initial activity effects are depressed, this period being followed by an increase in activity behavior. They attribute this effect to morphine tolerance. In our study, rats with morphine stimulation of the AT showed dramatic increases in activity over control animals. VMN stimulation with morphine failed to show this effect as did saline controls in both brain areas. At the termination of the experiment the animals were challenged via cannulae with nalorphine, a morphine antagonist. AT animals showed some withdrawal behavior as compared with control animals.

**57.8** EFFECTS OF REPEATED MORPHINE ADMINISTRATION ON LATERAL HYPOTHALAMIC SELF-STIMULATION IN RATS. Stanley A. Lorens* and Clifford L. Mitchell. Depts. Psychiatry and Pharmacology, College of Medicine, University of Iowa, Iowa City, Iowa, 52240.

Morphine (5, 10 and 20 mg/kg subcutaneously, calculated as the base) was investigated for its effects on lateral hypothalamic self-stimulation. On each of 5 days the animals received a 10 minute control self-stimulation period followed immediately by injection of morphine. Each animal then was tested for a period of 10 minutes at hourly intervals for six consecutive hours. The animals were placed in Wahman wheel-turning activity cages between self-stimulation sessions. The first administration of morphine suppressed self-stimulation 1-2 hours after injection but augmented it 3-6 hours post injection. The time-course and degree of effects were dose-dependent. 20 mg/kg produced effects of the greatest intensity and longest duration. With daily administration, tolerance was developed to the depressant effect on self-stimulation whereas the excitatory effect was enhanced. The increase in self-stimulation rates was not correlated with increased locomotor activity as measured by wheel running. The cortical EEG showed high voltage slow activity during morphine-induced suppression of self-stimulation, but reverted to low voltage fast activity when self-stimulation reappeared.

**58.1** SPONTANEOUS SEIZURE FREQUENCY AND AVOIDANCE CONDITIONING IN MONKEYS. Joan S. Lockard, Wendell Wilson* and Vladimir Uhlir*. Department Neurological Surgery, Sch. Med., University Washington, Seattle 98195

Emotional precipitation of seizures in epileptic patients has been an equivocal phenomenon. The problem is ruling out concomitant hyperventilation or sensory changes which may more directly influence seizure occurrence. These difficulties are circumvented if seizure frequency is tabulated at times other than during the emotional-inducing procedure. The aluminum-hydroxide, cerebrally injected, monkey model of chronic motor epilepsy (e.g., Epilepsia, 10: 305, 1969) was utilized here. Spontaneous seizures of 8 epileptic rhesus monkeys were automatically recorded (EEG, 22: 482, 1967; 27: 89, 1969) during weeks of short daily avoidance conditioning and during control weeks of no conditioning. Monkey motor activity triggered a video-tape recorder in a closed-circuit TV system for clinical verification of seizures. A clock mounted in view of the camera recorded time-of-day the seizures occurred. Seizure frequency was found to increase statistically significantly during weeks of avoidance conditioning but at times other than the conditioning itself. The data support a hypothesis in terms of an emotional activation of seizures since the increased number of seizures primarily occurred for all monkeys when the electric shocks of avoidance conditioning were absent. The increase in seizures was a temporary occurrence and the animals tended to re-establish their baseline frequencies during control weeks.

**58.2** A QUANTITATIVE ANALYSIS OF THE ANATOMICAL AND ELECTROPHYSIOLOGICAL CORRELATES OF CHRONIC EPILEPTOGENIC FOCI IN CATS. Marcos Velasco, M.D., Francisco Velasco, M.D.* and Xavier Lozoya, M.D.*, Division of Neurophysiology, Scientific Research Department, IMSS. México, D. F. (73-032).

Single microinjections of a critical amount of 0.03 ml. alumina cream into the cat's motor cortex, invariably produced epileptogenic foci with 3 consecutive stages: 1) Latent stage (LS), 2) Convulsive stage (CS) consisting in focally initiated clinical and EEG epileptiform signs, without interictal symptoms and independent EEG "mirror" foci. They initiated $34.4 \pm 2$ days after injection and lasted $16.8 \pm 4$ days. 3) Remission period to apparent normality. EEG spike density at epileptogenic focus during CS was larger ($p < 0.001$) than during LS and RS. Alumina cream lesions were similar in all animal brains, showing a central necrotic area, absence of both fibrotic capsule and gross perilesional abnormalities. However, remarkable differences in cortical thick and cellularity were found, depending upon the stage when brains were analyzed. LS brains showed slight reduction in cortical thick and cellularity and a small number of damaged neurons. CS brains showed a mild reduction in cortical thick and cellularity, a large number of partially damaged neurons and a small number of totally damaged neurons. RS brains showed a large cortical atrophy and almost complete neuronal depopulation. These results suggest that presence of clinical and EEG seizures may be dependent upon the number of partially damaged cortical neurons surrounding epileptic focus.

**58.3** SUPPRESSION OF PHOTICALLY ELICITED CORTICAL HYPERSYNCHRONY IN RATS BY TRIMETHADIONE. Charles E. Wilson* and Donnell J. Creel. Psychology Res. Lab., V.A. Hospital, Phoenix, Arizona 85012

The effects of the thalamically active anticonvulsant, trimethadione, on photically elicited electrocortical hypersynchrony were studied in order to better characterize the underlying mechanism of generation. Averaged visual evoked responses and the associated synchronous afterdischarge (AD) were recorded from chronic cortical electrodes in awake albino rats under various drug conditions. In agreement with earlier observations, pentylenetetrazol (10 mg/kg, i.p.) potentiated AD. Further, it was observed that trimethadione (50 mg/kg, i.p.) antagonized this potentiation but did not alter AD in rats injected with saline. At higher doses (100 mg/kg, i.p.) trimethadione did suppress AD in rats injected with saline. One of the suggested neuroanatomical generators of AD involves recurrent inhibitory pathways in the nonspecific thalamus. Schallek and Kuehn (PSEBM 112:813, 1963) have demonstrated that trimethadione is effective in raising the paroxysmal threshold in nonspecific thalamic nuclei. The present results are consequently regarded as supporting the notion of nonspecific thalamic involvement in AD generation. Some preliminary work with other anticonvulsants suggests that AD dimunition is specific to those agents which are effective in petit mal epilepsy.

**58.4** MULTIPLE UNIT ACTIVITY OF SPECIFIC AND NON SPECIFIC SYSTEMS DURING EXPERIMENTAL NON-FOCAL EPILEPSY. Francisco Velasco, M.D.* and Marcos Velasco, M.D. Division of Neurophysiology, Scientific Research Department. National Medical Center.IMSS México, D. F. (73-032)

---

The present report describes the temporal relationship between the changes in cortical EEG and multiple unit activity (MU) of various cortical and subcortical structures, occuring at the onset of non-focal Seizures induced by metrazol injection (10 mg/kg I.V. every 60 sec.) In 20 cats inmovilized with gallamine, simultaneous EEG and MU recordings, were obtained by means of 30 micron tip electrodes from specific structures (SS): medial and lateral geniculate bodies, and auditory and visual cortices and from non specific structures (NSS): pontine and mesencephalic reticular formation, intralaminar thalamic nuclei and prefrontal cortex. In addition, MU was recorded from the sciatic nerve as an index of the spinal cord and peripheral nerve output discharges. Smith Triggers and integrators were used to determine the number of active units with an amplitude of 100% above noise level. An increase of MU was observed in both SS and NSS prior the onset of cortical EEG seizures. MU simultaneously increased in reticular, thalamic and cortical NSS. They anticipated to changes observed in thalamic and cortical SS. MU changes in the sciatic nerve started lately and after the onset of cortical EEG seizures. It was assumed that metrazol has a primary effect on non specific reticulothlamo-cortical system.

**58.5** LOW LEVEL X-RADIATION AND AUDIO-SENSITIZATION SEIZURES. W. B. Iturrian* and L. J. Peacock, Depts. Pharmacol. and Psychol., Univ. Ga., Athens 30601

Recent reports (Iturrian and Fink, Dev. Psychobiol. 1: 230, 1968) add noise to the list of environmental factors having dramatic deleterious effects upon the immature but produce a mild reaction in the adult. Seizure susceptibility (SS) can be elicited in weanling mice genetically resistant to audiogenic crisis by a 30 sec (95 db) initial audio-sensitizing sound (IAS) exposure during a brief sensitive period. Seizures occur only when the sound stimulus is repeated after a critical sensitization-test interval of days. SS develops in 2 days and without additional sound only persists 5 days. Repeated auditory stimulation (every 12 hr) prior to the development of SS makes mice temporarily refractory. Audio-sensitization seizures are dramatically influenced by genetic factors as well as the neuro-ontogenetic stage.

This investigation was designed to assess the relative potential for low levels of X-radiation to induce audio-hypersensitivity or to alter the temporal parameters of induced SS. Acute exposure to irradiation (20 rad) as IAS did not induce audiosensitivity but (1) does prolong SS, (2) extends the "sensitive period" for sensitization, (3) will serve as the intermittent inhibitory stimulus and (4) induces a novel convulsant response to certain tranquilizers never observed in control littermates. Radiation has been the only nonauditory stimulus that appears to influence audio-sensitization.

**58.6** UNEQUAL PARTICIPATION OF NEURONAL DENDRITES AND SOMA IN SEIZURE ACTIVITY GENERATED BY DIFFERENT CONCENTRATIONS OF EPILEPTOGENIC AGENTS.
Emil C. Zuckermann. Dept. Neurol., Yale Univ. Sch. Med., New Haven 06510.

Simultaneous multi-microelectrode recordings were performed at various levels of the dorsal hippocampus in chronic awake cats after infusion of diverse amounts of epileptogenic agents (penicillin, pentylenetetrazol, strychnine, bemegride, acetylcholine) into the inferior horn of the lateral ventricle. The effects, similar in all the different drugs, are illustrated by penicillin experiments. At threshold concentration (100-150 U penicillin in 0.1 ml) no spontaneous discharges occur, but dendritic reactivity strongly increases on ipsi or contralateral hippocampal electrical stimulation. Trains of stimuli at 0.5-1/sec generated seizure activity during which somatic discharges occur late and transiently. Somatic paroxysmal depolarization shifts occur only at considerably higher concentrations of the drug (750-2000 U penicillin); still higher concentrations are needed before ictal events develop. The results suggest that a neuronal population can display multiple types of seizure activity and that dendrites have a considerably lower threshold for seizure than neuronal soma. The significance of these findings in connection with an adequate model for a clinical epileptic focus are discussed.

**58.7** DRUG EFFECTS ON EPILEPTIFORM ACTIVITY IN CHRONICALLY ISOLATED SLABS OF CEREBRAL CORTEX. A.J.Vazquez* and G.Krip* (SPON: H.C.Sabelli)Departments of Pharmacology, Chicago Medical School, Chicago, 60612 and University of Manitoba, Winnipeg, Manitoba, Canada.

We have studied the effects of cholinergic, adrenergic and serotonergic agents upon epileptiform afterdischarges (EAD) induced by electrical stimulation of chronically neuronally isolated slabs of cerebral cortex in unrestrained, unanesthetized cats. About 15 days after isolation, slabs respond to a train of stimulating pulses with a prolonged EAD. Muscarinic agents (pilocarpine, arecoline, oxotremorine and eserine) decrease EAD duration. Atropine or scopolamine antagonize these muscarinic effects and prolong EAD duration. Amphetamine, methamphetamine, tyramine and ephedrine decrease EAD duration. α-adrenergic blocking agents (phenoxybenzamine, phentolamine and tolazoline) neither modify EAD duration nor prevent its change by adrenergic agonists. β-adrenergic antagonists (pronethalol, propranolol) decrease EAD duration (probably because of their quinidine-like effects), but do not prevent the action of adrenergic agonists. Increasing brain serotonin levels by administering RO4-4602 ($N^1$[DL-seryl]$N^2$[2,3,4-trihydroxybenzyl]hydrazine) and 5-hydroxytryptophan (5HTP) decreases EAD duration. Methysergide, cyproheptadine, methergoline and p-chloro-phenylalanine not only increase EAD duration, but also prevent its decrease by 5HTP, by adrenergic and muscarinic agonists. Cyproheptadine prevents the shortening in EAD duration produced by amphetamine and by 5HTP, but not by cholinergic agents. On the basis of these results, we propose that the spread of epileptiform activity in the cortex is regulated by a series chain of inhibitory adrenergic-serotonergic-cholinergic linkages.

Supported by MA-2912 of the Medical Research Council of Canada, USPHS grant MH-14110 and the Epilepsy Foundation of America.

**58.8** Brainstem Section And Propagation Of Focal Paroxysmal Discharge In Rabbit. Michael L. Woodruff*, Fred H. Gage III* and Robert L. Isaacson. Center for Neurobiological Sciences, Univ. of Florida, Gainesville, Fla. 32601

Servit, et al. (Exptl. Neurol. 21: 383, 1968) demonstrated the importance of the mesencephalon both to the development of secondary foci and the seizure susceptibility of the frog forebrain. In the present investigation the influence of the mesencephalic reticular formation on the spread of focal, penicillin-induced seizure discharge was studied in the rabbit by sectioning the brainstem completely from the middle of the interquadrigeminal ridge, dorsally through prepontine tegmentum, ventrally. Control preparations consisted of animals sectioned through the posterior third of the pons, as well as intact, flaxedilized rabbits. Bipolar electrographic recordings indicated that seizures originated in the frontal cortex were more variable in duration and in the interseizure interval after section of the anterior brainstem. While seizures of the experimental subjects did propagate to the contralateral homotopic cortex (as well as to thalamus and hippocampus), these seizures did not consistently outlast the primary discharges at any time. Propagated seizures did last longer in the control subjects after approximately 8 to 12 propagated primary discharges. Brainstem section produced no apparent effect on the size, shape, or propagation of the interictal spikes. These results extend the observations of Servit, et al. to the mammal and support the hypothesis that both preferential and accesory pathways are involved in the propagation of focal epileptic activity. It would appear that sectioning the brainstem does not influence the spread of interictal spike discharges, but is important for the propagation of extended paroxysmal activity of focal cortical origin.

**59.1** ACTOMYOSIN LIKE PROTEIN IN BRAIN: A POSTULATED FUNCTION IN TRANSMITTER RELEASE. S. Berl, S. Puszkin* and W. J. Nicklas*. Dept. Neurol., College of Physicians & Surgeons, Col. Univ., New York, N.Y. 10032

Actomyosin-like protein (neurostenin; NS) has been isolated from bovine and rat brain synaptosomal fractions (Puszkin; Nicklas and Berl, J. Neurochem. 19, in press). It dissociates into actin-like (neurin, N) and myosin-like (stenin;S) proteins when centrifuged in sucrose gradients containing 0.6 M KI and 1 mM ATP. Similar to actin, N contains 3-methylhistidine and similar to myosin, S contains 3-methylhistidine and $\epsilon$-N methyllysine. SDS acrylamide gel electrophoresis indicates that the M.W. of N is ~47,000 and the major subunit of S ~240,000. $Mg^{2+}$-ATPase activity of synaptosomal NS is inhibited by 0.2 mM vinblastin or cytocholasin B. Uptake of dopamine, norepinephrine and GABA by synaptosomal preps. is inhibited by vinblastin or antiserum to NS. In contrast to synaptosomes a $Ca^{2+}$-ATPase similar to S is extracted from the vesicle fraction but little neurin. However, N is extracted from the synaptosomal membrane fraction but little S. Thus, S appears to be conc. in vesicles and N in membranes. A contractile mechanism for release of transmitter substance at synaptic junctions is suggested. At the site of contact between vesicles and presynaptic membrane, N and S interact to cause conformation changes in membranes which result in transient opening of vesicles and release of transmitter material. This is triggered by the entrance of $Ca^{2+}$ and ATP is hydrolyzed as it is in muscle for chemomechanical transformation. Supported in part by NIH Grant NS-04064 and Clinical Center for Research in Parkinson's and Allied Diseases NS-05184.

**59.2** NEUROFILAMENT-INTERSPACE IN FROG SCIATIC NERVE

P.H. Cooke*, R.E. Lindberg* and F.E. Samson, Jr. Department of Physiology and Cell Biology, University of Kansas, Lawrence, Ks. 66044.

Neurofilaments are among the most abundant ultrastructural elements in the cylinder of large caliber axons. If these filaments have a major skeletal role in the axoplasm, their arrangement should be modified by mechanical manipulation of nerve fibers. We have examined the effects of stretching segments of frog sciatic nerve on (1) the length-tension relationship, (2) overall ultrastructure of the fiber, and (3) the neurofilament-interspace in the cylinder of the large myelinated axons. When the length of the whole fiber is doubled by stretching, the myelin sheaths are fragmented and the axonal cylinders are markedly compressed, however no marked changes in the epineurial- or endoneurial sheaths could be identified. The "common" interspace between neurofilaments was determined by optical diffraction to be related to the extent of stretch. In highly stretched nerves the neurofilaments are fused into a reticulated mass. The relationship of stress-relaxation rates to length or tension suggests that the nerve fiber segment behaves like a "dilatant fluid". The observed reduction of the interspace between the neurofilaments correlates well with the onset of this mechanical behavior. These observations suggest that the neurofilaments are constant and structurally firm components of the axoplasm.

Supported by a Biomedical Sciences Support Grant (RR-07037) from the University of Kansas.

**59.3** AXONAL TRANSPORT OF DOPAMINE IN NIGRO STRIATAL NEURONS OF RATS.

H.C. Fibiger and E.G. McGeer. Kinsmen Laboratory of Neurological Research University of British Columbia, Vancouver, Canada.

Axonal transport of catecholamines in neurons whose cell bodies lie in the substantia nigra and whose projections terminate in the corpus striatum was studied by the stereotaxic injection of microlitre quantities of labelled precursor (tyrosine or dopa) into the substantia nigra according to a previously described method (Fibiger et al., J. Neurochem. in press). At various intervals thereafter (3-24 h), the animals were sacrificed, the brain was dissected, and the amounts of labelled catecholamines were measured in the midbrain, hypothalamus, thalamus, pons/medulla, hippocampus, cortex and corpus striatum. Significant quantities of labelled dopamine, but not of tyrosine or dopa, were recovered from the corpus striatum 3 to 6 h after the nigral injection. The amount of labelled striatal dopamine underwent a substantial decline between 6 and 24 h. The nigral injection of either precursor elicited striking contralateral turning during the early post-injection periods (3-6 h). This behaviour was not observed at 24 h. Destruction of nigral cells by pretreatment with tranylcypromine (5 mg/kg) in combination with intraventricularly administered 6-hydroxydopamine (200 µg in 25 µl) markedly impaired the transport of dopamine to the corpus striatum and also reduced the contralateral turning. These experiments suggest that axonally transported dopamine may be of functional significance in synaptic transmission. (Supported by grants from the Medical Research Council of Canada, MA-4674, MA-3633, MA-4013 and by a Medical Research Council Scholarship).

**59.4** NEURONAL AND GLIAL IONTOPHORESIS OF $H^3$ AMIN ACIDS IN LEECH GANGLION.
A. Globus, H. D. Lux*, and P. Schubert*. Human Morph., and Psychiatry, Univ. of Calif., Irvine, CA 92664

Iontophoresis of $H^3$ amino acids through a multi-barreled micropipette into glia or neurons of the leech ganglion followed by autoradiography make possible the study of glial-neuronal functions and neuronal morphology. The leech ganglion is divided into six packets. Each packet contains approximately 60 cells and a giant glia cell which envelopes them. The entire structure is visable under transmitted light allowing the impalement of neurons and glia while the ganglion rests in a cooled bathing solution. The dosage of $H^3$-glycine and leucine was calibrated by passing 50 nA for 2-5 minutes in Ringer's solution followed by scintillation counting. Glial cell resting potential was 30-70 mV. Label was never found in excess of background in glia cells with survival times in excess of 30 minutes. Within 2 minutes of glial iontophoresis, neurons and proximal axons were labeled indicating rapid transfer. Somas and axons were easily traced. Neurons had resting potentials of -40 to -50 mV. The injected neuron was heavily labeled. After long survival times adjacent neurons were labeled, but glia showed only background levels. Axoplasmic spread was in excess of 30 mm/day. The Retzuis cells showed a conical process roughly 20 $\mu$ in diameter on the axon near the Soma. It extended to the axon of the other Retzuis cell. The noninjected Retzuis cell was often labeled. The label was less dense than the injected Retzuis cell and more dense than the other neurons. Puromycin blocked uptake. Bloakage was confined to the injected neuron. These amino acids are transferred rapidly from the glia cell to the neurons where they are incorporated into water insoluble proteins. (Supported by NS grant # NS 08603-03).

**59.5** AXONAL TRANSPORT OF RNA IN GOLDFISH OPTIC SYSTEM.
N. A. Ingoglia, B. Grafstein, B. S. McEwen and I. G. McQuarrie*. Dept. Physiol., Cornell Univ. Med. Coll., New York, N.Y. 10021; New Jersey Coll. Med. Dent. at Newark, N.J. 07103; Rockefeller Univ., New York, N.Y. 10021

After injection of radioactive guanosine or uridine into goldfish eye, labeled TCA-soluble material (i.e., free nucleosides and nucleotides) and labeled RNA appeared in the optic tectum. The rate of transport along the optic nerve of the TCA-soluble material was faster than that of the RNA (average rates about 2 mm per day and $<$ 1 mm per day respectively). After the optic nerves had been crushed, neither component appeared in the tectum until the regenerating axons arrived. Since glial continuity would have been re-established earlier, these results show that the transport involved the axons and did not depend on the glia alone. In the earliest stages of regeneration, the ratio of RNA to TCA-soluble material was higher than in the normal tectum, which suggests that when the regenerating axons entered the tectum, they were already loaded with RNA. Thus at least part of the RNA appearing in the tectum was probably synthesized in the retinal ganglion cell bodies. This view was confirmed in experiments involving inhibition of retinal RNA synthesis by intraocular injection of actinomycin-D.

Supported by USPHS grants NS 09015, NS 2440-01 NSRB, NS 07080 and MH 13189.

(Note: TCA = trichloracetic acid)

**59.6** CALCIUM REQUIREMENT FOR AXOPLASMIC FLOW. Joel B. Kirkpatrick and R. E. Rose*. Dept of Path., Coll. of Med., Univ. of Ariz., Tucson 85724

The rapid migration of subcellular particles in peripheral axons in vitro can be observed directly by Nomarski differential interference contrast microscopy. The presence of 10 mM EGTA in calcium- and magnesium-free incubation medium stops movement within about 30 minutes. Smaller concentrations of EGTA or added calcium allow movement to continue for several hours. To determine the amount of calcium present in nerve when movement stops we performed the following experiments. Chicken sciatic nerve was removed from the perineurium, cut into 10-25 mg segments and incubated at 37°C in medium containing sucrose 233mM, glucose 10mM, $CaCl_2$ 1mM and tris base 26mM adjusted to pH 7.4 with HCl and bubbled with $O_2$. $^{45}Ca$ was added to a specific activity of $10^6$ cpm per μmole. After incubation the nerve segments were stirred for several hours with 1 ml Biosolve, and counted by liquid scintillation. Calcium entered the nerves to achieve in 1-2 hr an equilibrium concentration four times greater than the concentration of Ca in medium. When nerve segments labelled by 1 hr incubation in radioactive medium were transferred to medium containing no calcium and 10mM EGTA, the calcium was rapidly withdrawn from the nerve and bound to EGTA in the medium. After thirty minutes in EGTA medium the calcium content of nerve segments was 0.7 μmoles per mg wet weight. In this whole nerve, much of the calcium is probably bound to myelin, so the figure obtained represents only an upper limit of the true intraaxonal calcium content. Hodgkin and Keynes (J. Physiol. 276: 253, 1957) estimate that 98% of axonal calcium is bound to macromolecules. Using their figure we calculate that the ionized calcium concentration required to maintain axoplasmic flow is not more than 14 μM. (Supported by USPHS Grant No. NS 09503.)

**59.7** MEMBRANE PROPERTIES [EXCITABILITY AND OSMOTICITY] AND FAST AXOPLASMIC TRANSPORT IN VITRO, Sidney Ochs. Dept. Physiology, Indiana University Medical School, Indianapolis, Indiana 46202

A transport filament has been proposed to account for fast axoplasmic transport of the heterogenous group of materials carried down mammalian nerve fibers at a rate close to 410 mm/day. Oxidative metabolism supplies ATP to the transport mechanism and to the Na pump required to maintain excitability. The question arises as to whether changes in the membrane can affect fast transport. The L7 dorsal root ganglia of cats were injected with $^3H$-leucine and after 2-3 hrs for incorporation and downflow, the nerves were removed and placed into flasks containing Krebs-Ringer bubbled with 95% $O_2$ + 5% $CO_2$ at 38° C. The usual pattern of fast transport is maintained for at least 4 hrs in vitro. Phosphate buffer, $Ca^{2+}$, or $Mg^{2+}$, could each be removed without changing the pattern or rate of transport. KCl substituted for NaCl with a resulting depolarization of the membranes also did not alter fast axoplasmic transport. Finally, 300 mM of sucrose or glucose alone in the in vitro medium can maintain the usual fast transport pattern and rate. By adding 50-75 mM sucrose to make the nerve hypertonic, the rate decreased. The effect was greater with a 300 mM sucrose addition. Some differences in the degree and time of block were seen when the nerve was made hypertonic by adding NaCl or KCl as opposed to sucrose. Making the nerve hypertonic by reducing the sucrose concentration by 50 mM also diminished the rate with a much greater effect seen with a 140 mM decrease. These results plus earlier evidence that TTX and procaine did not affect fast transport, indicate that changes in the external medium which alter membrane excitability are not causal in altering fast transport, but a decrease in transport occurs when there is an alteration of the internal milieu. Supported by: NIH 080706, NSF 28664 and the John A. Hartford Foundation, Inc.

**60.1** RELATIONSHIP OF ANATOMY AND FUNCTION IN CNS: A NEURONAL MODEL STUDY. Photios A. Anninos* and Rafael Elul (SPON: J.D. French). BRI and Depts. Biomath., Anat., and Mental Retard. Center, NPI, UCLA, Los Angeles 90024

Phylogenesis has been characterized by development of new brain structures which, because of their particular geometry, imply different patterns of interconnection between neurons. The "closed nuclei" of the brain stem (Mannen, Arch. ital. Biol. 98: 333, 1960), in which neurons are arranged on the periphery, and all connections are made in the central neuropile provide an example. In this system distance on the periphery between two cells does not affect the likelihood of their forming a connection. This property can be expressed as a Poisson probability distribution. The neocortex appears to embody a rather different principle of structure; its planar arrangement implies that adjacent cells may be more likely to interconnect than remote ones. A number of probability distributions may express this greater probability of interaction with adjacent elements. For the present investigation we have chosen a normal (Gaussian) probability distribution to characterize neuronal connectivity in the neocortex.

We have explored the difference between the Poisson and Normal laws of connectivity in terms of activity of model nerve nets. The nets used follow Harth & Edgar (J. Biophys. 7: 689, 1967) and Anninos et al.(J. Theor. Biol. 20: 121, 1970). The principal finding is that nets with a Poisson law of connectivity can be activated by firing of a single neuron, and thereafter exhibit sustained activity which does not decay. In contrast, similar nets with the identical number of connections, but distributed following a Gaussian law, are activated only when a significant fraction of the population is extraneously fired and are incapable of long-term sustained activity. It is interesting to note that isolated cortical slabs in the cat are devoid of spontaneous activity and respond by a short burst to massive direct stimulation (Burns, J. Physiol. 111: 50, 1950; and 112: 156, 1951).

**60.2** DENDRITIC ORGANIZATION OF STELLATE CELLS IN LAYER IV OF CAT STRIATE CORTEX. Nell B. Cant* and L. T. Rutledge. Dept. Physiol., Univ. Mich., Ann Arbor, Michigan, 48104.

It has been emphasized that the organization of dendritic trees determines the types of input that a neuron receives. Preparatory to asking the question whether the organizations of dendritic trees may be changed by various environmental manipulations, we have studied the normal dendritic organization of stellate cells in cat striate cortex. Stellate cells were chosen for study because they presumably receive much of the afferent input to striate cortex. Tissue was taken from normal cats and stained with a Golgi-Cox method. Coronal sections were cut at 100μ and studied at 645X magnification. Dendritic organization was analyzed by determining values for number of dendrites per cell, number of dendritic segments per cell, number of branch points and terminations per cell, and number of branch points and dendritic segments per dendrite. Segment lengths were also measured. The ascending axon stellate cells were found to oriented perpendicular to the boundaries of layer IV and six frequently seen branching patterns were identified. Preliminary data from a second study of tissue from adult cats indicate that there may be changes in the dendritic organization of the layer IV stellate cells after enucleation of one or both eyes. If we assume that the denervated lateral geniculate cells project, at least in part, to layer IV stellate cells, these data would indicate that changes in afferent input could have an influence on dendritic organization in adult striate cortex. (Supported by NIH Grant NDS 04119.)

**60.3** PARKINSONIAN BEHAVIOR IN ARTIFICIAL NEURAL NETS. Ronald A. Cyrulnik* and Photios A. Anninos* (SPON: R. Elul). Depts. of Anat., Neurol., Biomath., Sch. Med. and Mental Retard. Center, NPI, UCLA, Los Angeles 90024

Neuropathology of parkinson's disease is presumed to involve an imbalance of complex servomechanisms incorporating the alpha motoneurons of the spinal cord. In an attempt to elucidate certain clinical features characterizing the development of this disease such as cogwheel rigidity, a neural net model (Anninos et al., J. Theor. Biol. 26: 121, 1970; Anninos, Kybernetik, in press, 1972) is proposed as representing the alpha motoneuron pool. There are both excitatory and inhibitory inputs converging upon this pool from upper centers. Peripheral inputs via the dorsal roots constitute excitatory input originating upon stretch in muscle spindles. Reaction to continuous passive stretch of a limb is characterized by cogwheel rigidity throughout its entire extent of movement. Patients with Parkinsonism manifest increased tone, and since dorsal rhizotomy abolishes the rigidity, it appears that the pathology is associated with decrease of descending inhibition. Thus, at rest the level of motoneuron activity is likely to be higher in parkinsonians than in normal individuals. In terms of our model, muscular stretch is represented by increased excitatory input to the net, resulting in an increase in instantaneous activity. In the following time interval most neurons will consequently be refractory, resulting in a very low level of activity. A net in this situation will not return to its original level of activity, but to a lower steady state. Thus, if the resting activity is sufficiently high, and inhibition level is low, the additional input to muscle stretch can cause a sudden "Give" in tone. At this point, however, there are now many non - refractory neurons, so that any additional input will cause the net to go to the high steady state level of activity resulting in a "Catch". The model also predicts that the "Catch" would be more gradual than the "Give" since there is a damped oscillation of activity around the high steady state as the net approaches it.

**60.4** PERIODICITY AND METACHRONISM IN NERVOUS SYSTEM ENSEMBLES? David A. Goodman and Chester L. Richards*. Newport Neuroscience Center, Irvine, California 92664

A year ago we suggested that individual receptor cilia and certain ciliated neurons in the central nervous system might show activity normally associated with functional ciliated epithelial cells. We now propose that ensembles of such nervous system elements might be periodically active and might operate in a metachronal mode. Metachronism refers to the synchronous activation of cells or cell columns and a phased sequence of activation in adjacent cell rows. Sequential activation of adjacent cells produces apparent travelling waves across the cell volume. Such wave activity might be supported by mechanical or electrical coupling of the synchronously active cells and might be sustained by neuroid conduction or propagated action potentials between adjacent cells; velocity and direction of wave propagation would depend on exact phasing of active cells in the ensemble Such coherent wave activity might be expected in those regions of metazoan nervous systems where neurons, receptor elements, or glia with pro - perties of ciliated ephithelial cells are closely apposed. Such loci might be the ependymal layers surrounding the ventricles, tightly packed receptor elements, certain granule cell fields, or wherever substantial numbers of candidate cells share a common substrate or a common "load". Magnitude of movement by participating cells in such a cell system might be described as low amplitude movement or as "micro-oscillations". Our postulation of synchronous and phased oscillations by cells in the metazoan neuropil derives from earlier speculations on CNS function by E. von Holst, N. Weiner, and C.J. Herrick. Additionally, such periodically active elements could parsimoniously underlie primitive rhythmic behaviors in Necturus maculosus, a neotenic salamander.

**60.5** SPIKE INTERVAL DISTRIBUTION CODING IN THE MAMMALIAN VISUAL PATHWAY. A. C. Sanderson*, W. M. Kozak, and T. W. Calvert*. Biotechnology Program, Carnegie-Mellon Univ., Pittsburgh, Pa. 15213

Experimental results are presented showing spike interval histograms recorded from retinal ganglion cells, optic tract, and lateral geniculate nucleus of the cat. These results exhibit a clear correlation between spike interval distribution and stimulus condition at the retina. The averaged mean rates of the cells studied were nearly the same in light as in darkness. We discuss the implications of these results using existing mathematical models of spike trains considered as stochastic point processes. It can be shown theoretically that distribution coding in an array of input fibers to a lateral inhibition network could be decoded in such a way as to directly affect the output mean rates from the network. Thus, distribution coding can be postulated as a mechanism involved in the spatial information processing capabilities of a structure such as the lateral geniculate nucleus in the visual pathway.

**60.6** A STEP IN THE ANALYSIS OF RETINAL CIRCUITRY BY MEANS OF EXTENSIVE THREE-DIMENSIONAL RECONSTRUCTIONS FROM ELECTRON MICROGRAPHS OF SERIAL SECTIONS. Fritiof S. Sjöstrand. Department of Zoology, University of California, Los Angeles, California 90024

Extensive three-dimensional reconstruction of an area in the outer plexiform layer in the rabbit retina has revealed very complex synaptic connections of the β-type receptor cells as compared to the α-type cells. The β-type cells, which are typical rod cells, therefore stand out as specialized cells with respect to their connections to the retinal circuitry. Possible patterned bipolar cell connections with receptor cells could furnish a basis for directional vision in these retinas. The new technique for extensive three-dimensional reconstructions from electron micrographs of serial sections will be described. This technique aims at a revealing of complete neuronal circuits in contrast to the fragmentary information obtained by the Cajal type of approach. A major problem has been to cut down to a reasonable level the time involved in making extensive enough three-dimensional reconstructions to include complete neuronal circuits.

**60.7** EVIDENCE AGAINST A STRONG RELATIONSHIP BETWEEN DENDRITIC TREE PATTERNING AND DIFFERENCES IN PHYSIOLOGY. Roger W. West and John E. Dowling*.
Dept. Biology, Harvard U., Cambridge, Mass., 02138.

Neurobiologists have often assumed that the vast diversity of dendritic tree patterns in retinal ganglion cells is necessary in order to establish different synaptic inputs and, thus, the diversity of receptive fields. A close examination of ground squirrel ganglion cells has yielded data that imply that differences in dendritic tree patterns may have little or nothing to do with establishing different receptive field properties in these cells. Light microscopy of Golgi-stained ground squirrel retinas reveals over 15 distinct dendritic tree morphologies. Since ground squirrel ganglion cells have been found to have only 5 types of ganglion cell receptive fields this is inconsistent with the assumption that each type of dendritic tree establishes a different physiology. Electron microscopy of Golgi-impregnated, serially sectioned ganglion cells also reveals that at least one class of dendritic tree pattern can have either 100% amacrine and no bipolar input, or 20% amacrine and 80% bipolar input. This leads to the almost certain consequence that light microscopically indistinguishable dendritic tree patterns can have very different physiologies. Thus, it is concluded that dendritic pattern diversity may be largely independent of receptive field class and may serve some other as yet unknown function.

**61.1** HIPPOCAMPAL NEURAL ACTIVITY: REGIONAL DIFFERENCES IN SLEEP AND WAKING. Phillip J. Best. Department of Psychology, University of Virginia, Charlottesville, Va. 22901

Dorsal Hippocampal single cell activity was recorded from 51 chronically implanted (62u nichrome) electrodes in unrestrained rats under the conditions of Quiet Awake (QA), Sleep with Slow Waves (SSW) and Paradoxical Sleep (PS). Electrodes were aimed at Cajal's Regio Superior (including Subiculum, CA1 and CA2), Regio Inferior (CA3 and CA4) and Facia Dentata. Significant differences in firing rates were found between regions, and between states for each region. Regio Superior shows its lowest rate during PS when Regio Inferior and Facia Dentata show their highest rates. The lowest rate for Regio Inferior occurs during SWS, while for Facia Dentata the lowest rate occurs in QA. If we ignore the Region of electrode placement the rate of activity is practically identical for each state.

The data suggest that apparent discrepancies between previous studies of hippocampal unit activity during PS are due primarily to differences in placement of recording electrode. The data also suggest the existence of an inhibitory pathway to Regio Superior, probably through the Fimbria, which is active during PS. Such a pathway has not yet been described.

**61.2** SEPTAL UNIT RESPONSES TO HIPPOCAMPAL STIMULATION. Henry M. Edinger, Raymond A. Troiano* and Allan Siegel. Depts. Physiology, Medicine and Anatomy, College of Med. & Dent. of N.J. - New Jersey Medical School, Newark, N.J. 07103.

The purpose of the present study was to determine the nature of the hippocampal projection to the septum in the cat. Bipolar stimulating electrodes were placed in the dorsal and ventral hippocampus using the hippocampal evoked potential, recorded by nichrome wire electrodes adjacent to the stimulating electrodes, as an indicator of effective hippocampal stimulation. Single unit discharges in the ipsilateral septum were recorded extracellularly with varnish coated tungsten microelectrodes and stored on magnetic tape. Biphasic stimuli yielded orthodromic action potentials in the septum at a minimum latency of 8 msec. Many units were driven at much longer latencies (up to 60 msec). The excitatory phase was followed by an inhibitory phase as indicated by the complete absence of spontaneous action potentials for 50 to 500 msec after the driven spike in neurons with high spontaneous firing frequencies. Units exhibiting long inhibitory periods without preceding excitation were seen in both the medial and lateral septum following stimulation of dorsal or ventral hippocampus. Inhibition was also prominent in the ventral septum and preoptic area, but excitatory driving showed a topographic restriction similar to the distribution of hippocampal efferents described by Siegel and Tassoni (Brain, Behav. & Evol. 4:185, 1971). Stimulation of the lateral hypothalamus also produced excitation-inhibition sequences in septal and preoptic neurons. (Supported by NIH Grant NS 07941-02 and by the Schizophrenia Research Program of the Supreme Council 33° A.A. Scottish Rite, Northern Masonic Jurisdiction.)

**61.3** THE TEMPORAL RELATIONSHIPS OF BRAIN STEM AND CORTICAL UNIT ACTIVITY TO THE EYE MOVEMENTS OF DESYNCHRONIZED SLEEP. J. Allan Hobson, Robert W. McCarley* and R. Terry Pivik*. Dept. Psychiatry, Harv. Med. Sch., Boston, 02115

Neurons of the gigantocellular tegmental field (FTG) in the pontine reticular formation concentrate their firing in desynchronized sleep (D); within D sleep, FTG firing is highly correlated with eye movement. We now present evidence that FTG neurons show phasic increases in rate prior to the individual eye movements of D. Extracellular action potentials were recorded from individual nerve cells in chronically implanted, unanesthetized cats. Identification of pontine brain stem neurons as belonging to the FTG was made on the basis of histology. Cortical neurons were located in the posterior half of the lateral and suprasylvian gyri. The activity of 10 FTG and 10 cortical neurons in relation to eye movement was quantified by means of sequential interval and cumulative histograms. For each cell, 10 isolated eye movements were identified in the EOG and time of onset ($t_0$) of each was established. The number of firings in 20 successive 50 msec bins beginning 500 msec before ($t_{-500}$) and ending 500 msec after ($t_{+500}$) each eye movement was calculated. Increases in rate were observed as inflection points occurring before eye movements in the individual curves of 8 of 10 FTG neurons (mean: $t_{-130}$ msec, range: $t_{-300}$ msec to $t_{+50}$ msec). Increases occurred after eye movements in all ten cortical neurons (mean: $t_{+55}$ msec, range: $t_0$ to $t_{+150}$ msec). In the pooled data, an inflection point occurred 100 msec earlier for the FTG neurons ($t_{-100}$) than for the cortical neurons ($t_0$). Peaks in the pooled sequential interval histograms were also separated by 100 msec, the FTG peak occurring at $t_0$, the cortical peak occurring at $t_{+100}$. Both neuronal groups had more firings after eye movement than before, but the proportion of firings occurring before eye movement was 2½ times greater for the FTG cells than for the cortical cells (0.37 vs 0.14).

**61.4** THE NEUROCHEMICAL BASES OF PONTO-GENICULATE-OCCIPITAL CORTEX (PGO) WAVES. Barry L. Jacobs. Dept. Psychol., Princeton Univ., Steven J. Henriksen and William C. Dement*. Dept. Psychiatry, Stanford Univ. Med. Sch.

PGO waves are an essential component of rapid eye movement sleep (REMS) in the cat. Since the entire REMS stage is easily disrupted by pharmacological intervention in a normal animal, we have adopted two experimental paradigms for studying the neurochemical bases of these waves. 1) Inhibition of serotonin synthesis following systemic injections of p-chlorophenylalanine (150 mg/kg s.c.) results in PGO waves being released into the waking state where they are more amenable to study. These waves were completely blocked for several hours by systemic injections of atropine (0.25-1.0 mg/kg). Reciprocally, eserine (0.05-0.10 mg/kg) increased PGO activity and at least partially reversed the atropine-induced blockade. On the other hand, the rate of occurrence of these waves was not suppressed by a variety of presumptive catecholamine receptor blockers. These results suggested the use of the second paradigm. 2) The propensity to have REMS is enhanced, and is made markedly refractory to disruption, by prior selective deprivation of this state. Following 2 control REMS periods in a 5 day REMS deprived animal, we administered either atropine (1-3 mg/kg) or scopolamine (0.5 mg/kg) and then studied the rate of occurrence of PGO waves in the subsequent REMS periods. The large PGO waves which normally occur regularly during REMS and the minute or so which immediately precedes it, were not suppressed by this treatment, while the clusters of these waves which normally accompany the bursts of rapid eye movements in REMS were abolished. These latter data strongly support the work of Pompeiano and his coworkers. Conclusions: In the normal animal, PGO waves occur at least partially as a result of an active cholinergic mechanism which is held under tonic serotonergic inhibition except during REMS.

**61.5** BRAIN STEM NEURONS: FIRING DURING REPEATED SLEEP-WAKING CYCLES. Robert W. McCarley*, J. Allan Hobson and R. Terry Pivik*. Dept. Psychiatry, Harv. Med. Sch., Boston, 02115

Neurons involved in generation of desynchronized sleep (D), when compared with other neurons, might be expected to show a greater concentration of firing during D and a longer lead time of rate increase prior to the electrographically defined onset of D. From 4 unanesthetized cats, we recorded extracellular action potentials from cells with the same stereotaxic coordinates (gigantocellular tegmental field) as those from which recordings of single sleep-waking cycles had demonstrated the greatest concentration of firing during D. In 4 units for which data analysis is complete, the firing rate increases and concentration of firing in D were consistent throughout all of the 50 cycles recorded (summary in table).

| Unit # | Hrs. Obs. | # D Cycles | Total Firings | Firings in D # | Firings in D % | % Time in D | Rate (s/s) D | Rate (s/s) Non-D | Rate Ratio D/Non-D |
|---|---|---|---|---|---|---|---|---|---|
| 531 | 5.0 | 10 | 11,831 | 10,685 | 90.3 | 17.5 | 3.387 | .07730 | 43.8 |
| 568 | 4.2 | 13 | 59,212 | 48,652 | 82.2 | 24.9 | 12.87 | .9255 | 13.9 |
| 585 | 5.3 | 11 | 4,365 | 4,255 | 97.5 | 16.7 | 1.326 | .006877 | 193 |
| 610 | 10.5 | 16 | 77,078 | 58,721 | 76.2 | 13.7 | 11.47 | .5644 | 20.3 |

Averages over multiple cycles showed 3 of the 4 units had rate increases beginning about 4 min prior to the onset of D. Rates accelerated rapidly in the minute before D, peaked within the first portion, then declined slowly, with an abrupt decrease as D ended. A still further decrease continued until about 3-5 min after D, with rates at this time reaching their lowest levels. This was followed by a gradual return to the average non-D firing rates. The curves describing the time course of changes in firing rate have implications for models of D sleep cycle regulation.

**61.6** CONTINUOUS MARKOV PROCESSES MODELLING 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 distributions as first passage time distributions through the neuron's threshold value.

**62.1** ROLE OF CEREBRO-PONTO-CEREBELLAR AND CEREBRO-RETICULO-CEREBELLAR PATHWAYS IN THE EARLY MOSSY FIBER RESPONSE. Gary I. Allen, Gian Battista Azzena* and Tadao Ohno*. Dept. of Physiology, State Univ. of New York at Buffalo, N. Y. 14226

The pons has been considered the most important relay for the early mossy fiber pathway from the motor cortex to the cerebellum, with minor significance attached to the cerebro-reticulo-cerebellar pathways. The present experiments were performed in an attempt to assess the relative contributions of the cerebro-ponto-cerebellar and cerebro-reticulo-cerebellar pathways. The mossy fiber field potentials evoked by stimulation of the sensorimotor cortex were examined in the pars intermedia of cats before and after controlled electrolytic lesions of individual cerebellar peduncles. The two components carried by the cerebro-ponto-cerebellar and cerebro-reticulo-cerebellar pathways were approximately the same size and reached the cerebellum with the same latency, a result obtained under nitrous oxide or thiopental anesthesia. Single unit recordings confirmed that these two inputs both contribute to the firing of Purkyně cells. Furthermore, the inputs provided by these two pathways converge onto common granule cells and either input by itself is ineffective in firing most granule cells, as shown with the $P_2$ and $N_3$ fields. By separately stimulating these two pathways, it was shown that activation of the granule cells requires that the two inputs reach the granule cells simultaneously. Therefore, it seems likely that these two pathways, probably carrying different signals, work together in the transfer of information from the cerebral cortex to the cerebellum.

**62.2** BEHAVIORAL, ELECTROPHYSIOLOGICAL, AND ULTRASTRUCTURAL EFFECTS OF COOLING ON THE GOLDFISH CEREBELLUM. Naiphinich Kotchabhakdi* and C. Ladd Prosser. Dept. Physiol., U. of Illinois, Urbana, Ill. 61801.

When goldfish, acclimated to 25°C, were placed in cold water brain temperature (measured by thermistor) reached that of the water in 1 minute. Initial behavioral hyperexcitability appeared below 14°C; after 2-5 minutes below 9°C motor incoordination, impaired postural and equilibrium control appeared; these losses were reversible on rewarming. After more than 30 minutes at 4°C irreversible loss of reflex responses, cessation of breathing and finally death occurred. Local cooling of the cerebellum by an implanted thermode produced the reversible deficits at the same temperature as whole body cooling. Spontaneous activity of Purkinje cells (PC) recorded extracellularly by implanted electrodes in unanesthetized fish and intracellularly in curarized fish decreased with cooling and was blocked reversibly at 8-9°C. Inhibition of PC spontaneity, caused by stimulation of cerebellar surface or by auditory or visual inputs, was blocked at about 12°C; excitatory responses to the same stimuli blocked below 10°C. Preliminary ultrastructural observations indicate changes in abundance of vesicles and other synaptic structures in cerebellum of fish exposed to cold. Evidence indicates that the reversible behavioral and electrical blocking by cold are due to synaptic effects and not to failure of peripheral functions. It appears that complex circuits with multiple synapses and interneurons are most sensitive to cooling and that cooling can aid in elucidating the integrating functions of cerebellum. [Supported by NSF GB4005 and a Rockefeller Foundation Fellowship.]

**62.3** RHYTHMIC ACTIVATION OF THE CEREBELLAR CLIMBING FIBER INPUT BY HARMALINE. Yves Lamarre and Claude de Montigny*. Dept. of Physiol., Med. Fac., Univ. Montreal, Quebec.

In decerebrate, paralysed cats, unitary recordings were obtained in the brain stem and cerebellum following administration of harmaline (5 mg/Kg). Rhythmic discharges at 8-12/sec in the inferior olive generated synchronous climbing fiber responses in Purkinje cells. Rhythmic bursting of cerebellar interneurones, most likely evoked by climbing fiber collaterals, was also observed. This activation of cerebellar interneurones resulted in a strong depression of Purkinje cell simple spike firing. The sustained rhythmic climbing fiber responses evoked inhibition-excitation sequences in the fastigial and Deiters nuclei and in the bulbar reticular formation, inducing muscle tremor via reticulo- and vestibulo-spinal pathways. It was also observed that decerebrate rigidity was markedly reduced by harmaline, due probably to a decreased gamma efferent activity. These results suggest that climbing fiber activity is related to a decreased antigravity muscle tone and, at the same time, to some phasic components of motor activation.

(Supported by the Medical Research Council of Canada).

**62.4** CEREBELLO-HIPPOCAMPO-CEREBELLAR INTERRELATIONSHIPS. J. Mitra and R. S. Snider. Center for Brain Research, Univ. of Rochester Medical Center, Rochester, New York 14642

Electrically induced seizure activity recorded in cerebral cortex following hippocampal stimulation can be reduced in severity and/or stopped by stimulation of ascending cerebellar systems especially those from nucleus fastigii. This has been demonstrated in both cat and monkey. Additional data on the diencephalic structures which mediate these effects are being studied. When seizure activity is induced in the hippocampus, microelectrode recordings in cerebellum of granule cell units (chloralose and urethane anesthesia) show increased discharges synchronous with hippocampal bursts while background activity is greatly reduced and remains reduced for several seconds after termination of seizure activity. The background activity in both the hippocampus and cerebellum returned about the same time. These changes are not related to minor fluctuations in blood pressure and heart rate. The inhibitory effects on granule cells are being investigated. (Supported in part by NIH Grant No. 06827-07 and No. 04592).

**62.5** SYNAPTIC CURRENTS PRODUCED IN CEREBELLAR CORTEX BY PROPRIOCEPTIVE INPUTS.[1] John T. Murphy and Hon Kwan*. Dept. of Physiology, University of Toronto, Faculty of Medicine, Toronto, Ont., Canada.

Current density, which is of primarily synaptic origin, is measured extracellularly in the cerebellar cortex of unanesthetized cats. During natural activation of propriocepters in individual muscles, a restricted focus of cortex is activated. We show that current flow occurs almost completely orthogonal to the plane defined by the Purkinje cell layer except at the fringes of this focus, where flow also occurs in directions parallel to this plane. By careful correlation of histologically determined recording locations with the observed spatial current density, the temporal sequence of synaptic activities in populations of the major neuron types of the three layers of the cerebellar cortex is determined. A striking new finding is that the cerebellar cortex acts as a high-pass filter for mossy fiber inputs. We also present evidence that climbing fibers synaptically activate Golgi and granule neurons in this physiological context.

[1]Supported by the MRC of Canada (MA 4140)

**63.1** TASTE OF WATER: NEURAL RECORDINGS FROM RAT, HAMSTER, CAT, AND SQUIRREL MONKEY. Linda M. Bartoshuk and Marion K. Frank*. John B. Pierce Foundation Laboratory, New Haven, Conn. 06519 and Rockefeller Univ., New York,N.Y. 10021.

Electrophysiological recordings were obtained from single fibers in the chorda tympani nerves of rat, hamster, cat, and squirrel monkey and in the glossopharyngeal nerve of rat. Responses to water were contingent on the nature of the preceding adapting solution. That is, responses were to water-after-NaCl, or water-after-HCl, etc. rather than to water per se. The percentages of fibers responsive to the various contingencies were not the same for all species. The failure to observe water responses in some species in earlier work was probably due to the use of Ringers solution as a rinse (i.e., adapting solution). The NaCl in the Ringers did not provide an optimal contingency for water responses in all species. The water-after-NaCl contingency appears to be uncommon in species strongly sensitive to NaCl because the water-after-NaCl responses correlate negatively with NaCl responses in all species tested. In man, water under various adaptation contingencies tastes like other substances. For example, water-after-NaCl tastes similar to quinine (i.e., bitter) and water-after-HCl tastes similar to sucrose (i.e., sweet). Correlation coefficients suggest that the water tastes for the species tested in this study are not always similar to the tastes they are similar to in man.

**63.2** CLASSIFICATION OF CAT GENICULATE GANGLION TONGUE UNITS. James C. Boudreau and Necip Alev*. Leech Farm VA Hospital, Pittsburgh, Pa. 15206

On the basis of single unit recordings the tongue units were divided into mechanically sensitive and chemosensitive units. The chemosensitive units were classified into three categories on the basis of spontaneous activity measures and their response to chemicals and electrical stimulation of the tongue. Electrical stimulation of excised fungieform papillae to which tongue units project elicited latencies of 7 to 9 msec from Group I units, 10 to 13 msec from Group II units and greater than 14 msec from Group III units. The intact tongue was stimulated with more than 150 different biochemical substances including amino acids, nucleotides and various metabolic intermediates. Group I and II units discharged to many of these substances, some of which activated members of both groups. Group I units were preferentially discharged by certain substances such as pyruvic, citric and malic acid, Group II units by cysteine and proline. Group III units were affected by fewer substances although some Group III units were among those maximally sensitive to nucleotide salts. Spontaneous activity measures also distinguished between the three groups, at least in part. The units in the three groups projected to fungieform papillae located in different regions of the tongue, although there was overlap in projection zones.

**63.3** A SOLUTION TO THE PROBLEM OF CEREBRAL CORTICAL LOCALIZATION OF TASTE IN THE CAT. Peter J. Hand, Adrian R. Morrison and Marvin I. Ruderman*, Department of Animal Biology, School of Veterinary Medicine, University of Pennsylvania, Phila., 19104

Outlining of a neocortical area in which natural gustatory stimuli evoke neural responses has proven difficult. We used a new approach to this problem. Single penetrations of the gustatory (parvocellular: pc) and somesthetic (lateral) regions of nucleus ventralis posteromedialis (VPM) were made with a vertically oriented electrode and activity evoked by natural stimulation (citric acid solutions and brush strokes). Electrolytic lesions were then made through the recording electrode and subsequent axonal degeneration studied with the Fink-Heimer I stain. Three cats were used for control lesions of surrounding nuclei, four for VPMpc, and three for lateral VPM lesions. Control lesions produced no degeneration in the cortical areas under investigation. Small lesions placed in the two VPM areas resulted in separate regions of cortical degeneration. Degeneration was found in either the lateral or both banks of the presylvian sulcus, and not in the coronal gyrus, following VPMpc lesions - the most medial areas projecting more medially. In contrast, lateral VPM lesions did not produce degeneration in the sulcus but did in the coronal gyrus, an area previously included in the gustatory region determined by electrical stimulation of the mixed (gustatory and tactile) chorda tympani nerve. The primary contribution of this study has been to demonstrate that the gustatory region of VPM, as defined by natural stimulation, projects to a restricted region of cortex hidden within the presylvian sulcus and not within the coronal gyrus as previous studies indicated. (Supported by NS-06716, 08410).

**63.4** STIMULUS-DEPENDENT MODIFICATION OF TASTE CELL MEMBRANE POTENTIALS BY ELECTRICAL STIMULATION OF SENSORY NERVE FIBERS. F.A. Kutyna* and R.A. Bernard., Dept. of Physiol., Mich. State Univ., E. Lansing, Mich. 48823

Previous work has shown that peripherally originating inhibitory interactions occur between taste papillae. Antidromic conduction of nerve impulses along the peripheral branches of taste fibers has been proposed to account for the inhibition. This study was done to determine whether electrical stimulation of the peripheral stump of the cut sensory nerve has an effect on the transmembrane potential of taste receptor cells. Intracellular recordings from cells of frog fungiform papillae were obtained using standard techniques. The sensory (IX) and motor (XII) nerves to the tongue were bilaterally severed and blood flow in the papillae was observed throughout the experiments. Application of taste solutions produced a depolarization of the cells similar to that reported by others. Electrical stimulation of the peripheral stump of the ipsilateral IX nerve produced a hyperpolarizing response whose magnitude was related to stimulus frequency. Prior application of chemical stimuli to the tongue affected the magnitude of this hyperpolarization, e.g. distilled $H_2O$ led to an increase, whereas buffered Ringer's to a decrease in the response. These effects were not associated with changes in papillary blood flow. Our results suggest that antidromic activity in peripheral taste fibers may produce a hyperpolarization of the receptor cells which can be modified by the presence of taste stimuli on the tongue. This hyperpolarization offers a possible mechanism for an inhibitory effect on the receptor cells.
(Supported in part by NIH grant NS 09168)

**63.5** Taste Bud Innervation and Lateral Interactions. Inglis J. Miller, Jr. Dept. Anat., Bowman Gray School of Medicine of Wake Forest University, Winston-Salem, North Carolina 27103

An interaction has been demonstrated physiologically among multiple taste bud inputs to single chorda tympani nerve fibers in the rat resulting in the depression or enhancement of an ongoing response (J. Gen. Phys. 57: 1, 1971) In the present study, branching of the afferent chorda tympani neurons is examined as the morphological basis of the physiological interaction by silver impregnation and light microscopy in the rat. In the normal animal the innervation of the lingual epithelium is dominated in number by trigeminal fibers of the lingual nerve. The organization and distribution of lingual fiber terminations is distinctly different from those of the chorda tympani nerve in the lingual epithelium. The lingual nerve was severed unilaterally at its emergence from the cranium, and these fibers were allowed to degenerate providing a lingual epithelium innervated by chorda tympani nerve fibers alone on one-half of the tongue. Myelinated chorda tympani fibers travel along the ventral portion of the tongue and course upward through muscle and connective tissue perpendicular to the epithelial surface in the region of individual papillae. Near the base of the fungiform papilla multiple branching occurs and unmyelinated branches ascend to innervate the taste bud. It is from the region at the base of the fungiform papilla that branches travel laterally to innervate adjacent papillae. Up to five myelinated chorda tympani nerve fibers innervate a single taste bud while many unmyelinated branches have been traced to neighboring taste buds, and ample morphological evidence is present to support an earlier hypothesis that branching in the dendritic arborization of the afferent fiber might provide a basis for lateral interactions in this system. (Supported by General Research Support Grant RR 5404)

**63.6** SURVIVAL AND TROPHIC FUNCTION OF NEURONS IN HOMOGRAFTS OF AG-B HISTOCOMPATIBLE RATS. Andrew A. Zalewski*. (SPON: Lloyd Guth). NIH, Bethesda, Md. 20014

The Ag-B histocompatibility gene locus of the rat determines antigens which greatly influence the survival of homografted organs. Organs which are exchanged between Ag-B compatible animals may survive whereas incompatible ones are rejected. The present study was performed to determine the importance of Ag-B locus antigens on neuron survival and function. Homografts of gustatory nodose ganglia from compatible (Fischer) or incompatible (Brown Norway) rats were combined with isografts of tongue's vallate papillae and placed into the anterior chamber of eyes of Lewis host rats to see if any neurons survived and could grow nerve fibers into the papilla and cause taste bud regeneration ( perform a trophic function). After 5 weeks, all ganglia were infiltrated by lymphocytic cells, and neurons were present in Ag-B compatible but not in Ag-B incompatible ganglia grafts. Furthermore, taste buds were found in some papillae reinnervated by surviving Ag-B compatible neurons. Papillae isografted alone lacked taste buds. The results demonstrate that Ag-B locus compatibility is required for neuron survival in homografts and that some surviving neurons are functional (can induce taste bud regeneration). Long-term studies are needed to determine if neuron survival and function can continue in nonimmunosuppressed animals.

**64.1** THERMOSENSITIVITY OF THE MEDULLA OBLONGATA: INFLUENCE ON THERMOREGULATORY BEHAVIOR AND BODY TEMPERATURE. J. M. Lipton. Psychol. Div., Univ. Tex. Southwestern Med. Sch., Dallas, 75235

Rats implanted with single water-perfused thermodes in the medullar region were trained to shift ambient air temperature from 50° to 10°C. by pressing a pedal. Air temperature rapidly returned to 50°C. when the pedal was released. When medullar temperature was controlled at levels over the range 34-43°C., the proportion of time spent pressing for cold air was positively correlated with medullar temperature. Electrolytic destruction of the preoptic/anterior hypothalamic (PO/AH) region resulted in an increase in the correlation between medullar temperature and the time spent in the cold air, indicating that the significance of medullar temperature to behavioral thermoregulation was enhanced. In other experiments on rats resting in a neutral environment (23°C.), heating the medullar region (40-43°C.) produced decreases in colonic temperature which were proportional to the degree of brain heating. Cooling the medulla (34-37°C.) produced shivering in most animals but did not result in significant changes in body temperature. Destruction of the PO/AH region did not alter these shivering and hypothermic responses to manipulation of medullar temperature. It is concluded that thermosensitive elements in the medulla oblongata contribute to the control of thermoregulatory behavior and physiological thermoregulatory processes and that these elements may be the central basis of the physiological and behavioral temperature regulation which persists following PO/AH injury. (Supported in part by NIH Grants No. 1 R01 NS10046 and No. 5 S01 RR05426).

**64.2** TEMPORAL SUMMATION IN THE WARMTH SENSE. Lawrence E. Marks. John B. Pierce Foundation Laboratory and Yale University, New Haven, Conn. 06519.

The way in which warmth sensation increases with duration of stimulus exposure was investigated in human subjects, who made magnitude estimations of the warmth sensation aroused by irradiation of the forehead. A stimulus of constant irradiance produces warmth that increases in near proportion to duration over the first three seconds of exposure. However, weak stimuli grow less rapidly in warmth than do strong ones. Given a constant low level of warmth, a stimulus half the duration of another must be twice as intense (complete summation), but given a constant high level of warmth, it need only be about 1.5 times as intense (partial summation). Thus temporal summation, like spatial summation, is a level-dependent phenomenon. Complete summation takes place only for threshold and low-level warmth. The transition between complete and partial summation is abrupt; it may be, therefore, that two different neural processes or mechanisms are involved in the mediation of warmth sensations. When the intensity of the stimulus is calculated in terms of the changes induced in superficial skin temperature, only partial summation occurs even at low levels of warmth. Calculation of changes induced in the temperature of tissue below the skin surface suggests that still less summation takes place. If warmth receptors are located at depths greater than about 0.2 mm below the surface, then no temporal summation occurs. In fact, given the same change in deep tissue temperature, a stimulus of relatively long duration produces less warmth than a stimulus of shorter duration.

**64.3** SPATIAL SUMMATION IN THE WARMTH SENSE. Joseph C. Stevens. John B. Pierce Foundation Laboratory and Yale University, New Haven, Conn. 06519.

The warmth sense has the capacity to sum the neural effects of infrared stimulation over large areal extents of the skin. Hence it is possible to trade the intensity of stimulation for its areal extent to preserve (1) a constant absolute threshold, (2) any constant level of supraliminal warmth, and (3) any constant reaction time. Psychophysical experiments on the forehead and the back (human subjects) reveal that area and intensity make approximately equal relative contributions to threshold (i.e., are reciprocally related), but with increasing level of warmth, the relative contribution of area diminishes continuously and eventually reaches zero near the threshold of pain. The degree of summation is, therefore, level-dependent. That summation can take place freely across dermatome boundaries was demonstrated by experiments that compared the perception of a split warmth field delivered to the two sides of the midline with the perception of a unitary field on one side. Split fields always felt unitary and their apparent strength was governed by the same rules of summation that apply to unitary fields. It would seem that the neural locus of summation is primarily central.

**64.4** RESPONSE TO HEAT OF VIBRATION-SENSITIVE MECHANORECEPTORS. Ira Wexler and Richard F. Mayer. Dept. of Neurol., Univ. of Md. Hosp. Sch. Med., Baltimore, Md., 21201.

Afferent impulses from slowly-adapting (SA) mechanoreceptors in cat hindlimb skin were monitored while the skin was vibrated at a rate of 100 Hz. with sinusoidal displacements. When the skin was cool (30-34$^{o}$ C.), vibration resulted in 2-5 per second trains of impulses. Within a train, spikes fired regularly at the 100 Hz. fundamental frequency. Heating the (vibrated) skin caused the number of spikes per train to fall off, consequently, total firing into the spinal cord (SC) was reduced. When the skin cooled to its preheated level the train pattern of spikes returned. In separate experiments spike activity in SC anterolateral (AL) and dorsal (DC) columns was recorded. In the AL, spike activity increased pari passu with skin heating. In the DC a train pattern of impulses induced by skin vibration and inhibited by skin heating was seen. The results indicate that a peripheral mechanism exists whereby heat interferes with the generation of vibratory nerve impulses. Electrophysiological confirmation is thus provided of preexisting psychophysical data showing, in humans, a raised threshold to vibration caused by skin heating.

# NOTES