Contents

General Conference Information

Shoreham Hotel Telephone No.: (202) 234-0700
Address: 2500 Calvert Street, N.W., Washington, D. C. 20036

Registration: The Registration Desk in the lobby of the Shoreham Hotel will be open as follows:

Wednesday, October 27	4:00 p.m. to 9:00 p.m.
Thursday, October 28	8:00 a.m. to 6:00 p.m.
Friday, October 29	8:00 a.m. to 6:00 p.m.
Saturday, October 30	8:30 a.m. to 11:30 a.m.

Registration for Members	$20.00
Registration for Non-Members	$25.00
Registration for Students	$ 5.00

Registration fee includes attendance at all meeting sessions and a copy of the Abstracts Program.

Single Day Registration	$10.00

Includes one day admission to meeting sessions and copy of Abstracts Program.

Message Center: A Conference Message Center will be in operation during the same hours as the Registration Desk. Please suggest that callers who wish to reach you during the day ask the hotel operator (202-234-0700) for the Neuroscience Conference Message Center. Please check the message board each day.

Hotel Reservations: The block of rooms at the Windsor Park Hotel has been filled. There are still rooms remaining in our block at the Shoreham Hotel. To insure confirmed reservations from this block, your reservation must be RECEIVED BY THE HOTEL NOT LATER THAN OCTOBER 6, 1971. Please call the Shoreham Hotel directly (202-234-0700). An advance deposit or written guarantee of payment is necessary to hold your room if arrival is scheduled after 6:00 p.m. Check out time for both the Shoreham and the Windsor Park is 3 p.m.

Opening Reception: A cash bar reception is scheduled for Wednesday, October 27, from 8:00 p.m. to 10:00 p.m. in the Diplomat Room, Shoreham Hotel. President Mountcastle, officers, members of the Council and Chapter officers and representatives will be there to greet you.

Abstracts Program: Each member of the Society for Neuroscience and all non-members who register in advance will be mailed a copy of the Meeting Abstracts Program. PLEASE BRING THIS WITH YOU TO THE MEETING as there will be a charge of $5.00 for additional copies of the program.

Discussion and Hospitality Lounge: A Discussion and Hospitality Lounge for Conference participants and their spouses will be set aside in the Marquee Lounge, Shoreham Hotel on Thursday and Friday from 9:00 a.m.

to 5:00 p.m. and Saturday from 9:00 a.m. to noon. This lounge is to provide an area for informal discussion as well as a central meeting location. Information about Washington sightseeing, shopping and special events will also be made available.

Kennedy Center Event: On Friday evening, October 29, there will be a reception and buffet in the Regency Ballroom, Shoreham Hotel and seats reserved at the Kennedy Center Opera House for the performance of "Candide." Tickets are $13.00 each to the reception and buffet and may be purchased either through pre-registration or at the current registration desk. Tickets are $10.50 to "Candide" and must be purchased through pre-registration not later than October 16. You may attend the reception and buffet without purchasing tickets for the performance of "Candide," or attend the Kennedy Center performance without going to the reception and buffet. Your ticket to "Candide" includes round trip bus transportation between the Shoreham Hotel and the Kennedy Center.

Press Room: The press facilities will be located in the Press Room, Shoreham Hotel. It will be opened on Wednesday from 4:00 p.m. to 9:00 p.m., Thursday and Friday from 8:00 a.m. to 6:00 p.m. and Saturday from 8:30 a.m. to 11:30 a.m.

Conference Business Office: The Conference Business Office will be located in the Caucus Room, Shoreham Hotel and will be open during registration hours.

Society Business Office: The Society for Neuroscience Business Office will be located in the Council Room, Shoreham Hotel and will be open during registration hours.

Luncheon Facilities: A special sandwich bar will be set up in the Marquee Lounge on Thursday and Friday between 11:30 a.m. and 1:00 p.m. for Conference participants. There are additional restaurants in the hotel and on nearby Connecticut Avenue.

Secretarial Service: Typing service may be obtained from the Shoreham Hotel's Public Stenographer. Contact through hotel house telephone.

Public Transportation: Public bus transportation via D. C. Transit Company is available on Connecticut Avenue, adjacent to the Shoreham Hotel and in front of the Windsor Park Hotel. Take L2 and L4 buses to downtown Washington and its shopping areas. Bus fare is $.40 and passengers must have exact change as bus drivers are not allowed to make change.

Meeting Schedule

All meeting rooms are at the Shoreham Hotel.

WEDNESDAY, OCTOBER 27, 1971

Meeting of the Council of the Society for Neuroscience—2:00 p.m. to 5:00 p.m.—Club Room A

Opening Reception—8:00 p.m. to 10:00 p.m.—Diplomat Room

THURSDAY, OCTOBER 28, 1971

SELECTED TOPIC SEMINARS

1. Sensation and Perception: Psychophysical Measurements and Brain Mechanics—9:00 a.m. to 11:30 a.m.—Regency Ballroom
2. Macromolecular Mechanisms—9:00 a.m. to 11:30 a.m.—Empire Room
3. Critical Periods in CNS Development—9:00 a.m. to 11:30 a.m.—Diplomat Room

SESSIONS OF CONTRIBUTED PAPERS

4. Non-cortical Visual Mechanisms—1:00 p.m. to 4:00 p.m.—Regency Ballroom
5. Metabolism—1:00 p.m. to 4:15 p.m.—Empire Room
6. Molecular Modification and Memory—1:00 p.m. to 4:00 p.m.—Tudor Room
7. Hypothalamic Functions—1:00 p.m. to 4:15 p.m.—Heritage Room
8. Neural Nets and Models—1:00 p.m. to 4:15 p.m.—Executive Room
9. EEG and Behavior—1:00 p.m. to 4:00 p.m.—Diplomat Room
10. Coding in Sensory Systems—1:00 p.m. to 4:00 p.m.—Blue Room
11. Drugs and Neural Function—1:00 p.m. to 4:15 p.m.—Forum Room
12. Problems of Pattern Recognition—1:00 p.m. to 4:00 p.m.—Club Room B
13. Morphology and Ultrastructure—1:00 p.m. to 4:00 p.m.—Ambassador Room

Presidential Addresses—4:30 p.m. to 5:30 p.m.—Regency Ballroom
Ralph W. Gerard, Honorary President
Vernon B. Mountcastle, President

FRIDAY, OCTOBER 29, 1971

SELECTED TOPIC SEMINARS

14. Education in the Neurosciences—9:00 a.m. to 11:30 a.m.—Diplomat Room
15. Order and Disorder in Movement—9:00 a.m. to 11:30 a.m.—Regency Ballroom
16. Synaptic Transmission—9:00 a.m. to 11:30 a.m.—Empire Room

SESSIONS OF CONTRIBUTED PAPERS

17. Mammalian Geniculo-striate Mechanisms—1:00 p.m. to 3:45 p.m.—Regency Ballroom
18. Biogenic Amines—1:00 p.m. to 4:15 p.m.—Empire Room
19. Memory and Motivation—1:00 p.m. to 4:00 p.m.—Diplomat Room
20. Cellular Mechanisms—1:00 p.m. to 4:15 p.m.—Forum Room
21. Sleep—1:00 p.m. to 3:30 p.m.—Tudor Room
22. Motor Control—1:00 p.m. to 4:15 p.m.—Blue Room
23. Receptor and Synaptic Processes—1:00 p.m. to 4:00 p.m.—Ambassador Room
24. EEG—1:00 p.m. to 3:45 p.m.—Executive Room
25. Behavior—1:00 p.m. to 4:15 p.m.—Heritage Room

Business Meeting: Society for Neuroscience (open to membership only)—4:00 p.m. to 5:30 p.m.—Ambassador Room

In addition to business items of concern to the membership, Edward F. MacNichol, Jr., Director, National Institute of Neurological Diseases and Stroke, will speak on Present and Future Prospects for Support of Research and Training in the Neurosciences.

Reception and Buffet—5:30 p.m. to 7:30 p.m.—Regency Ballroom

Performance of "Candide"—8:00 p.m.—John F. Kennedy Center for the Performing Arts

As reviewed by The Washington Post drama critic, Richard L. Coe, "Candide's" restrained elegance will be matched in setting by the Kennedy Center Opera House. Leonard Bernstein's score "by far his most sophisticated . . ." looks at the 18th century: "musically, mirroring and mocking its conventions with a subtlety striking on today's musical stages. . . . The romantic songs have the melodic verve of youthful Mozart; trios, quartets, quintets and choruses chuckle at Donizetti. Some songs have the later lilt of Gilbert and Sullivan. . . . Essentially, the score's triumph is its mastery of style."

SATURDAY, OCTOBER 30, 1971

SELECTED TOPIC SEMINARS

26. Nerve Nets—9:00 a.m. to 11:30 a.m.—Diplomat Room
27. Information Processing and Storage—9:00 a.m. to 11:30 a.m.—Empire Room
28. Brain, Consciousness, and the Control of Behavior—9:00 a.m. to 11:30 a.m.—Forum Room

Technical Sessions

THURSDAY, OCTOBER 28

Session 1. **9:00 a.m. to 11:30 a.m.** **Regency Ballroom**

SENSATION AND PERCEPTION: PSYCHOPHYSICAL MEASUREMENTS AND BRAIN MECHANICS

Chairman: Vernon B. Mountcastle, Johns Hopkins University School of Medicine

Introductory Lectures

1.1 A PSYCHOPHYSICAL YARDSTICK FOR SENSORY PROCESSES. Joseph Stevens, The John B. Pierce Foundation Laboratory

1.2 NEURAL MECHANISMS IN SENSATION, AND THE LINEARITY OF THE ACTION OF THE NERVOUS SYSTEM. Vernon B. Mountcastle

Selected Contributed Papers

1.3 PERIPHERAL NEURAL DETERMINANTS OF INTENSITY DISCRIMINATION FOR COOLING OF THE SKIN. Kenneth O. Johnson and Ian Darian-Smith, Department of Physiology, School of Medicine, Johns Hopkins University

1.4 THE DEPENDENCE OF THE DISTRIBUTION OF SLOW CORTICAL POTENTIALS RECORDED IN THE RHESUS ON THE TASK IMPOSED ON THE MONKEY. Emanuel Donchin, David Otto, Lauren K. Gerbrandt, and Karl Pribram, Department of Psychology, University of Illinois, Department of Psychology, Stanford

1.5 INTENSITY AND WAVE LENGTH ANALYSIS BY VISUAL SYSTEMS. Russell DeValois, University of California, Berkeley

Summarizing Lecture

1.6 FROM IMPINGEMENT TO ACQUISITION OF STIMULUS INFORMATION. Gerhard Werner, Department of Pharmacology, University of Pittsburgh School of Medicine

THURSDAY, OCTOBER 28

Session 2 **9:00 a.m. to 11:30 a.m.** **Empire Room**

MACROMOLECULAR MECHANISMS

Chairman: Francis O. Schmitt, Neurosciences Research Program, Massachusetts Institute of Technology

Invited Lectures

2.1 NEURONAL MEMBRANOLOGY. Francis O. Schmitt

2.2 NUCLEIC ACIDS AND PROTEINS IN LEARNING AND NEURONAL FUNCTION. Edward Glassman, Department of Biochemistry, University of North Carolina School of Medicine

2.3 ROLE OF CYCLIC AMP, CALCIUM AND MICROTUBULES IN NEUROPLASMIC DYNAMICS. Howard Rasmussen, Department of Biochemistry, University of Pennsylvania

2.4 MOLECULAR BIOLOGY OF THE SYNAPSE. Floyd E. Bloom, Laboratory of Neuropharmacology, NIMH

Selected Contributed Papers

2.5 FURTHER EVIDENCE ON THE ROLE OF MEMBRANE PROTEIN IN EXCITATION INITIATION IN AXONS. Alfred Strickholm and Hulda R. Clark, Anatomy-Physiology Department, Indiana University

2.6 THE EFFECT OF C-AMP ON IN VITRO NEURITE DEVELOPMENT. F. J. Roisen, W. G. Braden, M. Pichichero and R. Murphy, Department of Anatomy, Rutgers Medical School

2.7 FINE ULTRASTRUCTURAL FEATURES OF RIBOSOMES AND SYNAPTIC MEMBRANES IN BRAIN CORTEX. Vincenzo Di Carlo, Department of Anatomy, Loyola University of Chicago, Stritch School of Medicine, Maywood, Illinois, and L. B. Mendel Research Laboratory, Elgin State Hospital, Elgin, Illinois

THURSDAY, OCTOBER 28

Session 3. **9:00 a.m. to 11:30 a.m.** **Diplomat Room**

CRITICAL PERIODS IN CNS DEVELOPMENT

Chairman: Richard Held, Professor of Experimental Psychology, Massachusetts Institute of Technology

Invited Lectures

3.1 CONNECTIVITY IN THE VISUAL SYSTEM. Colin Blakemore, Physiological Laboratory, Cambridge, England

3.2 HORMONAL PROGRAMMING. Seymour Levine, Laboratory of Developmental Psychobiology, Stanford University School of Medicine

3.3 NECESSARY SEQUENCES OF BEHAVORIAL-ENVIRONMENTAL INTERACTIONS. Alan Hein, Associate Professor of Psychology, Massachusetts Institute of Technology

THURSDAY, OCTOBER 28

Session 4. **1:00 p.m. to 4:00 p.m.** **Regency Ballroom**

NON-CORTICAL VISUAL MECHANISMS

Chairman: W. Maxwell Cowan, Department of Anatomy, Washington University School of Medicine

Contributed Papers

1:00 p.m. 4.1 VISUAL DISCRIMINATION AND THE EFFECTS OF ABLATIONS OF THE CENTRAL VISUAL SYSTEM IN LEMON AND NURSE SHARKS. R. Curtis Graeber, Sven O. E. Ebbesson, J. A. Jane and P. J. Best, Departments of Psychology and Neurosurgery, University of Virginia, and Lerner Marine Laboratory, Bimini, Bahamas

1:15 p.m. 4.2 LIMULUS LATERAL EYE: HOW TO GAIN FIVE LOG UNITS OF SENSITIVITY. Robert B. Barlow, Jr. and Ehud Kaplan, Laboratory Sensory Communications, Syracuse University

1:30 p.m. 4.3 A COMPARATIVE STUDY IN THE NEUROPHYSIOLOGY OF VISION IN SQUID AND OCTOPUS. Peter H. Hartline and G. David Lange, Department of Neurosciences, School of Medicine, University of California, San Diego

1:45 p.m. 4.4 TRANSFER PROPERTIES OF THE ERG OF OCTOPUS. G. David Lange and Peter H. Hartline, Department of Neurosciences, School of Medicine, University of California, San Diego

2:00 p.m. 4.5 CHEMICAL ANALYSIS AND IN VITRO ACTIVITY OF RETINAL ROD OUTER SEGMENTS. William Robinson, Ann Gordon-Walker, Joan Dawes and Deric Bownds, Laboratory of Molecular Biology, University of Wisconsin

2:15 p.m. 4.6 SYNAPTIC INPUT ON GANGLION CELLS IN THE GROUND SQUIRREL RETINA. Roger W. West and John E. Dowling, The Johns Hopkins University

2:30 p.m. 4.7 THE RESPONSE OF MONKEY RETINAL GANGLION CELLS TO A FLASHING AND MOVING LUMINOUS SPOT. R. P. Scobey and J. M. Horowitz, Department of Behavioral Biology, School of Medicine and Department of Animal Physiology, University of California, Davis

2:45 p.m. 4.8 RETINAL RESPONSE LATENCY AS A FUNCTION OF FLASH RATE. Walter Salinger and Donald B. Lindsley, Departments of Psychology and Physiology, University of California, Los Angeles

3:00 p.m. 4.9 DIRECTIONALLY SELECTIVE VISUAL UNITS RECORDED IN THE OPTIC TECTUM OF THE GOLDFISH. Douglas Wartzok and William B. Marks, Department of Biophysics, Johns Hopkins University

3:15 p.m. 4.10 VELOCITY DEPENDENT DIRECTIONAL SELECTIVITY IN CAT SUPERIOR COLLICULUS. Barry E. Stein and Makanjuola O. Arigbede, Department of Anatomy, University of California, Los Angeles, Center for Health Science

3:30 p.m. 4.11 VISUAL LEARNING BY CATS AFTER LESIONS OF THE SUPERIOR COLLICULUS-PRETECTUM. J. S. Winterkorn, Anatomy Department, Cornell University Medical College

3:45 p.m. 4.12 VISUAL SYSTEM EXCITABILITY TEMPORALLY RELATED TO FAST AND SLOW COMPONENTS OF NYSTAGMUS IN THE CAT. Robert B. Graham, Department of Psychology, University of Florida

THURSDAY, OCTOBER 28

Session 5. **1:00 p.m. to 4:15 p.m.** **Empire Room**

METABOLISM

Chairman: Donald Tower, Laboratory of Neurochemistry, National Institute of Neurological Diseases and Stroke

Contributed Papers

1:00 p.m. 5.1 HIPPOCAMPUS AND ZINC: THE POSSIBLE ROLE OF ZINC IN THE CNS. Werner J. Niklowitz, Department of En-

vironmental Health, College of Medicine, University of Cincinnati

1:15 p.m. 5.2 FURTHER STUDIES ON A CORTICOSTERONE BINDING MACROMOLECULE FROM RAT BRAIN CYTOSOL. B. I. Grosser, W. Stevens, and D. J. Reed, Department of Psychiatry, Anatomy and Pharmacology, School of Medicine, University of Utah

1:30 p.m. 5.3 HYDROXYTRYPTAMINE-RELATED CHANGES IN CEREBRAL PROTEIN SYNTHESIS. Elihau Heldman and Walter B. Essman, Queens College of the City University of New York

1:45 p.m. 5.4 DISTRIBUTION OF AMINOTRANSFERASES IN RAT BRAIN. M. Benuck, F. Stern, and A. Lajtha, New York State Research Institute for Neurochemistry and Drug Addiction, Ward's Island, New York

2:00 p.m. 5.5 LYSOSOMAL ACID HYDROLASES IN NEONATAL RAT BRAIN AND IN MONOLAYER CULTURES DERIVED FROM NEONATAL BRAINS EXPOSED PRENATALLY TO ETHYLNITROSOUREA (ENU). H. H. Traurig and J. N. Allen, Division of Neurology, College of Medicine, Ohio State University

2:15 p.m. 5.6 EFFECTS OF DIBUTYRYL ADENOSINE CYCLIC 3′:5′-MONOPHOSPHATE ON EMBRYONIC RAT CEREBELLUM CULTURED IN VITRO. Robert S. Lasher and Ian S. Zagon, Department of Anatomy, University of Colorado Medical School

2:30 p.m. 5.7 CHARACTERIZATION OF RNA POLYMERASE ACTIVITY IN ISOLATED OLIGODENDROGLIA ENRICHED NUCLEI. Donald E. Slagel and Bobby C. Powell, Department of Surgery, Division of Neurosurgery, University of Kentucky College of Medicine

2:45 p.m. 5.8 ESR STUDIES OF SPIN-LABELLED NEUROBLASTOMA CULTURE CELLS. Howard H. Wang, Gregory Giotta and Dorothy Steele, University of California, Santa Cruz

3:00 p.m. 5.9 IN VIVO METABOLISM OF GALACTOSPHINGOLIPIDS IN THE BRAIN OF JIMPY AND CONTROL MICE. Mary J. Druse and Edward L. Hogan, Neurobiology Program, School of Medicine, University of North Carolina

3:15 p.m. 5.10 POSTNATAL PROTEIN-CALORIE DEFICIENCY EFFECTS ON LEARNING AND NEUROCHEMISTRY OF INFANT RHESUS MONKEYS. Ordy, J., Northern Illinois University

3:30 p.m. 5.11 CEREBRAL BLOOD FLOW AND CEREBRAL FUNCTION. James H. Salmon and Albert L. Timperman, Department of Neurosurgery, University of Cincinnati College of Medicine and the Veterans Administration Hospital

3:45 p.m. 5.12 EFFECT OF pH ON METABOLISM AND ULTRASTRUCTURE OF GUINEA PIG CEREBRAL SLICES IN VITRO. K. K. Patel, J. F. Hartmann and M. M. Cohen, Department of Neurological Science, Rush Medical College, Chicago

4:00 p.m. 5.13 AGE-SPECIFIC SUSCEPTIBILITY OF THE RAT BRAIN TO VIRAL INFECTION. Andrew A. Monjan, Neal Nathanson, Gerald A. Cole and Donald H. Gilden, Department of Epidemiology, School of Hygiene and Public Health, Johns Hopkins University

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Session 6. **1:00 p.m. to 4:00 p.m.** **Tudor Room**

MOLECULAR MODIFICATION AND MEMORY

Chairman: Bernard W. Agranoff, University of Michigan Medical School

Contributed Papers

1:00 p.m. 6.1 MOLECULAR BASIS OF LEARNING AND MEMORY. Edward M. Kosower, Department of Chemistry, State University of New York, Stony Brook

1:15 p.m. 6.2 UCB 6215 AND METAMPHETAMINE EFFECTS ON ACQUISITION. Otto L. Wolthuis, Medical Biological Laboratory TNO, Rijswijk, The Netherlands

1:30 p.m. 6.3 RESISTANCE OF FLUROTHYL-INDUCED RETROGRADE AMNESIA IN CHICKS TO THE REMINDER EFFECT. Arthur Cherkin, Veterans Administration Hospital, Sepulveda, California and University of California, Los Angeles, School of Medicine

1:45 p.m. 6.4 BRAIN SEIZURE ACTIVITY AND RETROGRADE AMNESIA IN RATS. Steven Zornetzer and James L. McGaugh, Department of Psychobiology, University of California, Irvine

2:00 p.m. 6.5 CYCLOHEXIMIDE: DELAYED DEVELOPMENT OF AMNESIA FOLLOWING DIFFERENT LEVELS OF TRAINING. L. R. Squire and S. H. Barondes, Department of Psychiatry, School of Medicine, University of California, San Diego, La Jolla

2:15 p.m. 6.6 RNA METABOLISM IN GOLDFISH BRAIN DURING ACQUISITION OF NEW BEHAVIORAL PATTERNS. V. E. Shashoua, McLean Hospital Research Laboratory, Belmont, Massachusetts and Harvard Medical School

2:30 p.m. 6.7 ACTIVITY IN GOLDFISH OF A SYNTHETIC LEARNING-LINKED RAT PEPTIDE. Rodney C. Bryant, Brain Research Institute, University of Tennessee

2:45 p.m. 6.8 SPECIFIC MODIFICATION OF BEHAVIOR OF RECIPIENT GOLDFISH WITH BRAIN EXTRACTS FROM DONORS TRAINED ON AN APPETITIVE SHAPE DISCRIMINATION TASK. Ronald B. Hoffman, Department of Biophysical Science, University of Houston

3:00 p.m. 6.9 MODIFICATION OF RECIPIENT BEHAVIOR BY INTRACRANIAL INJECTIONS OF EXTRACTS FROM BRAINS OF TRAINED DONOR GOLDFISH. William G. Braud, Department of Psychology, University of Houston

3:15 p.m. 6.10 PHOSPHORYLATION OF NUCLEAR PROTEINS DURING AVOIDANCE BEHAVIOR OF RATS. Barry J. Machlus, John Eric Wilson and Edward Glassman, Department of Biochemistry and Neurobiology Program, University of North Carolina

3:30 p.m. 6.11 BRAIN PROTEIN SYNTHESIS AFTER ELECTROSHOCK. Adrian J. Dunn, Department of Biochemistry and Neurobiology Program, University of North Carolina

3:45 p.m. 6.12 DENDRITIC SPINE FUNCTION AND SYNAPTIC ATTENUATION CALCULATIONS. Wilfrid Rall and John Rinzel, National Institutes of Health

THURSDAY, OCTOBER 28

Session 7. **1:00 p.m. to 4:15 p.m.** **Heritage Room**

HYPOTHALAMIC FUNCTIONS

Chairman: Philip Bard, Department of Physiology, Johns Hopkins School of Medicine

Contributed Papers

1:00 p.m. 7.1 CNS EFFECTS OF MELANOCYTE-STIMULATING HORMONE IN MAN. Abba J. Kastin, Marcos Velasco, Lyle H. Miller, David Gonzalez-Barcena, William D. Hawley, Kjell Dyster-Aas, Andrew V. Schally and Luisa Parra, Veterans Administration and Public Health Service Hospitals, and Tulane and Louisiana State University Medical Schools, New Orleans, IMSS, Centro Medico, Mexico, and University of Lund, Sweden

1:15 p.m. 7.2 A SPECTRAL AND DISCRIMINANT ANALYSIS OF EEG ACTIVITY IN LESIONED AND NON-LESIONED HYPOTHALAMIC SITES. Fred Abraham, Martin Gardiner and Jerome Maderdrut, Brain Research Institute, University of California, Los Angeles

1:30 p.m. 7.3 EFFECTS OF ELECTRICAL STIMULATION OF THE SEPTUM ON DRINKING ELICITED FROM ELECTRICAL STIMULATION OF THE HYPOTHALAMUS. G. J. Morgenson, W. Sibole and J. J. Miller, University of Western Ontario, London, Canada

1:45 p.m. 7.4 DRINKING BY RATS FOLLOWING LATERAL HYPOTHALAMIC DAMAGE. Edward M. Stricker, Department of Psychology, University of Pittsburgh

2:00 p.m. 7.5 THE ELUCIDATION OF HYPOTHALAMIC CONTROL OF FEEDING WITH C^{14} TRACER TECHNIQUES. Jaak Panksepp, Worcester Foundation for Experimental Biology

2:15 p.m. 7.6 EFFECT OF HABENULAR LESIONS ON FOOD ODOR PREFERENCE AND FOOD CONSUMPTION IN RATS. Lyle J. Rausch, Rebecca Rausch and Charles J. Long, Department of Psychology, Memphis State University

2:30 p.m. 7.7 A CENTRAL CIRCUIT INVOLVED IN CONTROL OF GASTRIC SECRETION. M. Kadekaro and C. Timo-Iaria, Department of Physiology, Michigan State University and University of Sao Paulo (Brazil)

2:45 p.m. 7.8 IMMEDIATE LIPEMIC RESPONSE TO CEREBRAL ACTIVITY. James W. Correll and Roger W. Countee, Department of Neurological Surgery, College of Physicians and Surgeons, Columbia University

3:00 p.m. 7.9 ANALYSIS OF THE EFFECTS OF POSTERIOR HYPOTHALAMIC LESIONS ON COPULATORY BEHAVIOR OF THE MALE RAT. Anthony R. Caggiula, Seymour M. Antelman and Michael J. Zigmond, Department of Psychology, University of Pittsburgh

3:15 p.m. 7.10 SEXUAL BEHAVIOR EVOKED BY HYPOTHALAMIC STIMULATION IN UNRESTRAINED MONKEYS. Adrian A. Perachio and Margery Alexander, Yerkes Regional Primate Research Center, Emory University

3:30 p.m. 7.11 BIOCHEMICAL AND RADIOAUTOGRAPHIC STUDIES OF ^{3}H-CORTICOSTERONE BINDING TO HIPPOCAMPUS. Bruce S. McEwen, John Gerlach and Darcy B. Kelley, The Rockefeller University

3:45 p.m. 7.12 BIOSYNTHESIS OF THE HYPOTHALAMIC TRIPEPTIDE-AMIDE TRF. Roger Guillemin, The Salk Institute for Biological Studies, La Jolla

4:00 p.m. 7.13 CHARACTERISTICS OF THE HERING-BREUER REFLEXES DURING EXPIRATION IN THE CAT. C. K. Knox, Laboratory of Neurophysiology, University of Minnesota Medical School

Session 8. **1:00 p.m. to 4:15 p.m.** **Executive Room**

NEURAL NETS AND MODELS

Chairman: Phillip G. Nelson, Behavioral Biology Branch, National Institute of Child Health and Human Development

Contributed Papers

1:00 p.m. 8.1 DIGITAL COMPUTER SIMULATION OF LARGE NERVE NET MODELS OF BRAIN CORTICES. Larry D. Wittie, Computer Science Department, University of Wisconsin

1:15 p.m. 8.2 EXCITATORY AND INHIBITORY INTERACTIONS IN LOCALISED POPULATIONS OF MODEL NEURONS. Hugh R. Wilson and Jack D. Cowan, Department of Theoretical Biology, University of Chicago

1:30 p.m. 8.3 A THEORY OF HIERARCHICAL ORGANIZATION IN PERCEPTION. Karl Kornacker and Leo E. Lipetz, Department of Biophysics, The Ohio State University

1:45 p.m. 8.4 COMPUTER ANALYSIS OF ACTIVITY PATTERNS IN SINGLE RESPIRATORY CELLS. Charles L. Webber, Jr. and Clarence N. Peiss, Department of Physiology, Loyola University, Stritch School of Medicine

2:00 p.m. 8.5 CONDITIONAL PROBABILITY MATRIX—A METHOD FOR THE ANALYSIS OF INTERSPIKE INTERVALS. C. J. Sherry and T. J. Marczynski, Department of Pharmacology, University of Illinois at the Medical Center

2:15 p.m. 8.6 HUMAN EPILEPTIC NEURONS: COMPARISON OF INTERICTAL FIRING PATTERNS TO THOSE OF "EPILEPTIC" NEURONS IN ANIMALS. William H. Calvin, George A. Ojemann and Arthur A. Ward, Jr., Department of Neurological Surgery, University of Washington School of Medicine

2:30 p.m. 8.7 FUNCTIONAL DEVELOPMENT OF INTRACORTICAL SYNAPTIC ORGANIZATIONS ACTIVATED BY INTERHEMISPHERIC AFFERENTS. Robert J. Shofer and Dominick P. Purpura, Department of Anatomy, Albert Einstein College of Medicine

2:45 p.m. 8.8 MEMBRANE POTENTIAL TRAJECTORY ALTERATIONS UNDERLYING MOTONEURON FIRING RATE CHANGES. Peter C. Schwindt and William H. Calvin, Departments of Neurological Surgery and Physiology/Biophysics, University of Washington

3:00 p.m. 8.9 ELECTROPHYSIOLOGY OF THE PRIMATE CEREBELLAR CORTEX. James R. Bloedel, Richard S. Gregory and Stephen H. Martin, Departments of Physiology and Neurosurgery, Minnesota Medical School

3:15 p.m. 8.10 SINGLE NEURON ACTIVITY IN THE CNS OF THE ACANTHOCEPHALAN MACRACANTHORHYNCHUS HIRUDINACEUS. Donald M. Miller, Tommy T. Dunagan and Kenneth R. Hightower, Department of Physiology, Southern Illinois University

3:30 p.m. 8.11 INFORMATION TRANSMISSION IN AND BY A CRAYFISH. Dale Harris and Lawrence Stark, University of California, Berkeley

3:45 p.m. 8.12 ELECTROPHYSIOLOGICAL ANALYSIS OF LOCAL REFLEXES IN A MOLLUSC. David J. Prior, Department of Biology, University of Virginia

4:00 p.m. 8.13 CENTRAL INTERACTIONS AMONG TOUCH-SENSITIVE NEURONS IN THE SURF CLAM. DeForest Mellon, Jr., Department of Biology, University of Virginia

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Session 9. **1:00 p.m. to 4:00 p.m.** **Diplomat Room**

EEG and Behavior

Chairman: Herbert H. Jasper, Department de Physiologie, Université de Montreal

Contributed Papers

1:00 p.m. 9.1 INTRACELLULAR RESPONSES OF STRIATAL NEURONS TO PAIRED AFFERENT STIMULI. N. A. Buchwald, C. D. Hull and D. D. Price, Department of Anatomy, Psychiatry, Mental Retardation Center, NPI, University of California, Los Angeles

1:15 p.m. 9.2 ACTION OF INTRAVENTRICULAR TETRODOTOXIN AND CELLULAR MECHANISM OF GENERATION OF EEG. Rafael Elul, Department of Anatomy, University of California, Los Angeles

1:30 p.m. 9.3 BASAL GANGLIA RESPONSES TO ANTIDROMIC PYRAMIDAL STIMULATION. G. Krauthamer, Department of Anatomy, Rutgers University Medical School

1:45 p.m. 9.4 THE STATISTICAL ANALYSIS OF EVOKED POTENTIALS. Donald C. Martin, Biomathematics Program, Statistics Department, North Carolina State University

2:00 p.m. 9.5 A METHOD FOR COMPUTER ANALYSIS OF EEG DESYNCHRONIZATION. Zaven S. Khachaturian, Joyce L. Kerr, Henry Gluck and Joseph Schachter, Division of Child Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, and Department of Psychiatry, School of Medicine, Case Western Reserve University

2:15 p.m. 9.6 IDENTIFICATION OF FUNCTIONAL BIOELECTRIC CONFIGURATIONS IN SPONTANEOUS ACTIVITY OF THE BRAIN. Stephen S. Fox and Hansook Ahn, Department of Psychology, University of Iowa

2:30 p.m. 9.7 THE EFFECTS OF STIMULUS UNCERTAINTY ON THE PUPILLARY DILATION RESPONSE AND THE VERTEX EVOKED POTENTIAL. David Friedman, Queens College

2:45 p.m. 9.8 HIPPOCAMPAL EVOKED POTENTIALS IN TASK SITUATIONS IN THE TEMPORAL-LOBE EPILEPTIC. Martin F. Gardiner, Anthony Dymond, Paul Crandall and Donald O. Walter, Departments of Physiology and Surgery (Neurology), University of California, Los Angeles, School of Medicine and Brain Research Institute, Los Angeles

3:00 p.m. 9.9 INTERACTIONS OF DISSIMILAR STIMULI ON HUMAN SLOW EVOKED POTENTIALS. Hallowell Davis, Poul A. Osterhammel, Craig C. Wier and Shirley K. Hirsh, Central Institute for the Deaf, St. Louis

3:15 p.m. 9.10 CORTICAL STEADY POTENTIAL CORRELATES OF INSTRUMENTAL PERFORMANCE. Roy A. Anderson, Department of Psychiatry, Case Western Reserve University, Cleveland

3:30 p.m. 9.11 SLOW POTENTIAL CORRELATES OF REACTION TIME PERFORMANCE IN MONKEYS. D. Symmes, M. Healy and K. Chase, National Institute of Child Health and Human Development

3:45 p.m. 9.12 ABOLITION OF BOTH THE CNV AND THE SLOW-POTENTIAL SHIFT ACCOMPANYING AUGMENTING RESPONSES DURING REVERSIBLE CRYOGENIC BLOCKADE OF THE NONSPECIFIC THALAMO-CORTICAL SYSTEM IN THE CAT. James E. Skinner, Neurophysiology Section, Physiology Department, Baylor College of Medicine

THURSDAY, OCTOBER 28

Session 10. **1:00 p.m. to 4:00 p.m.** **Blue Room**

CODING IN SENSORY SYSTEMS

Chairman: Lawrence Kruger, Department of Anatomy, University of California, Los Angeles

Contributed Papers

1:00 p.m. 10.1 RESPONSES OF FASTIGIAL NEURONS TO STIMULATION OF CUTANEOUS MECHANORECEPTORS. John C. Eccles, Nassir H. Sabah and Helena Táboríková, Departments of Physiology and Biophysics, State University of New York at Buffalo

1:15 p.m. 10.2 DEVELOPMENT OF NEURAL CODING CHARACTERISTICS IN PRIMARY CUTANEOUS AFFERENTS IN KITTENS. R. E. Beitel, J. M. Gibson and W. I. Welker, Laboratory of Neurophysiology, University of Wisconsin

1:30 p.m. 10.3 UNIQUE SENSORY CODING OF DIRECTIONAL MOVEMENTS BY MIDLINE VIBRISSA. Bruce Oakley, Zoology Department, University of Michigan

1:45 p.m. 10.4 SENSORY MODALITY REPRESENTATION IN THE ANTERO-LATERAL SYSTEM. James A. Mosso and Lawrence Kruger, Departments of Neurosurgery and Anatomy, University of California, Los Angeles, Center for Health Science

2:00 p.m. 10.5 RESPONSES OF CELLS IN CAT POSTERIOR THALAMUS TO STIMULATION OF CENTRAL AFFERENT PATHWAYS AND PERIPHERY. Karen J. Berkley, Department of Psychology, Florida State University

2:15 p.m. 10.6 SOMATOSENSORY CORTEX AND DISCRIMINATIVE BEHAVIOR IN THE RAT. Stanley Finger, Dept. of Psychology, Washington University, St. Louis

2:30 p.m. 10.7 PROJECTION IN THE CUNEATE FASCICULUS OF MECHANORECEPTIVE AFFERENT FIBERS INNERVATING THE RACCOON'S FOREPAW. Lillian M. Pubols and B. H. Pubols, Jr., Department of Anatomy, Hershey Medical Center, Pennsylvania State University

2:45 p.m. 10.8 VELOCITY AND ACCELERATION RESPONSE IN N. GRACILIS TO ANGULAR JOINT MOTION. W. J. Williams, S. L. BeMent, T. C. T. Yin and W. D. McCall, Jr., Bioelectronic Science Laboratory, E.C.E. Department and Bioengineering Program, University of Michigan

3:00 p.m. 10.9 SOMATOTOPIC MICRO-ORGANIZATION OF SmI FORELIMB AREA IN CEREBRAL NEOCORTEX OF THE CAT. C. Welker, Central Wisconsin Colony and Training School

3:15p.m. 10.10 DISCHARGE CHARACTERISTICS OF SINGLE UNITS IN THE ANTEROVENTRAL AND DORSAL COCHLEAR NUCLEI OF BARBITURATE-ANESTHETIZED CATS. Jay M. Goldberg, William E. Brownell and Robert A. Lavine, Department of Physiology, University of Chicago

3:30 p.m. 10.11 EFFECT OF PREADAPTING TEMPERATURE ON THE PHASIC RESPONSE OF TRIGEMINAL THERMORECEPTORS. D. A. Poulos and E. Leibowitz, Departments of Neurosurgery and Physiology, Albany Medical College

3:45 p.m. 10.12 INTENSITY DISCRIMINATION FOR LOCAL WARMING OF THE SKIN: PERIPHERAL NEURAL MECHANISM. I. Darian-Smith, K. O. Johnson and Carole LaMotte, Department of Physiology, School of Medicine, Johns Hopkins University

4:00 p.m. 10.13 CHARACTERISTICS OF SECOND PAIN INDICATIVE OF PROLONGED CENTRAL SUMMATION. Donald D. Price, Department of Physiology, Medical College of Virginia, Richmond

THURSDAY, OCTOBER 28

Session 11. **1:00 p.m. to 4:15 p.m.** **Forum Room**

DRUGS AND NEURAL FUNCTION

Chairman: Norman Weiner, Department of Pharmacology, University of Colorado Medical Center

Contributed Papers

1:00 p.m. 11.1 EFFECT OF PHENOBARBITAL ON A LEECH NEURON. James W. Prichard, Section of Neurology, Yale University School of Medicine

1:15 p.m. 11.2 COMPARISON OF THE EFFECTS OF SHORT, INTERMEDIATE AND LONG ACTING BARBITURATES ON SQUID AXON MEMBRANES. D. T. Frazier, K. Murayama, N. J. Abbott and T. Narahashi, University of Kentucky Medical Center and Duke University Medical Center

1:30 p.m. 11.3 EFFECTS OF NEREISTOXIN ON THE NEUROMUSCULAR TRANSMISSION OF THE FROG. Toshio Narahashi, Takehiko Deguchi and Hans G. Haas, Department of Physiology, Pharmacology, Duke University Medical Center

1:45 p.m. 11.4 ELECTROMYOGRAPHIC CHANGES IN LOCAL TETANUS FOLLOWING SUBCUTANEOUS INJECTION OF GLYCINE IN RATS. Alexander A. Fedinec, Robert S. Pozos and William C. Latham, Department of Anatomy and Department of Physiology and Biophysics, University of Tennessee Medical Units, and Biology Laboratory, Public Health Service, Boston

2:00 p.m. 11.5 CENTRAL NERVOUS SYSTEM CHANGES WITH α-γ-DIAMINOBUTYRIC ACID. T. Banerjee and W. E. Hunt, Department of Anatomy and Division of Neurosurgery, The Ohio State University College of Medicine

2:15 p.m. 11.6 ORAL INTAKE OF MORPHINE IN SUCROSE AND SALINE SOLUTIONS BY RATS. K. A. Khavari and Marc E. Risner, Department of Psychology, University of Wisconsin

2:30 p.m. 11.7 DO ATROPINIC DRUGS DISSOCIATE ELECTROCORTICAL ACTIVATION AND BEHAVIOR? C. H. Vanderwolf and Mary Cromien, Departments of Psychology and Physiology, University of Western Ontario, London, Canada

2:45 p.m. 11.8 EXCITATORY AND INHIBITORY EFFECTS OF PSYCHOTOMIMETIC DRUGS. Wagner H. Bridger, Irwin J. Mandel and David M. Stoff, Department of Psychiatry, Albert Einstein College of Medicine

3:00 p.m. 11.9 INTRAMEDULLARY INJECTIONS OF THE SPINAL CORD. Thomas B. Ducker and Phanor L. Perot, Jr., Department of Neurosurgery, Medical University of South Carolina

3:15 p.m. 11.10 MOVEMENT DISORDER IN CATS WITH CHRONIC METHAMPHETAMINE INTOXICATION. A Sudilovsky and E. Ellinwood, Duke University Medical Center

3:30 p.m. 11.11 LENGTH OF TREATMENT WITH CHLORDIAZEPOXIDE AND RESPONSE TO ITS SUDDEN WITHDRAWAL. Lino Covi, Ronald S. Lipman, Joseph H. Pattison, Leonard Derogatis and E. H. Uhlenhuth, Department of Psychology, School of Medicine, Johns Hopkins University

3:45 p.m. 11.12 THE DIFFERENTIAL EFFECTS OF DALMANE® ON THE CONTINGENT NEGATIVE VARIATION, AUDITORY EVOKED RESPONSE, AND REACTION TIME. Robert P. Borda and John H. Hablitz, Department of Physiology, Section on Neurophysiology, Baylor College of Medicine

4:00 p.m. 11.13 THE ASCERTAINMENT OF SIX YY MALES IN A PRIVATE NEUROLOGICAL PRACTICE. Fred A. Baughman, Jr. and Joseph D. Mann, Blodgett Memorial Hospital and Butterworth Hospital, Grand Rapids

THURSDAY, OCTOBER 28

Session 12. **1:00 p.m. to 4:00 p.m.** **Club Room B**

PROBLEMS OF PATTERN RECOGNITION

Chairman: Robert W. Doty, Center for Brain Research, University of Rochester

Contributed Papers

1:00 p.m. 12.1 CODING OF WEB-BUILDING MOVEMENTS IN THE SPIDER ARANEUS DIADEMATUS CL. Peter N. Witt, Division of Research, North Carolina Department of Mental Health

1:15 p.m. 12.2 HABITUATION TO VIBRATORY STIMULI IN THE WEB OF AN ORB-WEB SPIDER. Charles F. Reed, Department of Psychology, Temple University

1:30 p.m. 12.3 AN INTEGRATIVE SYSTEM: THE CRAYFISH ANTENNAE AND BRAIN. Robert C. Taylor, Department of Zoology, University of Georgia

1:45 p.m. 12.4 PATTERNS OF ELECTRIC ORGAN DISCHARGE IN MORMYRID FISH DETERMINED BY PATTERNS OF ELECTRICAL STIMULATION SIMULATING CONSPECIFICS. Peter Moller, Hunter College of the City University of New York

2:00 p.m. 12.5 ROLE OF THE LATERAL MEDULLA IN MATING AND RESPONSES TO GENITAL STIMULATION IN FEMALE CATS. James D. Rose and Jerome Sutin, Department of Anatomy, Emory University

2:15 p.m. 12.6 STORAGE OF COPULATORY STIMULATION IN THE FEMALE RAT. Susan Craig, Stephen Zoloth and Norman Adler, Department of Psychology, University of Pennsylvania

2:30 p.m. 12.7 SOMATOSENSORY UNIT RESPONSE HABITUATION: CONTRASTING EFFECTS OF STIMULUS INTENSITY. Solon B. Holstein, Jennifer S. Buchwald and Judith Schwafel, Department of Physiology, School of Medicine, University of California, Los Angeles, and Veterans Administration Hospital, Long Beach

2:45 p.m. 12.8 AUDITORY THRESHOLDS IN THE KANGAROO RAT BEFORE AND AFTER REDUCTION OF MIDDLE EAR VOLUME. Douglas B. Webster and Molly Webster, Department of Biology, New York University

3:00 p.m. 12.9 TRIGEMINAL DEAFFERENTATION AND FEEDING BEHAVIOR IN PIGEONS: SENSORY AND MOTIVATIONAL EFFECTS. H. Philip Zeigler, Department of Psychology, Hunter College

3:15 p.m. 12.10 TEMPORAL PROCESSING AND PERCEPTUAL LATENCIES. Ruth Rutschmann, Department of Psychology, Queens College, City University of New York

3:30 p.m. 12.11 AUDITORY INFORMATION PROCESSING BY CVA HEMIPLEGIC ADULTS. Glenn E. Snelbecker and William Fullard, Temple University and Moss Rehabilitation Hospital, Philadelphia

3:45 p.m. 12.12 MEDIATION OF VISUAL FEAR VIA THE CORPUS CALLOSUM. Robert W. Doty, Kenichi Yamaga and Nubio Negrão, Center for Brain Research, University of Rochester

Session 13. **1:00 p.m. to 4:00 p.m.** **Ambassador Room**

MORPHOLOGY AND ULTRASTRUCTURE: DEMONSTRATION AND DISCUSSION LOUNGE

Chairman: Ray S. Snider, Center for Brain Research, University of Rochester

Contributed Papers

13.1 FUNCTIONAL ULTRASTRUCTURE OF THE CANINE ARACHNOID VILLUS. John F. Alksne and Ethel T. Lovings, Division of Neurosurgery, University of California, San Diego, La Jolla, California, and Division of Neurosurgery, Medical College of Virginia

13.2 EXPERIMENTAL MODIFICATION OF CEREBELLAR CIRCUITRY DURING DEVELOPMENT AND ITS BEHAVIORAL CONSEQUENCES. Joseph Altman and William J. Anderson, Laboratory Developmental Neurobiology, Department of Biological Science, Purdue University

13.3 DEVELOPMENT OF NEURONS AND SYNAPSES IN CULTURES OF DISSOCIATED CELLS OF EMBRYO MOUSE CNS. A LIGHT AND ELECTRON MICROSCOPIC STUDY. Murray B. Bornstein and Pat G. Model, Departments of Neurology and Anatomy, Albert Einstein College of Medicine

13.4 ALTERATIONS AT NODES OF RANVIER PRODUCED BY TREATMENT WITH TRYPSIN. Richard P. Bunge and Riley C. Yu, Department of Anatomy, Washington University School of Medicine, St. Louis

13.5 MATURATION OF THE POSTMIGRATORY NEURON: A RADIOAUTOGRAPHIC AND ULTRASTRUCTURAL STUDY. A. B. Butler, Department of Neurosurgery, School of Medicine, University of Virginia

13.6 IS THERE A SEX DIFFERENCE IN THE NUMBER OF MAMMALIAN CENTRAL NEURONS? Franco R. Calaresu and James L. Henry, Department of Physiology, University of Western Ontario, London, Canada

13.7 ON THE ORGANIZATION OF CEREBELLAR EFFERENT PATHWAYS IN THE NURSE SHARK, GINGLYMOSTOMA CIRRATUM (BONNATERRE). C. B. G. Campbell and Sven O. E. Ebbesson, Center for Neural Sciences, Indiana University, Department of Neurosurgery, University of Virginia Medical School, and Lerner Marine Laboratory, Bimini, Bahamas

13.8 ROLE OF THE VAGUS IN CARDIAC PATHOLOGY. K. C. Corley, F. O'M. Shiel, H. P. Mauck and J. H. Greenhoot, Departments of Physiology, Pathology, Med. and Neurosurgery, Medical College of Virginia

13.9 TRANSPLANTATION OF PRECURSORS OF NERVE CELLS IN THE CEREBELLUM OF YOUNG RATS. Gopal D. Das and Joseph Altman, Department of Biological Science, Purdue University

13.10 PROJECTIONS OF THE OPTIC TECTUM IN THE NURSE SHARK, GINGLYMOSTOMA CIRRATUM (BONNATERRE). Sven O. E. Ebbesson, Department of Neurosurgery, University of Virginia Medical School, and Lerner Marine Laboratory, Bimini, Bahamas

13.11 RECENT OBSERVATIONS ON THE STRUCTURAL ORGANIZATION OF THE SPINAL V NUCLEUS IN THE CAT: THE DEEP FIBER BUNDLES. Stephen Gobel, Neural Mechanisms Section, National Institute of Dental Research

13.12 DEGENERATION AND REGENERATION PHENOMENA IN OLFACTORY RECEPTOR NEURONS. P. P. C. Graziadei and J. F. Metcalf, Department of Biological Science, Florida State University

13.13 ALTERATIONS IN SYNAPTIC PARAMETERS PRODUCED BY REARING ENVIRONMENT IN RATS. William T. Greenough, Roger West and T. Blaise Fleischmann, Department of Psychology, University of Illinois

13.14 BINOCULAR COMPETITION IN THE CONTROL OF GENICULATE CELL GROWTH. R. W. Guillery, Department of Anatomy, University of Wisconsin

13.15 DEGENERATION FROM ALUMINA CREAM EPILEPTOGENIC FOCI—RELATION TO SEIZURES. A. Basil Harris, Department of Neurological Surgery, University of Washington School of Medicine

13.16 EVIDENCE FOR RECYCLING OF MEMBRANE ACCOMPANYING TRANSMITTER RELEASE AT THE FROG NEUROMUSCULAR JUNCTION. John E. Heuser, Laboratory of Neuropathology and Neuroanatomical Sciences, National Institute of Neurological Diseases and Stroke

13.17 VISUAL FUNCTION OF RAT RETINAS MALFORMED BY IRRADIATION AT BIRTH. Samuel P. Hicks and Constance J. D'Amato, Department of Pathology, University of Michigan Medical Center

13.18 FREEZE-ETCH AND FINE STRUCTURE OF PERIPHERAL NERVE. S. J. Hubbard, Department of Anatomy, Rutgers Medical School

13.19 THE FUNCTIONAL RELATIONSHIP OF NEURONS AND SATELLITE CELLS IN METABOLICALLY ACTIVE GANGLIA. A. O. Humbertson, Jr. and J. E. Zimmerman, Department of Anatomy, The Ohio State University College of Medicine and Department of Surgery, School of Medicine, University of California, Los Angeles.

13.20 AN EXPERIMENTAL ULTRASTRUCTURAL APPROACH TO THE IDENTIFICATION OF SYNAPTIC ENDINGS IN THE OPOSSUM RED NUCLEUS. James S. King, George F. Martin and Richard Dom, Department of Anatomy, College of Medicine, Ohio State University

13.21 PRIMATE PERIPHERAL NERVE REGENERATION AFTER LOSS OF COLLATERAL BLOOD SUPPLY. David G. Kline and Earl R. Hackett, Surgery/Neurosurgery, Louisiana State University School of Medicine

13.22 NEURAL NET AND SELECTIVE OUTGROWTH FROM INSECT NERVE CELLS IN VITRO. Rita Levi-Montalcini, Washington University, St. Louis

13.23 LOCALIZATION OF THYROXINE I ^{125} IN DEVELOPING CNS TISSUE IN CULTURE. ELECTRON MICROSCOPIC AUTORADIOGRAPHY. Laura Manuelidis, Yale University School of Medicine

13.24 EFFECTS OF EARLY HYPO- AND HYPERTHYROIDISM ON CELL DIFFERENTIATION AND SYNAPTOGENESIS IN RAT CEREBELLUM. Jean L. Nicholson and Joseph Altman, Department of Biological Science, Purdue University

13.25 ESTRADIOL-H^{3} CONCENTRATION BY CELLS IN A LIMBIC-HYPOTHALAMIC SYSTEM IN THE FEMALE RAT BRAIN. AN AUTORADIOGRAPHIC STUDY. Donald Pfaff, Melvyn Keiner and Ellen Warren, Rockefeller University

13.26 SYNAPTIC REORGANIZATION IN THE DEGENERATING LATERAL GENICULATE NUCLEUS OF THE RABBIT. Henry J. Ralston, III and Kao L. Chow, Department of Anatomy, University of Wisconsin, Madison, and Department of Neurology, Stanford University

13.27 DOES DENERVATION OF CEREBRAL CORTEX PRODUCE PROLIFERATION OF NEURONAL PROCESSES? L. T. Rutledge, Joyce Duncan and Nell Cant, Department of Physiology, University of Michigan Medical School

13.28 PRE AND POST JUNCTIONAL LOCALIZATION OF ACETYLCHOLINESTERASE BY QUANTITATIVE E.M. AUTORADIOGRAPHY. Miriam M. Salpeter and Andrew W. Rogers, Cornell University

13.29 THE ORGANIZATION OF THALAMIC NUCLEI AND THEIR EFFERENT PATHWAYS IN THE NURSE SHARK, GINGLYMOSTOMA CIRRATUM (BONNATERRE). D. M. Schroeder and Sven O. E. Ebbesson, Department of Neurosurgery, University of Virginia Medical School, and Lerner Marine Laboratory, Bimini, Bahamas

13.30 NEURONAL GROUPS AND FIBER PATTERNS IN CEREBELLAR TISSUE CULTURES. Frederick J. Seil, Department of Neurology, Stanford University, Veterans Administration Division

13.31 POSTNATAL CHANGES IN THE ARRANGEMENT OF NEUROFILAMENTS AND MICROTUBULES IN CLARKE'S NUCLEUS IN THE KITTEN. Diane E. Smith, Department of Anatomy, Jefferson Medical College, Thomas Jefferson University, Philadelphia

13.32 ROLE OF THE GROWTH CONE AND CELL JUNCTIONS IN VENTRAL-ROOT FORMATION. Henry J. Wehman and Barbara A. Plantholt, Research Department, Rosewood State Hospital, and Department of Pediatrics, University of Maryland

FRIDAY, OCTOBER 29

Session 14. **9:00 a.m. to 11:30 a.m.** **Diplomat Room**

EDUCATION IN THE NEUROSCIENCES

Chairman: Horace W. Magoun, University of California, Los Angeles

Invited Lectures

14.1 INTRODUCTORY SURVEY. Horace W. Magoun

14.2 NEUROPHYSIOLOGY AND NEUROANATOMY. Dominick P. Purpura, Albert Einstein College of Medicine, New York

Selected Contributed Paper

14.3 NEUROSCIENCE FOR MEDICAL STUDENTS. Louise H. Marshall, National Research Council, Washington, D. C.

Invited Lectures

14.4 PANEL DISCUSSION: INTERDISCIPLINARY EDUCATION IN NEUROSCIENCE—PRE-COLLEGE, COLLEGE, GRADUATE, HEALTH PROFESSIONAL, POSTDOCTORAL. Chairman of

Panel—Robert L. Thompson, Hunter College of the City of New York; Participants—Eliot Stellar, University of Pennsylvania Medical School; Richard F. Thompson, University of California, Irvine

FRIDAY, OCTOBER 29

Session 15. **9:00 a.m. to 11:30 a.m.** **Regency Ballroom**

ORDER AND DISORDER IN MOVEMENT

Chairman: Edward V. Evarts, Laboratory of Neurophysiology, National Institute of Mental Health

Invited Lectures

15.1 THE MOTOR UNIT: HISTOCHEMICAL AND PHYSIOLOGICAL STUDIES. Robert E. Burke, Laboratory of Neural Control, National Institute of Neurological Diseases and Stroke

15.2 ACTIVITY OF OCULOMOTOR NEURONS DURING EYE MOVEMENT. David A. Robinson, Department of Medicine, Johns Hopkins University

15.3 INPUTS AND OUTPUTS OF THE CORPUS STRIATUM. Walle Nauta, Department of Psychology, Massachusetts Institute of Technology

15.4 ACTION OF L-DOPA ON MOVEMENT DISORDERS IN MAN. Thomas N. Chase, Laboratory of Clinical Science, National Institute of Mental Health

Selected Contributed Papers

15.5 MECHANISM OF ACTION OF L-DOPA IN PARKINSON'S DISEASE. Kenneth G. Lloyd and Oleh Hornykiewicz, Department of Pharmacology, University of Toronto and Clarke Institute of Psychiatry

15.6 FUNCTIONAL ZONES IN THE CAT VENTROLATERAL THALAMUS. Peter L. Strick, Department of Anatomy, University of Pennsylvania School of Medicine

Invited Lecture

15.7 PROGRAMS FOR RESEARCH ON CENTRAL CONTROL OF MOVEMENT. John C. Eccles, Laboratory of Neurobiology, Department of Physiology, State University of New York at Buffalo

FRIDAY, OCTOBER 29

Session 16. **9:00 a.m. to 11:30 a.m.** **Empire Room**

SYNAPTIC TRANSMISSION

Chairman: Stephen W. Kuffler, Department of Neurobiology, Harvard Medical School

Invited Lectures

16.1 VISUAL IDENTIFICATION OF LIVING SYNAPSES AND STUDIES ON THEIR FINE STRUCTURE. U. J. McMahan, Department of Neurobiology, Harvard Medical School

16.2 THE RELEASE OF TRANSMITTER SUBSTANCES AT NERVE TERMINALS. A. R. Martin, Department of Physiology, University of Colorado Medical School

16.3 DUPLICATION OF SYNAPTIC TRANSMISSION BY APPLIED ACETYLCHOLINE TO THE POSTSYNAPTIC MEMBRANE. Stephen W. Kuffler

FRIDAY, OCTOBER 29

Session 17. **1:00 p.m. to 3:45 p.m.** **Regency Ballroom**

MAMMALIAN GENICULO-STRIATE MECHANISMS

Chairman: Carl Kupfer, National Eye Institute

Contributed Papers

1:00 p.m. 17.1 THE RECEPTIVE FIELD CHARACTERISTICS OF PRINCIPAL AND ASSOCIATION CELLS IN THE RAT LATERAL GENICULATE NUCLEUS. William R. Mead and Mary Emily Bussey, Department of Psychology, University of Illinois

1:15 p.m. 17.2 ELECTROPHYSIOLOGICAL CORRELATES OF FLICKER PERCEPTION IN THE CAT. Arthur S. Schwartz, Division of Neurobiology, Barrow Neurological Institute, Phoenix

1:30 p.m. 17.3 SUPERIOR COLLICULUS: INTERACTIONS OF CORTICAL AND RETINAL PROJECTIONS ON SINGLE NEURONS IN THE CAT. James T. McIlwain and Howard L. Fields, Brown University, Providence, Rhode Island and Boston City Hospital

1:45 p.m. 17.4 LINE ORIENTATION DISCRIMINATION DEFICITS FOLLOWING PARTIAL ABLATION OF THE GENICULO-CORTICAL SYSTEM IN CATS. Mark A. Berkley, Department of Psych., Florida State University

2:00 p.m. 17.5 INTERACTION BETWEEN THE VISUAL CORTEX AND SUPERIOR COLLICULUS OF THE CAT DURING LEARNING. Bonnie J. Shubart, Department of Anatomy, Cornell University Medical College

2:15 p.m. 17.6 LATE INTRACELLULAR EVOKED RESPONSE. Ronald A. Cyrulnik and Rafael Elul, Brain Research Institute and Department of Anatomy, University of California, Los Angeles

2:30 p.m. 17.7 A DORSOMEDIAL VISUAL AREA ADJOINING V II IN THE OWL MONKEY (AOTUS TRIVIRGATUS). John M. Allman, Jon H. Kaas and F. M. Miezin, Laboratory of Neurophysiology, University of Wisconsin

2:45 p.m. 17.8 RESPONSES OF MONKEY LGN CELLS TO LUMINANCE AND COLOR FIGURES. D. Max Snodderly, Jr., Russell L. De Valois, William E. Yund and Norva K. Hepler, Department of Psychology, University of California, Berkeley

3:00 p.m. 17.9 COLOUR AND CONTOUR DETECTION BY CELLS REPRESENTING THE FOVEA IN MONKEY STRIATE CORTEX. John Boles, Psychology Department, University of Western Ontario, London, Canada

3:15 p.m. 17.10 FUNCTIONAL PROPERTIES OF NEURONS IN THE STRIATE CORTEX OF THE MACAQUE MONKEY SUBSERVING THE FOVEAL REGION OF THE RETINA. G. F. Poggio, R. J. W. Mansfield and A. M. Sillito, The Johns Hopkins University

3:30 p.m. 17.11 PATTERN EVOKED RESPONSES FROM PRIMARY AND ASSOCIATION AREAS IN MAN. Earle G. Wallingford, Jr. and Donnell J. Creel, Neuropsychology, Duke University, Durham, North Carolina, and Neuropsychology, Veterans Administration Hospital, Kansas City

FRIDAY, OCTOBER 29

Session 18. **1:00 p.m. to 4:15 p.m.** **Empire Room**

BIOGENIC AMINES

Chairman: Julius Axelrod, National Institute of Mental Health

Contributed Papers

1:00 p.m. 18.1 A COMMON ERROR IN THE MEASUREMENT OF BRAIN DOPAMINE FOLLOWING L-DOPA. J. C. de la Torre and William O. Boggan, Departments of Neurosurgery and Psychiatry, Pritzker School of Medicine, Chicago

1:15 p.m. 18.2 TOPICAL PHARMACOLOGY OF MONOAMINE-SENSITIVE STRUCTURES IN THE RAT BRAIN. D. Bieger, L. Larochelle and O. Hornykiewicz, Clarke Institute of Psychiatry and Department of Pharmacology, University of Toronto

1:30 p.m. 18.3 HYPOTHALAMIC AND MEDIAN EMINENCE CATECHOLAMINES AND THYROID FUNCTION. Gregory M. Brown and Oleh Hornykiewicz, Clarke Institute of Psychiatry and Department of Psychiatry, University of Toronto

1:45 p.m. 18.4 CATECHOL-O-METHYL TRANSFERASE: REDUCTION BY CHRONIC L-DOPA THERAPY. James L. Weiss, Cal K. Cohn and Thomas N. Chase, Laboratory of Clinical Science, National Institute of Mental Health

2:00 p.m. 18.5 FURTHER STUDIES ON CATECHOLAMINE (CA) BIOSYNTHESIS IN MOUSE NEUROBLASTOMA TUMORS AND IN CULTURED MOUSE NEUROBLASTOMA CELLS. B. Anagnoste, L. S. Freedman, M. Goldstein and J. Broome, Departments of Psychiatry and Pathology, New York University Medical Center

2:15 p.m. 18.6 MULTIPLE FORMS OF RAT BRAIN TYROSINE HYDROXYLASE. Ronald T. Kuczenski and Arnold J. Mandell, Department of Psychiatry, School of Medicine, University of California, San Diego, La Jolla

2:30 p.m. 18.7 COMPENSATORY CHANGES IN BRAIN TYROSINE HYDROXYLASE ACTIVITY FOLLOWING CHRONIC ALTERATIONS IN CENTRAL NORADRENERGIC TRANSMISSION. David S. Segal and Arnold J. Mandell, Department of Psychiatry, School of Medicine, University of California, San Diego, La Jolla

2:45 p.m. 18.8 ADDICTIVE DRUG EFFECTS ON THE ACTIVITY OF SEPTAL SYNAPTOSOMAL SEROTONIN BIOSYNTHETIC ENZYMES. Suzanne Knapp and Arnold J. Mandell, Department of Psychiatry, School of Medicine, University of California, San Diego, La Jolla

3:00 p.m. 18.9 NEUROAMINE METABOLISM IN THE CENTRAL NERVOUS SYSTEM. Michael J. Walsh, Department of Pharmacology, Bowman Gray School of Medicine, Wake Forest University

3:15 p.m. 18.10 CELL-FREE STUDIES ON CATECHOLAMINE-STIMULATED ADENYL CYCLASE FROM RAT CEREBRAL CORTEX. Kern von Hungen and Sidney Roberts, Department of Biological Chemistry and Brain Research Institute, University of California, Los Angeles, School of Medicine

3:30 p.m. 18.11 THE EFFECTS OF PRENATAL INJECTIONS OF D-AMPHETAMINE SULFATE ON ACTIVITY AND ON CATECHOLAMINES IN THE BRAINS OF YOUNG MICE. Lawrence D. Middaugh, L. Ann Blackwell and John W. Zemp, Departments of Biochemistry and Psychiatric Research, Medical University of South Carolina

3:45 p.m. 18.12 PREFERENTIAL PROTECTION OF MONOAMINES IN THE BRAIN: BIOCHEMICAL AND BEHAVIORAL EFFECTS. Dell L. Rhodes and Larry L. Butcher, Department of Psychology, University of California, Los Angeles

4:00 p.m. 18.13 DECREASES IN REWARDING BUT NOT AVERSIVE BRAIN STIMULATION FOLLOWING ALPHA-METHYL-P-TYROSINE. Barrett R. Cooper and Ronald M. Paolino, Department of Pharmacology and Toxicology, Purdue University

FRIDAY, OCTOBER 29

Session 19. **1:00 p.m. to 4:00 p.m.** **Diplomat Room**

MEMORY AND MOTIVATION

Chairman: J. L. McGaugh, Department of Psychobiology, University of California, Irvine

Contributed Papers

1:00 p.m. 19.1 NEUROANATOMICAL CORRELATES OF TIME RECONSTRUCTION IN THE RAT. Robert W. Thatcher, Department of Anatomy, Albert Einstein College of Medicine

1:15 p.m. 19.2 ELECTROENCEPHALOGRAPHIC CORRELATES AND PREDICTORS OF PERFORMANCE DURING LEARNING AND MEMORY IN THE MONKEY. Samuel L. Moise, Jr. and Anatol Costin, Department of Anatomy, School of Medicine, University of California, Los Angeles

1:30 p.m. 19.3 UNIT ACTIVITY IN THE FRONTAL GRANULAR CORTEX OF THE MONKEY IN A CLASSICAL DELAYED RESPONSE TASK. Joaquin M. Fuster, Department of Psychiatry and Brain Research Institute, School of Medicine, University of California, Los Angeles

1:45 p.m. 19.4 CORTICAL STEADY POTENTIAL CORRELATES OF TRANSIENT MEMORY IN MONKEYS. Steven C. Rosen and John S. Stamm, Psychology Department, SUNY at Stony Brook

2:00 p.m. 19.5 SPEECH AND SHORT TERM VERBAL MEMORY ALTERATIONS WITH HUMAN VENTROLATERAL THALAMIC STIMULATION. George Ojemann and Arthur Ward, Jr., Neurological Surgery Department, University of Washington, Seattle

2:15 p.m. 19.6 OPERANT CONTROL OF LAMBDA WAVE PRODUCTION IN NORMAL AND PARALYZED CATS. Paul School and Vernon Rowland, Departments of Psychology and Psychiatry, Case Western Reserve University, Cleveland

2:30 p.m. 19.7 LONG-TERM OBSERVATIONS OF PATTERNS OF SELF-STIMULATION. George Koob and Zoltan Annau, Department of Environmental Medicine, Johns Hopkins University

2:45 p.m. 19.8 BEHAVIORAL STUDIES OF ANALGESIA RESULTING FROM ELECTRICAL STIMULATION OF THE BRAIN. David J. Mayer, Huda Akil and John C. Liebeskind, Department of Psychology, University of California, Los Angeles

3:00 p.m. 19.9 PAIN SUPPRESSING EFFECTS OF REWARDING BRAIN STIMULATION. Mitchel D. Rose and C. R. Gallistel, Department of Psychology, University of Pennsylvania

3:15 p.m. 19.10 COMPARISONS OF SUBSTANTIA NIGRA AND CAUDATE NUCLEUS LESIONS ON THREE LEARNING MEASURES IN RATS. Judson C. Mitcham and Roger K. Thomas, Department of Psychology, University of Georgia

3:30 p.m. 19.11 TIME FACTORS IN RECOVERY OF FUNCTION FOLLOWING FRONTAL LOBE LESIONS IN THE RAT. Geoffrey A. Patrissi and Donald G. Stein, Department of Psychology, Clark University, Worcester

3:45 p.m. 19.12 RETENTION OF THE SECOND OF TWO PRE-OPERATIVELY LEARNED BRIGHTNESS DISCRIMINATIONS FOLLOWING POSTERIOR NEODECORTICATION IN THE ALBINO RAT. Lois O. Stratton, Department of Psychology, Louisiana State University, New Orleans

FRIDAY, OCTOBER 29

Session 20. **1:00 p.m. to 4:15 p.m.** **Forum Room**

CELLULAR MECHANISMS

Chairman: Sidney Ochs, Department of Physiology, Indiana University Medical Center, Indianapolis

Contributed Papers

1:00 p.m. 20.1 BIDIRECTIONAL AXOPLASMIC FLOW IN FROG SCIATIC NERVE IN VITRO. Lester M. Partlow, C. David Ross and David B. McDougal, Department of Pharmacology, School of Medicine, Washington University, St. Louis

1:15 p.m. 20.2 RAPID AXONAL TRANSPORT OF GLYCOPROTEINS LABELED WITH ^{3}H-FUCOSE IN THE GOLDFISH OPTIC SYSTEM. David S. Forman, Bruce S. McEwen and Bernice Grafstein, Rockefeller University, and Cornell University Medical College

1:30 p.m. 20.3 TRANSPORT OF RADIOACTIVE PROTEIN FROM EYE TO VISUAL CORTEX. Bernice Grafstein and Robert Laureno, Department of Physiology, Cornell University Medical College

1:45 p.m. 20.4 AXONAL TRANSPORT IN OPTIC NERVES OF MICE LACKING VISUAL RECEPTORS. Marion Murray and Bernice Grafstein, Department of Anatomy, University of Chicago, and Department of Physiology, Cornell University Medical College

2:00 p.m. 20.5 A RAPID QUANTITATIVE METHOD FOR ASSESSING THE EFFECT OF DRUGS UPON AXOPLASMIC TRANSPORT: STUDIES WITH ANTIMITOTIC AGENTS. Anne L. Cahill, James C. Paulson and William O. McClure, Department of Biochemistry, University of Illinois

2:15 p.m. 20.6 AXOPLASMIC TRANSPORT OF AChE, LDH AND MAO IN MAMMALIAN NERVE FIBERS. M. A. Khan, N. Ranish and S. Ochs, Department of Physiology, Indiana University Medical Center

2:30 p.m. 20.7 AMINO ACID TRANSPORT IN VITRO BY RAT BRAIN SYNAPTOSOMES. N. A. Peterson and E. Raghupathy, Brain-Behavior Research Center, Sonoma State Hospital, Eldridge

2:45 p.m. 20.8 NEURAL REGULATION OF MUSCLE GANGLIOSIDE BIOSYNTHESIS. Stephen R. Max, Department of Neurology, University of Maryland School of Medicine

3:00 p.m. 20.9 DEPENDENCE OF SYMPATHETIC REINNERVATION OF THE RAT IRIS IN ORGAN CULTURE ON NERVE GROWTH FACTOR. S. D. Silberstein, D. G. Johnson, I. Hanbauer and I. J. Kopin, National Institute of Mental Health

3:15 p.m. 20.10 ^{45}Ca AND ^{40}Ca UPTAKE AND EXCHANGE IN LEG NERVES OF "LIBINIA EMARGINATA." C. Paul Bianchi, Department of Pharmacology, School of Medicine, University of Pennsylvania

3:30 p.m. 20.11 ROLE OF ADENOSINE TRIPHOSPHATE AND CERTAIN CATIONS IN MEMBRANE FUNCTION OF NORMAL AND MUTANT PARAMECIUM AURELIA. John Nurnberger and Jorgen Fex, Center for Neural Sciences, Indiana University

3:45 p.m. 20.12 ARE CILIATED NEURONS FUNCTIONAL? David A. Goodman and Chester L. Richards, Newport Neuroscience Center and University of California, Irvine

4:00 p.m. 20.13 POSTWEANING GROWTH OF CHOROID PLEXUSES AND A REGIONALLY SPECIFIC EFFECT OF A LOW SODIUM AND POTASSIUM DIET. W. B. Quay, Department of Zoology, University of California, Berkeley

Session 21. **1:00 p.m. to 3:30 p.m.** **Tudor Room**

SLEEP

Chairman: Elliot D. Weitzman, Division of Neurology, Montefiore Hospital and Medical Center, Bronx

Contributed Papers

1:00 p.m. 21.1 EFFECT OF PROBE-PENETRATION LESIONS ON SLEEP-AWAKE BEHAVIOR IN PIGEONS. Samuel M. Church and Irving J. Goodman, Department of Psychology and Psychiatry, West Virginia University

1:15 p.m. 21.2 RESPONSES OF DIENCEPHALIC NEURONS TO OLFACTORY BULB STIMULATION, ODOR, AND AROUSAL. B. R. Komisaruk and C. Beyer, Institute of Animal Behavior, Rutgers University

1:30 p.m. 21.3 EYE MOVEMENTS AND LATERAL GENICULATE NUCLEUS SPIKES IN SLEEPING AND AWAKE CATS FOLLOWING UNI- AND BILATERAL LABYRINTHECTOMY AND CEREBELLECTOMY. John B. Munson and Ron A. Waldorf, Department of Physiology, College of Medicine, University of Florida

1:45 p.m. 21.4 MOVEMENT DISORDERS INDUCED IN SLEEP BY COMBINED CEREBELLAR-SPINAL CORD LESIONS IN CATS. Adrian R. Morrison and Robert M. Bowker, Department of Animal Biology, School of Veterinary Medicine, University of Pennsylvania

2:00 p.m. 21.5 OPERANT CONDITIONING OF LATERAL GENICULATE SPIKES IN OWL MONKEYS. LaNelle Linnstaedter and Adrian A. Perachio, Yerkes Regional Primate Research Center, Emory University

2:15 p.m. 21.6 RELATIONSHIPS BETWEEN FIRING RATE AND FIRING PATTERN OF CEREBELLAR PURKINJE CELLS. Robert W. McCarley and J. Allan Hobson, Department of Psychiatry, Harvard Medical School

2:30 p.m. 21.7 NEURONAL ACTIVITY OF THE PONTINE BRAIN STEM DURING SLEEP AND WAKING. J. Allan Hobson, Department of Psychiatry, Harvard Medical School

2:45 p.m. 21.8 ACTIVITY OF SINGLE RAPHE NEURONS DURING SLEEP AND WAKEFULNESS. Dennis J. McGinty and Ronald M. Harper, Veterans Administration Hospital, Sepulveda, and Departments of Psych. and Anatomy, University of California, Los Angeles

3:00 p.m. 21.9 EXCITABILITY CHANGES IN VISUAL CORTICAL NEURONS IN NATURAL TRANSITIONS OF SLEEP AND WAKING. T. Kasamatsu and W. Ross Adey, Space Biology Laboratory, Department of Anatomy, University of California, Los Angeles

3:15 p.m. 21.10 CHANGES IN INHIBITORY EVENTS ELICITED IN CORTICAL PRECENTRAL UNITS OF BEHAVING MONKEY DURING SLEEP AND WAKING. M. Steriade, M. Deschênes, P. Wyzinski and J. Y. Hallé, Laboratory of Neurophysiology, Department of Physiology, School of Medicine, University of Laval, Quebec

FRIDAY, OCTOBER 29

Session 22. **1:00 p.m. to 4:15 p.m.** **Blue Room**

MOTOR CONTROL

Chairman: Earl Eldred, Professor of Anatomy, Center for the Health Sciences, University of California at Los Angeles

Contributed Papers

1:00 p.m. 22.1 QUANTITATIVE ANALYSIS OF MECHANORECEPTOR DISCHARGE PATTERNS IN RESPONSE TO CHANGES IN MUSCLE LENGTH. John T. Murphy, Elward J. Davison, Frank Johnson, Hon C. Kwan and William A. Mackay, Departments of Physiology and Electrical Engineering, University of Toronto

1:15 p.m. 22.2 ON STRUCTURAL CORRELATES OF CODING MECHANISMS IN MUSCLE SPINDLES. Ulf L. Karlsson, Elizabeth G. Bendeich and William M. Hooker, Dental Research Laboratory and Department of Anatomy, College of Dentistry and Medicine, University of Iowa

1:30 p.m. 22.3 SOME FUNCTIONAL PROPERTIES OF STATIC AND DYNAMIC FUSIMOTOR INNERVATION OF CAT SOLEUS MUSCLE SPINDLES. Russell Durkovic and James B. Preston, Department of Physiology, SUNY Upstate Medical Center, Syracuse

1:45 p.m. 22.4 EFFECTS ON MUSCLE SPINDLES OF DISUSE AND INCREASED USE OF THE GROSS MUSCLE. Alfred Maier and Earl Eldred, Department of Anatomy, School of Medicine, University of California, Los Angeles

2:00 p.m. 22.5 MEASUREMENT OF THE % OF DISCHARGE OF A MOTONEURON POOL BY MEANS OF MONOSYNAPTIC REFLEX, EMG AND TWITCH TENSION. H. P. Clamann and E. Henneman, Department of Physiology, Harvard Medical School

2:15 p.m. 22.6 RANKING OF MOTOR UNITS IN THE MEDIAL GASTROCNEMIUS MUSCLE ACCORDING TO REFLEX THRESHOLD, SUSCEPTIBILITY TO INHIBITION AND SPEED OF CON-

TRACTION. E. Henneman and J. D. Gillies, Department of Physiology, Harvard Medical School

2:30 p.m. 22.7 MECHANICAL EVIDENCE FOR A SINGLE POPULATION OF FAST CONTRACTILE ELEMENTS IN EXTRAOCULAR MUSCLE. N. H. Barmack and B. G. Rence, Laboratory of Neurophysiology, Good Samaritan Hospital and Medical Center, Portland

2:45 p.m. 22.8 BEHAVIOR OF ABDUCENS MOTONEURONS DURING VESTIBULARLY INDUCED EYE MOVEMENTS. Alexander A. Skavenski and David A. Robinson, Department of Biomedical Engineering, Johns Hopkins University

3:00 p.m. 22.9 LOSS OF OPTOKINETIC AFTER-NYSTAGMUS AFTER BILATERAL LABYRINTHECTOMY. Bernard Cohen and Takuya Uemura, Department of Neurology, Mount Sinai School of Medicine

3:15 p.m. 22.10 PUPILLARY CONSTRICTION AND UNIT ACTIVITY. Kyozo Watanabe, Max-Planck Institut für Psychiatrie, Müchen, Germany

3:30 p.m. 22.11 SENSORY-MOTOR FUNCTION AFTER DORSAL COLUMN LESIONS IN MACAQUES. Charles J. Vierck, Jr., Jack E. Maniscalco and Alexander A. Manning, Department of Neuroscience and Center for Neurobiological Sciences, University of Florida College of Medicine

3:45 p.m. 22.12 PROPRIOCEPTIVE INFLUENCES ON INFERIOR OLIVARY CELLS DURING PHASIC REFLEX MOVEMENT IN CATS. M. A. Clendenin, A. J. Szumski and J. Astruc, Medical College of Virginia—Virginia Commonwealth University

4:00 p.m. 22.13 CEREBRAL CORTICAL CONTROL OF JAW REFLEXES IN THE SQUIRREL MONKEY (SAIMIRI SCIUREUS). Michael H. Chase, Departments of Anatomy and Physiology, University of California, Los Angeles, School of Medicine and the Veterans Administration Hospital, Sepulveda

FRIDAY, OCTOBER 29

Session 23. **1:00 p.m. to 4:00 p.m.** **Ambassador Room**

RECEPTOR AND SYNAPTIC PROCESSES

Chairman: Dominick P. Purpura, Department of Anatomy, Albert Einstein College of Medicine

Contributed Papers

1:00 p.m. 23.1 KINETICS OF ACETYLCHOLINE RECEPTOR PRODUCTION AND INCORPORATION INTO MEMBRANES OF DEVELOPING MUSCLE FIBERS. H. Criss Hartzell and Douglas M.

Fambrough, Department of Biology, Johns Hopkins University and Department of Embryology, Carnegie Institute

1:15 p.m. 23.2 SYNAPTIC TRANSMISSION BETWEEN NEURONS AND MUSCLE FIBERS IN CELL CULTURES DERIVED FROM CHICK EMBRYOS. G. D. Fischbach, National Institute of Child Health and Human Development

1:30 p.m. 23.3 ACh SENSITIVITY OF NON-INNERVATED AND INNERVATED MYOTUBES IN CELL CULTURES. S. Cohen and G. Fischbach, National Institute of Child Health and Human Development

1:45 p.m. 23.4 ACETYLCHOLINE RESPONSES IN NEUROBLASTOMA CELL CULTURES: BLOCKING EFFECTS OF ATROPINE VERSUS TUBOCURARINE. J. Peacock, P. G. Nelson, J. Minna and M. Nirenberg, National Institutes of Health

2:00 p.m. 23.5 SYNAPTIC TRANSMISSION IN THE CHICK CILIARY GANGLION DURING EMBRYOGENESIS. G. Pilar and Lynn Landmesser, Department of Physiology, University of Utah, and Department of Regulatory Biology, University of Connecticut

2:15 p.m. 23.6 THE EFFECTS OF HIGH [Ca++] ON THE ACTIVITY OF NEURONS OF THE ISOLATED SPINAL CORD OF THE FROG. G. E. Dambach and S. D. Erulkar, Department of Pharmacology, School of Medicine, University of Pennsylvania

2:30 p.m. 23.7 L-GLUTAMATE: POSSIBLE EXCITATORY TRANSMITTER IN CNS OF LAMPREY. Burgess N. Christensen, Division of Bio-Medical Sciences, Section on Neurosciences, Brown University, Providence

2:45 p.m. 23.8 EFFECTS OF STRYCHNINE, BICUCULLINE AND PICROTOXIN ON LABYRINTHINE-EVOKED INHIBITION IN NECK MOTONEURONS OF THE CAT. Leslie P. Felpel, The Rockefeller University

3:00 p.m. 23.9 TRANSMISSION AT SYNAPSES OF ELECTRORECEPTORS. M. V. L. Bennett, Albert Einstein College of Medicine

3:15 p.m. 23.10 ANTIDROMIC INHIBITION: A POSSIBLE NEURAL MECHANISM TO ACCOUNT FOR PERIPHERAL INTERACTIONS BETWEEN TASTE STIMULI. R. A. Bernard, Department of Physiology, Michigan State University

3:30 p.m. 23.11 EFFECTS OF CARBOXYLATE MODIFICATION ON FROG NEUROMUSCULAR TRANSMISSION. S. Stuesse, N. Katz and C. Edwards, Department of Biological Science, SUNY, Albany

3:45 p.m. 23.12 FALSE NEUROCHEMICAL TRANSMITTERS IN THE CNS. Ross J. Baldessarini, Neuropharmacology Laboratory, Psychiatry Research Laboratories, Massachusetts General Hospital and Harvard Medical School

Session 24. **1:00 p.m. to 3:45 p.m.** **Executive Room**

EEG

Chairman: Theodore H. Bullock, Department of Neurosciences, University of California, School of Medicine, San Diego, La Jolla

Contributed Papers

1:00 p.m. 24.1 THE ELECTROENCEPHALOGRAM DURING VOLUNTARY BREATH HOLDING IN MAN. Robert Lansing, Peter Crown and John Thomas, Department of Psychology, University of Arizona

1:15 p.m. 24.2 ELECTROCORTICAL WAVES ASSOCIATED WITH DYSKINETIC MOVEMENTS PRODUCED BY LESIONS OF THE CAUDATE NUCLEUS IN CATS. Samuel L. Liles, Louisiana State University Medical School

1:30 p.m. 24.3 COMPUTER-ANALYSIS OF 40 Hz EEG IN NORMAL AND MBI CHILDREN. Daniel E. Sheer and Lyllian Hix, Department of Psychology, University of Houston

1:45 p.m. 24.4 VARIABILITY OF THE EEG IN RELATION TO REACTION TIME IN NORMAL CHILDREN. Walter W. Surwillo, Department of Psychiatry, University of Louisville School of Medicine

2:00 p.m. 24.5 OBSERVATIONS ON FREQUENCY CHANGES AND ON SYNCHRONIZATION OF THETA WAVES. Clara Torda, Mt. Sinai School of Medicine

2:15 p.m. 24.6 A COMMON NEURONAL PATTERN IN SEIZURES. Emil C. Zuckermann, Division of Neurology, Yale University School of Medicine

2:30 p.m. 24.7 THE FASTIGIAL PRESSOR RESPONSE: SIMILARITY TO CARDIOVASCULAR ADJUSTMENT TO POSTURE. Nobutaka Doba and Donald J. Reis, Department of Neurology, Cornell University Medical College

2:45 p.m. 24.8 SPLANCHNIC REPRESENTATION IN THE FASTIGIAL NUCLEUS OF THE CEREBELLUM. Charles H. Hockman, Brain Research Laboratory, Department of Pharmacology, University of Toronto

3:00 p.m. 24.9 FOCAL REFLEX MYOCLONUS. Richard F. Mayer and Granger G. Sutton, Department of Neurology, School of Medicine, University of Maryland

3:15 p.m. 24.10 CEREBELLAR ACTIVITY IN EMOTIONAL BEHAVIOR. Robert G. Heath, Department of Psychiatry and Neurology, School of Medicine, Tulane University

3:30 p.m. 24.11 THE ASSOCIATION OF CEREBRAL AMINE DEFECTS AND ABNORMAL VISUAL EVOKED RESPONSES IN PHENYLKETONURIA. Charles M. McKean, Marilyn M. Marcus and Edward W. P. Schafer, Brain-Behavior Research Center, Sonoma State Hospital, Eldridge

FRIDAY, OCTOBER 29

Session 25. **1:00 p.m. to 4:15 p.m.** **Heritage Room**

BEHAVIOR

Chairman: Ethel Tobach, Department of Animal Behavior, American Museum of Natural History, New York

Contributed Papers

1:00 p.m. 25.1 NEW EVIDENCE CONCERNING REFRACTORY PERIOD IN SELF-STIMULATION NEURONS. Mary C. Wetzel, Department of Psychology, University of Arizona

1:15 p.m. 25.2 BEHAVIORAL TYPES OF NEURONS IN HIPPOCAMPAL FORMATION OF RAT. James B. Ranck, Jr., Department of Physiology, University of Michigan

1:30 p.m. 25.3 ELECTROMICTURITION IN MAN AND ANIMALS. Blaine S. Nashold, Jr. and Harry Friedman, Department of Surgery, Division of Neurosurgery, Duke University Medical Center

1:45 p.m. 25.4 TOPOGRAPHY OF LONG-LATENCY SOMATOSENSORY RESPONSES IN THE HUMAN BRAIN: A REEXAMINATION. Merlin W. Donald, Neuropsychology Laboratory, Veterans Administration Hospital, West Haven

2:00 p.m. 25.5 EFFECTS OF EARLY WEANING AND DIFFERENTIAL HOUSING ON EMOTIONAL REACTIVITY AND BRAIN BIOCHEMISTRY IN THE RAT. S. Michael Plaut and Jimmie M. Davis, Galesburg State Research Hospital, Galesburg

2:15 p.m. 25.6 EFFECT OF NEONATAL SPLIT-BRAIN SURGERY ON SHOCK THRESHOLDS AND AVOIDANCE LEARNING IN RATS. Jeri A. Sechzer, Department of Psychiatry, Cornell Medical College

2:30 p.m. 25.7 CLINICAL RECONSTRUCTION OF NATAL MEMORY AND NEUROBEHAVIORAL RESEARCH. Virginia Johnson, Private Practice, 1516 Westwood Boulevard, Los Angeles

2:45 p.m. 25.8 ESCAPE TRAINING IN PARAMECIA. Thomas E. Hanzel and William B. Rucker, Department of Psychology, Mankato State Hospital, Minnesota

3:00 p.m. 25.9 ALTERATION OF BLOOD PRESSURE FOLLOWING INSTRUMENTAL CONDITIONING IN RATS. S. N. Dutta and S. N. Pradhan, Department of Pharmacology, Howard University College of Medicine

3:15 p.m. 25.10 ANALYSIS OF EMOTIONAL HYPERGLYCEMIA IN MONKEYS. Benjamin H. Natelson, Peter E. Stokes and Gerard P. Smith, Bourne Behavior Research Laboratory, Department of Psychiatry, New York Hospital-Cornell Medical Center, Westchester Division, and Department of Neurology, Albert Einstein College of Medicine

3:30 p.m. 25.11 EEG ALPHA PATTERNS ASSOCIATED WITH NEUROPROCESSING DYSFUNCTION IN CHILDREN. Juan de Dios Pozo-Olano, Division of Biological Sciences, University of Georgia

3:45 p.m. 25.12 THE NEUROPSYCHOLOGY OF PSYCHOSIS AND SOMATIC TREATMENT. I. F. Small and J. G. Small, Department of Psychiatry, Indiana University Medical Center

4:00 p.m. 25.13 CEREBRAL TRAINING AS A REHABILITATIVE MODALITY. Ernst Schmidhofer, Cerebral Training Institute, Columbus

SATURDAY, OCTOBER 30

Session 26. **9:00 a.m. to 11:30 a.m.** **Diplomat Room**

NERVE NETS

Chairman: Donald M. Maynard, Department of Biology, University of Oregon

Invited Lectures

26.1 PATTERN FORMATION AND NEURAL CONNECTIVITY. Donald M. Maynard

26.2 GENETIC SPECIFICATION OF AN INSECT NEURONAL NETWORK. David Bentley, Department of Zoology, University of California, Berkeley

Selected Contributed Papers

26.3 MOTOR CONTROL OF THE ABDOMEN IN FLYING AND FLIGHTLESS LOCUSTS. J. M. Camhi and M. Hinkle, Section of Neurobiology and Behavior, Cornell University

26.4 CYCLING ACTIVITY IN ARTIFICIAL NERVE NETS. Photios A. Anninos, Department of Anatomy, University of California, Los Angeles

26.5 DEVELOPMENT OF ORGANOTYPIC BIOELECTRIC ACTIVITIES IN CULTURED REAGGREGATES OF RODENT CNS CELLS AFTER COMPLETE DISSOCIATION. S. M. Crain and

M. B. Bornstein, Departments of Physiology and Neurology, Albert Einstein College of Medicine and Rose F. Kennedy Center

Invited Lectures

26.6 ACCURACY OF NEURONAL CONNECTIONS. G. A. Horridge, Research School of Biological Sciences, Australian National University, Canberra

26.7 NEURAL ORGANIZATION OF THE VERTEBRATE RETINA. John Dowling, Biological Laboratories, Harvard University

SATURDAY, OCTOBER 30

Section 27. 9:00 a.m. to 11:30 a.m. Empire Room

INFORMATION PROCESSING AND STORAGE

Chairman: Walter A. Rosenblith, Professor of Communications, Biophysics, Massachusetts Institute of Technology

Invited Lectures

27.1 INVOLVEMENT OF PROTEIN SYNTHESIS IN MEMORY FORMATION. R. B. Roberts, Biophysics Section, Department of Terrestial Magnetism, Carnegie Institute

27.2 CENTRAL PROCESSING IN THE AUDITORY SYSTEM. N. Y. S. Kiang, Electrical Engineering, Massachusetts Institute of Technology

27.3 HOW MUCH PROCESSING SHOULD OCCUR BEFORE VISUAL INFORMATION IS "READY" TO BE STORED? D. A. Pollen, Department of Surgery, Harvard Medical School

27.4 PSYCHOBIOLOGICAL ANALYSIS OF LEARNING AND MEMORY. M. S. Gazzaniga, Department of Graduate Psychology, New York University

Selected Contributed Papers

27.5 AN INFORMATION THEORY ANALYSIS OF THE AUDITORY LOCALIZATION OF A LATERAL SOUND SOURCE. Terence W. Barrett, Department of Physiology and Biophysics, University of Tennessee Medical Units, Memphis

27.6 NEURONAL CODING OF COMPLEX LOW FREQUENCY STIMULI AT SUBCORTICAL AUDITORY SITES IN CAT BRAIN. James L. Walker and Edward S. Halas, Department of Psychology, University of North Dakota, Grand Forks

27.7 CODING OF SPECIES-SPECIFIC VOCALIZATION IN THE AUDITORY CORTEX OF AWAKE SQUIRREL MONKEYS. Z. Wollberg and J. D. Newman, National Institute of Child Health and Human Development

27.8 AUDITORY EVOKED POTENTIALS DURING SPEECH PERCEPTION. Charles C. Wood, William R. Goff and Ruth S. Day, Neuropsychology Laboratory, Veterans Administration Hospital, West Haven

SATURDAY, OCTOBER 30

Session 28. **9:00 a.m. to 11:30 a.m.** **Forum Room**

BRAIN, CONSCIOUSNESS, AND THE CONTROL OF BEHAVIOR

Chairman: Karl H. Pribram, Department of Psychiatry, Stanford University School of Medicine

Invited Lectures

28.1 Edward V. Evarts, Laboratory of Neurophysiology, National Institute of Mental Health

28.2 Walle Nauta, Department of Psychology, Massachusetts Institute of Technology

28.3 John C. Eccles, Laboratory of Neurobiology, State University of New York, Buffalo

Abstracts of Contributed Papers

Submitted to Society for Neuroscience

1.3 PERIPHERAL NEURAL DETERMINANTS OF INTENSITY DISCRIMINATION FOR COOLING OF THE SKIN. Kenneth O. Johnson and Ian Darian-Smith. Dept. Physiol., Sch. Med., Johns Hopkins Univ., Baltimore, Md. 21205

The human capacity to discriminate sudden cooling steps was determined by the method of paired comparisons for temperature steps varying from 0 to 8°C (T-STEP) and for background temperatures from 29° to 41°C (T-BASE). The difference limen is independent of the background temperature over that range and is related to T-STEP by the generalized Weber law, DL = 0.07+0.017T-Step. The discharge of the Adelta thermoreceptive afferent population in response to rapid cooling steps, which is also independent of the background temperature, is approximately linear with respect to T-STEP. Discharge sensitivity (the slope of the intensity function) is, however, strongly related to the stimulus history. Preceding stimuli have a strong suppressive effect on the fiber's response to the present stimulus. At the interstimulus interval used in the discrimination studies these effects combine to produce a constant average discharge over most of the T-STEP range. This implies that the Weber function is not determined by CNS mechanisms. The trial-to-trial variability of the cold afferent discharge is also independent of T-STEP which leaves the fiber sensitivity as the sole determinant of the Weber function. The average neural response increment corresponding to the DL, the fiber sensitivity times the DL, is constant and independent of T-STEP as well as T-BASE.

1.4 THE DEPENDENCE OF THE DISTRIBUTION OF SLOW CORTICAL POTENTIALS RECORDED IN THE RHESUS ON THE TASK IMPOSED ON THE MONKEY. Emanuel Donchin, David Otto*, Lauren K. Gerbrandt*, and Karl Pribram. Dept. Psych. Univ. of Ill., Urbana, Ill., 61801; Dept. Psych., Stanford, Calif.

Event related potentials were recorded using an array of transcortical platinized platinum--iridium electrodes from 7 Macaca mullata performing three different reaction time tasks. Potentials were extracted from the ongoing EEG using a signal averaging technique. All monkeys were trained to press a lever following a warning stimulus (tone or light) and hold the lever down until a second stimulus (light or tone) appeared. Very prompt responses to both stimuli and depressing the switch during the interstimulus interval were rewarded by a food pellet. Four monkeys were subsequently trained to press a lever without a preliminary signalling stimulus, hold lever down until a stimulus appeared and then release the lever as promptly as possible. In addition three monkeys were trained to press a lever and release immediately after the presentation of a stimulus. However, a warning stimulus was presented a second before the imperative stimulus. The monkeys were not to respond to this first warning stimulus with any motor response. The data show an exquisite dependence of the distribution of slow negative and positive potentials on the scalp on the task the monkey is performing. Specifically, a slow negative potential resembling Grey Walter's CNV appeared over the frontal cortex when the monkey waited for the imperative stimulus without executing any response (task 3). However, when the monkey was performing a response (holding down the lever) during the waiting interval little, if any, negativity appeared over the frontal area, though prominent negative-positive waves could be recorded over the posterior parietal area.

1.5 INTENSITY AND WAVE LENGTH ANALYSIS BY VISUAL SYSTEMS. Russell DeValois. University of California, Berkeley, California.

Visual objects are partially detectable by their differences from the background in either intensity or wave length. These (usually redundant) types of information are usually analyzed in very different ways by the orimate visual system.

Prime wave-length differences are detected by spectrally opponent cells, which differences are signalled by the outputs of cones containing different but broadly overlapping pigments. Location on the black-white dimension is signally by spectrally non-opponent cells, which sum the outputs of the same cones. Pure intensity differences in white or monochromatic light are signalled by all cell types. The spatial and temporal characteristics of these two types of analysis are quite different. Detection of wave-length differences improves as stimulus size increases, since it is based on comparison of the outputs of receptors lying in different retinal regions. Detection of intensity differences is optimal for small stimuli because of the opposing center-surround spatial organization of the receptors of most cells. The optimal temporal characteristics of pure luminance and pure color stimuli are also different.

2.5 FURTHER EVIDENCE ON THE ROLE OF MEMBRANE PROTEIN IN EXCITATION INITIATION IN AXONS. Alfred Strickholm, and Hulda R.Clark*
Anatomy-Physiology Dept., Indiana University, Bloomington, Indiana, 47401

Considerable evidence exists that membrane bound protein is essential for the generation of action potentials in nerve. Thus proteases applied internally to axons abolish the action potential prior to any loss in resting membrane potential. When proteases are applied externally, the action potential is generally unmodified but specific resting ionic membrane conductances are changed. Further characterization of the membrane protein's role in permeability regulation was obtained by measuring membrane resistance in crayfish giant axons as a function of pH. pH was varied over the range of 4 to 10 for nerve in normal saline and in elevated potassium which depolarized the axon by an amount normally sufficient to produce excitation. These pH studies have indicated that ionic conductance in resting crayfish axons decreases with increasing protonation of the outer membrane surface. The variation of membrane resistance with pH suggests that several exposed groups on protein are involved in ionic permeability regulation. In axons depolarized by potassium, the relation between pH and membrane resistance is altered. At around pH 6.3, a marked transition in membrane resistance occurs over a few tenths of pH that suggests a cooperative phenomena which probably involves the unmasking of buried histidine groups. These results suggest that a conformational change in membrane protein is involved in the mechanism of the action potential.

2.6 THE EFFECT OF C-AMP ON IN VITRO NEURITE DEVELOPMENT. F. J. Roisen*, W.G. Braden*, M. Pichichero* and R.Murphy* (SPON: A.R. Freeman) Dept. Anat. Rutgers Med. School, New Brunswick, N.J. 08903

Cell aggregation, differentiation, secretion, morphological expression, and pigment migration have recently been shown to be dependent on intracellular levels of 3'5' adenosine monophosphate (cyclic AMP); the role of cyclic AMP in stimulating cellular and intracellular movements prompted our study of embryonic chick dorsal root ganglia. Test substances were applied to the cultures during the routine feeding procedure. High resolution time lapse ciné recordings employing differential interference microscopy allowed precise continuous observation. The following parameters were evaluated quantitatively: explant size, overall outgrowth; rates of elongation; distribution of growth; the number, length, diameter and degree of neurite aborization. Eighty percent (170) of the 5'AMP treated cultures showed a significant decrease in all of the above factors, while the remaining twenty percent showed no significant deviation from the controls. Cultures treated with either cyclic AMP, dibutyryl cyclic AMP or Nerve Growth Factor (NGF) exhibited marked increases compared to controls with respect to the surface area of the outgrowth, rates of neurite elongation, and the number of neurites per culture as well as significant increases in the diameters, lengths and degree of arborization of the neurites. Since it has been suggested that microtubules (neurotubules) play important roles in many of the parameters previously discussed, the effects of cyclic AMP, dibutyryl cyclic AMP and NGF have been investigated in the presence of colcemid. In all three cases the arrest of neurite development due to the specific disruptive action of colcemid on microtubules was reversed. Our studies support the notion that cyclic AMP stimulates neurite growth by mediating in some way the process of microtubule assembly.

2.7 FINE ULTRASTRUCTURAL FEATURES OF RIBOSOMES AND SYNAPTIC MEMBRANES IN BRAIN CORTEX. Vincenzo Di Carlo, Dept. Anat., Loyola Univ. of Chicago, Stritch Sch. of Med., Maywood, Ill. and L. B. Mendel Res. Lab., Elgin State Hosp., Elgin, Ill.

Utilizing high-resolution electron microscopic techniques on osmium-fixed and Epon-embedded mammalian and amphibian brain cortex specimens, it was possible to identify some new fine ultrastructural features in neuronal organelles and membranes. In studying perikarya and dendrites, it was observed that a complex internal structural organization can be resolved in ribosomes. One of the main recognizable patterns inside ribosomes was found to be a right-handed helix, comprising as many as 7 or 8 turns, wound around the major axis of the particle. The main structural element which makes up the helical pattern appears to be a thin osmiophilic filament attached to minute osmiophilic granules. Larger granules, measuring approximately 30-40 Å in diameter, which are clearly distinct from the filament, are also evident inside ribosomes, especially in axial or close-to-axial projections. They appear to be the center of hexagonal or elliptical formations (about 90 Å in diameter) similar to the polyhedric-globular units previously described in membranes (Nature 213, 833; 1967). In studying axodendritic synapses, it was possible to observe clear-cut morphological differences between pre-synaptic and sub-synaptic membranes: the pre-synaptic membrane is often wavy and appears to consist essentially of a row of relatively large osmiophilic granules, measuring approximately 40 Å, which can frequently be recognized as the centers of polyhedric-globular units; the sub-synaptic membrane is usually straight and appears to be composed of smaller, closely spaced osmiophilic granules, approximately 30 Å in diameter.

Session 3

No Contributed Papers

Session 4

4.1 VISUAL DISCRIMINATION AND THE EFFECTS OF ABLATIONS OF THE CENTRAL VISUAL SYSTEM IN LEMON AND NURSE SHARKS. R. Curtis Graeber*, Sven O.E. Ebbesson, J.A. Jane and P.J. Best. Depts. Psych. and Neurosurgery, Univ. of Virginia, Charlottesville, Virginia 22901, and Lerner Marine Lab., Bimini, Bahamas.

An instrumental conditioning procedure was developed to examine the abilities of individual juvenile lemon sharks (Negaprion brevirostris) and nurse sharks (Ginglymostoma cirratum) to learn black-white and pattern discriminations. The sharks were required to choose the correct one of two target doors at the end of a straight alley for food reinforcement. In spite of their relatively simple nervous system, the results indicate that these animals can learn to discriminate black versus white and horizontal versus vertical black and white stripes as rapidly as most mammals. Subsequent experiments examined the effects of tectal and forebrain ablations. It was found that extensive bilateral damage to the optic tectum does not severely affect the nurse shark's ability to learn such discriminations. Although these results do not deny the importance of the optic tectum as a center for the integration of visual information in the shark, they do emphasize that other areas such as the lateral geniculate nucleus and telencephalon play important roles.

Supported by: 1 R01-EY00154-01A1; 1-K4-NS-46,292-01A1; Lucille Sebrell Memorial Fund and James A. Baur Research Fund. First author carried out this research while a member of the Army Graduate Psychology Program.

4.2 LIMULUS LATERAL EYE: HOW TO GAIN FIVE LOG UNITS OF SENSITIVITY. Robert B. Barlow, Jr. and Ehud Kaplan*. Lab. Sensory Comm., Syracuse Univ., Syracuse, N. Y. 13210.

Since 1928 experiments on the Limulus lateral eye have followed Hartline's original procedure of excising the eye from the animal and placing it in a recording chamber. This procedure often produces a preparation in which the sensitivity of ommatidia to light declines steadily. We overcame this difficulty by recording from the optic nerve fibers without removing the eye from the animal. We found significant physiological differences between the excised and intact lateral eyes: (1) single ommatidia in the intact eye respond without saturation over a range of 10 log units of light intensity, whereas receptors in the excised eye normally respond over a 5 log unit range of light intensity; (2) ommatidia in the intact eye are spontaneously active in the dark, whereas receptors in the excised eye are not. High sensitivity to light and spontaneous activity can be maintained in the intact preparation for at least one week. The sensitivity of units in the excised eye decreases roughly by a factor of 10 every four hours. Two mechanisms may enable ommatidia in the intact eye to respond over such large ranges (10^{10}) of light intensity. This possibility is suggested by studies on light adaptation and on the variability of the interspike intervals, and by the plateau in the intensity characteristic.

4.3 A COMPARATIVE STUDY IN THE NEUROPHYSIOLOGY OF VISION IN SQUID AND OCTOPUS. Peter H. Hartline and G. David Lange. Dept. Neurosciences, Sch. Med. UCSD, San Diego 92038.

ERG, optic nerve and optic lobe recordings were made in intact animals and in in vitro preparations. An isolated eye-optic nerve - optic lobe preparation was developed. Eye, optic nerve, and optic lobe are removed from octopus (O. bimaculoides, anesthetized with ethanol or chilling to 5° C) or from squid (Loligo opalescens) and placed in chilled circulated sea water or physiological saline. Suction electrodes can be applied to sclera for ERG or to optic nerves in their course between eye and optic lobe. Both afferent and efferent activity can be seen on optic nerves. Efferent spikes are largest and are identified by double electrode and cutting techniques. In both species these can be either spontaneous or normally silent and can be affected by lights on the retina. Both excitatory and inhibitory effects have been seen. Afferent spikes usually have the character of "on" units. Microelectrodes have been used to probe the optic lobe. So far squid and octopus results have been remarkably similar in most particulars even though in the long run we expect differences correlatable to their generally different life styles.

This investigation supported by PHS grant NS09342.

4.4 TRANSFER PROPERTIES OF THE ERG OF OCTOPUS. G. David Lange and Peter H. Hartline., Dept. Neurosciences, Sch. Med. UCSD, San Diego 92038.

Input output relations (transfer functions) were obtained for the transduction of sinusoidally modulated light intensity to gross electrical responses on the eye. Both intact animal and isolated eye - optic nerve - optic lobe preparations (see Hartline and Lange these abstracts) were used. No essential differences were found. Linearity holds reasonably well with small modulations. The transfer function shows a typical bandpass characteristic with the best frequency being at between 0.5 and 2 Hz. Responses are down approximately 40 db at 10 and 0.01 Hz. Responses to steps and short flashes of light intensity have also been measured. There is a facilitation phenomenon wherein the response to the second of a pair of flashes is greatly enhanced when they are 50-100 msec apart. Oscillations at 10-50 Hz can be elicited when bright lights are shown on the dark adapted eye. Responses are in general much more complex than those seen by Tasaki et al (Vis. Res. 3:61-75, 1963) in isolated retina.

This investigation supported by PHS grant NS09342.

4.5 CHEMICAL ANALYSIS AND IN VITRO ACTIVITY OF RETINAL ROD OUTER SEGMENTS.
William Robinson, Ann Gordon-Walker, Joan Dawes and Deric Bownds.*
Laboratory of Molecular Biology, University of Wisconsin, Madison, Wisconsin 53706.

Retinal rod outer segments are a favorable preparation for studying nerve membrane excitation in vitro for they maintain their ability to transduce light into a sodium conductance change even after extensive purification. Molecular mechanisms underlying both excitation and adaptation can then be investigated by characterizing the protein components of these photoreceptor membranes as well as the conductance changes which they modulate. These membranes contain 50-54,000 grams of protein/mole of retinal, 40,000 grams of which is the visual pigment. This was determined by fractionating detergent solubilized outer segments by SDS gel electrophoresis and agarose and hydroxyapatite column chromatography. Purified rhodopsin was analyzed for amino acid content. The amount of retinal was determined from the reported value of 42,000 for the molar extinction coefficient, which we are re-determining. Purified outer segments can be assayed for a light induced sodium conductance decrease using a modification of the procedure of Korenbrot and Cone. This decrease is normally irreversible if more than 0.3% of the visual pigment is bleached. The conductance is restored in less than 20 min. in the presence of 10^{-6}M cyclic AMP even if as much as 50% of the rhodopsin has been bleached. The outer segments regain their original sensitivity, responding to 100 quanta/outer segment/second with a conductance decrease, even though no rhodopsin regeneration occurs. Calcium ions appear to also play a role in the conductance change.

4.6 Synaptic Input on Ganglion Cells in the Ground Squirrel Retina

Roger W. West and John E. Dowling
The Johns Hopkins University
Baltimore, Maryland

Ganglion cells in the ground squirrel retina integrate visual information either spacially or temporally. Electron microscopy of Golgi impregnated, serially sectioned ganglion cells reveals two patterns of synaptic input. One set of ganglion cells has a large dendritic field and a primarily bipolar input. Their size correlates well with the large receptive fields of the spacially integrating cells and offers a direct path from receptors to the ganglion cells giving this simple response. The other set of ganglion cells has a small dendritic field and a primarily amacrine input. This smaller size correlates well with the small receptive fields of the temporally integrating cells, and the amacrine cells would serve as interneurones in governing the complex responses recorded from these ganglion cells. At least one subtype of ganglion cell in this latter group has only amacrine input. Thus, not all ganglion cells are third order neurones as is usually stated. Some of the complexly responding cells are at least fourth order neurones.

Little correlation has been found between gross morphology and synaptic input other than width of dendritic tree. Cells with high bipolar or amacrine input can have either highly stratified or diffuse dendritic trees. However, only ganglion cells with high amacrine input are multi-stratified.

4.7 THE RESPONSE OF MONKEY RETINAL GANGLION CELLS TO A FLASHING AND MOVING LUMINOUS SPOT. R.P. Scobey and J.M. Horowitz*. Dept. Behavioral Biology, Sch. Med. and Dept. Animal Physiol., Univ. of Cal., Davis, Cal. 95616.

Action potentials from 22 retinal ganglion cells in the peripheral visual fields of rhesus macaque monkeys were evoked by both spatial and temporal changes of a small luminous spot. The spot was less than ten minutes of arc in diameter and was imposed against a constant background illumination of 0.3 cd./m^2. First the sensitivity of sites along a diameter through the receptive field was measured as a reference for additional measurements of displacement and increment thresholds. A displacement threshold was then obtained at a series of sites along the same diameter by rapidly displacing the spot of light from a fixed site to a test site, any by adjusting the displacement to the minimum value just sufficient to evoke a noticeable increase in the ongoing activity of the ganglion cell. Typically the minimum displacement threshold was about 1/100 of the diameter of the receptive field center. In addition, along the same locus of points the minimum value of intensity change needed to evoke a noticeable increase in the ongoing activity was measured. The displacement threshold at any site in the receptive field was found to be related simply to both increment changes in spot intensity at the same site and to the location of the site within the receptive field. Therefore, the keenness of the vision of movements in the visual periphery can be accounted for by the basic receptive field characteristics.

4.8 RETINAL RESPONSE LATENCY AS A FUNCTION OF FLASH RATE. Walter L. Salinger* and Donald B. Lindsley, Depts. Psychol. and Physiol., UCLA, L.A. 90024.

Response latency in the visual pathways from eye to cortex varies inversely with flash intensity and is due mainly to receptor level processes. Response latency also varies as a function of flash frequency when intensity is held constant. This study has sought to contrast the retinal loci and mechanisms underlying latency shifts due to flash frequency and intensity. In cats under Nembutal anesthesia flash evoked responses were recorded from the optic tract (both gross and unit responses) and in association with the extra-ocular ERG. With intensity constant, the latency of evoked responses in the optic tract increased with increasing frequency, whereas simultaneously recorded ERGs did not change systematically in latency. Thus the latency shift as a function of frequency appears to be proximal to the receptor level and possibly also to the bipolar cell level. Both "on" and "off" unit responses in the optic tract reflected similar latency shifts as a function of flash frequency. All units showed some latency shift but only about half showed shifts corresponding in magnitude to those of the gross evoked response. These results will be discussed in terms of the relationship of unit to gross evoked responses in the optic tract and with respect to possible retinal mechanisms responsible for the latency change as a function of flash rate.

4.9 DIRECTIONALLY SELECTIVE VISUAL UNITS RECORDED IN THE OPTIC TECTUM OF THE GOLDFISH. Douglas Wartzok* and William B. Marks. Department of Biophysics, Johns Hopkins University, Baltimore, Maryland, 21218.

Metal-filled micropipettes were used to record from the tectal afferent endings of individual directionally selective retinal ganglion cells in the goldfish. Ten characteristics of the directional units were observed in order to determine their mechanism and function. The stimulus was a light pipe attached to a computer controlled x-y recorder. In 87 units 68% of the preferred directions were nasal or nasal-dorsal with the six remaining directions all about equally represented. There was no correlation between preferred direction and location in the visual field. The receptive field diameters ranged from 2 to 8.5 deg. with a mean of 4.4 ± 1.4 deg. (s.d.;n=40). The response was decreased by 50% at angles of 79 ± 18 deg. (s.d.;n=108) from the preferred direction. Two spots of light, one moving in the preferred direction and one moving in the null direction, were made to collide within the receptive field. The separation at which the response to the one moving in the preferred direction was inhibited by the one moving in the null direction was 1.4 ± 0.6 deg. (s.d.;n=4). This experiment delimited the size of the directionally selective subunit and showed that inhibition is a factor in the directionally selective mechanism. Background light limited to the periphery almost eliminated the response to movement in three out of four units tested, implying the existence of an inhibitory surround. The response was linear with speed up to a mean optimal speed of 11.7 ± 4.2 deg./sec. (s.d.;n=6). There was correlation with goldfish eye movements (Easter, S.S., personal communication) for three of the characteristics of the single units. The inhibitory mechanism of directional selectivity and the possible function of eye movement control in the goldfish appear to be similar to that postulated for several mammals.

4.10 VELOCITY DEPENDENT DIRECTIONAL SELECTIVITY IN CAT SUPERIOR COLLICULUS. Barry E. Stein * and Makanjuola O. Arigbede* (SPON: L. Kruger). Dept. Anat., UCLA Ctr. Hlth.Sci., L.A. 90024

Neurons in the superior colliculus of cats were studied with metal microelectrodes under different anesthetic conditions. The limits of visual receptive fields of individual collicular units were determined. Light and dark rectangular stimuli (bars) were mounted on a hydraulically driven apparatus so that stimulus orientation, position and velocity could be duplicated accurately in successive stimulus presentations. These bars were repeatedly presented in 8 directions, at 45 degree intervals, in order to determine the optimum direction of movement. For most units, an optimum direction was determined for a given stimulus velocity, but in many cases the optimum direction was markedly altered at other velocities. Several units were encountered which responded best to movement in a given axis rather than a given direction. The response to repeated stimulus presentations displayed marked fluctuations, without consistent diminuition of responsiveness, sometimes interpreted as habituation.

4.11 VISUAL LEARNING BY CATS AFTER LESIONS OF THE SUPERIOR COLLICULUS-PRETECTUM. J.S. Winterkorn. Anatomy Dept., Cornell Univ. Med. Coll., New York, N.Y. 10021.

Cats can be initially trained or retrained after bilateral complete lesions of the superior colliculus-pretectum to perform light-dark and horizontal-vertical line discriminations in a V-shaped maze with a food reward. Using door pushes as the criterion for correct performance, lesioned animals are comparable to unoperated animals. However, using an alley entry criterion of correct performance, the unoperated animals achieve criterional performance without difficulty whereas the lesioned cats remain at chance performance levels unless special training methods are employed. These data suggest that the superior colliculus-pretectum of the cat is not essential to spatial orientation in the V-maze but implicate these structures in other processes underlying visual learning.

4.12 VISUAL SYSTEM EXCITABILITY TEMPORALLY RELATED TO FAST AND SLOW COMPONENTS OF NYSTAGMUS IN THE CAT. Robert B. Graham, Department of Psychology, University of Florida, Gainesville, Florida 32601.

This work studies the temporal relationship between eye nystagmus and excitability changes in the visual system of chronically implanted cats. Previous authors have noted enhanced potentials in visual cortex (VC) and superior colliculus (SC) during tracking eye movements. Hyperexcitability in these structures has also been noted following lateral geniculate nucleus (LGN) spikes (Munson and Graham, Exp. Neurol. 1971). The LGN spikes characteristically occur at the transition point between fast and slow components of caloric (CN) and optokinetic (OKN) nystagmus in cats which exhibit LGN spikes in the waking state. Two questions arise: 1) does the eye movement-related hyperexcitability occur specifically at the time of the LGN spike; and 2) do cats which do not exhibit the LGN spikes when awake still show the hyperexcitability. Potentials in VC, SC and pontine reticular formation evoked by shocks to optic nerve were recorded during CN and OKN, both in cats which showed LGN spikes while awake and in those which did not. Both groups of cats exhibited LGN spikes during fast-wave sleep and following reserpine administration. Potentials were enhanced over a period of about 100 msec, commencing just before the fast-slow inflection point and attaining a maximum about 50 msec after that point. This hyperexcitability occurred at the time of the LGN spike in cats which exhibited waking LGN spikes and occurred at the corresponding time in the cats which did not exhibit waking LGN spikes. No such enhancement was seen at the transition from slow to fast phase and, indeed, in some cases excitability was depressed at that time. Thus, LGN spikes seem to signal a brief increase in central excitability which is related not to nystagmus in general but to some event occurring as the eyes stop at the end of a fast movement and begin the slow return. Fixation is such an event. (Supported by NSF Grant GB-7622)

Session 5

5.1 HIPPOCAMPUS AND ZINC: THE POSSIBLE ROLE OF ZINC IN THE CNS. Werner J. Niklowitz. Dept. Environ. Health, Coll. Med., University of Cincinnati

The hippocampal formation contains the highest concentration of zinc in the CNS (MASKE, Naturw. 32:424, 1955 and others). Histochemical methods revealed that Zn^{2+} is found in the mossy fiber layer and cytochemically it was shown that Zn^{2+} is located in the boutons. Experiments to relate Zn^{2+} to metallo-enzymes were not successful. The questions remain what endogenous substances Zn^{2+} is related to and what functional role it may have in the CNS. Our phase and electronmicroscopic investigations of the hippocampus in experimental epilepsy (produced by 3-acetylpyridine, methoxypyridoxine, metrazol) revealed that the granular cell system of the hippocampal gyrus dentatus and in particularly the mossy fiber boutons show significant structural alterations which antedate the development of convulsions. It has been suggested that some changes are related to a release of neurotransmitters. Recently, it has been shown that at least some boutons and pharmacological receptors contain a metal in or near sites of neurotransmission. Chelation is considered to play a prominent role in stabilizing certain neurotransmitters (catechol- indolamines). COLBURN a.MAAS (Nature 208:37,1965) developed the hypothesis that biogenic amines are stored in an ATP-metal-monoamine complex. On the basis of work by COLBURN et al. and our own studies on the possible functional role of certain trace metals in CNS metabolism the following is proposed: Zn^{2+} in proper concentration in the hippocampus is important in a specific storage mechanism for neurotransmitters. Certain metals such as lead or mercury may competitively interfere with Zn^{2+} or other essential trace metals with resultant biochemical, functional, and morphological alterations. As it has been shown that Zn^{2+} content of the hippocampus in cases of schizophrenia is lower, we are studying Zn^{2+} concentrations in the hippocampus in cases of lead encephalopathy, in which there is preferential hippocampal deposition of lead. (Supported by USPHS 5 P10 ES00159)

5.2 FURTHER STUDIES ON A CORTICOSTERONE BINDING MACROMOLECULE FROM RAT BRAIN CYTOSOL. B.I. Grosser, W. Stevens*, and D.J. Reed*. Dept. Psychiatry, Anatomy and Pharmacology, Sch. Med., U of Utah, S.L.C. 84112.

The association *in vivo* of ^{3}H-corticosterone to macromolecules from the whole brain cytosols of adrenalectomized male rats has been reported. This interaction appears to be specific since prior administration of 3 mg of non-radioactive corticosterone almost completely inhibits the binding of ^{3}H-corticosterone administered 30 min later by ventriculocisternal perfusion, whereas prior administration of non-radioactive cortisol, cortisone and 11-dehydrocorticosterone only partially inhibits the uptake of ^{3}H-corticosterone. Estradiol, testosterone and progesterone do not interfere with the association of ^{3}H-corticosterone to macromolecules in the brain cytosol. Further studies have been performed which indicate that the binding of ^{3}H-corticosterone to macromolecules of whole brain cytosol from adrenalectomized rats occurs rapidly at 4° C. Scatchard plots of the data following 1 h incubation of whole brain cytosols at 4° C demonstrate that the K(assoc) was 4.0×10^{11} and that 1.9×10^{-12} moles of corticosterone were bound per mg of protein. Examination of different regions of rat brain with respect to their capacity to bind ^{3}H-corticosterone *in vivo* indicates that the greatest concentration of cytosol binding molecules are localized in the hippocampus. Partial analysis of the proteins that bind corticosterone indicates that they are excluded from the gel phase on Sephadex G-100 and G-200. Evidence was obtained that the corticosterone binding molecule in brain cytosol is not corticosteroid binding globulin (CBG). (Supported by NIH 5 K02 MH-18,270, NS 07761, NSF GB19040, NIH 1-K3-NB 7779, and NB 04553.)

5.3 5-HYDROXYTRYPTAMINE-RELATED CHANGES IN CEREBRAL PROTEIN SYNTHESIS. Elihau Heldman and Walter B. Essman. Queens College of the City University of New York, Flushing, N.Y., 11367.

It has been shown that brain 5-hydroxytryptamine (5-HT) elevation, as a consequence of electroconvulsive shock (ECS) can be related to the fixation and/or storage of information. In several studies the effects of ECS upon incorporation of ^{14}C-amino acids into whole brain protein indicated, based upon a 5 min. rate function derived from kinetic studies, over 40% inhibition immediately following treatment; graded inhibition of protein synthesis followed a time course wherein effects were no longer apparent beyond 15 min. after treatment. Regional and subcellular studies indicated that protein synthesis after ECS was maximally inhibited in cerebral cortex (59%), as compared with basal ganglia and thalamus (33%) or cerebellum (27%); for cerebral and cerebellar cortex maximum inhibition was shown in synaptosomal fractions (72 and 34%, respectively). Differences in the mode by which cytoplasmic protein synthesis inhibition occurred may reside in a correlated ATP depletion. Consistent with ECS-induced brain 5-HT elevation, intracranial 5-HT produced inhibition of ^{14}C-leucine incorporation into whole brain protein (15%) by 10 min. after injection. Cerebral cortex was again confirmed as the region of maximal 5-HT-induced inhibition. Subcellular studies of this tissue indicated that 5-HT, administered *in vivo*, accounted for differential inhibition within 10 min., with maximum effect in the synaptosomal fraction (34%). *In Vitro* studies of ^{14}C-leucine incorporation into cytoplasmic and synaptosomal proteins support 5-HT-induced differences in that site of inhibition.

(Supported by Grant HD-03493 from the N.I.H.).

5.4 Distribution of Aminotransferases in Rat Brain. M.Benuck, F.Stem, and A.Lajtha. New York State Research Institute for Neurochemistry and Drug Addiction, Ward's Island, N.Y.10035.

A survey in our laboratory (J.Neurochem., in press) using rat brain homogenate showed that 17 of the 22 amino acids tested donated their amino groups to several keto acids. We investigated the more active enzyme reactions with respect to their subcellular localization and regional distribution in the nervous system of the rat. The reactions studied were glutamate with oxaloacetate; alanine, GABA, leucine, phenylalanine, tyrosine, asparagine and methionine with 2-ketoglutarate; and glutamate, glutamine and ornithine with glyoxylic acid. The regions investigated were sciatic nerve, spinal cord, cerebral cortical grey matter, corpus callosum (white matter) and midbrain of adult rats. Aminotransferase activity in the sciatic nerve was generally very low, although glutamate oxaloacetic aminotransferase activity was significant, and asparagine 2-ketoglutarate aminotransferase activity was only slightly lower than in other brain areas. Activity in general was found to be higher in cortical grey matter and mid brain than in the corpus callosum and spinal cord. Exceptions to this pattern of distribution existed; e.g., glutamate glyoxylate aminotransferase activity was similar or higher in the corpus callosum than in other areas. Values in midbrain were close to those in cortex, again with some exceptions such as alanine 2-keto-glutarate aminotransferase, which was twice as active in cortical grey matter than in midbrain. Subcellular distribution studies showed little activity in purified nuclei, whereas aminotransferase activity was high in mitochondria and also in the cerebral supernatant fractions. GABA-aminotransferase and aromatic aminotransferase activity was present predominantly in the mitochondrial fraction.

5.5 LYSOSOMAL ACID HYDROLASES IN NEONATAL RAT BRAIN AND IN MONOLAYER CULTURES DERIVED FROM NEONATAL BRAINS EXPOSED PRENATALLY TO ETHYLNITROSOUREA (ENU). H. H. Traurig* and J. N. Allen. Div. of Neurol., Coll. of Med., Ohio State Univ., Columbus, Ohio. Supported by N.C.I. Grant #CA 08543.

Transplacental exposure of fetuses to ENU induces tumors postnatally, usually derived from glial cells or their precursors. These tumors are characterized by marked increases in lysosomal acid hydrolases activity compared to normal brain. The objective of this study was to determine the activity of certain lysosomal acid hydrolases in primary monolayer cultures of glial cells derived from brains of neonates prenatally exposed to ENU. Results are compared to cultures derived from unexposed neonatal brains and to brains during neonatal development. Data are expressed as μmoles substrate hydrolyzed/hr/mg protein. During neonatal development β-glucuronidase (β-G) activity gradually declined from day one through 30. Acid phosphatase (AP) was unchanged through day 10, then gradually declined through day 30 to adult levels. Aryl sulfatase A & B (AS) activity increased markedly between days 3 and 6, less markedly between days 6 and 15 and gradually declined through day 30. N-acetyl-β-D-glucosaminidase (GAD) activity increased markedly between days 6 and 20, then declined by day 30. In cultures derived from neonatal brains and neonatal brains prenatally exposed to ENU, β-G, AS and AP activities reached their maxima by 14 days incubation and changed little throughout 49 days incubation. GAD activity increased throughout the 49 day incubation period. In conclusion, maximal activities in neonatal brain were 2-4x's greater than those of adult cerebrum. Activities of primary monolayer cultures of glial cells derived from neonatal brain were 5-10x's greater than neonatal whole brain and more than 10x's greater than normal adult cerebrum. Transplacental exposure of prenatal rats to ENU had no effect on lysosomal acid hydrolase activities in subsequent primary cultures derived from their brains through 49 days incubation.

5.6 EFFECTS OF DIBUTYRYL ADENOSINE CYCLIC 3':5'-MONOPHOSPHATE ON EMBRYONIC RAT CEREBELLUM CULTURED IN VITRO.[1] Robert S. Lasher and Ian S. Zagon*. Dept. Anat., Univ. Colorado Med. Sch., Denver 80220.

While the role of adenosine cyclic 3':5'-monophosphate (CAMP) in the metabolism and function of the mature nervous system has been investigated extensively, no studies have examined the possible role of CAMP in neural differentiation. In light of this, partially dissociated cultures of 16 day prenatal rat cerebellum, growing on a collagen coated substrate in 2 ml of a modification of Ham's medium F12 for 1 week, were fed with medium containing 5 X 10^{-4}M dibutyryl CAMP for 3 days. At the end of this time, cultures growing in the presence of dibutyryl CAMP demonstrated a much more extensive outgrowth of neuronal processes than untreated controls. In addition dibutyryl CAMP appeared to promote increased survival of the dispersed neurons. These preliminary data suggest a possible role for CAMP in promoting neuronal differentiation. Data from experiments currently underway to further determine the effects of CAMP on neural differentiation at the cellular and ultrastructural levels will be discussed.

[1]Supported by NIH grant NS09641-01.

5.7 CHARACTERIZATION OF RNA POLYMERASE ACTIVITY IN ISOLATED OLIGODENDROGLIA ENRICHED NUCLEI. Donald E. Slagel and Bobby C. Powell*.Dept. Surg. Div. Neurosurg.,Univ. of Ky. Col. of Med., Lexington, Ky. 40506.

Nuclei isolated from sheep centrum semiovale were used to characterize nuclear RNA polymerase activity in oligodendroglial cells with respect to $(NH_4)_2SO_4$ activation, pH maximum, optimum incubation time, presence of nucleases, and the U/G base ratio of newly synthesized RNA. Nuclei were isolated from sheep brain by homogenization, centrifugation in 0.32M buffered sucrose and purified by centrifugation through 2.39M buffered sucrose. The nuclear pellet was suspended in an assay buffer containing in mmole/ml : tris-HCl 0.1, sucrose 0.24, $MgCl_2$ 0.008, KCl 0.07,NTP's (UTP,CTP,&ATP) 0.1,phosphoenolpyruvate 1.6, pyruvate kinase 9.2 enzyme units,$(NH_4)_2SO_4$ 0.2, and labelled NTP (usually H^3GTP) 2.5 µc. Polymerase reaction mixture was incubated at 37 C. for 10 min. Reaction was stopped by precipitation with 10% TCA. Precipitate was washed,solubilized, and placed in scintillation solution. Solution was counted in a Packard scintillation spectrophotometer 3375 at a H^3 counting efficiency of 46%. Ammonium sulfate showed peak stimulation occurred at 0.2M . At this concentration the percent stimulation was 537% of the control activity with no ammonium sulfate.Optimum pH for the reaction occurred with a broad maximum at pH 7.8. Reaction kinetics gave a biphasic curve having a steep slope from 0 to 20 min.The reaction continued linear,decreased rate to 60 min. The presence of nucleases in the reaction could not be detected by increased U.V. absorbance of added RNA or by an actinomycin experiment designed to measure nuclease degradation of newly synthesized RNA. The U/G ratio of newly synthesized RNA and the measurement of all these characteristics using neuronal enriched nuclei will be reported. Experiments using specific inhibitors for RNA polymerase I,II,&III will also be discussed.

5.8 ESR STUDIES OF SPIN-LABELLED NEUROBLASTOMA CULTURE CELLS. Howard H. Wang, Gregory Ciotta* and Dorothy Steele*. University of California, Santa Cruz, California 95060.

Membrane properties of neuroblastoma culture cells (clone N-18) were studied with 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO), various fatty acids and steroid spin labels, and a tetracaine spin-label. Similar studies were also carried out on crab and lobster nerve membranes and a fibroblast culture cell preparation for comparison. Neuroblastoma cells grown in Dulbecco's modified Eagle's medium with 10% fetal calf serum, washed with a balanced salt solution and then incubated in a balanced salt solution containing TEMPO showed an ESR spectrum indicative of both hydrophobic and hydrophilic low viscosity environments. This result is similar to that found for the rabbit vagus (Hubbell and McConnell, PNAS 61:12). Since neuroblastoma cells contain no associated neuroglia, the above results can only be due to the neuroblastoma cells and the bathing medium. Washing with a balanced salt solution containing no TEMPO readily removed the hydrophilic component of the ESR spectrum. The hydrophobic component of the spectrum is only removed with prolonged washing. Such results indicate an extracellular origin of the hydrophilic component of the ESR spectrum. Preliminary results also indicate the presence of reducing agents at the membrane surface.

5.9 IN VIVO METABOLISM OF GALACTOSPHINGOLIPIDS IN THE BRAIN OF JIMPY AND CONTROL MICE. Mary J. Druse and Edward L. Hogan. Neurobiol. Prog., Sch. Med., UNC, Chapel Hill, N.C. 27514

A striking deficiency of brain cerebroside (C) and sulfatide (S) content characterizes the Jimpy mutant (Jp) which manifests a sex-linked recessive disorder in formation of CNS myelin. We have examined the in vivo incorporation of U-^{14}C-glucose into brain C and S at 7, 10, 13 and 16 days post partum, comparing the Jp with littermate controls. Animals were sacrificed 1, 6 and 24 hours following IP injection of 5 microcuries of U-^{14}C-glucose and brain lipids extracted according to Folch-Pi et al. C and S were purified on a Florisil column followed by TLC. Gluco and galactosphingolipids were resolved on borate-impregnated silica gel plates. In control brain, the maximal total activity of labelled hexose occurred at 16 days which is in accord with Moser and Karnovsky (1958). In Jp brain, the total activity of the C and S was comparable to that in littermate controls at 7-10 days post partum but reduced to 13% of the control value at 13 days and 6% at 16 days. The total activity in the mutant C and S at 13-16 days was less than at 7-10 days. The time course of incorporation in the mutant did not indicate an increased turnover of brain C and S. Similar incorporation of hexose into mutant and control C and S of brain at ages prior to and at the inception of active myelination does not accord with a primary defect in the biosynthesis of C and S in Jp. The significant decrease in incorporation at older ages could be due to a decrease in the number of the oligodenrocytes and thus a secondary effect. (Supported by USPHS Grants NB-06926 and MH-1107)

5.10 POSTNATAL PROTEIN-CALORIE DEFICIENCY EFFECTS ON LEARNING AND NEUROCHEMISTRY OF INFANT RHESUS MONKEYS, Ordy, J., Northern Illinois University, DeKalb, Illinois, 60115.

The aims of this study were to examine the effects of early protein malnutrition on visual discrimination learning in relation to neurochemical changes in frontal and visual areas of the neocortex, the caudate and hippocampus of infant rhesus monkeys. Eighteen 90 day old infant monkeys were assigned to a high (25%), medium (12.5%) or low (3.5%) isocaloric protein diet from 3 to 9 months after birth. All infants were tested daily for visual discrimination learning. They were sacrificed at 9 months of age for biochemical, histochemical and electron microscopic evaluations of the brain, pituitary, adrenals, pancreas and liver. During the 6 month period on the 3 different protein diets, the low protein monkeys became progressively inferior in the acquisition and reversal of 2-choice visual discrimination learning problems. Chemical evaluations indicated that the low protein diet resulted in significant decreases of RNA concentrations and acetylcholinesterase activity in the visual cortex and hippocampus. The low protein diet also produced significantly lower norepinephrine and serotonin concentrations in the hypothalamus. Morphologically, the low protein diet resulted in significantly lower postnatal increases in the weight of the body, brain adrenals, pancreas and liver, but not the pituitary. Observations with the electron microscope indicated qualitative differences in the free and membrane bound ribosomes of the endoplasmic reticulum and in the organization of synaptic membranes in neurons of the visual cortex and hippocampus. The experimental findings demonstrated significant learning and brain vulnerability to postnatal protein-calorie deficiency which was related to the age at which the deficiency was established, the protein value of the diet and the duration of the protein-calorie deficiency.

5.11 CEREBRAL BLOOD FLOW AND CEREBRAL FUNCTION. James H. Salmon, Albert L. Timperman* Dept. of Neurosurg. Univ. of Cinti. Col. of Med. and the Veterans Administration Hospital, Cincinnati, Ohio 45220

Cerebral blood flow studies using the inert gas Xenon^{133} were performed in 25 demented patients. The Xenon was injected via the internal carotid artery and the radioactivity recorded from an extracranial scintillation detector. The washout curve obtained was submitted to compartmental analysis. With this technique the blood flow through the gray (CBF_G) and the white matter (CBF_W) can be estimated. Of greater importance, the relative weight of the gray matter (W_G) can be calculated. CBF_G was decreased in each of these patients. The relative weight of gray matter, W_G, was also decreased in each of these patients. The first part of the study was an attempt to correlate W_G with other tests of cerebral function such as the Wechsler Adult Intelligence Scale, clinical evaluation and the patient's capacity to care for himself. There was a good correlation between W_G and I.Q. No patient whose W_G was below 25% had an I.Q. greater than 50. Higher values of functional gray matter were associated with higher I.Q. scores. The estimation of W_G shows promise as an objective measurement of the anatomical substrate of intelligence.

5.12 EFFECT OF pH ON METABOLISM AND ULTRASTRUCTURE OF GUINEA PIG CEREBRAL SLICES IN VITRO. K.K. Patel, J. F. Hartmann and M. M. Cohen, Dept. Neurol. Sci., Rush Med. Coll., Chicago, 60612

The effect of pH in the range of 6.2 to 9.0 on in vitro rates of O_2 and glucose utilization as well as on the ultrastructure of cerebral tissue was studied. Guinea pig cortex slices were incubated at 37°C in 31 mM-K^+-phosphate medium. Control slices were incubated in medium at pH 7.4. Following results are expressed as per cent deviation, in rates of O_2 and glucose consumption in acidic and basic media, from those at pH 7.4.

µmol/g/h	pH 6.2	6.4	7.0	8.4	9.0
Oxygen	-26.1	-19.3	-10.4	+2.1	+0.6
Glucose	-60.5	-66.8	-10.2	+20.1	+12.8

The data indicated that (1) Metabolic rates decreased during acidic incubations and increased during basic incubations (2) Effect of acidic pH was greater than an equal change in pH from 7.4 toward the basic (3) Both acidic and basic media affected glucose consumption to a higher degree than O_2 uptake. Ultrastructural changes from relatively normal structure involved principally swelling of astrocytic and neuronal cell bodies and processes. As with the chemical effect, acidosis had much more severe effect on the fine structure than alkalosis. Accompanying the cellular swelling a general loss of cytoplasmic density occurred at low pH, whereas density was preserved at basic pH despite swelling of contained mitochondria and cisterns of endoplasmic reticulum. Extracellular space was enlarged throughout the pH range studied. In conclusion, from pH 7.0 to 6.2 the glycolytic and structural effects were progressively more severe and at pH 6.2 the fine structure showed gross deterioration.

5.13 AGE-SPECIFIC SUSCEPTIBILITY OF THE RAT BRAIN TO VIRAL INFECTION.

Andrew A. Monjan*, Neal Nathanson, Gerald A. Cole*, and Donald H. Gilden*.
Dept. Epidemiology, Sch. Hyg. & Pub. Hlth., JHU, Baltimore, Md. 21205.

Changes in susceptibility to lymphocytic choriomeningitis (LCM) virus infection of various nuclei in the developing rat brain were systematically studied by direct immunoflourescent staining. In the neonatally infected rat, LCM virus produces a non-fatal and long lasting infection of the central nervous system (CNS) which is generally not cytopathic. As such, it is a valuable model in determining regional susceptibilities of brain areas to viral infection. Litters of rats were inoculated with a standard dose of LCM virus at various postnatal ages and were sacrificed at periodic intervals after infection to determine the distribution of viral antigen. This distribution was found to be primarily determined by the age at inoculation of the virus and not by the duration of infection. Areas of the brain which showed high levels of immunoflourescence were the granule cell layers of the cerebellum, hippocampus, hypothalamus, periventricular region, and the olfactory bulb. Cells in these areas have been shown to undergo postnatal replication and migration. These cells were found to be insusceptible to infection in older animals, at a time when migration has ceased. Once infected, viral antigen could be detected for at least several months. These studies indicate that cellular systems within the CNS have a susceptibility to LCM virus which is dependent upon their developmental state at time of infection. It is possible that such a model could be used to identify cells in studies of CNS organogenesis and to determine whether these infected brain regions function normally.

Session 6

6.1 MOLECULAR BASIS OF LEARNING AND MEMORY. Edward M.Kosower, Dept.Chem.,State Univ. New York, Stony Brook, N.Y. 11790 (SPON: S. H. Snyder)

Disulfide bonds are implicated as the storage element in labile memory and synaptic expansion through addition of synaptomeric protein is suggested as the storage mode for permanent memory. Treatment of frog myoneural junctions with the thiol-oxidizing agent, "diamide"($(CH_3)_2NCON=NCO-N(CH_3)_2$), produces a dramatic increase in MEPP rate and in the size of the EPP.(R.Werman,P.L.Carlen,M.Kushnir, and E.M.Kosower,(Nature,in press). From this and other facts, Werman and Kosower(Nature,in press) derived a microscopic theory of transmitter release, in which contraction of presynaptic vesicle sites led to transmitter release. The contraction is produced by Ca^{++} in normal depolarization and by disulfide formation in diamide-induced release at dithiol sites. We propose that the Ca^{++}-dithiolate salts can be oxidized by intraneuronal glutathione disulfide(GSSG) to yield a disulfide at the vesicle release site(VRS). The number of VRS-disulfide links can be estimated as a small integer per neurone for each stimulus trace, if 10^2 reverberations are included. The VRS-disulfides can be repaired either by reaction with glutathione(GSH) to form the normal state or by reaction with a synaptomeric protein and then GSH to produce an expanded VRS, i.e., an expanded presynaptic site. Possible postsynaptic effects have not been considered. Given our calculations, reverberations emerge as an extremely important factor in efficient learning and memory formation.

6.2 UCB 6215 AND METAMPHETAMINE EFFECTS ON ACQUISITION. Otto L. Wolthuis*. (SPON: W. L. Byrne). Medical Biological Laboratory TNO, Rijswijk, The Netherlands.

The behavioral effects of UCB 6215 and metamphetamine were studied in rats. When injected 30 minutes before training, both drugs considerably enhanced acquisition in a Y-maze and an automated drinktest. Memory disruptive effects of electroconvulsive shock and pentylenetetrazole treatment after one trial passive avoidance learning were not affected by UCB 6215; nor was Y-maze learning if UCB 6215 or metamphetamine was injected daily immediately after training. When fully trained animals were injected twice daily during a period of rest, results of retention tests 24 hours after the last injection were not different in UCB 6215, metamphetamine or saline-treated animals. However, when retention tests took place under the influence of these drugs injected 30 minutes in advance, scores in the metamphetamine-treated groups were much higher, whereas they were equal in UCB 6215 and saline-treated groups. By a newly developed technique, automatically scored horizontal movements and rearing appeared not to be affected by UCB 6215; metamphetamine, however, increased both. "Flinch" thresholds as a result of footshock were not altered by UCB 6215 and were almost significantly elevated by metamphetamine. From these results it is concluded that UCB 6215 does not enhance acquisition by its effects on consolidation, memory decay or retrieval. Neither does this drug act as a CNS stimulant. It seems, therefore, that UCB 6215 does enhance acquisition through its effects on registration mechanisms. Although responsiveness to footshock is not affected, preliminary results suggest that the drug exerts its effects on acquisition through its action on visual registration.

6.3 RESISTANCE OF FLUROTHYL-INDUCED RETROGRADE AMNESIA IN CHICKS TO THE REMINDER EFFECT. Arthur Cherkin. VA Hospital, Sepulveda, Ca. 91343 and UCLA School of Medicine, Los Angeles, Ca. 90024.

Retrograde amnesia (RA) provides the major experimental evidence for the memory consolidation theory but reminder-stimulated restoration of memory has been interpreted as negating the consolidation interpretation of RA induced in foot-shocked rodents by electroconvulsive shock (ECS) [SCIENCE 169:683, 1970]. We investigated the generality of the reminder effect using one-trial learning of peck suppression in the neonate chick (N=459), with RA induced by strong and moderate flurothyl treatments. Suppression training was effected by allowing spontaneous pecking at a target coated with a strongly aversive liquid, methyl anthranilate (MeA). Four min later, RA was induced by a strong amnesic treatment (inhalation of 1.7% v/v flurothyl vapor for 8 min). A retention test 24 hr post-training showed RA in 94% of the chicks; these received a concurrent reminder since the test target that they pecked was coated with a moderately aversive liquid, MeA diluted 1:400 in water. A second retention test 48 hr post-training showed no restoration of memory. To enhance sensitivity to any reminder effect, the RA treatment was moderated by halving the flurothyl concentration and delaying its administration, thereby inducing RA in only 62% of the chicks. Also, the reminder was delayed for 2 hr after the 24-hr test. Under these conditions, the 48-hr test revealed a weak restoration of memory. The latter may reflect the summation of two sub-threshold engrams: (1) a partial engram of the original training that survived moderate RA treatment and (2) a residual weak engram of the reminder treatment. This interpretation appears compatible with the rodent results and suggests that the reminder effect does not necessarily negate consolidation theory; rather, it adds to the evidence that ECS typically induces only partial RA.

6.4 BRAIN SEIZURE ACTIVITY AND RETROGRADE AMNESIA IN RATS. Steven Zornetzer* and James L. McGaugh. Dept. Psychobiology, Univ. Calif., Irvine. 92664.

In a recent series of experiments we investigated the relationship between electrical stimulation of frontal cortex and retrograde amnesia (RA). Frontal cortex-initiated primary afterdischarge (PAD) activity was always a sufficient condition for subsequent RA. Rats received different intensities of frontal cortex stimulation immediately following an aversive experience (shock). We found an inverse relationship between motivational intensity of the aversive experience and frontal cortex-induced disruption. Thus, under learning conditions of weak motivational intensity, all frontal cortex current intensities, at brain seizure threshold and above, produced complete RA. There was no current intensity-RA gradient. In contrast, under conditions of strong motivational intensity there was a graded relationship between current intensity (and concomitantly the severity of the resulting brain seizure) and RA magnitude. Further, EEG analyses suggested that the spontaneous secondary afterdischarge (SAD) contributed to the RA associated with the PAD. Reduced silver stains indicated that the region of frontal cortex stimulated was motor cortex. In addition to the classical motor projection system, however, collateral fibers were found leaving the cerebral peduncle at the rostral portion of the substantia nigra and terminated in the ventral tegmental region of the midbrain. Bilateral bipolar electrical stimulation of this region of midbrain indicated that RA resulted only if the brain's response to the stimulation included both a PAD and SAD. Midbrain-elicited PADs alone were not sufficient to result in RA. These data suggest that 1) under certain conditions brain seizures and RA can be uncoupled, and 2) electrical stimulation of ventral tegmental midbrain was less efficient in producing RA than similar stimulation of frontal cortex. Neuroanatomical and electrophysiological implications of these data will be discussed.

6.5 CYCLOHEXIMIDE: DELAYED DEVELOPMENT OF AMNESIA FOLLOWING DIFFERENT LEVELS OF TRAINING. L. R. Squire and S. H. Barondes.
Dept. Psychiatry, Sch. Med., UCSD, La Jolla, Calif. 92037.

Mice given cycloheximide before receiving 15 or 21 training trials in a 2-choice, object discrimination task were totally amnesic 24 hours later. When 15 trials were given amnesia developed within 3 hours. In contrast, amnesia developed between 6 and 12 hours after training when training consisted of 21 trials. These results are difficult to reconcile with an "intermediate-term," protein synthesis-independent, memory process having a fixed lifetime of a few hours. The significance of these findings will be considered in the light of single and multiple trace theories of memory storage.

6.6 RNA METABOLISM IN GOLDFISH BRAIN DURING ACQUISITION OF NEW BEHAVIORAL PATTERNS. V. E. Shashoua, McLean Hospital Research Laboratory, Belmont, Mass. 02178 and Harvard Medical School, Boston, Mass. 02115, U.S.A.

Base composition measurements were used as a criterion of RNA changes in goldfish brain. The RNA synthesized during acquisition of new swimming skills was compared to RNA formed in a variety of behavioral situations including intense physical exercise, convulsive seizures, passive behavior, and under conditions of anoxia. RNA synthesized during acquisition of new behavioral patterns was found to have a uridine/cytidine ratio 20-80 per cent higher than that formed under non-learning conditions. A number of drugs, including dibutyl cyclic AMP, were also found to cause changes in the uridine/cytidine ratio in the newly synthesized RNA. A study of the pattern of RNA synthesis during the acquisition of new behavioral skills by sucrose density gradient analysis showed that a class of RNA molecules with a sedimentation constant of 13-14s was formed. The time course of the synthesis of this RNA and its breakdown was investigated. The RNA changes were produced by two behavioral situations; (1) during the process of acquiring new swimming skills and (2) as a result of attempts to master an impossible task. The results suggest that the modified RNA synthesis taking place during acquisition of new behavioral patterns is probably not specific with respect to the particular information content being stored. The changes appear to be required for the consolidation step of new information storage. (Supported by the Grant Foundation).

6.7 ACTIVITY IN GOLDFISH OF A SYNTHETIC LEARNING-LINKED RAT PEPTIDE. Rodney C. Bryant.
Univ. of Tennessee, Brain Research Institute, Memphis, 38103.

The isolation and synthesis of a molecule ("scotophobin," SP) formed in the brains of rats trained to avoid dark, and its reported activity in mice (G. Ungar et al., Nature, in press), raise the question of its activity in other vertebrates. Common goldfish (carrasius auratus), 7-10 cm in length, were injected intracranially with 25 nanograms SP or with control solution (C). To protect against SP storage degradation, methanol (0.125 µl/10.0 µl injection volume) was present in both solutions; dilution to volume was with distilled water. Among fish with no innate dark preference, light avoidance learning (begun 2 days post-injection and continued for 10 days) was inhibited in SP-injected fish compared with C fish, who learned normally; in dark avoidance learning, SP fish were superior to C fish, though differences were smaller. Among fish with innate dark preference, light avoidance learning was markedly stimulated in those injected with SP; but dark avoidance was markedly inhibited, this effect being overcome with prolonged training. In unselected fish overtrained to avoid light and then injected, extinction was inhibited in SP fish compared with C. In summary, the activity of SP in fish without dark preference, learning to avoid light or dark, may be considered consistent with its reported effect in mice, but in fish preferring dark, the effects are strongly reversed. An effect of methanol per se on vision is discounted in view of gross observation and differential performance among groups. Competition between SP, a rat peptide, and an analogous fish molecule, may be involved in some of the above conditions.

6.8 SPECIFIC MODIFICATION OF BEHAVIOR OF RECIPIENT GOLDFISH WITH BRAIN EXTRACTS FROM DONORS TRAINED ON AN APPETITIVE SHAPE DISCRIMINATION TASK. Ronald B. Hoffman* (SPON: W.G. Braud). Dept. Biophy. Sci., Univ. of Houston, Houston, Tex. 77004.

The specificity of behavioral modification through brain extracts in a shape discrimination task and the nature of the active substances mediating the phenomenon were investigated. 6-7 inch goldfish were trained to discriminate between an upright isosceles triangle and an inverted isosceles triangle for food reinforcement in each of two phases of the study. In phase I, a crude RNA extract was prepared from the pooled brains of each experimental group and a control group. In phase II, a protein extract, a dialyzate extract, and a retentate extract were prepared for each group. Extracts were injected intracranially into naive 3-4 inch goldfish which were tested at 24, 48, 72, 96, and 120 hr. following injection. Each recipient fish received ten non-reinforced test trials per day. Wilcoxon Matched-Pairs Signed-Rank tests were applied to the differences of preference scores over days compared to baseline measures. Recipient fish displayed significant shifts in shape preference which correlated with the training of the donors in both phases. The refined extracts used in phase II indicated that a complex of RNA and protein may be involved in the learning and retention of this task in goldfish.

6.9 MODIFICATION OF RECIPIENT BEHAVIOR BY INTRACRANIAL INJECTIONS OF EXTRACTS FROM BRAINS OF TRAINED DONOR GOLDFISH. William G. Braud. Dept. Psychol., Univ. of Houston, Houston, Tex. 77004.

Extracts rich in ribonucleic acid (RNA) and protein, prepared from brains of trained donor goldfish, were injected into naive recipient fish to determine whether recipient behavior would be modified in a manner consistent with the training of the donors. In Experiment 1, separate RNA-protein extracts were prepared from whole brains of fish which had received either (a) 11 days of acquisition training in a shuttle-box avoidance task, (b) 11 days of acquisition followed by 7 days of extinction training, (c) 11 days of "training" but did not learn the correct response (superstitiously learned "incorrect" behavior), or (d) no training whatever (naive control). The four types of extract were injected intracranially into four groups of 8 naive recipient fish which were tested via nonreinforced "acquisition" trials 1, 2, 3, and 4 days after injection. One and two days after injection, recipients of acquisition extract avoided significantly more frequently than recipients of the other three extracts, which latter did not differ among themselves. In a second phase, either acquisition, extinction, or naive extracts were injected into three groups of 8 fish which had already partially acquired the response (65% correct responding). These recipients were given "extinction" test trials 1, 2, and 3 days after injection. During extinction, recipients of acquisition extract evidenced significantly less, and recipients of extinction extract significantly more extinction behavior than recipients of control extract. In two replications of Experiment 2, recipients of extract from fish whose striking response had been habituated for 8 days showed significantly fewer striking responses on the first two of four post-injection days than did recipients of control extracts. The combined results of these experiments suggest specific modification of recipient behavior via brain extracts from trained donors.

6.10 PHOSPHORYLATION OF NUCLEAR PROTEINS DURING AVOIDANCE BEHAVIOR OF RATS. Barry J. Machlus*, John Eric Wilson, and Edward Glassman. Dept. of Biochemistry and The Neurobiology Program. University of North Carolina, Chapel Hill, North Carolina, 27514.

Previous work in this laboratory has shown an increase in the incorporation of uridine into nuclear RNA, polysomal RNA and polysomes in the brains of mice (Zemp, et al., PNAS 55:1423, 1966, and Adair et al., PNAS 61:606, 1968) or rats (Coleman, et al., Brain Res. 26:349, 1971) during 15 min. of avoidance training. In light of recent ideas concerning the possible functions of nuclear proteins, the incorporation of orthophosphate into the proteins from isolated nuclei of rat brain cells during avoidance behavior was investigated. One rat of a pair was injected intracranially with ^{32}P phosphate while the other rat was injected with ^{33}P phosphate. Thirty min. later one of the rats was randomly selected to receive 5 min. of avoidance training, while the other served as a quiet control. The animals were sacrificed after training and the brains were combined and homogenized. Nuclei were extracted in 0.2 N HCl and the proteins were pptd. from the extract by addition of acetone. Proteins were then dried and resolved by chromatography on Amberlite IRC-50, using a gradient of guanidinium chloride. Four main peaks appeared in the eluate. The first consisted of non-histone nuclear protein (RP), and there was approx. 100% greater phosphorylation of these proteins in the trained than in the quiet rat. Further fractionation of RP showed that only some of the components were phosphorylated, and after proteolysis nearly all of the increased incorporation of phosphate was found in phosphoserine. Dissection of the brain indicated that the RP response occurred in the nuclei of the basal forebrain. Further behavioral studies on performing, extinguishing, and prior trained rats all indicated an increase in labeled phosphate in the RP in trained rats when compared with quiet control rats, whereas shock alone did not elicit a response.

6.11 BRAIN PROTEIN SYNTHESIS AFTER ELECTROSHOCK. Adrian J. Dunn. Dept. Biochem. & Neurobiology Program, Univ.N.C., Chapel Hill, 27514.

Brain protein synthesis was estimated by the incorporation of intraperitoneally injected (U-^{14}C)leucine in a 5 min pulse after a single electroconvulsive shock (ECS) in male Swiss Webster mice. Immediately after the ECS there was a ca. 50% decrease in the incorporation corrected for free leucine pool labelling. The decrease recovered to about normal (sham-ECS controls) in 15 min. Occasional mice (ca. one third) showed increased incorporations 20-30 min after the ECS and the data suggest a slight stimulation 30-60 min. after the ECS. The leucine incorporation immediately after electroshock showed a linear correlation with the shocking current used. The presence or absence of convulsions did not distort this correlation. This shows that the inhibition of incorporation is not dependent on the convulsions *per se* and is therefore probably not due to anoxia. It is suggested that electroshock alters the ion balance of the brain and that this in turn affects protein synthesis which is known to be very sensitive to ion concentrations. The significance of this effect of electroshock is interpreted in relation to the characteristics its amnesic effect and those of other agents.

6.12 DENDRITIC SPINE FUNCTION AND SYNAPTIC ATTENUATION CALCULATIONS. Wilfrid Rall and John Rinzel*. NIH, Bethesda, Md. 20014.

The functional significance of dendritic spines is not yet known. Anatomical studies have shown that some neurons receive most of their synaptic contacts upon their dendritic spines (Colonnier, 1968), and that long, thin spine stems occur more frequently on distal dendritic branches of small caliber, while stubby spines occur more frequently on proximal dendritic branches of large caliber (Laatsch & Cowan, 1966; Jones & Powell, 1969; Peters & Kaiserman-Abramof, 1970). Does it not seem paradoxical that synaptic attenuation due to distal dendritic location is compounded with attenuation by high stem resistance? We have computed the effects of synaptic input received by a dendritic spine. Our neuron model consists of several idealized dendritic trees with passive membrane properties. Rigorous mathematical solutions (steady state and transient) were obtained for current injection at a single dendritic branch. These solutions were coupled computationally with a spine model whose spine-head membrane received synaptic excitatory conductance input. We varied the ratio, R_{ss}/R_{in}, of spine stem resistance to dendritic input resistance, over a wide range of values (0.01 to 100). Our results indicate that only a portion of this range is particularly favorable for adjustment of synaptic potency (i.e. contribution to somatic EPSP). Over this favorable range, we suggest that fine adjustments of the stem resistances of many spines, as well as changes in dendritic caliber (Rall, 1962), could provide an organism with a way to adjust the relative weights of the many synaptic inputs received by such neurons; this could contribute to plasticity and learning of a nervous system. It is interesting that resistance estimates for both thin, distal and stubby, proximal dendritic spines indicate that many R_{ss}/R_{in} values lie in this favorable range.

Session 7

7.1 CNS EFFECTS OF MELANOCYTE-STIMULATING HORMONE IN MAN. Abba J. Kastin, Marcos Velasco*, Lyle H. Miller*, David Gonzalez-Barcena*, William D. Hawley*, Kjell Dyster-Aas*, Andrew V. Schally*, and Luisa Parra*. VA and PHS Hosps., and Tulane and LSU Med. Schools, New Orleans, La.; IMSS, Centro Medico, Mexico, D.F.; and Univ. Lund, Sweden.

Experiments in animals indicate that administration of melanocyte-stimulating hormone (MSH) results in changes in the electroencephalogram (EEG) and learning behavior. Only one study reported CNS effects of MSH in the human being, and these were rather non-specific (Kastin et al., Lancet 1: 1007, 1968). The present investigation examined the changes produced by MSH in man with respect to the averaged somatosensory cortical evoked response (SER), reaction time, EEG, galvanic skin potential (GSP), and 2 tests of memory. Ten mg of synthetic alpha MSH was infused intravenously for 4 hours into 3 hypopituitary patients (2 hypophysectomized and 1 with Sheehan's syndrome) and 2 normal controls. The effects of threshold electrical stimulation of the median nerve were recorded over 3 cortical sites. In all subjects, the increase in SER, particularly the late components, was dramatic. In several cases, the SER could be seen directly in the EEG recording on single trials. Changes in SER after MSH administration occurred during attention and were not evident when the subject was relaxed or distracted by another task. There also appeared to be increased high voltage alpha activity in the EEG, decreased reaction times, increased GSP, and improvement in visual, but not verbal, memory. Infusion of 3-5 units of ACTH as a control did not produce any of the described CNS changes. Plasma cortisol levels at the completion of the MSH infusion were normal but did increase after appropriate ACTH stimulation, thus further ruling out any mediation of the adrenal gland. In summary, administration of MSH to man produced CNS changes which suggest increased attentiveness depending on the demands of the situation.

7.2 A SPECTRAL AND DISCRIMINANT ANALYSIS OF EEG ACTIVITY IN LESIONED AND NON-LESIONED HYPOTHALAMIC SITES. Fred Abraham, Martin Gardiner,* and Jerome Maderdrut.* Brain Research Institute, UCLA, L.A., California 90024

Previous cospectral work with learning studies had shown changes in 36-40 Hz phases and coherences involving hypothalamic areas in chronic cats. This experiment attempted to determine the extent to which this activity was local or remote by comparing monopolar to bipolar recordings, and by comparing cospectral, phase, and coherence measures within hypothalamus before and up to two weeks after lesioning medial and lateral areas contralaterally. Spectral and cospectral similarities, high coherences, and bipolar rejection of 36-38 Hz activity revealed a great pattern of homogeneity of activity throughout this area, whether generated locally or remotely. Discriminant analyses selected different measures depending on whether they were given immediate postlesion, final postlesion, or all postlesion conditions to compare with prelesion conditions. The types of variables selected as well as the relationships between the canonical variables revealed a pattern of induced slow wave and other changes after lesioning followed by recovery of most measures except monopolar coherences involving lesioned areas, suggesting generally that at least the high frequency activity is mainly remote or more pervasive than the locality of a particular electrode. Amygdala and pyriform areas are good possibilities; our research shows a good coherence to pyriform, and phase leads over hypothalamus, consistent with Freeman's (1969) earlier reports of slow wave conduction velocities within the pyriform (about 2mm/msec). The significance of these results is as much to show how randomized and validity checks on the discriminant procedure reveal its limitations as well as its potentialities, especially in cautioning against a current trend to reify the selected variables.

7.3 EFFECTS OF ELECTRICAL STIMULATION OF THE SEPTUM ON DRINKING ELICITED FROM ELECTRICAL STIMULATION OF THE HYPOTHALAMUS. G. J. Mogenson, W. Sibole* and J. J. Miller*, University of Western Ontario, London, Canada.

Drinking was induced in rats when stimulated (rectangular pulses: duration 0.1 msec, 50 Hz) by means of chronic electrodes implanted in the hypothalamus. A second chronic electrode was then implanted in the septum of each rat. Evoked potentials (E.P.) were recorded from the hypothalamic electrode to septal stimulation as the septal electrode was placed stereotaxically to ensure that there was a functional link between the two electrodes. The E.P.s had two main components with latencies of 10-14 and 18-23 msec. In subsequent behavioral tests, beginning one week later, a pulse of stimulation was delivered to the septum 5 msec prior to each pulse of stimulation to the hypothalamus. Drinking induced by hypothalamic stimulation was facilitated in most of the animals when accompanied by septal stimulation, although in three cases septal stimulation reduced water intake. When septal stimulation facilitated drinking the septal electrodes were in the region of the dorsal fornix and the 10-14 msec was prominent in the E.P., whereas when septal stimulation suppressed drinking, the septal electrodes were at more ventral sites in the vicinity of the bed nucleus of the stria terminalis and the 18-23 msec component was prominent in the E.P. It is concluded that septal stimulation both facilitates and inhibits drinking elicited by hypothalamic stimulation and it appears that the effects are mediated by different pathways, facilitation of induced drinking by means of the fornix and suppression of drinking by the stria terminalis.

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7.4 DRINKING BY RATS FOLLOWING LATERAL HYPOTHALAMIC DAMAGE. Edward M. Stricker. Dept. Psychol., Univ. Pittsburgh, Pittsburgh, Pa. 15213.

Bilateral destruction of the lateral hypothalamus of rats is usually followed by prolonged periods of adipsia, following which most animals eventually resume water drinking. The basis for the recovery of drinking still is uncertain, although it is generally believed that rats recovered from lateral hypothalamic damage ("recovered laterals") are not responsive to physiological stimuli for thirst but instead respond to oropharyngeal sensations, associated with the consumption of dry food, that result from a presumed impairment of salivary flow. The present findings indicate that recovered laterals are, in fact, responsive to various thirst stimuli. For example, they drank increased amounts of water when they were made hypovolemic by subcutaneous treatment with a hyperoncotic colloidal PEG solution, or when circulating levels of angiotensin were increased following infrahepatic ligation of the inferior vena cava. However, their drinking responses, although substantial, were sluggish and generally were smaller than those of normal control rats given identical treatments. Furthermore, recovered laterals did not increase drinking following i.p. injection of hypertonic NaCl solution, as did control rats. It thus seems doubtful that systemic dehydration, as produced by feeding, contributes significantly to their ad libitum water intake since recovered laterals mostly drink in proximate association with meals. On the other hand, water drinking is not needed for swallowing dry food, as has been suggested previously, since, unlike totally desalivated rats, recovered laterals ate in the absence of drinking water and did not punctuate their feeding with frequent drinking episodes when water was available. Instead, it is suggested that lateral hypothalamic damage may cause food-associated drinking by disrupting the reflex secretion of saliva due to food stimuli.

7.5 THE ELUCIDATION OF HYPOTHALAMIC CONTROL OF FEEDING WITH C^{14} TRACER TECHNIQUES. Jaak Panksepp* (SPON: J.D. Davis). Worcester Foundation for Experimental Biology, Shrewsbury, Mass. 01545.

After injection of C^{14}-D-glucose, radioactivity was found to decrease more slowly in the ventromedial (VMH) than the lateral hypothalamus (LHA) of the rat. That this difference has behavioral significance is indicated by the finding that intraperitoneal injections of C^{14}-glucose, which depress feeding more than equivalent intragastric injections, lead to higher levels of radioactivity in the VMH than do intragastric injections. Diabetes induced by alloxan attenuates the increased incorporation of C^{14} in the VMH, suggesting that insulin sensitive cells in the VMH mediate adjustments of feeding as a consequence of intracellular nutrient metabolism. The integration of nutrients by VMH cells probably mediates long-term regulation of food intake rather than short-term satiety, for direct injections of glucose and/or insulin into the VMH depresses daily food intake but not the size of immediate post-injection meals. Similarly, VMH lesions affect long-term adjustments of feeding rather than post-meal satiety (Panksepp, PHYSIOL BEHAV 7:In Press, 1971). Presently we are attempting to identify the substance(s) which account for the increased incorporation of C^{14} in the VMH after radioactive glucose loads.

7.6 EFFECT OF HABENULAR LESIONS ON FOOD ODOR PREFERENCE AND FOOD CONSUMPTION IN RATS. Lyle J. Rausch*, Rebecca Rausch* and Charles J. Long. Dept. Psych., Memphis State Univ., Memphis, Tn. 38111.

Recent data have implicated the habenula in food and water consumption. The present study examined the effects of habenular lesions on (1) food consumption, and (2) preference for food odor. Twenty rats were placed on a 1-hr daily feeding schedule of powdered Purina lab meal with water always available. Food consumption data was obtained by weighing food cups and spillage before and after feeding. Food-odor preference was measured in a double-lever situation where either odor of wet mash or air presentation was contingent upon a lever press. Preference was evaluated in 3 sessions: prior to surgery, 3 days post-surgery, and 10 days post-surgery. After collection of pre-surgical data, 10 rats received bilateral habenular lesions and 10 rats were sham-operated. Following surgery habenular rats were found to have a dramatic and significant decrease in food consumption accompanied by weight loss while controls maintained normal weights and consumption rates. However both groups demonstrated a significant preference for food odor over air in the 2-lever situation. Analysis of responses during preference testing indicated that decreases in food consumption (weight loss) resulted in greater motivation for food odor. Thus it appears that although the sensory (olfactory) and motivational aspects of food consumption are intact in rats with habenular lesions, consumption of powdered food declines. This may be due to either an impairment of motor capacities or some reduction in integrative function of the habenular nuclei with respect to the many facets of consummatory behavior.

7.7 A CENTRAL CIRCUIT INVOLVED IN CONTROL OF GASTRIC SECRETION. M. Kadekaro* and C. Timo-Iaria* (SPON: R.A. Bernard). Dept. Physiol., Mich. State Univ. and Univ. of Sao Paulo (Brazil).

The site of action of 2-deoxy-d-glucose (2-DG) responsible for the gastrosecretory response was investigated in 102 cats with implanted cannulae for chronic collection of gastric juice. Intercollicular decerebration suppressed water and pepsin responses to 60 mg/kg of the drug and strongly reduced acid secretion. The latter was elicited by 100mg/kg. Bilateral destruction of the medial forebrain bundle (MFB) area in hypothalamus provoked aphagia and almost abolished volume and pepsine response; acid secretion was less affected. Bilateral lesion of globus pallidus also strongly reduced volume and pepsin responses whereas acid secretion was only delayed. Lesioning areas which contribute to the MFB did not impair response to 2-DG. Topical stimulation of the MFB area with 2-DG caused secretion to occur but stimulation of the globus pallidus was ineffective. These results lend support to previous statements that the lateral hypothalamus contains neurons (receptors) sensitive to lack of metabolizable glucose and suggest that their excitation provokes gastric secretion by activation of a reflex arc whose efferent side is located in globus pallidus. The neural control of secretion seems to be differentially organized as to water, pepsin and acid. The lower brain stem probably also contains receptors sensitive to lack of glucose and more involved in control of acid secretion than of pepsin and water.

7.8 IMMEDIATE LIPEMIC RESPONSE TO CEREBRAL ACTIVITY. James W. Correll, and Roger W. Countee. Dept. Neurol.Surg., College of Physicians & Surgeons, Columbia University, 10032

Cerebral activity evoked by electrical stimulation (stim) of certain basal diencephalic and limbic structures in chronic unanesthetized dogs and cats results in a dramatic increase in absorptive lipemia (Correll, Nature,223:415,1969) and the present intent is to report the results of continued investigations. The animals are prepared with stereotoxically implanted stainless steel bipolar electrodes insulated to their tips and stim accomplished by delivering a 7.5 to 15V biphasic 0.4 ms. square wave pulse at a frequency of 50/sec. It is shown that the increase in lipemia, usually grossly visible as increased plasma milkiness or turbidity (turb), can occur within seconds and is associated with an increase in plasma triglyceride concentrations (trigl), decrease in free fatty acids (FFA) but no change in phospholipid or cholesterol. The magnitude of the increase in turb and in the trigl is not consistently correlated, suggesting that while the trigl may be important in the turb response other factors also participate. It is shown that cerebral stim, in large part, promptly reverses the lipemic-clearing effect of heparin, suggesting an effect on the lipoprotein lipase enzyme system. The lipemic response can be elicited under chloralose anesthesia, but is prevented by pentobarbitol. It has been found that the lipemic response can be elicited in the starved state with an increase in the plasma trigl and a decline in FFA but with little or no change in turb. Adrenalectomy and hypophysectomy does not prevent the response. Stim of several sites with known hypothalamic connections have elicited the lipemic response. In the hypothalamus it appears that active sites are well localized, with closely adjacent areas being inactive. It is concluded that the CNS is able to exert a profound and almost instantaneous influence on the circulating lipids.

7.9 ANALYSIS OF THE EFFECTS OF POSTERIOR HYPOTHALAMIC LESIONS ON COPULATORY BEHAVIOR OF THE MALE RAT. Anthony R. Caggiula*, Seymour M. Antelman* and Michael J. Zigmond*(SPON: Edward M. Stricker). Dept. Psychol., Univ. Pittsburgh, Pittsburgh, Pa. 15213.

Lesions of the posterior hypothalamus in the area of the medial forebrain bundle (MFB) reduce or abolish copulatory behavior of the male rat. Several hypotheses were tested regarding the nature of this copulatory deficit. The pattern of sexual loss indicated impairment of the initiation component of copulation. However, an hypothesis based on reduction of "non-specific arousal" was found to be untenable following several manipulations which increased behavioral arousal but did not reinstate copulation. Manipulations included handling of the animal, replacement of the female and tail shock. Attempts were made to reinstate copulatory behavior by reversing the deficits in biogenic amines which accompany MFB lesions. Lesions were also made in the locus ceruleus and the raphe area in order to determine the extent to which a particular biogenic amine may have contributed to the effect obtained. Additional experiments were done in an effort to mimic the effects of electrolytic lesions by selective pharmacological manipulation of endogenous biogenic amines. Selective lesioning of catecholamine-containing neurons in the CNS was accomplished by intraventricular administration of 6-hydroxydopamine. Depletion of brain catecholamines without the use of lesions was obtained by administration of alphamethylparatyrosine.. Brain serotonin was depleted through the use of parachlorophenylalanine. Detailed behavioral, anatomical and biochemical analyses of effective and ineffective lesions were included.

7.10 SEXUAL BEHAVIOR EVOKED BY HYPOTHALAMIC STIMULATION IN UNRESTRAINED MONKEYS.' Adrian A. Perachio and Margery Alexander. Yerkes Regional Primate Research Center, Emory University, Atlanta, Georgia 30322.

Sexual behavior was evoked by remotely controlled electrical stimulation of the hypothalamus in unrestrained male monkeys (Macaca mulatta). The evoked response occurred as a stimulus related effect. Most mounts were accompanied by pelvic thrusting, and a series of stimulations produced ejaculation. The mean number of thrusts per stimulated mount exceeded the normal thrust rate. The number of mounts and number of ejaculations were significantly increased over control values. The interval between ejaculations was significantly shorter for evoked than for spontaneous sexual performance. Social variables qualitatively and quantitatively affected the nature of the responses. Inhibition of evoked and spontaneous sexual behavior was observed when a dominant male was present. Evoked mounting would occur with the female that was preferentially chosen during spontaneous behavior. Responses evoked from a number of other hypothalamic and extrahypothalamic sites will be discussed. A film will demonstrate the described responses.

7.11 BIOCHEMICAL AND RADIOAUTOGRAPHIC STUDIES OF ^{3}H-CORTICOSTERONE BINDING TO HIPPOCAMPUS. Bruce S. McEwen, John Gerlach,* and Darcy B. Kelley.* The Rockefeller Univ., New York, N. Y. 10021.

In virtually all steroid hormone target tissues which have been studied so far, there are proteins which bind the appropriate hormone in a stereospecific manner and which are located in the cell nucleus. We have found such binding sites which bind radioactive corticosterone (McEwen et al., Brain Res. 1970, 17, 741) and estradiol (Zigmond and McEwen, J. Neurochem. 1970, 17, 889) differentially distributed in the rat brain. The highest concentration of corticosterone-binding sites occurs in the hippocampus, and these sites have been studied by biochemical techniques and radioautography. Subcellular fractionation of hippocampus labeled *in vivo* by ^{3}H-corticosterone reveals that binding is due to a soluble protein and to proteins tightly bound to the cell nucleus. The soluble protein is distinguishable from transcortin (corticosteroid-binding globulin) in serum on the basis of precipitation by protamine sulfate, sedimentation properties, and movement on polyacrylamide gels. The relative rates of exchange of bound ^{3}H-corticosterone with excess unlabeled corticosterone *in vitro* show serum >> brain soluble > brain nuclear. Radioautography reveals that neurons in Ammon's horn and dentate gyrus are heavily labeled with radioactivity injected as ^{3}H-corticosterone, and that the heaviest labeling occurs over neuronal cell nuclei. The labeling pattern among these neurons is heterogeneous: high in some neurons and low in others, and high in occasional clusters of neurons. This is particularly evident in the CA2 region where a heavily-labeled cluster of neurons occurs. Data from two other small mammals, the mouse and hamster, indicate that the hippocampus in these species is also the principal site of ^{3}H-corticosterone binding in the brain. (Supported by grants NS 07080 and MH 13189 from the USPHS.)

7.12 BIOSYNTHESIS OF THE HYPOTHALAMIC TRIPEPTIDE-AMIDE TRF. Roger Guillemin, The Salk Institute for Biological Studies, La Jolla, California, 92037.

The molecular structure of hypothalamic TRF (Thyrotropin Releasing Factor) has been established as pyroGlu-His-Pro-NH_2 (C.R.Acad.Sci.(Paris), 269, 1870, 1969; Nature, 226, 321, 1970). To elucidate the mechanisms of biosynthesis of this tripeptide, in several experiments 1 or 2 fragments of rat ventral hypothalamus (2-5 mg wet weight) were minced and incubated (37.5C, 60 min) in Eagle's fluid added with 100 μCi ^{3}H-Pro (45 Ci/mM). At the end of the incubation period, tissues and fluids, following addition of 1-5 μg synthetic TRF as carrier, are extracted in 90% EtOH, the dry extract dissolved in H^2O for chromatography on a microcolumn (3x2mm) of Norit; most of the free ^{3}H-Pro is not retained and TRF is eluted by 100 μl 45% EtOH. Following reduction of the volume by evaporation to 20 μl, aliquots are chromatographed on successive TLC's (silica gel) in several systems or on a microcolumn (2 mm x 20 cm) Sephadex G-25 in 0.2 N HOAc. ^{3}H-Pro is incorporated in several peptides separating on TLC; furthermore, in all cases, some ^{3}H-Pro is located in a (ninhydrin -, Pauly +) zone corresponding to the TRF carrier. The incorporation of ^{3}H-Pro in the TRF zone is not prevented by preincubation of the hypothalamic tissues with 10 or 100 μg/ml cycloheximide (30 min), prior to addition of ^{3}H-Pro. These results are compatible with the proposal that TRF (pyroGlu-His-Pro-NH_2) is synthesized in hypothalamic tissues by a mechanism not necessarily involving a ribosomal transcription.

7.13 CHARACTERISTICS OF THE HERING-BREUER REFLEXES DURING EXPIRATION IN THE CAT. C. K. Knox, Laboratory of Neurophysiology, Univ. of Minnesota Medical School, Minneapolis, Minnesota 55455, USA.

The use of controlled pulse and step changes of lung volumes during expiration in cats, both lightly and deeply anesthetized with sodium pentobarbital, shows that there are two central components of inspiratory inhibition in response to lung inflation. The first component has the characteristics of an almost ideal integration of receptor feedback and is suppressed by deep levels of anesthesia. The second is less influenced by anesthetic, is phasic and is nonlinearly related to lung volume. Lung inflations produce expiratory prolongation when applied only during the first 70% of the expiratory phase, this fraction being independent of both level of anesthesia and alveolar CO_2 tension. Controlled deflations shorten expiration so long as they fall within approximately the first 85% of a normal expiratory time and reveal an on going linear decay of inhibition of inspiratory activity. Neither deflations nor inflations during an expiration influence the following inspiration. The results support the hypothesis that within the brain stem there is a linearly increasing and decreasing inhibition of inspiratory neurons. Inflation receptor activity would appear to act to further inhibit inspiratory neurons through rather direct and indirect mechanisms, the former possessing phasic characteristics while the latter might be associated with pontine phase-spanning neurons. Further, inflation receptor input appears to be inhibited within the brain stem by central activity occurring late in expiration. (Supported by NIH Postdoctoral Research Fellowship 1 F0 2 NS41662-01 NSRB.)

Session 8

8.1 DIGITAL COMPUTER SIMULATION OF LARGE NERVE NET MODELS OF BRAIN CORTICES. Larry D. Wittie* (SPON: Ramon E. Moore)
Computer Sciences Department, Univ. of Wisconsin, Madison, 53706

A system to simulate the firing interaction of nets of up to 8000 neurons, interconnected by up to 40,000 synapses of which 500 may contact the dendritic tree of any one neuron, has been coded in Fortran on the Univac 1108. Two tables define such a nerve net during simulation: an internal state table giving for each neuron its class, location, excitation, refractoriness, and the shape of its post firing refractory curve; a connection table giving for each neuron the location, strength, activity level, propagation delay, and dendritic attenuation characteristics of all of its axonal (pre-) and dendritic (post-) synapses. Experiments with simple planar nets, in which each neuron contacts half of its nearest 25 neighbors, showed that inhibitory neurons are needed for the net to remain active at less than maximal levels. Without inhibition, activity in such a net rapidly dies out if it is below a critical level; activity above that level rapidly mushrooms until all neurons are firing as fast as their absolute refractory periods allow. To study nets organized more like real brain cortices, a general cortex initializer has been added to the simulation system. Given for each class of neurons in the cortical model the 3-D spatial distribution of its somas, the shape, extent, and synaptic density of its axonal and dendritic fields, and its firing/refractory characteristics, the system finds all synapses and calculates all the locations, delays, connections, and other entries in the two tables needed to simulate the model. This simulation system is currently being used to study how the cerebellar cortex acquires and executes learned motor reflexes.

8.2 EXCITATORY AND INHIBITORY INTERACTIONS IN LOCALISED POPULATIONS OF MODEL NEURONS. Hugh R. Wilson* and Jack D. Cowan. Dept. Theor. Biol., Univ. of Chicago, Chicago, Ill. 60637.

Coupled nonlinear equations are derived for the dynamics of spatially distributed populations of both excitatory and inhibitory model neurons. In the case of uniformly stimulated populations, phase plane and numerical methods are used to determine the nature of the responses. The results obtained show simple and multiple hysteresis phenomena, and limit cycle activities. Non-uniform stimulation results in spatially organised activities which generalise the purely temporal phenomena. The role of such activities in information processing is discussed.

8.3 A THEORY OF HIERARCHICAL ORGANIZATION IN PERCEPTION. Karl Kornacker* and Leo E. Lipetz. Dept. of Biophysics, The Ohio State University, Columbus, Ohio 43210.

A major problem of neuroscience is to develop a definition of hierarchical organization which: (1) defines the important phenomena at each organizational level of the nervous system, (2) provides the basis for a deductive theory of the interrelations between phenomena at different levels.

A satisfactory solution cannot be achieved unless the definition of each phenomenon specifies the lower level behavior necessary for the existence of that phenomenon. Such specification is particularly difficult in neuroscience because different sets of concepts and experimental methods are used to characterize the phenomena occurring at successive organizational levels of the nervous system.

A solution, based on the "theory of inherently macroscopic processes" (see reference), will be outlined. Examples will be given to show how the phenomena of pattern-sensitive perception can be related to a biophysical description of nerve membrane activity.

Reference: Theory of inherently macroscopic processes, with application to heat and active transport. Karl Kornacker, Nature 219, 1283-1284, 1968.

8.4 COMPUTER ANALYSIS OF ACTIVITY PATTERNS IN SINGLE RESPIRATORY CELLS. Charles L. Webber, Jr.* and Clarence N. Peiss. Department of Physiology, Loyola University, Stritch School of Medicine, 2160 South First Avenue, Maywood, Illinois 60153.

Current experiments in our laboratory are investigating the statistical firing patterns of single medullary units which exhibit an in-phase relationship with peripheral respiratory parameters. Experiments are carried out on spontaneously breathing cats. Single unit medullary recordings are made with metal microelectrodes. Peripheral respiratory parameters including airflow, intrapleural pressure and end expiratory pCO_2 are continuously monitored. All experiments are recorded on FM magnetic tape for subsequent data analysis on a Digital PDP-12 computer. Various experimental manipulations are performed in order to alter respiration rate and patterns, and these are repeated after bilateral cervical vagotomy. Data analysis includes generation of interspike interval histograms and frequency modulation curves of single medullary units. From the former, a hyperbolic relationship between modal firing times and respiration rate can be shown. The latter relates the time interval between spikes in a train and the sequence in which they occur in that train. The averaged data over many respiratory cycles demonstrate that respiratory trains exhibit an initial frequency increase, a plateau at maximum frequency, and final frequency decrease. An inverse relationship can be shown between respiration rate and the time for medullary units to reach maximum firing levels. Discharge patterns are significantly altered by bilateral cervical vagotomy. This procedure increases the correlation between respiration rate and time to reach maximum firing levels. This suggests that medullary unit discharge patterns are regularized by removal of vagal afferent feedback. *(Supported by HE 08682 and GM 999)*

8.5 CONDITIONAL PROBABILITY MATRIX—A METHOD FOR THE ANALYSIS OF INTERSPIKE INTERVALS. C. J. Sherry* and T. J. Marczynski, Dept. of Pharmacology, Univ. of Illinois at the Medical Center, Chicago, Illinois 60612.

The relationship between immediately adjacent interspike intervals (INT-I) was analyzed by generating a conditional probability matrix. This was accomplished in three steps by a program for the IBM computer. In the first step, the INT-I were read in milliseconds and stored. In the second step, a matrix was constructed in the computer such that the 'i', or column values, and the 'j', or row values, run from 1 to 1000 msec by steps of 10. One additional column and row was used to collect interval pairs in which one or both members of a pair had a value greater than 1000 msec. The INT-I were then read in and a one was added to the value of the cell whose name (i-j value) was equal to the value of two adjacent INT-I. If upon examining this 1000 by 1000 millisecond matrix it was noted that a particular square of 10 column-rows was differentially filled in over any other set, then the third step of this program was performed. A new matrix was generated such that the column and row values were increased by steps of 1 instead of 10 msec; e.g., if the first ten column-rows of the first matrix were filled more than any other set, then the matrix would have the value of 1 to 100 msec for the columns and rows by steps of 1. The data was read in again and the resulting matrix was examined to note any patterns in the filling of the matrix cells which reflect the firing patterns of the investigated neuron. The advantages of the proposed method over other currently used methods will be discussed. Supported by Grants from NIH NB-6385 and PHS MH-8396.

8.6 HUMAN EPILEPTIC NEURONS: COMPARISON OF INTERICTAL FIRING PATTERNS TO THOSE OF "EPILEPTIC" NEURONS IN ANIMALS. *William H. Calvin, George A. Ojemann, and Arthur A. Ward, Jr.* Department of Neurological Surgery, University of Washington School of Medicine, Seattle, Washington 98105

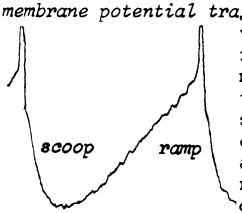
Human cortical neurons have been studied with extracellular single unit recording techniques prior to surgical excision of epileptic foci in more than a dozen patients, who were typically awake under local anesthesia. The interictal firing patterns of neurons in and near the electrographicly located epileptogenic focus demonstrate the high-frequency bursting behavior earlier seen in artifical "epileptic" foci in awake animals; they occasionally show the high-frequency spike trains which wax and wane, similar to data obtained in some anesthetized animal foci. Detailed analysis of several dozen human epileptic neurons was performed in order to compare their firing patterns to data obtained from monkeys in which chronic epilepsy had been produced by alumina (Calvin, Sypert, and Ward, *Exptl. Neurol. 21:535, 1968*). Not only are human epileptic and monkey "epileptic" neurons remarkably similar in the overall pattern of high-frequency (200-500/sec for 5-50 msec) bursts of spikes separated by variable interburst periods of silence or normal firing, but the detailed timing pattern within the bursts are similar. One of the most unique features of the awake monkey data is the "long-first-interval" burst where the first spike fluctuates in time relative to the rest of the spikes, which behave as a group. This unique pattern has now been seen on several occasions in human epileptic neurons. This suggests that the long-first-interval burst is not an artifact of the alumina method. Thus, human epilepsy and the alumina-induced "epilepsy" are similar not only in the chronic seizure disorder itself, but also similar at the level of the interictal firing patterns of the single cortical neurons themselves. [Supported by grant NS 04053 from the National Institutes of Health.]

8.7 FUNCTIONAL DEVELOPMENT OF INTRACORTICAL SYNAPTIC ORGANIZATIONS ACTIVATED BY INTERHEMISPHERIC AFFERENTS. Robert J. Shofer* and Dominick P. Purpura. Dept. Anat., Albert Einstein College of Medicine, Bronx, New York, 10461.

Transcallosal responses (TCRs) evoked in anterior suprasylvian gyrus of young kittens (<10 days old) exhibit restricted distribution indicative of limited intracortical spread of callosal projections. The prominent negativity of the initial component of the TCR elicited by weak stimuli is succeeded by a complex predominantly surface positive response following stronger stimulation even in very young kittens. Threshold responses to low-frequency (0.5 cps) stimulation are markedly facilitated for long periods following transient increases in stimulus intensity and resumption of minimal stimulation. This facilitation is evident before the second week and is characterized by enhancement and regularization of all components of the TRC. In contrast relatively small increments in stimulus frequency result in depression of TCRs which may be a prelude to convulsant activity. Intracellular and extracellular recordings reveal low frequency spontaneous and evoked discharges during TCRs during the first few postnatal weeks. IPSPs are prominent in the synaptic events elicited by interhemispheric afferents in very young kittens. Such IPSPs coincide with the surface negativity of TCRs in a manner similar to that of specific responses of immature sensorimotor cortex. The changing statistical properties of unit discharges and correlative transmembrane potentials, taken together with studies of the spatial distribution of TCRs are considered in relation to morphogenetic features of elements involved in the production of interhemispheric activities.

8.8 MEMBRANE POTENTIAL TRAJECTORY ALTERATIONS UNDERLYING MOTONEURON FIRING RATE CHANGES. *Peter C. Schwindt* and William H. Calvin.* Departments of Neurological Surgery and Physiology/Biophysics, University of Washington, Seattle, Washington 98105.

The rhythmic firing of cat spinal motoneurons to synaptic drive may be mimicked by injecting steps of transmembrane current. The initial firing rate adapts to a lower steady rate. For both rates, the plot of firing rate vs. current (the *f-I curve*) is piecewise linear over two regions: The primary range and, in some cells, a steeper secondary range. The *membrane potential trajectory between spikes* is characterized by the voltage scooping downwards after a spike and then rising linearly towards the firing level for the next spike. Omitting delayed depolarizations from the present characterizations, it may be said that such trajectories alter in two major ways to effect changes in the firing rate. Some rate changes are associated with alterations in the steepness of the ramp (its slope may be proportional to current). In other cases, the ramp does not alter with current strength; the depth and duration of the preceding scoop are altered when the firing rate is changed. The decline in firing rate during adaptation is typically effected by such changes in the scoop, with the ramps remaining superposable. In such cases, it may be said that the firing rate changes are correlated with events immediately following a spike rather than with how the firing level is subsequently approached. In those motoneurons with ramp slope alterations, they are most impressive at the lower firing rates. In motoneurons with a secondary range, trajectory alterations are more complex; however, rate changes are typically effected by scoop alterations. [Supported by NIH grants NS 04053 and GM 00260]



8.9 ELECTROPHYSIOLOGY OF THE PRIMATE CEREBELLAR CORTEX. James R. Bloedel, Richard S. Gregory* and Stephen H. Martin*. Depts. Physiol. and Neurosurg., Minn. Med. Sch., Minneapolis, Minn. 55455

The cerebellar cortex of squirrel monkeys was studied by recording unitary activity and field potentials evoked by electrodes placed on the cerebellar surface, in the cerebellar white matter, and in the inferior olive. The purpose of the experiments was to compare the interactions of neurons in the primate cerebellar cortex with those previously studied in cats. By analyzing the changes in the depth profile of the antidromic field response produced by a conditioning surface stimulus and by studying the responses of single Purkinje cells to the activation of parallel fibers, it was found that superficial stellate cells in the cerebellar cortex of primates may have a greater effect on the activity of Purkinje neurons than in the feline cerebellar cortex. As expected, the inhibitory action of basket cells was shown to be distributed lateral to the beam of activated parallel fibers. Of particular interest was the finding that the inhibition of the antidromic field response by a conditioning surface stimulus increased markedly as the electrode was moved toward and just past the end of the parallel fiber beam. At these same locations the surface stimulus evoked a negative field potential deep in the molecular layer whose latency was longer than that of the direct parallel fiber response. These data suggest that some fiber system other than parallel fibers may activate basket cells located in this position. It is tentatively suggested that these fibers may be the axons of Lugaro cells, since they contact these interneurons and project in the same direction as the parallel fibers.

8.10 SINGLE NEURON ACTIVITY IN THE CNS OF THE ACANTHOCEPHALAN MACRACANTHORHYNCHUS HIRUDINACEUS. Donald M. Miller, Tommy T. Dunagan* and Kenneth R. Hightower*. Dept. Physiol., SIU,

The CNS of the female Acanthocephalan was investigated to (1) delineate all the cells and nerves of the system, and (2) determine the activity of single neurons with respect to the ensemble. Potentials were detected from single cells using micropipette electrodes and from nerves using silver silver-chloride electrodes. After recording the potentials on magnetic tape, the cell was marked by iontophoretic injection of Procion Yellow dye(Dichloro-s-triazine). The activity of the cell which was identified by fluorscence microscopy of serial sections was then correlated with the potentials recorded from the nerves. The entire ganglion consists of 86 cells, and gives rise to 6 pairs of nerves containing a total of 72 neurons. The ganglion cells consist of several varieties of cells differentiated from one another by size, number of nuclei, number of nucleoli, granulation and their affinity for stains. Several cells have been injected by iontophoresis and this aspect of the work continues. However as more cells are marked, more axon-cell body connections can be determined and additional correlations can be accomplished. This CNS is perhaps the smallest with respect to number of cells and the inputs and outputs are restricted enough to allow for the analysis of the entire system as a 10X10 matrix.

8.11 INFORMATION TRANSMISSION IN AND BY A CRAYFISH

Dale Harris* and Lawrence Stark. University of California, Berkeley

Our experimental approach has been to measure information rate in a photoreceptor nerve channel and in the photokinetic behavioral responses of the crayfish mediated by that channel. Dispersion curves of conduction times were obtained for nerve pulses following short, medium, and long intervals. Similar statistical studies showed how probabilities of duration of walks and pauses in crayfish behavior were conditioned upon the seven light intensities used as input stimuli.

Mathematical communication theory developed by Shannon is used as the theoretical basis of the further analysis of our experimental results; these are presented as computed information rates and capacities. Information rates of 280, 140 and 80 bits/second were calculated for one centimeter of nerve channel for three static light intensities. After allowance for the two parallel channels and the total length of fiber involved in this system, capacity is 144 bits/second. Information theoretic calculations with respect to the behavioral responses shows a maximum information rate of approximately 0.1 bits/second.

The large discrepancy can partly be explained by experimental findings of lower capacities for sensory transducer and synaptic elements of the channel, as well as multiplexing of information on the nerve channel. Neurological signal processing probably utilizes a long 'b' code, such as average frequency, as discussed in an earlier paper postulating discrete codes.[1] It would be advantageous to drive the behavioral system with higher bandwidth inputs and to observe higher bandwidth responses. Interestingly, the time function of information rate during behavioral response showed significant time dependence; habituation and dishabituation are postulated as neurophysiological mechanisms underlying behavior in this crayfish system.[2]

1. L. Stark, Neurological Control Systems, Plenum Press (1968)

2. With partial support from NINDS Grant #NS08546

8.12 ELECTROPHYSIOLOGICAL ANALYSIS OF LOCAL REFLEXES IN A MOLLUSC.

David J. Prior. Dept. Biol., Univ. Virginia, Charlottesville, Va. 22903

The surf clam responds to weak tactile stimulation of the siphons with local muscular contractions. Stronger tactile stimulation elicits local reflex activity and, furthermore, siphon retraction. Only local reflex activity persists following severance of connections between the siphons and the central nervous system. Clusters of neuron somata occur at the peripheral branching points of the siphonal nerves. Intracellular records from these cluster cells indicate they are efferents to the siphon wall musculature involved in local reflexes. Cluster cells receive synaptic input from touch sensitive afferents. The neural correlate of the behavioral stimulus discrimination was obtained by simultaneous intracellular recording from pairs of cluster cells and efferents to the retractor muscles. The cluster cells produce action potentials at stimulus intensities sufficient to produce only excitatory post synaptic potentials (EPSP) in the retractor efferents. The values of spike threshold potential and rheobasic injected current for cluster cells were found to be lower than those for retractor efferents. Measurements of the 'central delay' between an extracellulary recorded input volley and onset of the EPSP in cluster cells indicate monosynaptic input. Thus with lower 'critical firing level' and monosynaptic input, the cluster cells are well suited for a role in the efferent limb of local reflexes. (Grant NS-04989 U.S.P.H.S. to DeForest Mellon Jr.).

8.13 CENTRAL INTERACTIONS AMONG TOUCH-SENSITIVE NEURONS IN THE SURF CLAM. DeForest Mellon, Jr. Dept. of Biol., Univ. of Virginia, Charlottesville, Virginia 22903.

The cell bodies of one population of touch-sensitive neurons (TSN's) in the surf clam are located in a defined region of the surface of the visceroparietal ganglion. Axons of these cells innervate the siphons and posterior mantle, and intracellular recordings of electrical activity have permitted analysis of their response characteristics and have revealed two kinds of interaction among individual TSN's. Each TSN possesses a restricted, well-defined receptive field, within which adequate stimulation generates bursts of nerve impulses which propagate toward the soma. Tactile stimulation of the siphon regions outside of this receptive field evokes bursts of small (1-3 mV) constant-amplitude depolarizing potentials in the impaled neuron. These responses apparently reflect impulse activity in one or more neighboring TSN's and, by various criteria, are attributed to a weak electrical coupling between the sensory neurons. Tactile stimulation over a much broader region generates inhibitory postsynaptic potentials in the TSN's. These are accompanied by a large, presumably chemically-mediated increase in the conductance of the postsynaptic membrane and can block invasion of the soma by an approaching nerve impulse. Both types of sensory cell interaction are presumably important in the integration of tactile input by the central nervous system and may complicate present interpretations of the physiological basis for behavioral habituation in molluscs. (Grant NS-04989, USPHS)

Session 9

9.1 INTRACELLULAR RESPONSES OF STRIATAL NEURONS TO PAIRED AFFERENT STIMULI. N.A. Buchwald, C.D. Hull and D.D. Price*. Dept. of Anatomy, Psychiatry, Mental Retardation Center, NPI, UCLA, Los Angeles, Calif. 90024

Intracellular recordings were made from striatal neurons in cats. Averaged synaptic responses of these cells were constructed by first filtering out action potential spikes by means of a low pass filter and then averaging the resultant potentials. Responses of more than 200 individual cells to stimulation of cortical, thalamic and brain stem sites and to peripheral stimuli were classified according to the sequence, duration and amplitude of postsynaptic potentials. Eighty percent of responses to these stimuli in striatal neurons consisted of EPSP-IPSP sequences. An exception occurred with stimulation of the region of the CM nucleus of the thalamus which evoked "pure" EPSPs in 40% of the cells recorded. Responses of the striatal neurons to temporally separated stimuli applied to the cortex and to one of the other sites were then studied. When cortical inputs competed with subcortical sites for regulation of the neuron, the cortex seemed to prevail. If the interval between the stimuli were such that the EPSPs coincided and therefore were not competitive, the amplitude of the resultant response was essentially a linear sum of the two EPSPs. However, if an excitatory response to a thalamic or nigral stimulus occurred during the IPSP phase of a cortically evoked potential the former was greatly reduced or failed to appear. In contrast, preceding thalamic or brain stem stimuli failed to inhibit the excitatory components of cortically evoked potentials regardless of the pairing intervals. The prepotence of cortical stimuli was particularly marked by their ability to abolish the "pure" EPSPs elicited by excitation of the centre median nucleus. It seems reasonable to suggest that afferent information reaching the striatum by way of the interlaminar thalamic nuclei may be modulated at the striatal level by corticofugal inputs.

Aided by USPHS MH07097, HD04612 and Cal. State Dept. of Mental Hygiene.

9.2 ACTION OF INTRAVENTRICULAR TETRODOTOXIN AND CELLULAR MECHANISM OF GENERATION OF EEG. Rafael Elul. Dept.Anat.,Univ.Cal.,Los Angeles,Cal.90024

Intraventricular injection of tetrodotxin (TTX) in 0.5-5 µg dose produces either complete or intermittent flattening of EEG over both hemispheres. Intracellular recordings from cortical neurons adjacent to the gross EEG electrode reveal normal spike firing which persists during EEG flattening. Although the firing rate is somewhat reduced during the episodes of EEG flattening, subthreshold wave activity continues on a level only slightly under that in presence of EEG. Moreover the intracellular inhibition of firing does not precisely coincide with flattening of the EEG. That these results do not represent a peculiar resistance to TTX of cortical neurons, is demonstrated in control experiments involving topical application of this drug in same concentration, leading to complete disappearance of all spike activity in cortex within 30-60 min.

These results indicate that the disappearance of EEG is not due to a direct effect of TTX; in intraventricular application the drug apparently acts on periventricular structures. Because subthreshold wave activity in single neurons persists during episodes of EEG flattening, it appears that the mechanism responsible for flattening involves modification of interneuron relations rather than action on individual generators of EEG. The present results may be interpreted to suggest that: (i) EEG is produced by synchronization of cortical neurons, and (ii) periventricular structures provide the synchronizing impulses. Taken together with previous results, the present data also suggest that although cortical neurons are synchronized in space, they are desynchronized in time, i.e. subcortical influence synchronizes from the total cortical population different groups of neurons in successive instants in time, perhaps resulting in "scanning" of the cortex as originally proposed by Pitts and McCulloch.

9.3 BASAL GANGLIA RESPONSES TO ANTIDROMIC PYRAMIDAL STIMULATION. G. Krauthamer. Department of Anatomy, Rutgers University Medical School, New Brunswick, N. J. 08903.

To determine whether selective stimulation of the corticospinal pathway evokes responses in the basal ganglia, the medullary pyramids were exposed by a ventral approach in cats anesthetized with Dial and immobilized with Flaxedil. A closely spaced array of bipolar concentric electrodes was used to systematically explore the basal ganglia and adjacent white matter for responses evoked by single shocks applied to the medullary pyramids. The antidromic response of the pericruiate cortex was monitored for comparative purposes. Single pyramidal shocks yielded the typical multiphasic cortical response; simpler, large amplitude potentials of short duration could also be recorded in portions of the internal capsule. Within the basal ganglia, prominent responses occured in the globus pallidus; small amplitude responses were dispersed throughout the striatum. In some striatal locations the initial, brief deflection was followed by a larger slow potential. The early striatal responses and the pallidal potentials had response latencies between 0.4 to 0.8 msec.; like the pericruciate response, they followed repetitive pyramidal stimulation at rates well above 100Hz. While a contribution by corticopinal fibers of passage cannot be entirely ruled out in every instance, these preliminary observations suggest that the corticostriatal projections consist, in part, of axon collaterals of corticospinal fibers. Pyramidal activity would thus be obligatorily relayed to portions of the extrapyramidal system. (Supported in part by NIH grant no. FR-05576.)

9.4 THE STATISTICAL ANALYSIS OF EVOKED POTENTIALS. Donald C. Martin Biomathematics Program, Statistics Dept., N.C. State University 27607

Several methods for the analysis of digitized evoked responses are considered. The basic procedure is to reduce the dimensionality of the signal record from the original 100 to 500 observations to a reasonably small vector, 10 to 50 elements, by specific linear transformations based upon least squares approximations. The suitability of the approximating function is checked by an analysis of the average evoked response. The transformed vectors are then suitable for analysis by several conventional multivariate statistical procedures. Experimental data will be used to illustrate these procedures.

9.5 A METHOD FOR COMPUTER ANALYSIS OF EEG DESYNCHRONIZATION. Zaven S. Khachaturian, Joyce L. Kerr, Henry Gluck+ and Joseph Schachter*.
Div. Child Psychiat., Univ. Pitt. Sch. Med., Pgh., Pa. 15213
+ Dept. Psychiat., Sch. Med., Case Western Reserve Univ., Cleve., O.

Often behavioral arousal is not well correlated with EEG desynchronization and the relationship between these two variables is not well understood. To further study this relationship a method was developed for on-line computer (PDP-12) analysis of levels of EEG desynchronization. At the beginning of a test the experimenter can specify epoch length, sampling rate, time window (which is moved) and its increment. During the specified time window the computer calculates a ratio which takes into account both the frequencies and the amplitude of the EEG. The window is incremented and a new desynchronization index (DI) is calculated. The same procedure is repeated through the entire length of the epoch. The DI is low when the EEG is made up of high voltage and low frequency activity, and it is high when the waves are of low voltage and fast frequency. This method of analysis has been used on three types of data. a) A parametric study was conducted where a sinusoidal signal simulated all possible combinations of EEG amplitude and frequencies. b) EEG recorded from indwelling electrodes in rats during the injection of various types of drugs. c) EEG recorded from human neonates during different stages of sleep. The results have shown that this method of analyzing EEG activation provides several advantages. The experimenter can rapidly obtain a quantitative and objective measure of EEG arousal. Furthermore, if several electrode loci are analyzed simultaneously, this measure provides a means for comparing changes occurring at different sites and the time course of these changes.

9.6 IDENTIFICATION OF FUNCTIONAL BIOELECTRIC CONFIGURATIONS IN SPONTANEOUS ACTIVITY OF THE BRAIN. Stephen S. Fox and Hansook Ahn*. Department of Psychology, University of Iowa, Iowa City, Iowa 52240

Prior studies from this laboratory with Rudell and Rosenfeld have indicated the feasibility of directly validating functional representation or coding in components and combinations of components of the sensory evoked potential. In those studies under direct control of reinforcement evoked potential components were demonstrated to be functionally independent and state dependent as were transforms between closely related sensory structures. The operant method of analysis has been extended in the present study to spontaneous activity of brain. Spontaneous activity from the brains of chronically implanted cats was recorded with computer aid. Individual 20-millisecond long units of spontaneous activity were identified, which occurred on the average of one/minute. Activity preceeding and following these brief bioelectric events was also recorded. For four animals large sequential potentials similar to evoked potentials followed these selected events but no regular potentials preceeded them. Averaging revealed dramatic similarity of this spontaneous event from day to day within each animal. Functional relevance of these events was demonstrated by increasing their probability independent of changes in frequency of EEG under reinforcement control. The significance of such repeatable functional units of bioelectricity for a theory of spontaneous bioelectric coding will be discussed.

9.7 THE EFFECTS OF STIMULUS UNCERTAINTY ON THE PUPILLARY DILATION RESPONSE AND THE VERTEX EVOKED POTENTIAL. David Friedman* (SPON: S. Sutton) Queens College, Flushing, N.Y.

Peak pupillary dilation, the late positive component (P_3) of the auditory evoked potential, and slow baseline shifts, were recorded simultaneously and studied as a function of degree of stimulus uncertainty. All responses were averaged using a Computer of Average Transients. Degree of stimulus uncertainty was manipulated by varying the probability of occurrence of two stimuli from 20 to 80 percent probabilities of occurrence. N_1-P_3, an overall measure of evoked potential amplitude, and peak dilation amplitude both decreased monotonically with the rareness of event occurrence. This relationship held for N_1-P_3 in both uncertain (S guessed the identity of the upcoming stimulus) and certain (S was told the identity of the upcoming stimulus) conditions, but only in the uncertain condition for peak dilation. Contingent Negative Variation (CNV) and pupillary slope (pre-stimulus events) did not vary as a function of probability in either condition. Contrary to Naatanen's (1970) and Karlin's (1970) arguments, no relationship between CNV and evoked potential amplitude was found. All response measures differed markedly in amplitude between certain and uncertain conditions. N_1-P_3 and peak dilation were larger in the uncertain condition than in the certain condition. CNV was more negative in the uncertain condition than in the certain condition, and pupillary slope showed more sympathetic activity in the uncertain than in the certain condition. Results for probability manipulation were interpreted in terms of Sokolov's (1963) theory of the orienting reflex, while findings for the effects of uncertainty were interpreted as indicative of greater arousal associated with the uncertain condition.

9.8 HIPPOCAMPAL EVOKED POTENTIALS IN TASK SITUATIONS IN THE TEMPORAL-LOBE EPILEPTIC. Martin F. Gardiner,* Anthony Dymond,* Paul Crandall,* and Donald O. Walter. Depts. of Physiol. and Surg. (Neurol.), UCLA Sch. Med. and Br. Res. Inst., Los Angeles, Calif. 90024.

We have been studying averaged sensory evoked potentials (AEPs) recorded simultaneously at the scalp and from indwelling electrodes in temporal-lobe epileptics under the UCLA Clinical Neurophysiology Program. Depth placements in each patient were dictated by clinical requirements, to assist in localizing an epileptic focus, in order to assess potentialities for remedial surgery. We report here on hippocampal AEPs to low intensity short duration-tone bursts presented by earphone as the patients lay in a darkened room with eyes closed. For some stimulus presentations (trials) the patients were not given specific instructions relating to the tones. AEPs averaged across blocks of such trials were often small, and were variable in waveform. In other trials the patients were required to count stimulus presentations. AEPs averaged from such trials were less variable than AEPs from instruction-free trials and were characterized by prominent late components (at lags greater than 200 ms). Two other types of tests were given to some patients: counting combined with pitch discrimination, and counting combined with loudness discrimination. Late components in hippocampal AEPs were usually larger in such task conditions than under the simple counting tasks. In all subjects, the late components in task trials showed significant variability in amplitude, and also in waveform, across hippocampal leads. Leads where late components had minimum amplitude corresponded well with locations where an epileptic focus was indicated by seizure records.

9.9 INTERACTIONS OF DISSIMILAR STIMULI ON HUMAN SLOW EVOKED POTENTIALS. Hallowell Davis, Poul A. Osterhammel*, Craig C. Wier* and Shirley K. Hirsh*. Central Institute for the Deaf, St. Louis 63110

When pairs of similar stimuli are presented at 500 msec (ISI), the slow vertex potential evoked by the 2nd stimulus is depressed to about 1/3 of its amplitude after a 5 sec interval. A similar but less severe depression is produced if the 1st stimulus is in a different modality. In one experiment with 6 adult subjects, the stimuli were filtered clicks (1200 Hz) to left ear, electric shocks to left median nerve at wrist and vibration of middle finger of left hand (enclosed in a sound-treated box). In a 2nd experiment (n=7) flashes from a photostimulator were substituted for the vibrations. The stimuli were carefully matched by each subject to produce comfortably-strong equal sensation magnitudes. Responses in blocks of 32 were averaged to each of the 6 cross-modal pairings and the 3 intra-modal pairs in each experiment. The average 2nd response (ISI = 500 msec) of intra-modal pairs was 39% of the response at ISI = 5.5 sec: for the cross-modal pairs it was 64%. The relations were all symmetrical, i.e. flash depressed click or shock as much as click or shock depressed flash. Vibration of fingers and shocks to the median nerve of the same hand interacted like different modalities, although they both activated the left hand somatosensory system.

9.10 CORTICAL STEADY POTENTIAL CORRELATES OF INSTRUMENTAL PERFORMANCE Roy A. Anderson, Dept. Psychiatry, C.W.R.U., Cleveland, 44106

Steady potential (SP) shifts were recorded from freely-moving rats during fixed-interval (FI-30 sec., -1 min., -2 min.) bar-pressing for food rewards. Cortical surface placements in visual, motor, and somatosensory areas all yielded active loci. Arousal with orienting response was associated with negative shifting at most loci, but some showed positive shifting. The development of stable FI performance corresponded to the acquisition of a systematic pattern of SP shifting. Bar-pressing was anticipated and accompanied by a sustained SP shift terminating with an abrupt increase in amplitude on reward delivery. Eating and subsequent absence of bar-pressing were associated with return of the SP baseline to a stable background level and, at times, ECoG synchrony. Shifting was minimal to absent during the first to second third of each interval, but recurred as the animal resumed bar-pressing. Continuous records of behavior revealed systematic patterns of movement (feeder licking, grooming, etc.) during periods between bar-pressing. The probability of this behavior was inversely related to mean amplitude of SP shifting. This finding supports the concept that noncontingent (collateral) behavior reduces tension under conditions where activation (drive) is present, but specific, food-contingent responses are ineffective as a means of reducing it. By contrast, there was a direct correspondence between the probability of a bar-press and amplitude of SP shifting. The overall findings are consistent with the view SP shifts reflect gradients of diffuse activation and deactivation relevant to timing of response.

9.11 SLOW POTENTIAL CORRELATES OF REACTION TIME PERFORMANCE IN MONKEYS. D. Symmes*, M. Healy* and K. Chase*. (SPON: P. G. Nelson). NIH, NICHD, Bethesda, Md. 20014

Cortical activity has been recorded from four monkeys previously trained to a high level of performance on a reaction time task. The monkeys had to pull and hold a lever for periods between 2 and 6 sec. during which time a light in the lever was on. Prompt releases to light out were rewarded. Force and position readouts from the lever permitted an accurate description of the motor response, and revealed minimum reaction times (to beginning of force removal) of about 140 msec. Recordings with 9.5 sec time constants from Ag/AgCl cortical or epidural electrodes were digitized and averaged with a PDP-12 computer. Three sources of slow potentials have been identified in association with this behavior: 1) a source of negativity arising in central areas contralateral to the hand used which correlates positively with the force applied to the lever; 2) a less distinct but bilateral source of negativity which correlates inversely with reaction time; 3) a bilateral source of positivity of shorter duration which appears to correlate with the monkey's awareness of forthcoming reward. The spatial and temporal distribution of these potentials will be discussed.

9.12 ABOLITION OF BOTH THE CNV AND THE SLOW-POTENTIAL SHIFT ACCOMPANYING AUGMENTING RESPONSES DURING REVERSIBLE CRYOGENIC BLOCKADE OF THE NONSPECIFIC THALAMO-CORTICAL SYSTEM IN THE CAT. James E. Skinner, Neurophysiology Section, Physiology Dept., Baylor College of Medicine, Houston, Texas 77025.

Directed attention and expectancy have been shown to elicit a negative, steady-potential shift in the frontal and vertex regions of the cortex in both man (Walter et al., 1964, Nature) and animal (Low et al. 1966, Per. Mot. Skills). This negative potential, called the contingent negative variation (CNV), is similar in cortical distribution and electrical polarity to the slow-potential shift reported to be elicited by repetitive thalamic stimulation (Goldring and O'Leary, 1967, Electroenceph. clin. Neurophysiol.). In the present study the results show in three chronic cat preparations that reversible cryogenic blockade in the nonspecific thalamo-cortical system at the level of the inferior thalamic peduncle produces two effects: 1) it abolishes the steady-potential shift in the frontal cortex produced by expectancy (a 1000 cps tone forewarning the onset of mild electric shock) and 2) it abolishes the negative slow potential accompanying augmenting responses but does not affect the positive-negative augmenting response itself. Recruiting responses were found not to be accompanied by a negative steady-potential. These results show that the nonspecific thalamo-cortical system mediates or influences both of the above types of steady-potential shifts, suggesting that they are related.

Session 10

10.1 RESPONSES OF FASTIGIAL NEURONS TO STIMULATION OF CUTANEOUS MECHANORECEPTORS. John C. Eccles, Nassir H. Sabah* and Helena Táboríková. Depts. of Physiology and Biophysics, State Univ. of N. Y. at Buffalo, N. Y. 14226.

Neurons of the fastigial nucleus receive excitatory inputs from collaterals of the two types of afferents to the cerebellar cortex -- the mossy fibers and the climbing fibers -- and are inhibited by cerebellar Purkyně cells located mainly in the vermal zone. The rapidly adapting receptors and the slowly adapting receptors of the pads of the cat hindfoot and forefoot, as well as the hair follicle receptors in the adjacent hairy skin, were selectively activated by means of precisely controlled mechanical stimuli. The unitary responses of fastigial neurons were recorded extracellularly in decerebrate preparations, the stimuli being accurately timed so that successive responses could be summated to obtain post-stimulus time histograms and cumulative frequency distributions. Strong responses to the activation of the three types of mechanoreceptors could be recorded in the lateral region of the ipsilateral fastigial nucleus, the hindfoot area being in the anterior portion of the nucleus and the forefoot area posterior thereto. Units in the intermediate zone respond to activation of mechanoreceptors of both forefoot and hindfoot. The response patterns are quite diverse, ranging from simple excitation or inhibition to much more complex patterns. In accordance with their latencies these responses are attributable to the synaptic excitatory effects of the mossy fiber and climbing fiber collaterals, and to the inhibitory and disinhibitory effects of Purkyně cells that converge onto the fastigial neuron under investigation.

10.2 DEVELOPMENT OF NEURAL CODING CHARACTERISTICS IN PRIMARY CUTANEOUS AFFERENTS IN KITTENS. R. E. Beitel*, J. M. Gibson* and W. I. Welker. Lab. of Neurophysiol., Univ. of Wis., Madison, Wis., 53706.

Between the time of birth and weaning, domestic kittens develop a complex repertoire of tactile behavior. To determine if neural coding to the CNS from cutaneous afferents changes during this critical postnatal period, we have investigated several characteristics of first order cutaneous receptive fields of neurons which innervate the glabrous forepaw in kittens of 1 to 46 days postnatal age. Single neurons in cervical dorsal root ganglia were recorded extracellularly with tungsten microelectrodes in anesthesized kittens, and the force threshold, size and location of receptive fields were determined with a series of wires of graded diameters (von Frey technique). Other data taken included refractory periods, conduction velocity, and unit response patterns to controlled mechanical displacement of skin by pulse, trapezoidal, parabolic and sinusoidal waveforms. Mechanical stimuli were delivered by a metal probe driven by a feedback-controlled axial displacement generator. A LINC-computer was used to program stimulus delivery and analyze resultant neural discharge patterns. It was found that newborn kittens already possess tiny, sensitive receptive fields associated with "slow" and "rapid" adapting mechanoreceptors. First spike latencies varied inversely with postnatal age, but, with the exception of a limited capacity to follow sinusoidal stimuli 1:1 in the youngest kittens, temporal discharge patterns were essentially invariant through the postnatal period studied. It is concluded that the peripheral neurons examined are functionally mature in newborn kittens, and that the development of complex tactile behavior is not limited by the capability of cutaneous afferents to code characteristics of mechanical stimuli. (Supported by USPHS Grants 5326 and 6225.)

10.3 UNIQUE SENSORY CODING OF DIRECTIONAL MOVEMENTS BY MIDLINE VIBRISSA.[a] Bruce Oakley. Zoology Dept., Univ. of Michigan, Ann Arbor, 48104.

Bilateral innervation of the midline area provides an opportunity for strikingly different neural input with left-right hair movements. On the rat chin the central member of a row of three small vibrissae lies on the midline and is bilaterally innervated by the mylohyoid nerve. The adjacent left and right vibrissae, each 1mm off the midline, receive unilateral innervation from their respective mylohyoid nerves. Directional displacement of any vibrissa generates a phasic-tonic whole nerve discharge. Simultaneous recording from both left and right mylohyoid nerves indicated that movement of the midline vibrissa in the left direction produced vigorous activity in one mylohyoid nerve, whereas, movement to the right discharged the other mylohyoid nerve. Thus, slight differences in directional movement are translated into spatially separate activity in the brain. There was no evidence of functional reinnervation of a denervated right vibrissa by collateral sprouting of intact fibers from the midline vibrissa 1mm away. The partially denervated midline vibrissa, however, did remain accessible to reinnervation by the axons of the transected right nerve, which later formed functional contacts.

[a]Supported by NIH Grant NS-07072.

10.4 SENSORY MODALITY REPRESENTATION IN THE ANTERO-LATERAL SYSTEM. James A. Mosso* and Lawrence Kruger. Depts. Neurosurg. and Anat., UCLA Centr. for Health Sci., L.A. 90024.

The modality characteristics of neurons of the spinal trigeminal nucleus, pars caudalis were studied, and their fiber latencies following intradermal electrical stimulation within the receptive fields were determined. High threshold mechanoreceptors with long latencies and uniquely responsive to noxious stimuli were prominently represented amongst the peri-cornual cells. Thermo-sensitive neurons and neurons with corneal receptive fields responsive to a variety of stimuli also belong to the long latency class. However, most commonly encountered were short latency units responsive to low threshold stimulation of hair and skin mechanoreceptors. Hair receptor categories included: vibrissae, directionally sensitive and responsive to high vibratory frequencies; G_1 insensitive guard hairs; and exquisitely sensitive G_2 and D hairs. Skin mechanoreceptors included sensitive, rapidly adapting field units, Pacinian receptors responsive to vibration at 500 Hz, and slowly adapting mechanoreceptors, with punctate fields, which displayed a graded discharge frequency in response to rectangular displacements of varying amplitudes. The striking discriminative capacity of quintothalamic neurons was sufficiently similar to those of lemniscal neurons to suggest a rejection of the 'protopathic' concept for tactile neurons in this system.

10.5 RESPONSES OF CELLS IN CAT POSTERIOR THALAMUS TO STIMULATION OF CENTRAL AFFERENT PATHWAYS AND PERIPHERY. Karen J. Berkley. Dept. Psychol., Fla. St. Univ., Tallahassee, Fla. 32306.

In barbiturate-anesthetized cats, responses of cells were recorded extracellularly to the following electrical stimuli: contralateral dorsal column nuclei; ipsilateral "lateral spinothalamic tract" (or reticular formation) at medulla level; ventral surface of paws; and light flashes; clicks; combinations of above; and mechanical stimulation of skin surface. The cells' response characteristics were divided in two major groups--convergent (C) and non-convergent (NC). C-cells had one or more of the following properties: 1) responded to more than one paw, 2) both of the brain stimuli, 3) more than one stimulus "modality"; 4) had non-occlusive interactions between any two or more stimuli; 5) had a bilateral receptive field. Comparisons of cells in several nuclei are compared in the table below (VB, ventrobasal complex; PO, posterior group; PUL, pulvinar; LGN, lateral geniculate). The unexpected result was 29% C-cells in VB. Such cells, however, do not exhibit as much convergence as those in other nuclei; there was a mean of only 1.2 C-properties per C-cell. Their existence is compatible with anatomic evidence of specific and non-specific sensory pathway convergence in VB. (Supported by USPHS NS-02992, NB-7468, MH-11218 and NSF GU-2612.)

NUCLEUS	# CELLS	% C-CELLS	# C-PROPERTIES/C-CELL
VB	58	29	1.2
PO	117	44	1.6
PUL	26	35	1.8
LGN	46	11	1.9

10.6 SOMATOSENSORY CORTEX AND DISCRIMINATIVE BEHAVIOR IN THE RAT. Stanley Finger, Dept. Psychol., Wash. Univ., St. Louis 63130.

Blinded rats were tested for acquisition or retention of a series of five two-choice tactile discriminations.

Lesions of one or both electrophysiologically defined somatosensory areas of the cortex severely impaired acquisition of tactile habits, but animals that had been exposed to all five tactile discriminations prior to surgery performed normally even after the entire somatosensory projection had been ablated. The retention sparing was found to be a function of extended preoperative testing (overlearning), and the acquisition deficits diminished significantly when the hemispheres were damaged seriatim, or when small bilateral lesions of the somatosensory cortex were enlarged to full size in a second operation after a 35 day recovery period.

10.7 PROJECTION IN THE CUNEATE FASCICULUS OF MECHANORECEPTIVE AFFERENT FIBERS INNERVATING THE RACCOON'S FOREPAW. Lillian M. Pubols and B. H. Pubols, Jr. Dept. Anat., Hershey Med. Ctr., Penn. State Univ., Hershey, 17033.

Properties of myelinated first-order afferent fibers arising from cutaneous mechanoreceptors in the raccoon's ventral forepaw were studied at the level of the cuneate fasciculus, and the results were compared with those obtained from fibers of the median nerve (Pubols and Pubols, Exp. Neurol., 1971, 31). More than 200 units have been examined with tungsten microelectrodes at C_1-C_2 and C_5-C_6 spinal cord levels in pentobarbital sodium anesthetized preparations, and all recording loci have been histologically verified. Manually and electronically controlled mechanical stimuli have been applied to cutaneous receptive fields. The ratio of rapidly adapting (RA) to slowly adapting (SA) to Pacinian (Pc) units is approximately 3:1:1, compared to 1:1:0 in the median nerve. Two types of SA unit were identified, differing in duration of response to a prolonged stimulus. Both RAs and SAs have receptive field areas of less than 1 mm^2. Median indentation threshold is approximately 30 μ for RA and 20 μ for SA units. Discharge rate during skin movement is a power function of indentation velocity for both RAs and SAs, with exponents less than 1.0. However, for the majority of SAs examined, a logarithmic function predicts with the highest correlation coefficient the discharge rate during the first half-second of static displacement as a function of displacement amplitude. (Supported by NINDS grant NS-06371.)

10.8 VELOCITY AND ACCELERATION RESPONSE IN N. GRACILIS TO ANGULAR JOINT MOTION W. J. Williams, S. L. BeMent, T. C. T. Yin* and W. D. McCall, Jr.* Bioelec. Sci. Lab., E.C.E. Dept. and Bioengr. Prog., Univ. of Mich., Ann Arbor, Mich. 48105.

Dynamic response characteristics of the knee-joint proprioceptive system in sodium pentobarbitol anesthesized cats were analyzed at the second order cell level (nucleus gracilis). Changes in average firing frequency of certain cells were correlated with dynamic changes in knee angle. Two basic types of cell response were observed: (1) a small number of cells responded only at the limits of flexion or extension, (2) a greater number of cells responded over a wide intermediate angular range. Both types responded with high pass filter transfer characteristics (Bode plot result from 0.1 to 7 Hz. The first type of cell exhibited a transfer function of the form $K(s+z)\exp(-sT)$ and the second type of cell exhibited a transfer function of the form $K(s+z)^2\exp(-sT)$. The pure time delay T was about 12 msec and the corner frequency z was about 1 Hz. Since the first type of cell exhibited first order "derivative" response to joint motion and the second type exhibited second order "derivative" response to joint motion (above 1 Hz), it is postulated that these cells are capable of conveying angular velocity and acceleration information to higher levels. No second order cells were found with dynamic responses similar to those of slowly adapting knee joint receptors (McCall and Williams, Fed. Proc. 30:709 abs 1971.), in agreement with the findings of Burgess and Clark (J. Physiol. 28:301. 1969). Therefore, knee joint velocity and acceleration information may travel in the dorsal columns whereas positional information is probably mediated by other pathways. Supported by PHS-NIH Grant NS 08470.

10.9 SOMATOTOPIC MICRO-ORGANIZATION OF SmI FORELIMB AREA IN CEREBRAL NEOCORTEX OF THE CAT. C. WELKER, Central Wisconsin Colony and Training School, Madison, Wis. 53704

The boundary between the SmI forelimb area and adjacent primary motor area, and the fine grain somatotopic organization within SmI, were determined by means of microelectrode recording, micromapping, and cyto-architectural techniques. The postcruciate sulcus, although varying in location, length, and depth, marks the sensory-motor boundary in regions receiving projections from the arm and forearm. No distinctive surface feature, such as a sulcus or dimple, marks the sensory-motor boundary in the forepaw area. Within the SmI forepaw region, there are highly organized somatotopic patterns in very small cortical areas. In the 4 mm^2 area to which digit V projects, there is a distinct medio-lateral and rostro-caudal organization. The ventral glabrous pad and claw of the digit project rostral to the area for the hairy surfaces, and the ventral hairy surface projects medial to the dorsal hairy surface. The "hairy distal skin flaps" located on each side of a digit project to adjacent, but non-overlapping loci, which are larger than the area to which the glabrous pad of the digit projects. The somatotopic organization for the other digits is similar, but they project further laterally and caudally into the curving cortex of the coronal sulcus. The most rostral projections within the forepaw area are from the large glabrous pad on the ventral palm. The total cortical surface area for this palm pad, however, is smaller than that for digit V. This somatotopic micro-organization found within the SmI forepaw area suggests that the hairy, rather than the glabrous, cutaneous surfaces of the forepaw are most important in the localization of peripheral somatic sensory stimuli in the cat. (Supported by NIH Grant NS 07295.)

10.10 DISCHARGE CHARACTERISTICS OF SINGLE UNITS IN THE ANTEROVENTRAL AND DORSAL COCHLEAR NUCLEI OF BARBITURATE-ANESTHETIZED CATS. Jay M. Goldberg, William E. Brownell* and Robert A. Lavine*. Dept. Physiol., University Chicago, Chicago 60637

The cochlear complex may be divided into several subnuclei, differing in cellular and synaptic morphology. Two regions will be considered. The oral pole of the anteroventral nucleus (AVCN) consists almost exclusively of spherical shaped cells. Their major innervation consists of two to five auditory-nerve fibers, terminating as bulbs of Held. The dorsal nucleus (DCN) has a more complicated organization. There are many interneurons. The projection cells receive a highly convergent bouton innervation, representing direct auditory-nerve inputs and indirect inputs via interneurons. The present study explored the notion that the AVCN may function more or less like a simple relay nucleus, whereas the DCN should be a site of complicated synaptic processing. AVCN units have restricted excitatory receptive fields, usually with no inhibitory sidebands. The spacing of action potentials is irregular. Tone-burst responses have a simple time course. Firing rate is almost always monotonically related to stimulus intensity. Discharge may be phase-locked for tonal frequencies exceeding 3kHz. In all these respects, AVCN units resemble first-order fibers in discharge characteristics. DCN cells, in contrast, may have complicated receptive fields, including prominent inhibitory sidebands. Steady-state discharge patterns may be regular. Tone-burst responses provide evidence for complex excitatory-inhibitory interactions. Discharge rate may be a non-monotonic function of intensity. Phase-locking is seldom seen for tonal frequencies exceeding 1.0-1.5 kHz.

10.11 EFFECT OF PREADAPTING TEMPERATURE ON THE PHASIC RESPONSE OF TRIGEMINAL THERMORECEPTORS. D.A.Poulos and E.Leibowitz*, Depts. of Neurosurgery and Physiology, Albany Medical College, Albany, New York, 12208.

The response of trigeminal ganglion neurons to cooling of oral-facial regions was studied in anesthetized squirrel monkeys (S.sciureus). Thermal stimuli covering a range of 45-15C were applied in a steplike sequence above and below a series of preadapting reference temperatures. The reference temperatures used were: 43, 39, 35, 31 and 27C. Specific thermoreceptors (T units) gave increased phasic responses to progressively larger cooling steps down to 29-23C. The phasic response to any given stimulus temperature was increased when starting from a warmer reference temperature. However, for a given reference temperature, the range of cooling stimuli that produced progressive increases in the phasic response was limited. The range of linearly increasing phasic responses observed was related to the reference temperature. For example, the averaged range of phasic response increase was 16 degrees when cooling from 43C, and 4 degrees when cooling below 27C. Thus, single trigeminal T units appear capable of discriminating temperature changes over only a limited range below any reference temperature used in this study (with the range being progressively limited when starting from colder reference temperatures). A second neuronal type responsive to both thermal and mechanical stimulation (T+M unit) was also tested. T+M units gave phasic rate increases that were proportional to the degree of cooling over the entire stimulus range for each of the reference temperatures studied. Assuming that the squirrel monkey is capable of discriminating temperature changes below 27-23C, the detection of extreme cooling may in part depend on the activity of T+M units. (Supported by NIH Grant NB05976)

10.12 INTENSITY DISCRIMINATION FOR LOCAL WARMING OF THE SKIN: PERIPHERAL NEURAL MECHANISM. L.Darian-Smith, K.O. Johnson, and Carole LaMotte. Dept. Physiol., Sch. Med., Johns Hopkins Univ., Baltimore, Md 21205

The capacity to differentiate small incremental changes in localized warming pulses applied to the palmar skin was examined in human subjects using the method of paired comparisons. Stimulus parameters that influenced the difference limen(DL) were the baseline temperature(T-base),and the amplitude of the warming step (T-step).At normal resting skin temperatures and above(T-base=34-39^{o}C) the DL changed little with the intensity level at which the discrimination was made.However, when T-base equalled 29^{o} the DL was elevated at T-step values below 4^{o}C. Slowly conducting 'warm' fibers (cond. vel = 0.7-4.5m/sec) were isolated in the median nerve of the rhesus monkey, and their response characteristics compared with human discriminative capacities.The intensity functions of these fibers required specification not only of the test stimulus, but also of those stimuli occurring in the 30 seconds preceding it, as these stimuli were found to have a weighted suppressive action.The main factors determining the form of the Weber function were apparently peripheral, including the 'warm' fiber sensitivity to incremental stimulus changes (altering with both T-base and T-step), and the trial-to-trial variability of the fiber response. Central neural factors also limited discriminative capacity, but this effect was unrelated to either T-base or T-step, and did not modify the form of the Weber function.

10.13 CHARACTERISTICS OF SECOND PAIN INDICATIVE OF PROLONGED CENTRAL SUMMATION. Donald D. Price, Dept. Physiol., MCV, Richmond, Va. 23219.

Characteristics of second pain were studied in 15 naive human subjects (Ss) to assess their consistency with dorsal horn cell responses to C fiber stimulation (Mendell, E.N. 16: 316, 1966; Price and Wagman, E.N. 29: 833, 1970 and J.N. 32: 803, 1969). Selective block of ulnar n. impulses necessary for first (pricking) pain was achieved by pressure to the ventral forearm. Stimuli applied to the fifth finger were constant current 9 msec shocks, Von Fry hairs (.01 to 4.0 gms), and other mildly noxious stimuli. Shocks optimal for producing single and double pain were 4 and 9 mA respectively. Sensation thresholds to shock and graded Von Fry hairs increased progressively during blockade. After more than 40 mins, touch, first pain, and pin prick were no longer perceived but long latency (>1 sec) burning sensations due to 9 mA shocks and strong pinch persisted. Differences between reaction times to first and second pain (means ranged between .57 and 1.03 sec in 4 Ss) persisted throughout the course of blockade and indicated that second pain was related to impulses conducting between 0.9 and 1.6 m/sec. Five trains of 6 shocks were given with 5 different frequencies. After each train, Ss were asked if successive shocks in the train felt less intense, similar, or more intense. Before block of first pain and with 9 mA shocks, the no. of Ss reporting progressive increases in sensations during trains having the following frequencies were: 0.2/sec-1,0.3/sec-1,0.5/sec-10,0.75/sec-14, and 1.0/sec-14. Very few sensation increases occurred with 4 mA shocks. After block of first pain, the no. of Ss reporting increases to 9 mA shocks were: 0.2/sec-0,0.3/sec-1,0.5/sec-11,0.75/sec-14, and 1.0/sec-14. Results from 0.3/sec and 0.5/sec stimulation were significantly different ($p>.01$). The stimulus intensity and frequencies of shocks producing progressively more intense second pains are consistent with previously observed increases in dorsal horn cell responses to iterative C fiber stimulation.

Session 11

11.1 EFFECT OF PHENOBARBITAL ON A LEECH NEURON. James W. Prichard. Section of Neurology, Yale University School of Medicine, New Haven, 06510.

Sodium phenobarbital, 10 mM, caused a characteristic sequence of changes in the intracellularly recorded activity of the Retzius cells of leech segmental ganglia. An initial period of slight depolarization associated with greatly increased excitatory synaptic impingement and firing rate was followed by a 10-15 mv hyperpolarization which was interrupted every 10-12 seconds by large depolarizations which lasted 1-3 seconds and were surmounted by small, rapidly repeating action potentials. The hyperpolarized phase was associated with decreased input resistance; it was unaffected by substitution of propionate for chloride in the bathing fluid but was abolished by elevation of external potassium from 4 to 20 mM, which procedure also abolished the undershoots of the action potentials. When synaptic transmission was suppressed with 20 mM magnesium sulfate, the excitatory events of the phenobarbital response usually did not appear, but the hyperpolarization developed as usual. All the above phenomena were reversible and repeatable. These data suggest that a selective and reversible increase in membrane permeability to potassium is a principal direct effect of phenobarbital on this particular neuron. The excitatory portions of the response appear to be secondary to drug-induced changes in neurons synapsing on the Retzius cell.

11.2 COMPARISON OF THE EFFECTS OF SHORT, INTERMEDIATE AND LONG ACTING BARBITURATES ON SQUID AXON MEMBRANES. D. T. Frazier, K. Murayama*, N. J. Abbott*, and T. Narahashi. University of Kentucky Medical Center, Lexington, Kentucky 40506 and Duke University Medical Center, Durham, N.C. 27710.

Experiments utilizing both internal and external perfusion of squid giant axons have been carried out to determine if membrane penetration or receptor affinity can explain the duration of anesthesia obtained from phenobarbital, pentobarbital and hexobarbital. These barbiturates were applied either outside or inside the squid axon at concentrations which produced approximately equivalent depression of the amplitude of the action potential. The time needed to reach 1/2 the magnitude of the block and, similarly, the time required to reach 1/2 recovery following washing, were compared for all three drugs. The results were in agreement with our findings concerning pentobarbital (J. Pharm. Exp. Therap. 177:25, 1971) in that all three barbiturates were more potent from inside the squid axon than from the outside. When applied either outside or inside (10^{-2}M), there was no statistically significant difference between any of the three drugs with respect to onset of block or recovery. The recovery time was closely related to the degree of block produced. The time to block and time to recovery were much shorter when the drugs were applied to the inside. Using the squid axon as a model, it was concluded that neither differences in penetration or recovery at the membrane level could be used to explain the differential effects of these barbiturates on the central nervous system. (Supported by NIH grant NS03437 and a grant from the Grass Foundation.)

11.3 EFFECTS OF NEREISTOXIN ON THE NEUROMUSCULAR TRANSMISSION OF THE FROG. Toshio Narahashi, Takehiko Deguchi* and Hans G. Haas*. Dept. Physiol. Pharmacol., Duke Univ. Med. Ctr., Durham, N. C. 27710.

Nereistoxin (NTX), 4-N,N-dimethylamino-1,2-dithiolane, is the toxic principle from the marine annelid Lumbriconereis. There was evidence that NTX blocked certain cholinergic junctions. The mechanism of neuromuscular blocking action of NTX in the frog has been studied by means of intracellular microelectrode and voltage clamp techniques. After application of NTX, the neuromuscular transmission was blocked without any depolarization of the end-plate membrane, and a small end-plate potential was observed by nerve stimulation. Spontaneous miniature end-plate potentials decreased in both frequency and amplitude, and the quantum content of the end-plate potential tended to decrease also. The sensitivity of the end-plate membrane to iontophoretically applied acetylcholine was markedly reduced. Under voltage clamp conditions, the amplitude of both sodium and potassium components of the end-plate current was suppressed and their falling phase slightly accelerated after application of NTX. However, NTX exerted no differential action on the two components of the end-plate current. It was concluded that the major action of NTX responsible for the neuromuscular blockade is the inhibition of the mechanisms whereby the end-plate membrane undergoes conductance increases to sodium and potassium ions upon transmitter action. (Supported by NIH grants NS09272 and NS06855.)

11.4 ELECTROMYOGRAPHIC CHANGES IN LOCAL TETANUS FOLLOWING SUBCUTANEOUS INJECTION OF GLYCINE IN RATS. Alexander A. Fedinec, Robert S. Pozos and William C. Latham*. Dept. Anat. and Dept. Physiol. and Biophys.,Univ.Tenn. Med. Units, Memphis, Tenn.38103 and Biol. Lab. P.H.S., Boston, Mass.02130

Glycine has the properties of an inhibitory neurotransmitter substance released from spinal interneurones (Neurosciences Res. 1:143,1968). Iontophoretically administered glycine reduces the tetanus-induced hyperactivity of spinal motor neurones (Brain Res. 10:208, 1968). The present study examined the effect of subcutaneously injected glycine (2.5 M. pH 7.35, 2.5 ml./100 g.) on the electromyographic activity of Wistar rats during local tetanus. Tetanus was produced in the left gastrocnemius muscle by prior injection (24 h.) of 1000 mouse M.L.D./100 g. of purified tetanus toxin. Surface electromyograms were recorded from saline (0.1 M. NaCl), beta-alanine (2.5 M. pH 7.35, 2.5 ml./100 g.), and glycine injected normal and tetanus treated rats. Saline and beta-alanine had no effect on the electrical activity of normal or tetanus toxin injected muscles. Twenty minutes after injection of glycine, the electrical activity of normal muscles was reduced; the afterdischarge following toepad pinch was prolonged. Within 5 hours the electrical activity of the muscles returned to normal. Glycine also temporarily abolished the exaggerated electrical activity of muscles during local tetanus and reduced the prolonged afterdischarge to toepad pinch. In animals with transected spinal cords (T_{4-5}), glycine had a similar, depressing effect on the electromyographic activity of muscles during local tetanus. Single injections of glycine did not prolong the survival of tetanus treated animals.

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11.5 CENTRAL NERVOUS SYSTEM CHANGES WITH α-γ-DIAMINOBUTYRIC ACID. T. Banerjee* and W.E. Hunt, Dept. Anat. and Div. of Neurosurg., The Ohio State Univ. Coll. of Med., Columbus, Ohio 43210

Rats were used to produce an experimental model for neurolathyrism by injecting either L-2-4 Diamino butyric acid, an active ingredient of lathyrus latifolius, or lyophilized, freeze-dried aqueous extract of L. latifolius seeds, 10 mg/100 gm. body weight intraperitoneally for 3-4 weeks. Injection of water extract produced changes within the brain and spinal cord which were quite similar to those produced with DABA injection. Experimental and control rats were weighed weekly and comparative weight curves were made. Twenty out of thirty rats showed a progressive loss of weight and paresis of the hind limbs. Ten rats died without clinically detectable paresis. The signs of disease were the following: (1) drowsy, inactive and docile (2) paresis of hind limbs (3) sphincter disturbance (4) S-shaped deformity of tail (5) progressive loss of weight and (6) wasting of muscles. Withdrawal to pain was intact in spite of considerable paresis. EMG examination revealed fibrillation potential in only two animals. All animals were killed when the disease reached its peak clinically. The cerebral cortex, cerebellum, spinal cord and peripheral nerves were examined by light microscopy. The larger neurons appeared to be more affected. There was vacuolisation of cytoplasm, loss of Nissl substance and swelling of the nuclei of neurons of the cerebral cortex, cerebellum and anterior horn cells. The pyramidal tract appeared intact. Not all animals wer affected and of those that manifested the disease the symptoms varied greatly in degree. It is possible that autoradiography may be helpful in locating the possible site of neuronal damage.

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11.6 ORAL INTAKE OF MORPHINE IN SUCROSE AND SALINE SOLUTIONS BY RATS. K.A. Khavari and Marc E. Risner. Dept. of Psychology, Univ. of Wisconsin-Milwaukee, 53201.

One group of rats was given ad libitum access to 0.5 mg./cc. morphine in tap water. Food and solution intake were measured daily along with body weight. The animals were kept on this regimen until their solution intake approached stability, at which time they were given a choice between two bottles, one containing the morphine solution and the other containing tap water. Only one rat showed any amount of preference for morphine over water. There was a significant drop in body weight and food intake during the first few days of the choice test, indicating the effects of withdrawal following oral addiction. In an attempt to attenuate the aversive taste properties of morphine two groups of rats were subsequently given ad libitum access to morphine: either 1.0 mg./cc. in 10% sucrose solution or 1.0 mg./cc. in 0.6% saline. Both groups were maintained on this regimen until their solution intake approached stability. Asymptotic intake for the sucrose rats was approximately 65 ml. of solution and 15 g. of food per day; intake for the saline group was 35 ml. of solution and 25 g. of food per day. (Note that these data provide evidence for the rats' ability to meter the caloric intake per day.) The animals were then given a choice for 10 days between two bottles, one containing the drug solution and the other containing the respective vehicle. The sucrose morphine animals consistently chose the drug solution over the vehicle. In contrast, the saline morphine animals chose the vehicle over the drug solution. It is concluded that morphine dependency can be induced in the rat through forced oral ingestion. However, best results are obtained when morphine solutions are adulterated with 10% sucrose.

11.7 DO ATROPINIC DRUGS DISSOCIATE ELECTROCORTICAL ACTIVATION AND BEHAVIOR?[1]

C. H. Vanderwolf and Mary Cromien*, Depts. Psychology and Physiology, University of Western Ontario, London, Canada.

Hippocampal and neocortical activity was recorded during observation of behavior in chronically prepared rats. Hippocampal rhythmical slow activity (RSA) accompanied walking, running, jumping, struggling and head movement (voluntary movement) but disappeared during behavioral immobility, and during face-washing, scratching, chewing, gnawing, and chattering of the teeth (automatic movement). Neocortical activity did not show a clear relation to behavior. Following large doses of atropine SO_4 (25 mg/kg or more, i.p.) behavior-hippocampal relations persisted although RSA was less regular than normal. Neocortical activity became closely related to movement independent of stimulus input. During voluntary movement low amplitude slow waves (3-10 Hz) were continually present in frontal, parietal, and occipital cortex. During immobility or automatic movement, neocortical activity consisted of large amplitude slow waves (down to 1 Hz) similar to the pattern during deep slow wave sleep. Thus, although neocortical activity was clearly abnormal, it was more "activated" during voluntary movement than during behavioral immobility or automatic movement. The electrocortical abnormalities were related to behavioral deficits. Heavily atropinized rats are hyperactive, tremorous, squeal when touched, and often fall when placed on a narrow shelf. One-way avoidance acquisition is depressed in proportion to the $\log_{10}$ of the dose over the range of 5-150 mg/kg.

The data indicate that neocortical and hippocampal "activation" is related to concurrent motor activity. Atropine-induced slow waves appear related to a disturbance of cortical control of movement.

1 Supported by grant APA118 from the National Research Council.

11.8 EXCITATORY AND INHIBITORY EFFECTS OF PSYCHOTOMIMETIC DRUGS.

Wagner H. Bridger, Irwin J. Mandel* and David M. Stoff*. Dept. of Psychiatry, Albert Einstein College of Medicine, Bronx, N.Y. 10461.

Several experiments were performed which demonstrate that LSD and mescaline facilitate the acquisition of new conditioned avoidance behavior of rats but disrupt the same behavior when it is well established or old. In addition, chronic administration of these drugs produce tolerance for the disruptive effects but enhance the excitatory effects. Mescaline 50 mg/kg and LSD .5 mg/kg were administered to rats for 4 days prior to training on 2-way shuttle box shock avoidance procedure. The same dose was administered on the training day to these rats and controls that did not have chronic drug administration. All groups demonstrated significant facilitation of acquisition compared to rats given saline. Thus there is no tolerance to the excitatory effects of these drugs.

In the next experiment, mescaline 100 mg/kg was administered to rats for 4 days after each training session on the same avoidance procedure. On the fifth day the drug was given prior to the training session. Other rats were given the drug only on the fifth day. This latter acute drug group showed inhibition while the chronic drug group showed excitation as compared to saline controls. Thus there is pharmacological tolerance to the inhibitory effects of the drug.

The results of these experiments suggest that the inhibitory and excitatory effects of psychotomimetic drugs may be mediated by different mechanisms.

11.9 INTRAMEDULLARY INJECTIONS OF THE SPINAL CORD. Thomas B. Ducker and Phanor L. Perot, Jr., Dept. Neurosurg., Medical University of South Carolina, Charleston, 29401.

In the treatment of spinal cord diseases, it appears desirable to give drugs locally in high concentrations, concentrations which may not be tolerated systemically. Thus, we have studied the effect of intramedullary spinal cord injections in dogs. Trans-spinal cord conductions (measured from peripheral nerve stimulation), averaged somatosensory evoked potentials, spinal cord blood flow (determined from computer averaged Xenon 133 desaturation curves), carotid artery blood flow (measured by electromagnetic flow meters), blood pressure and pulse were simultaneously monitored. The distribution of the injection was recorded by radioactive counting film. With the completion of each experiment, the spinal cord was removed for pathologic study.

The results of the experiment showed that injections of saline to 0.5cc given through a 30 gauge needle at 0.1cc/minute were tolerated. There was no interference in electrical function. Blood flow in the cord, in the carotids, and systemically was not altered; and there was no distructive pathology. With injections at a more rapid rate of 1.0cc/minute, cord conduction was altered with amounts of 0.2cc, cord blood flow was reduced with 0.3cc, a systemic hypertensive response was produced with 0.4cc, and marked changes in systemic blood pressure and carotid blood flow occurred at 0.5cc. Since both slow and fast injections resulted in similar amounts and distribution of the solutions within the cord, only the slower injection is recommended.

11.10 MOVEMENT DISORDER IN CATS WITH CHRONIC METHAMPHETAMINE INTOXICATION. A. Sudilovsky* and E. Ellinwood*. (SPON: Joan C. Martin, Ph.D.) Duke Univ. Med. Ctr., Durham, N.C. 27706.

Video tape recordings and detailed multivariate rating charts were used in the analysis of posture, motor patterns and activity of 52 cats intoxicated with methamphetamine over a period of 11 days. Dosage was gradually increased from 15 mg/kg/day to 35 mg/kg/day injected i.p. Comparison between general activity level and abnormal postural attitude (relatioship significant at $P < 0.001$) showed higher dyssynchrony with high activity levels. At different times of the drug cycle the average number of individual movements in the three body ensembles, head-neck (HN), shoulder-forelegs (SF) and hip-hindlegs (HH), were relatively more independently active: HN activity receeded whereas SF dramatically increased over the latter days of drug administration; HH activity made its appearance on day 3 but never becoming as active as the other body ensembles. In addition, dyssynchrony continued to increase in frequence after motor stereotypies reached their peak on day 3. Postural dysjunction showed a falloff between 30 and 90 min. after day 3 ($P < 0.01$) but an increase during the same interval on day 1 ($P < 0.05$). Discussion will be made of a hypothesis that the breakdown of movement patterns and posture is due to methamphetamine stimulation of dopamine systems in the relative absence of coordinating and inhibiting effects of the norepinephrine systems, thus allowing a relative autonomy of lower level organizational CNS substrates.

11.11 LENGTH OF TREATMENT WITH CHLORDIAZEPOXIDE AND RESPONSE TO ITS SUDDEN WITHDRAWAL. Lino Covi, Ronald S. Lipman*, Joseph H. Pattison*, Leonard Derogatis* and E. H. Uhlenhuth*. Dept. Psych., Sch. Med., J. Hopkins Univ., Balto. 21205.

This study explored the possible occurrence of barbiturate-type abstinence phenomena of the minor kind following the abrupt withdrawal of a therapeutic dose regimen of chlordiazepoxide administered to anxious neurotic outpatients. While it is clear that the abstinence syndrome will occur following the abrupt withdrawal of intoxicating dose levels of the barbiturates and minor tranquilizers, only one study (Covi, et al, Drug Abuse: Chpt. 6, 1969) has systematically examined (and found evidence for) the possible occurrence of minor symptoms of physical dependence of the barbiturate-type following the abrupt withdrawal of CDP when administered in a therapeutic dosage (40 mg/d). In the present double-blind study, anxious neurotic outpatients were randomly assigned to a regimen of either 90 mg/d of phenobarbital (PHB) or 300 mg/d of diphenylhydantoin (DPH) for 10 weeks whereupon they were switched (blindly) to 45 mg/d of CDP for an additional 10-weeks followed by an identical placebo for 2-weeks. Since PHB is cross-tolerant to CDP while DPH is not, one group of patients had received the equivalent of 20-weeks of CDP prior to abrupt placebo substitution while the second group had received CDP for only 10-weeks. Clinical status as monitored bi-weekly by a symptom distress check list showed (a) therapeutic equivalence of the two treatment regimens after 20-weeks and (b) a reliable worsening of minor symptoms of abstinence (e.g., trembling, poor appetite, faintness or dizziness, etc.) in the PHB-CDP group than in the DPH-CDP group. These results, in conjunction with the results of an earlier study, support the likely occurrence of a minor abstinence syndrome of the barbiturate-type following the abrupt withdrawal of CDP when administered in therapeutic doses to anxious neurotic outpatients for periods longer than 16-weeks.

11.12 THE DIFFERENTIAL EFFECTS OF DALMANE® ON THE CONTINGENT NEGATIVE VARIATION, AUDITORY EVOKED RESPONSE, AND REACTION TIME. Robert P. Borda and John H. Hablitz.* Dept. Physiology, Sect. Neurophysiology, Baylor College of Medicine, Houston, Tex. 77025.

Six normal adult male volunteers were subjects in a study which assessed the effects of a new hypnotic, Dalmane® (flurazepam HCl), on reaction time, the auditory evoked response, and the contingent negative variation (CNV). Dalmane was administered orally for two weeks in the usual clinical dose of 30 mg h. s. and was replaced by a placebo for an additional two weeks. The EEG was recorded every other day throughout the four-week study, and CNVs and evoked responses were recorded while the subjects performed a disjunctive reaction-time task with auditory cues. CNV amplitude and the secondary positive component of the evoked response were found to be reduced during Dalmane administration, while reaction time was unaffected. It was concluded that whereas Dalmane does not impair performance of a simple, well-learned task, its effect on the CNV suggests that the subjects' capacity for sensory-motor integration was reduced.

11.13 THE ASCERTAINMENT OF SIX YY MALES IN A PRIVATE NEUROLOGICAL PRACTICE. Fred A. Baughman, Jr.* and Joseph D. Mann*. (SPON: Morris B. Bender). Blodgett Memorial Hospital and Butterworth Hospital, Grand Rapids, Mich.

Six YY males, five XYY and one XXYY, were ascertained in the private neurological practice of the senior author. Excessive height importantly contributed to the suspicion of the YY abnormality in four of the six cases. In two, the chief complaint was tremor of the hands; two were referred because of "spells"; one because of violent temper, and one because of mental deficiency. Bias in regard to behavior was a factor in the ascertainment of only two of the six cases. Intelligence was subnormal in all but one. Four of the six have been free of antisocial behavior and three are notably mild mannered. The concept, set forth by Court-Brown, that the XYY genotype confers aberrant behavior with little or no defect of intelligence, is further questioned.

Session 12

12.1 CODING OF WEB-BUILDING MOVEMENTS IN THE SPIDER ARANEUS DIADEMATUS CL.
Peter N. Witt, Division of Research, N. C. Department of Mental Health, Raleigh, N. C. 27611.

To identify factors which influence the orb-web pattern, the daily reconstructed web of each spider is recorded through photography. Measurements of web size, shape, and regularity are computed and correlated with age, sex, species, (early) development, and family of the builder. An individual shows characteristic changes of the geometric pattern during its life, partially with changes in body weight and leg length, partially with age (baby, mature, and old age webs), different for each sex. At a given time of life (or development) of spiders, the inter-family component of variance significantly exceeded the interindividual component in full sibs in some web measures. In contrast, a relatively high repeatability of measures in duplicate webs from the same individuals was found. This makes genetic precoding of some web characteristics likely. Size measures in the web appear to be most specific for a family; previously established relationship between web-size and silk production make level of productivity of silk glands probably a family characteristic. - Web-measures can be interpreted as a consequence of the movements of the builder when it lays the thread. The movements are guided from the central nervous system, which in turn receives information from probing legs, filled silk glands, using precoded neuronal patterns and possibly some experience. The present study is used as an example for obtaining insight into level of coding of movements through establishing correlations between the ontogeny of a behavior pattern with development of individuals. (Supported in part by National Science Foundation grant number GB 25274).

12.2 HABITUATION TO VIBRATORY STIMULI IN THE WEB OF AN ORB-WEB SPIDER.
Charles F. Reed. Dept. Psychol., Temple Univ., Phila. 19122.

A vibratory stimulus applied to the orb web produces either retreat or approach by the spider (Araneus sp.). As Szlep (Behaviour 23: 3, 1964) has shown, the approach response extinguishes with repeated presentations of the stimulus, but can be restored by applying the stimulus elsewhere in the web. These observations were extended for a range of frequencies and amplitudes, the course of extinction within and between days examined, and generalization of the habituated response tested. A progressive decline in the number of trials required for habituation occurs for blocks of trials separated by three-minute intervals. A relative readiness for habituation is apparent 24 hours later, but considerably less apparent at 48 hours. Generalization of response to other sectors of the web is narrow; sectors external to the generalized range appear to be equally effective in restoring the response, i.e. in requiring equivalent repetition for return to cessation of the approach response.

12.3 AN INTEGRATIVE SYSTEM: THE CRAYFISH ANTENNAE AND BRAIN.
Robert C. Taylor. Dept. Zool., Univ. of Ga., Athens 30601.

The crayfish (Cf) can distinguish other individual Cf through antennal mechanoreceptor input. It also appears to function in an analogous manner to a blind man's cane. To explain this discrimination a study was initiated on antennal mechanoreceptors, the 3-D anatomy of the Cf brain and integrative mechanisms in the various neuropiles. Large mechanoreceptors in the antennal flagellum are divided into 3 classes: 1) Position, 2) intermediate (movement and adapting position), 3) vibration (with best frequencies scattered among different cells and responding to resonant frequencies). Phasically responding hairs are scattered on the basal segments and a large chordotonal organ is located in the two basal flagellar segments. Proprioceptors are located in some of the basal segments again showing the same type of response (i.e. position, movement, vibration). In the brain (supraesophageal ganglia) the antennal motor region is separate from the more anteriorly located sensory region. The antennal neuropile is continuous medially with the tegumentary and antennulary neuropiles and the trio is connected via a large, medial neuropile to the contralateral trio. Large tracts connect all regions and every neuropile feeds into the accessory lobes. Integrative activity within specific neuropiles was recorded with tungsten carbide and stainless steel electrodes and the position marked using M. Perls' ferrocyanide reaction (Virchow Arch. path. Anat. 39: 42 (1867). Anatomically the antennal sensory neuropile is divided into linear arrays of "modules" which appear to classify and reclassify inputs into signals meaningful to the Cf, e.g., posterior movement (acceleration) of the flagellum, vibration frequencies, etc. A modular integration theory based on McCulloch's model of the reticular formation will be presented. (Support by NSF & NIH Grants.)

12.4 PATTERNS OF ELECTRIC ORGAN DISCHARGE IN MORMYRID FISH DETERMINED BY PATTERNS OF ELECTRICAL STIMULATION SIMULATING CONSPECIFICS. Peter Moller* (SPON: R. L. Thompson). Hunter College of the City University of New York, N. Y. 10021.

Electric organ discharges (EODs) of weakly electric fish may serve as communicating signals as well as in object location. Four mormyrids (1 Marcusenius, 3 Gnathonemus) were systematically stimulated with 30-sec tape recorded samples of low frequency (2-5 H_z) or high frequency (10-20 H_z) species-typical discharge patterns converted to square wave pulses. Low stimulus intensity (0.7 mV/cm) evoked initial cessation of EOD at both low and high frequencies. At low frequency, EOD remained surpressed or returned to control level during and following stimulation. At high frequency, EOD recovered to correlate positively with momentary variations in stimulus frequency and remained elevated in rate after stimulus offset. High stimulus intensity (57.2 mV/cm) evoked brief EOD acceleration at both low and high frequencies. At low frequencies, EOD rate was postively correlated with variations of stimulus frequency and returned to control level at stimulus offset. At high frequencies, EOD rate was negatively correlated with stimulus frequency variations. At stimulus offset, EOD briefly ceased, then entered a highly regular phase. Similar results were obtained using a live conspecific as the stimulus (Moller & Bauer, in prep.).

12.5 ROLE OF THE LATERAL MEDULLA IN MATING AND RESPONSES TO GENITAL STIMULATION IN FEMALE CATS. James D. Rose* and Jerome Sutin. Dept. Anat., Emory Univ., Atlanta, Ga. 30322.

In previous work, we have identified a population of cells in the region of the lateral reticular nucleus which respond specifically to vaginal probing. In this study, we examined the effect of destruction of these cells upon aspects of reproductive behavior such as the estrous cry and afterreaction which are elicited by vaginal probing or mating in the estrous cat. Bilateral radiofrequency current lesions were stereotaxically placed in the ventrolateral medulla of seven ovariectomized cats. Behavioral responses to vaginal probing and mating with a male cat were assessed with the animals in the anestrous state and after induction of estrous by estradiol injections given both before and after placement of the lesions. Post-lesion observation periods extended up to 52 days. Recording locomotor behavior on film and the estrous cry on magnetic tape aided the analysis of lesion effects. The lesions produced an ataxia, most pronounced in the hindlimbs, which abated within a few days. The estrous cry and afterreaction to vaginal probing and mating were either attenuated or abolished throughout the post-lesion observation period. Lateral tail deflection, treading, and lordosis in response to perineal tapping were not impaired. These results indicate that neurons in the ventrolateral medulla which respond to vaginal probing are concerned with the manifestation of the estrous cry and afterreaction of the female cat. (Supported by USPHS Grant FR-5364, NIH Postdoctoral Fellowship 1F2NB42889-01, and NIH Training Grant 5T01-NS 05669)

12.6 STORAGE OF COPULATORY STIMULATION IN THE FEMALE RAT. Susan Craig*, Stephen Zoloth* and Norman Adler. Department of Psychology, University of Pennsylvania, Philadelphia, Penna. 19104.

During copulation, the male rat mounts and dismounts from the female a number of times; during some mounts penile intromission occurs, and on the final intromission, the male ejaculates. The accumulated stimulation derived from the male's multiple intromissions is necessary for successful pregnancy; the intromissions initiate a neuroendocrine reflex resulting in the secretion of gestagen (state of pseudopregnancy). Since the probability of inducing pseudopregnancy increases as a function of the number of intromissions (J. Comp. Physiol. Psychol., 69:613, 1969), there must be some mechanism by which the stimulation from each of the intromissions can be stored. This storage of excitation in the female rat, as a function of the interval between intromissions, was studied in work presented here. Each female rat received either 2, 3, 5, or 10 intromissions. The spacing between intromissions was also systematically varied, from approximately 40 seconds to 1 hour. There was prolonged storage of copulatory stimulation. Between 80% and 100% of the females receiving 10 intromissions became pseudopregnant, even though the inter-intromission-interval was as long as 1 hour. Moreover, in the groups where females received 3 or 5 intromissions, more females became pseudopregnant if the intromissions were spaced apart by several minutes than if they were delivered ad libitum (40 sec.). Thus, the female rat is capable of storing copulatory stimulation over prolonged periods of time. This storage capability may be related to the normal copulatory pattern of the rat in its natural environment.

12.7 SOMATOSENSORY UNIT RESPONSE HABITUATION: CONTRASTING EFFECTS OF STIMULUS INTENSITY. Solon B. Holstein*, Jennifer S. Buchwald, and Judith Schwafel*. Dept. Physiol., Sch. Med. UCLA, L.A. 90024 and VA Hospital, Long Beach, Ca.

Multiple unit discharges of ventralis posterolateralis (VPL) were recorded in unanesthetized, chronically implanted cats. Natural cutaneous stimulation elicited distinctive patterns of increased discharge frequency, which reflected restrictive contralateral somatotopic fields. Repeated elicitation of contralateral forelimb flexion by 0.5 sec shock train to the paw was used to investigate systematic modifications in VPL discharge patterns and reflex behavior. Each animal experienced repeated habituation tests of 50 trials presented at an inter-trial interval of 15 sec. Each test utilized one of 3 levels of stimulus current selected from a random series. Statistically significant inverse relationships were found between the current intensity and magnitude of habituation, i.e., the weaker the stimulus the greater the progressive decrement in flexion response and VPL discharge. Post-habituation tests of dishabituation or spontaneous recovery typically resulted in a restoration of the magnitude of both the behavioral and electrophysiological measures. A second sequence of experiments examined generalized responsiveness by comparing the effects of habituation on test trials of each of 3 intensities, randomly presented, before and after habituation. It was found that the higher the intensity of the habituating stimulus, the greater the loss of responsivity to the test stimuli. While the former results suggest that the magnitude of response decrement is inversely related to the intensity of the habituating stimulus, the latter data indicate that generalized loss of responsivity is directly related to the intensity of the habituating stimulus.

12.8 AUDITORY THRESHOLDS IN THE KANGAROO RAT BEFORE AND AFTER REDUCTION OF MIDDLE EAR VOLUME. Douglas B. Webster and Molly Webster.* Dept. Biol., New York University, Bronx, N.Y. 10453.

Binaural, free field hearing thresholds for pure tones between 125 and 8000 Hz were determined for Dipodomys merriami in a shock avoidance tilt cage apparatus. Animals were trained to respond to a 70 dB (re. 0.0002 dynes/cm^2) tone. The sound level was then systematically attenuated and the intensity at which the % correct responses was half that at 70 dB was arbitrarily defined as threshold. The following mean thresholds were determined: at 125Hz, 21 dB; at 250 Hz, 16 dB; at 500 Hz, 10 dB; at 1000 Hz, 9 dB; at 2000 Hz, 10 dB; at 4000 Hz, 17 dB; at 8000 Hz, 19 dB. These thresholds indicate better hearing than humans at frequencies up to 1000 Hz, and poorer hearing above that. They are consistent with cochlear microphonic and evoked potential studies which also have indicated kangaroo rats are low frequency hearers. Previous field studies have shown that primary predators of kangaroo rats (rattlesnakes and owls) produce a low frequency noise during strikes and that normal kangaroo rats can avoid these strike attempts. Kangaroo rats whose hypertrophied middle ear cavities have been surgically reduced, and whose vision is also impaired, cannot avoid these predatory strikes. The present study demonstrates that reduction of middle ear volume raises the behaviorally determined threshold by an average of 16.5 dB at frequencies up to 1000 Hz, but by only 7 dB above 1000 Hz. (Supported by grant NS 05800 from NIH.)

12.9 TRIGEMINAL DEAFFERENTATION AND FEEDING BEHAVIOR IN PIGEONS: SENSORY AND MOTIVATIONAL EFFECTS. H. Philip Zeigler. Dep't. Psychol., Hunter College, CUNY, N. Y. 10021.

The peripheral distribution of the pigeon's trigeminal nerve permits deafferentation without disrupting motor function. Deafferentation affects both food intake and mandibulation--the process by which grain is moved from beak tip to back of mouth. In 8 birds bilateral section of trigeminal sensory nerves produced periods of aphagia which persisted for several weeks and were followed by prolonged periods of reduced intake (hypophagia). No such effects were seen in surgical controls and there were no effects upon drinking. Mandibulation deficits were assessed in 6 birds by calculating the number of feeding responses required to obtain a unit quantity of grain. Pecking and swallowing were unaffected by deafferentation but food/response ratios increased significantly and remained high for many weeks. Automatic monitoring of eating in aphagic and hypophagic birds indicates that the reduced food intake is due to the absence or reduction of feeding responses rather than to mandibulation deficits. We conclude that in addition to producing somatosensory deficits trigeminal deafferentation of the oral region affects motivational processes underlying responsiveness to food. The results are consistent with previous studies implicating central trigeminal structures in the neural control of hunger in the pigeon.

12.10 TEMPORAL PROCESSING AND PERCEPTUAL LATENCIES. Ruth Rutschmann. Dept. Psych., Queens Coll. CUNY, NY 11367

The studies are based on a model which a) assumes that maximal indeterminacy of the perceived order of two events (subjective simultaneity) occurs at interstimulus intervals producing approximately synchronous central processing, and b) attempts to relate two measures of temporal processing to variations in stimulus conditions. Relative latencies to paired stimuli in different modalities (visual, auditory, tactile) were estimated from psychophysical functions relating frequency of temporal order judgments to stimulus asynchronies, and from simple reaction time responses to the same stimuli obtained with the same subjects in the same session. In general, the psychophysical and psychomotor measures reflect comparable changes in perceptual latency as a function of variations in stimulus conditions, as e.g. sensation level of flash or click. There are individual differences in the absolute amount of latency difference to a particular pair, but qualitatively subjects perform similarly and do not show evidence of systematic biases for inputs processed in the hemisphere dominant for speech. The experiments do not support the notion that correct detection of temporal order is associated with relatively fixed interstimulus delays and is independent of sensory parameters of stimulation.

12.11 AUDITORY INFORMATION PROCESSING BY CVA HEMIPLEGIC ADULTS. Glenn E. Snelbecker* and William Fullard* (SPON: A. Finck). Temple University and Moss Rehabilitation Hospital, Phila., Pa., 19140.

This series of studies uses human operant research procedures and information theory techniques to delineate optimal conditions for presenting information to brain-damaged patients. Data from normal adults and children are used as reference groups to evaluate the performance of hemiplegic adult patients whose above-midbrain lesions have resulted from CVA. Pure tone stimuli from 100 to 8000 Hz equally spaced on a log frequency scale were presented to individual subjects. Three levels of stimulus uncertainty were used, involving 3, 4, or 5 tones. The subject "matched" each stimulus tone with the appropriate button on a 16-key console panel, with unused keys excluded from the subject's view. At all levels of stimulus uncertainty, the hemiplegic adults had substantially lower scores than the normal adults and moderately lower scores than 8- to 11-year-old children. The differences were most dramatic on the higher levels of stimulus uncertainty. Under experimental conditions used thus far, no significant differences have been detected between right- and left-hemiplegic patients. This experimental technique provides a feasible means for assessing the auditory information processing capabilities of brain-damaged patients.

12.12 MEDIATION OF VISUAL FEAR VIA THE CORPUS CALLOSUM. Robert W. Doty, Kenichi Yamaga* and Nubio Negrão*. Center for Brain Research, University of Rochester, Rochester, New York 14620.

In three macaques the right optic tract, anterior commissure and all of the corpus callosum rostral to the splenium were cut, and a "snare" placed around the remaining 5 - 7 mm of the splenium and psalterium. The left amygdala was subsequently removed by aspiration (extent not yet verified). Fear reactions remained normal, flight occurring to the slightest human approach or threat. Transection of the splenium by pulling the snare under local anesthesia (5, 45 and 120 days after amygdalectomy) effected an immediate and dramatic transformation in which the animals displayed no apprehension until touched, although they would blink or duck "reflexly" from a rapidly approaching object. Thus, confirming work of Downer and of Horel and Keating, the splenium transmits information between the visual and motivational systems permitting identification of threatening stimuli. Some recovery occurs after 10 - 14 days, apparently over subcortical paths since removal of the other amygdala then reprecipitates the absence of visually evoked fear. (Supported by Grant NS 03606 from NINDS and Grant GB-7522X1 from NSF)

Session 13

13.1 FUNCTIONAL ULTRASTRUCTURE OF THE CANINE ARACHNOID VILLUS. John F. Alksne, and Ethel T. Lovings*. Div. of Neurosurg., Univ. Calif. San Diego, La Jolla, Calif. 92103 and Div. of Neurosurg., Med. Coll. of Va., Richmond, Va. 23219.

Prior studies with the electron microscope have failed to identify the 8-12 micron pores in the arachnoid villus postulated to explain physiological flow studies. In order to further elucidate the morphology of spinal fluid absorbtion horseradish peroxidase has been injected into the cistern magna of dogs and arachnoid villi have been studied at sequential time intervals of ten minutes to three hours. In a second series of animals increased intracranial pressure has been maintained in order to maximize CSF to blood transport. The majority of the tracer appears to enter arachnoid cells rather than pass across the covering endothelium of the villus suggesting that some revision in the concepts of spinal fluid absorbtion may be necessary.

13.2 EXPERIMENTAL MODIFICATION OF CEREBELLAR CIRCUITRY DURING DEVELOPMENT AND ITS BEHAVIORAL CONSEQUENCES. Joseph Altman and William J. Anderson*. Lab. Devel. Neurobiol., Dept. Biol. Sci., Purdue, Lafayette, Ind. 47907.

In the rat, the precursors of the microneurons of the cerebellar cortex, the basket, stellate, Lugaro and granule cells, come into existence after birth. The chronology of the sequential differentiation of these different cell types during the first three weeks of postnatal life has been established. Because multiplying cells are extremely radiosensitive, they can be destroyed selectively with low-level focal x-ray, without visibly harming the differentiating and mature nerve cell population. Thus, using different schedules of irradiation it has become possible to produce different "species" of cerebellar cortices characterized by (a) total absence of all microneurons and absence of cortical lamination; (b) subtotal elimination of all microneurons with normal lamination; (c) selective elimination of the early-forming microneurons (basket and early granule cells); (d) selective elimination of the late-forming microneurons (stellate and late granule cells); (e) selective reduction of the granule cell population; (f) displacement of the granule cells (ectopia), and (g) preferential retardation of vermis and hemispheres. The behavioral testing of these animals with special reference to the development of motor skills was begun and some of the results will be described.

13.3 DEVELOPMENT OF NEURONS AND SYNAPSES IN CULTURES OF DISSOCIATED CELLS OF EMBRYO MOUSE CNS. A LIGHT AND ELECTRON MICROSCOPIC STUDY. Murray B. Bornstein and Pat G. Model* Depts. Neurol. & Anat., Albert Einstein Coll. Med., Rose F. Kennedy Center, Bronx, N.Y. 10461.

13-14 day mouse embryo spinal cord and brain stem were dissociated by exposure to 0.25% trypsin and repeated pipetting. Suspensions of cells, in concentrations of from 1 to $6x10^6$ cells/ml, were explanted on to 2 kinds of collagen-coated coverslips -- those carrying fragments of other tissue (cord, heart, fibroblasts) or not. They were maintained in Maximow slide assemblies for 2-4 weeks. The leaner suspensions appeared to survive better on coverslips which carried fragments of tissue, whether CNS or not. Single cells and reaggregates of from 2 to hundreds of cells attached to the collagen and differentiated into neurons, neuroglia and ependyma. Numerous neurites grew out to form a complex neuropil, rich in axo-dendritic synapses. Axo-dendritic and axo-somatic synapses were also present within the reaggregates. During the 3rd week in vitro, myelin formed in the larger reaggregates.

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13.4 ALTERATIONS AT NODES OF RANVIER PRODUCED BY TREATMENT WITH TRYPSIN. Richard P. Bunge and Riley C. Yu*. Dept. Anat., Washington Uni. School of Medicine, St. Louis, Mo. 63110.

Long term tissue cultures of rodent sensory ganglia provide an opportunity for direct microscopic observations on the reaction of the peripheral myelin sheath to various agents. We have observed that treatment of well myelinated mature cultures with 0.2% trypsin(bovine, cryst., Mann) for several hours causes substantial change in the region of the node of Ranvier. These alterations have been studied by light and electron microscopy. The initial change observed is a retraction of the Schwann cell processes that normally interdigitate in the nodal region. The nodal region then begins to lengthen and the myelin internode is foreshortened until extensive portions of the axon are bared. As this occurs the myelin becomes abnormally redundant in the paranodal region. Electron microscopic observations indicate that the terminal myelin loops remain in close proximity to the axon. With periods of treatment up to 4 hours, neurons and axons are notably resistant to trypsin application and may be maintained for extended periods after being returned to normal medium. After several weeks denuded portions of the axon may display newly formed myelin internodes; at the same time they retain segments of myelin grossly distorted by the initial trypsin treatment. It is concluded that trypsin may affect the special Schwann cell-axon contacts near the node without irreversible damage to the neuron, axon or Schwann cell itself.

Supported by the National Multiple Sclerosis Society

13.5 MATURATION OF THE POSTMIGRATORY NEURON: A RADIOAUTOGRAPHIC AND ULTRASTRUCTURAL STUDY. A. B. Butler* (SPON: J.A. Jane) Dept. Neurosurgery, Sch. Med., Univ. of Virginia, Charlottesville, Va. 22901

As a continuation of the study of the development of the parietal cortex of the Syrian hamster (Butler, A.B., and Caley, D.W., Anat. Rec. 169:287, 1971), neurons labeled in the ventricular zone at birth have been traced by radioautographic methods to their destination in lamina II and III. These labeled cells have been studied with the electron microscope from the time they cease migration until they are mature neurons. Labeled neurons were identified on semi-thin radioautographs with the light microscope. Identical cells were visualized on adjacent ultrathin sections with the electron microscope. Labeled neurons on postnatal day 6 have completed migration and typically exhibit a large apical process and an oblong or round nucleus. The cytoplasm contains numerous organelles the most characteristic being the complex RER. Differentiation of early post-migratory labeled neurons (PND 8-12) is characterized by a continued proliferation of RER begun during migration, a decreasing number of microtubules and filaments in the perikaryon and proximal processes compared to the late migratory stages, and a further increase in the size of the cell body and nucleus. Basal dendrites are identified in some cells at this stage. The number and complexity of organelles change little up to 130 days other than a further proliferation of RER in some labeled cells. By PND 30, labeled neurons were identified as stellate or small pyramidal neurons, with the latter predominating. A definite sequence of synaptic development was found with axo-dendritic synapses developing on the apical dendrites during the 10-20 day period, followed by axo-somatic synapses present by PND 30.

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13.6 IS THERE A SEX DIFFERENCE IN THE NUMBER OF MAMMALIAN CENTRAL NEURONS? Franco R. Calaresu and James L. Henry*. Dept. Physiology, Univ. Western Ontario, London 72, Canada.

It is established that the mean weight of the central nervous system of men is greater than that of women. At least four possibilities may be suggested to account for this difference : a difference in the number of neurons, a difference in their size, a difference in the number of glial cells, or a difference in the neuropil/perikaryon ratio. To test the possibility of a difference in the number of neurons serial transverse sections of the spinal cord of eight adult cats were stained with thionin and the neurons of the thoraco-lumbar intermediolateral nucleus were counted. A statistically significant ($p < 0.02$) difference was demonstrated between the mean count in four female cats (35,543 ± 1,411) and the mean count in four males (45,765 ± 2,556). This finding suggests that the number of neurons in the mammalian central nervous system may be different in the two sexes. It is further suggested that the greater number of neurons in the male may be related to the statistical expectation of a greater body mass in the fully developed animal. These results raise interesting questions regarding the influence of genetic and environmental factors on the developmental dynamics of neurogenesis in the two sexes.

(Supported by the Medical Research Council of Canada).

13.7 ON THE ORGANIZATION OF CEREBELLAR EFFERENT PATHWAYS IN THE NURSE SHARK, GINGLYMOSTOMA CIRRATUM (BONNATERRE). C.B.G. Campbell and Sven O.E. Ebbesson. Center for Neural Sciences, Indiana Univ., Bloomington, Ind. 47401; Dept. Neurosurgery, Univ. of Virginia, Med. Sch., Charlottesville, Va. 22901, and Lerner Marine Lab., Bimini, Bahamas.

Unilateral suction lesions were placed in the corpus cerebelli and auricles of sixteen nurse sharks. After survival periods of 10 days to 8 weeks the animals were killed by perfusion with 10% formalin, the brains processed by several modifications of the Nauta experimental silver impregnation method, and the degenerating efferent cerebellar pathways charted. Efferent fibers from the cerebellar cortex were found to terminate in the homolateral lateral cerebellar nucleus and via commissural fibers to be distributed to corresponding cortical areas of the opposite side and the contralateral lateral cerebellar nucleus. Lesions which involved the lateral cerebellar nucleus revealed two efferent systems: (1)a brachium conjunctivum system which projects to the contralateral medial medullary reticular formation via ascending and descending fibers, nucleus ruber, oculomotor nucleus, and trochlear nucleus, and (2)an uncrossed tract which descends to terminate in the lateral rhombencephalic reticular formation. No cerebello-hypothalamic pathway and no tractus cerebello-motorius cruciatus et rectus were demonstrable with experimental methods. In contrast with the notions of earlier workers, the present study indicates that at least Purkinje cell axons in this species of shark do not directly innervate neurons of the non-cerebellar brainstem or spinal cord.

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13.8 ROLE OF THE VAGUS IN CARDIAC PATHOLOGY. K.C. Corley, F.O'M. Shiel*, H.P. Mauck*, and J.H. Greenhoot, Dept. Physiol., Pathol., Med. and Neurosurg., Med. Coll. Va., Richmond, Va. 23219.

Consideration of the central nervous system involvement in the pathology of the heart has concentrated on the sympathetic innervation. While parasympathetic influences on cardiac function are recognized, cardiovascular pathology associated with this innervation has been generally overlooked. Experiments have shown that vagal stimulation can induce myocardial degeneration and sudden death, but these studies have not excluded indirect sympathetic involvement as a possible mechanism for these effects. The following study was designed to determine the effects of vagal stimulation on the heart when sympathetic responses shown to produce morphologic changes have been eliminated. In cats anesthetized with Na thiamylal, the spinal cords were sectioned at the cervical level (C_2), and the animals artificially respirated. Both vagii were sectioned, and electrodes placed on the distal cut-end. Blood pressure and heart rate were continuously monitored, and a stimulus (0.5-2.0 mA, 30 hz, 0.5 msec biphasic pulses) sufficient to reduce heart rate by 50%, without significant change in arterial pressure, was applied to the nerve. As additional control of sympathetic effects, propranolol (l mg/kg) was used in some cats to block heart beta-receptors. After stimulation for 60-90 minutes over a 3-hour period, cats were sacrificed, and the hearts studied. All experimental animals showed focal myocytolysis and in some instances fuchsinophilic changes of the myocardium, whereas minimal changes were found in sham operated controls. These data indicate in cat the potential for enhanced vagal discharge to produce myocardial cellular damage. (Supported by USPHS grants NS-01024, NS-07839, and HE-13454).

13.9 TRANSPLANTATION OF PRECURSORS OF NERVE CELLS IN THE CEREBELLUM OF YOUNG RATS. Gopal D. Das and Joseph Altman. Dept. Biol. Sc., Purdue University, Lafayette, Ind. 47907.

In the cerebellum of 7-day old rats, slabs of cerebellum from the donors of the same age were transplanted. One hour prior to the surgery, the donor animals were injected with thymidine-H^3 (dose: 10 μ C/gm. body weight; specific activity: 6.7 C/mM) in order to label the mitotically active cells of the external granular layer of the cerebellum. This facilitated identification of the transplanted elements, and determination of their survival, migration and differentiation in the host cerebellum. The host animals were kept for survival periods of 3 hrs, 1, 2, 4, 6, 10 and 16 days, at the end of which they were sacrificed and their brains were processed for autoradiography. The cells of the external granular layer of the donor tissue appeared to remain viable at least for 2 days. These cells showed active migration into the host cerebellum along three main paths, and they were the molecular layer, external granular layer and internal granular layer. In the long survival animals intensely as well as lightly labeled cells in the molecular and internal granular layers were found. The lightly labeled cells helped establish that the transplanted precursors of nerve cells were able to migrate into the host cerebellum, undergo mitosis and differentiate into the stellate, basket and granule cells.

13.10 PROJECTIONS OF THE OPTIC TECTUM IN THE NURSE SHARK, GINGLYMOSTOMA CIRRATUM (BONNATERRE). Sven O.E. Ebbesson. Dept. Neurosurgery, Univ. of Virginia, Med. Sch., Charlottesville, Va. 22901 and Lerner Marine Lab., Bimini, Bahamas.

Axons undergoing Wallerian degeneration following tectal lesions were demonstrated with modified Nauta and Fink-Heimer methods and traced to their termination in 10 nurse sharks. The postoperative survival times ranged from 7-35 days and the lesions varied in size from very small to total unilateral removal. Four distinct fiber paths originating in the optic tectum were identified. The largest is a massive diffuse pathway that ascends to terminate in several distinct ipsilateral thalamic nuclei, including the lateral geniculate nucleus and a large, more medially located nucleus, reminiscent of nucleus rotundus of birds and reptiles. A second pathway distributes to the deep layers of the contralateral optic tectum whereas the remaining two descend in the tegmentum as far as the medulla. One of these is crossed and issues fibers to dorsomedial reticular cell groups along its course, whereas the ipsilateral one terminates in the ventrolateral reticular zone. These findings are very similar to those we have seen in other vertebrate classes and support the notion that the principal pattern of central visual system organization was established very early in vertebrate evolution.

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13.11 RECENT OBSERVATIONS ON THE STRUCTURAL ORGANIZATION OF THE SPINAL V NUCLEUS IN THE CAT: THE DEEP FIBER BUNDLES. Stephen Gobel* (SPON: R. Dubner). Neural Mechanisms Section, National Institute of Dental Research, NIH, Bethesda, Md. 20014.

The most prominent feature of the spinal V nucleus is the presence of numerous small bundles of axons, ~ 40-60μ in diameter. These deep fiber bundles emanate from all levels of the spinal V tract and run longitudinally through the nucleus. A typical deep fiber bundle consists of myelinated and unmyelinated axons in an approximate 1:1 relationship. About three fourths of the myelinated axons fall between 0.5 and 1.5μ in diameter and, with the exception of a small number of large myelinated axons (5-6μ), the remaining one quarter fall between 1.5 and 3.0μ in diameter. The fine caliber unmyelinated axons (0.1-0.3μ) are found throughout the bundle either singly or in small fascicles. Light and electron microscopical analyses of the deep fiber bundles reveal three distinct patterns of axonal degeneration within 1 week following either V nerve rhizotomy or transection of the spinal V nucleus and tract either at the level of subnucleus oralis or subnucleus caudalis. After V nerve rhizotomy each deep fiber bundle contains a few large degenerating myelinated axons and an occasional small one. Caudal to the point of transection of the tract and subnucleus oralis, the deep fiber bundles exhibit many more small degenerating myelinated axons than after V nerve rhizotomy. Most of these small degenerating axons run in the periphery of the bundles. Rostral to the point of transection of subnucleus caudalis, the deep fiber bundles contain numerous small degenerating myelinated axons which are most numerous in the center of the bundle. These findings indicate that the deep fiber bundles, in addition to conveying some V nerve axons caudally, contain numerous axons which run rostrally as well as caudally and constitute a major intranuclear pathway in the spinal V nucleus.

13.12 DEGENERATION AND REGENERATION PHENOMENA IN OLFACTORY RECEPTOR NEURONS. P. P. C. Graziadei and J. F. Metcalf*. Department of Biological Science, Florida State University, Tallahassee, Florida 32306.

The observation that olfactory receptor neurons are continuously replaced during the adult life of vertebrates has been established with the aid of morphological and autoradiographic techniques. A second fact of interest was also observed, namely that in the olfactory receptor neurons the cutting of their axons (which normally extend to the olfactory bulb, where they synapse with the mitral cells) is not followed by the regeneration of the proximal stump, as commonly observed in other peripheral or CNS neurons. Instead, the severing of the axons is followed by the total degeneration of the neuronal cell bodies. When an olfactory nerve of one side is totally severed, degeneration of homolateral olfactory receptor neurons is observed. Contemporary to this degenerative phenomenon, a burst of mitotic figures are observed in the so called "basal cells" which divide and differentiate into mature receptor neurons. The basal cells are in reality neuroblasts with the capacity of becoming fully differentiated neurons. The degeneration of the mature cells experimentally obtained with the cutting of the olfactory nerves and followed by the regeneration of new receptors may represent an artifactural exaggeration of those degenerative-regenerative phenomena that have been shown to occur in normal animals with the aid of autoradiographic techniques. This phenomenon of degeneration and regeneration following the cutting of the olfactory nerves represents an ideal system for the study of morphological and biochemical correlates of neuronal plasticity in adult vertebrates.

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13.13 ALTERATIONS IN SYNAPTIC PARAMETERS PRODUCED BY REARING ENVIRONMENT IN RATS. William T. Greenough*, Roger West*, and T. Blaise Fleischmann* (SPON: E. Donchin). Dept. Psychol., Univ. Illinois, Urbana/Champaign, Ill. 61820.

Past studies have indicated that the distribution and size of synapses in various brain regions may be altered by changes in sensory stimulation. We have obtained similar effects by varying the complexity of the environment in which the animals are raised. Male littermate sets of rats were assigned (at 23 days of age) to either large group cages containing "toys", with a daily opportunity for free play in a toy-filled field, or to isolation cages with no view of other rats. After 30 days of environment, the animals were sacrificed and sections from visual cortex prepared, by conventional methods (stained with lead citrate and uranyl acetate), for electron microscopic examination. Micrographs (43,300x) were analyzed, without knowledge of the group to which they belonged, for total contact area and length of post-synaptic opaque region in asymmetric, round-vesicle synapses. The enriched-reared animals were found to have considerably larger area per synapse in layer 3 of the visual cortex. The distribution of synapses in other areas also seems to be altered by the rearing environment. Preliminary results indicate these effects involve an enhancement from the level of a socially-housed control, rather than a deprivation or impoverishment effect. The differences may represent a residue of information processing by the nervous system.

13.14 BINOCULAR COMPETITION IN THE CONTROL OF GENICULATE CELL GROWTH. R.W. Guillery, Dept. Anat., University of Wisconsin, Madison, Wisconsin 53706.

It has been shown previously that in kittens geniculate laminae that are visually deprived by a unilateral lid-suture grow less than normal. However, cell growth is affected only where the deprived laminae lie opposite a normally innervated lamina. The most lateral part of lamina A, which is innervated from the monocular crescent of the visual field and which extends beyond the edge of lamina A1, is not affected by lid-suture. One interpretation of this result is that a binocular competition controls geniculate cell growth and that the normal competitive balance is upset by the lid-suture. In order to test this interpretation further four kittens had the lids of one eye sutured and in the other eye a patch of temporal hemiretina was destroyed. After 5.5 to 12 weeks' survival lamina A1 showed a patch of transneuronal degeneration produced by the ipsilateral retinal lesion. Most of lamina A showed a reduced cell growth contralateral to the suture. However, the part lying opposite the zone of transneuronal degeneration contained cells that were larger than would be expected if there were no competitive effect ($p<0.01$). These results suggest that geniculate cells may compete for available synaptic surfaces upon cortical cells and that success in this competition may depend upon the nature of the visual input. They provide no evidence that visual deprivation can change geniculate cell growth by any direct, non-competitive effect.

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13.15 Degeneration from Alumina Cream Epileptogenic Foci - Relation to Seizures.
A. Basil Harris, M.D., Department of Neurological Surgery, University of Washington School of Medicine, Seattle, Washington 98105.

Acute and chronic epileptogenic sensorimotor cortical lesions were created by minute injections of aluminum hydroxide gel in adult macaca rhesus monkeys. Axon and terminal degeneration in this experimental animal model of epilepsy was assessed by Nauta-Gygax and Fink Heimer reduced silver methods on serial whole brain sections. Seizure development was followed with EEG, and cortical epileptogenic foci were verified by transdural electrocorticographic localization. Such foci consistently abutted alumina injection sites. Animals with acute, intermediate or chronic lesions were compared to a group treated with anticonvulsants. Studies in the first group showed that axon and terminal degeneration from alumina followed closely the distribution from electrolytic lesions reported by others. Acute degeneration products disappeared by one year. Chronic animals (1-5 yrs.) having seizures continue to show degeneration of axons and terminals so that this form of seizures is a continuum of events. In the second group of animals, anticonvulsants were given in a sufficient dosage to control seizures. When this control was absolute for a sufficient time period to allow residual degenerative products to be removed, the axon and terminal degeneration markedly diminished or was absent. Thus the evidence in this study is that seizures contribute to degeneration in the nervous system.

13.16 Evidence for recycling of membrane accompanying transmitter release at the frog neuromuscular junction

John E. Heuser, Research Associate, Laboratory of Neuropathology and Neuroanatomical Sciences, NINDS, NIH, Bethesda, Md.(SPON:Phillip G.Nelson)

It was recently found that exposing frog neuromuscular junctions to La^{++} ions leads to a massive spontaneous release of transmitter accompanied by drastic morphologic changes in the internal membrane compartments of the presynaptic terminals: the usual clusters of synaptic vesicles are replaced by membrane bound cysternae apparently linked to the cell surface by "coated vesicles" (Heuser & Miledi, Proc.Roy.Soc.1971). Since La^{++} blocks evoked transmitter release irreversibly, it was not possible to relate these morphologic changes to normal transmitter release. It has now been found that identical morphologic changes accompany transmitter release evoked by nerve stimulation at 10Hz for 15 minutes or exposure to 40mM K^{+} for 15 minutes at 10°C. Furthermore, following these treatments the morphologic changes are entirely reversible; the terminals revert to normal appearance during the 30-60min. rest period required for full recovery of transmitter release at 10°C. Several features of this morphological recovery have led to the hypothesis that transmitter release at the neuromuscular junction involves recycling of membrane, in which the membrane of synaptic vesicles merges with presynaptic membrane during transmitter release, and then is recovered as "coated vesicles" and transferred to internal membrane-bound cysternae (analogous to Golgi apparati) before returning to synaptic vesicles. These features include: (1) these various membrane forms are so located in the presynaptic terminal that they appear to form a structural sequence; (2) each membrane form predominates at a particular stage of recovery, so that membrane appears to pass through these forms in a clear temporal sequence; and (3) the tracer horseradish peroxidase applied during stimulation fills "coated vesicles", then membrane-bound cysternae, and finally synaptic vesicles, in an apparently sequential fashion.

13.17 VISUAL FUNCTION OF RAT RETINAS MALFORMED BY IRRADIATION AT BIRTH. Samuel P. Hicks and Constance J. D'Amato. Department of Pathology, University of Michigan Medical Center, Ann Arbor, Michigan 48104.

Opportunities to observe function of abnormally developed nervous tissues are rare. Radiation induces developmental abnormalities whose patterns are highly reproducible and dependent on dose and stage of development. Two hundred R to eyes at birth produces deficient retinas with "doubled" bipolar layer and photoreceptor rosettes; 600 R produces extremely deficient, chaotically structured retina with few photoreceptors. Rats bearing these types of retinas and trained from weanling age (Method: Exptl. Neur., 29:416-438, 1970) discriminated reciprocal pairs of patterns, such as stripes, triangles, and fractions of triangles, were not confused by triangles of unequal size or brightness, jumped from a platform to a stationary or moving platform in different positions, and to a dimly lighted platform in darkness. Six hundred R rats learned slower than normals, were less accurate in jumping to a moving platform.

When rats with one eye irradiated (600 R) learned to discriminate a pattern through that irradiated eye alone, they promptly discriminated the same pattern when it was presented to the opposite normal eye which had never seen the pattern. Thus, in what ever way the chaotic retina may have coded visual information for the brain, the brain was able to recognize the information in normal code.

Control rats made blind at birth learned to jump to the stationary platforms in fixed situations, but performed none of the other "visual" tasks.

13.18 FREEZE-ETCH AND THE FINE STRUCTURE OF PERIPHERAL NERVE. S.J.Hubbard. Dept.Anat., Rutgers Medical School, New Brunswick, N.J.08903.

The fine structure of nerve fibres in the sciatic plexus of the frog was examined in replicas obtained by the freeze-etch technique. The endoneurium, myelin, axolemma and axoplasm were seen in a variety of fractures. The two orientations, circular and longitudinal, of the small collagen and reticular fibres of the endoneurium were clearly demonstrable in a single photomicrograph. In the same preparation the outer Schwann cell membrane was seen pushing through the interstices of the fibre network thus sharing the environment of other nerve fibres. The collagen period was estimated as 660 Å. Schwann cell cytoplasm was seen both at the periphery, where it contained many cell organelles, and close to the axolemma where it was relatively homogeneous. Distortion of the myelin, presumably near clefts and nodes, showed cytoplasmic inclusions at various levels within the myelin sheath and, hence, intracellular continuity. The myelin period was estimated to be 180 Å corresponding well with X-ray diffraction measurements on fresh preparations. Myelin fractures showed several faces with different particle populations which might be related to different cleavage planes through the myelin. The myelin-axolemmal junction was resolved and the spacing estimated to be 200 Å. Axoplasm, either in cross or transverse fracture showed neurofilaments and neurotubules together with some vesicles and mitochondria. It is concluded that freeze-etch techniques can confirm and extend knowledge gained from conventional E.M. methods and should prove useful when combined with physiological studies.

13.19 THE FUNCTIONAL RELATIONSHIP OF NEURONS AND SATELLITE CELLS IN METABOLICALLY ACTIVE GANGLIA. A. O. Humbertson, Jr. and J. E. Zimmerman*. Dept. Anat., The Ohio State Univ. Coll. Med., Cols. Oh. 43210 and Dept. Surg., Sch. Med. UCLA, Los Angeles, Calif. 90024.

Proliferation of satellite cells in metabolically active sensory ganglia have been extensively studied. The chronological pattern of the proliferative response to nerve injury has been established and is affected by the distance of the ganglia from the peripheral nerve lesion. There was a close correlation temporally between the severity of neuronal chromatolysis and the extent of the satellite cell response. Using intratheal colchicine mitotic activity was demonstrated in satellite cells proliferating after nerve injury, while no such activity was observed in sensory ganglia with uninjured nerves. The degree of mitotic activity paralleled the magnitude of the satellite cell proliferation. Satellite cell proliferation was associated with the increased neuronal metabolism and neuronal hypertrophy produced by axotomy. However, proliferation did not accompany increased neuronal metabolism in the absence of neuronal hypertrophy as produced by intratheal colchicine. Therefore, neuronal hypertrophy rather than neuronal metabolism may be the initiating event in the satellite cell hyperplasia that frequently accompanies chromatolysis in sensory ganglia.

13.20 AN EXPERIMENTAL ULTRASTRUCTURAL APPROACH TO THE IDENTIFICATION OF SYNAPTIC ENDINGS IN THE OPOSSUM RED NUCLEUS. James S. King, George F. Martin and Richard Dom. Dept. Anat., Coll. Med., Ohio State University, Col., Oh. 43210

The purpose of the present investigation was to determine the precise location of synaptic endings in the red nucleus whose cell bodies of origin are in the cerebral cortex and the deep cerebellar nuclei. A series of lesions were placed in the "motor cortex" by cautery and suction or in the deep cerebellar nuclei by stereotaxic placement of electrodes. Postoperative survival times included 2, 3, 4, 5, 7, 8, 10 and 12 days. The brains were fixed by perfusion and the tissue subsequently processed for electron microscopy. Data from a cytoarchitectonic, Golgi and electron microscopic study of the normal cellular morphology and synaptalogy of the red nucleus (King, Anat. Rec. 166: 331, 1970) served as a control for the present study. Following cortical lesions, particularly at days 5, 7 and 8, small (1-2μ) synaptic endings demonstrated an electron-dense type of degeneration. These corticorubral synaptic terminals ended predominately, but not exclusively, on distal dendrites and dendritic spines of neurons in the red nucleus. In contrast, at days 3 and 4 after lesions in the deep cerebellar nuclei, large (5-9μ) synaptic terminals showed a filamentous type of degeneration. The cerebellorubral synaptic terminals contacted the proximal dendritic trunks and occasionally the somata of neurons in the red nucleus. These findings support the physiological postulations of Tsukahara, et al. (J. Neurophys. 31: 467, 1968) which state that the synapses for the cortically induced EPSP's are located on distal dendrites while the synapses for the cerebellar induced EPSP's are located on the proximal dendritic trunks of neurons within the red nucleus.

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13.21 PRIMATE PERIPHERAL NERVE REGENERATION AFTER LOSS OF COLLATERAL BLOOD SUPPLY, David G. Kline, M. D., and Earl R. Hackett, M. D. *
Surgery/Neurosurgery, L. S. U. School of Medicine, New Orleans, La 70112

While it is known that intact nerves can be completely mobilized without functional loss, the effect of removal of collateral blood supply on an injured nerve has been less certain. Both tibial nerves were partially crushed in 6 monkeys, completely crushed in 10, severed and sutured in 12, and left intact in 4. Evoked nerve action potentials (NAP) and electromyograms (EMG) were monitored to document the extent of injury. The nerve on one side was then completely mobilized with removal of all collateral blood supply while the opposite nerve was not mobilized. At intervals from one week to one year later, electrical studies were repeated and extremities perfused with micropaque-gelatin for x-ray studies of macro- and micro-circulation.

Mobilized nerves kept clinical, electrical, and histologic pace with those not mobilized. Post-injury NAP velocities were expressed as percent of baseline values. Velocities in partially crushed nerves averaged 92.1% of baseline in the mobilized and 91.6% of baseline in those not mobilized. With complete crush, the values were 35.2 vs. 37.2, 67.1 vs 72.0, and 75.5 vs. 79.7 at 3, 6, and 12 months for nonmobilized vs mobilized. With suture, values were 19.4 vs 20.6, 42.3 vs 45.0, 60.0 vs. 54.4, and 58.6 vs. 61.1% at 3, 6, 8, and 12 months, respectively.

Patterns of re-vascularization were indentical in both series except at 1 to 4 weeks where there was a larger quantity of collateral and intraneural vessels in non-mobilized nerves than in those mobilized. With crush, new vessels spanned the injury site in a longitudinal fashion whereas with severance and suture, the vascular pattern was disorganized and more small vessels were seen. Mobilization of injured nerves should be minimal but is safe since functional regeneration does not depend on the initial preservation of collateral blood supply.

13.22 NEURAL NET AND SELECTIVE OUTGROWTH FROM INSECT NERVE CELLS IN VITRO. Rita Levi-Montalcini. Washington Univ., St. Louis, Mo. 63130.

Nerve cells from embryo of the cockroach, Periplaneta americana, grow and survive in vitro for many months in a chemically defined medium. Dissociated nerve cells from brain and ganglia of 16-day old embryos produce a dense fibrillar network when cultured in the presence of foregut explants from the same donors. Radial fiber bundles emerging from this fiber network converge toward the explant and establish synaptic connection with it. Nerve cells, dissociated and cultured alone, survive for some weeks but never produce a fibrillar network and undergo progressive and complete deterioration between the second and third months in vitro. The marked difference in survival and nerve fiber production by dissociated nerve cells cultured in the presence or absence of foregut explants, suggests the release by these explants of a humoral factor which would enhance growth and differentiation of dissociated nerve cells. Ganglionic explants from 16-day embryos cultured in this medium produce a vigorous nerve fiber outgrowth and cell migration. When combined with other ganglia or leg primordia, fibers make connection with both types of explants, while they do not connect with other tissues or organs from the same donor. The results will be discussed in reference to the problems of axonal growth and neuronal specificity.

13.23 LOCALIZATION OF THYROXINE I ^{125} IN DEVELOPING CNS TISSUE IN CULTURE. ELECTRON MICROSCOPIC AUTORADIOGRAPHY. Laura Manuelidis*

Organotypic cultures of developing mammalian spinal cord and cerebellum were exposed to thyroxine I ^{125} for 15 minutes to 22 hours. Glutaraldehyde fixation of hormone was analyzed by "Sephadex G-25" and thin layer chromatography of supernatant solutions, and was compatible with fixation of hormone bound to non-extractable tissue sites; no free I ^{125} or thyroxine I ^{125} were fixed with these methods.

Bound hormone in the cell increased dramatically within the first two hours, and by 22 hours accounted for 25% of the total radioactive hormone in the cell. Electron microscopic autoradiography revealed that the major sites of hormone binding were the cell membrane, mitochondria, ribosomes, "mixed" endoplasmic reticulum, nucleus and synapse in that order of decreasing intensity. These organelles were all labelled as early as 15 minutes, and there was increasing accumulation of hormone at all these sites with longer exposures. Both glial cells and neurons were labelled at all times. Glial cells incorporating thymidine H^3 for 2 hours prior to exposure to thyroxine I showed the same distribution and number of cytoplasmic grains as other glial cells. The notion that thyroxine may act at multiple cell sites in developing cells of the CNS will be discussed in light of these findings.

13.24 EFFECTS OF EARLY HYPO- AND HYPERTHYROIDISM ON CELL DIFFERENTIATION AND SYNAPTOGENESIS IN RAT CEREBELLUM. Jean L. Nicholson and Joseph Altman. Dept. Biol. Sci., Purdue Univ., Lafayette, Ind. 47906.

Cell differentiation and synaptogenesis were studied following injections of thyroxine (hyperthyroid) and propylthiouracil (hypothyroid) from birth. Termination of cell proliferation in the external granular layer was found to be accelerated in hyperthyroidism and retarded in hypothyroidism, as determined by H^3-thymidine autoradiography. Synaptogenesis was also studied using the ethanolic-phosphotungstic acid method for staining synaptic profiles. The developmental increase in synaptic profiles/unit area was found to be accelerated by hyperthyroidism and retarded by hypothyroidism until 30 days of age when control values were approached. This was in contrast to the effect on total number of synapses at 30 days, which was markedly reduced in both groups as determined by calculation from planimetric areal measurements of the molecular layer and counts of synaptic profiles/unit area. Therefore, although hyperthyroidism accelerates the formation of synapses, the total number of synapses is reduced at 30 days, presumably because it also leads to early termination of cell proliferation and hence to decreased cell number and cerebellar size. In contrast, the primary effect of hypothyroidism seems to be a reduction in the extent of cell differentiation, resulting in fewer neuronal arborizations rather than decreased cell number. In either case, a significant reduction in the number of synapses occurs at 30 days, presumably leading to behavioral deficits and reduced learning ability.

13.25 ESTRADIOL-H^3 CONCENTRATION BY CELLS IN A LIMBIC-HYPOTHALAMIC SYSTEM IN THE FEMALE RAT BRAIN. AN AUTORADIOGRAPHIC STUDY. Donald Pfaff, Melvyn Keiner* and Ellen Warren*. Rockefeller University, New York, N.Y. 10021.

Direct mounting of unfixed frozen sections onto emulsion-coated slides was used to determine by autoradiography the locations of estradiol-concentrating cells in the female rat brain. Ovariectomized females were injected, i.p., with physiological doses of estradiol-17B-H^3 and sacrificed 2 hr. later. In the darkroom frozen sections cut in a cryostat were mounted onto NTB-3 emulsion-coated slides, for an exposure period of 6 months before developing. Significant grain concentrations were found over the cell bodies of cells - primarily neurons - in the septum, amygdala (cortical and medial nuclei), medial preoptic area, olfactory tubercle, medial anterior hypothalamus, arcuate nucleus, ventromedial nucleus of the hypothalamus, and in certain periaqueductal structures in the midbrain. In most other regions of the brain, only occasional, scattered cells concentrated the radioactive hormone. The locations of estradiol-cells described here confirm conclusions based on autoradiograms of osmium-formalin fixed brain sections (Pfaff, Endocrin. 82:1149, 1968) and scintillation counting of dissected brain regions (McEwen & Pfaff, Brain Res. 21:1, 1970). Many of the sites having the greatest number of estradiol-concentrating cells are hormone-sensitive, as demonstrated in previous studies using hormone implant, lesion and electrical stimulation techniques. The observed distribution provides clues to the location of cells mediating estradiol effects on pituitary function and mating behavior.

13.26 SYNAPTIC REORGANIZATION IN THE DEGENERATING LATERAL GENICULATE NUCLEUS OF THE RABBIT. Henry J. Ralston, III and Kao L. Chow. Dept. Anat., U.Wis.,Madison, 53706 and Dept. Neurol.,Stanford U.,Stanford,94305.

The neurons of the lateral geniculate nucleus of the rabbit undergo rapid cell death following removal of the visual cortex. The degenerated nucleus thus provides an excellent model for the study of retrograde neuronal degeneration and the consequent changes in synapses in the nucleus. In the first few days following cortical ablation, electron microscopy demonstrates orthograde degeneration of small synaptic knobs of cortical origin, followed by extensive degeneration of dendrites and cell bodies of geniculate neurons. At longer survival times of 3 months to 1 year, there are very few remaining geniculate cells, and consequently the retinal and other afferents to the nucleus are deprived of normal postsynaptic sites. This results in large fields of axonal terminals which synapse upon each other, rather than upon dendrites, as in the normal nucleus. The synaptic terminals include retinal afferents and at least 2 other synaptic types of unknown origin. Despite the tendency towards axo-axonal contacts, retinal afferents appear not to synapse with each other. It is concluded that extensive synaptic reorganization may take place but some degree of specificity of contact can be maintained.

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13.27 DOES DENERVATION OF CEREBRAL CORTEX PRODUCE PROLIFERATION OF NEURONAL PROCESSES? L.T. Rutledge, Joyce Duncan and Nell Cant*. Dept. of Physiol., Univ. of Mich. Med. Sch., Ann Arbor, Mich. 48104

In Cajal's studies of undercut cerebral cortices in young animals he observed proliferation of axon collaterals of cortical pyramidal cells. No quantitative study has since been made to consider the exact nature and extent of proliferation, the critical factor of brain age at denervation, or changes in synaptic loci or cortical organization. We denervated the cerebral cortices of cats (4-day olds, 40-day olds and adults) by unilaterally undercutting them. After several months pieces of undercut cortices were removed and stained with a modified Golgi-Cox. Studies were made of neuronal processes and data compared with that from adult intact cortex. Average length of the two longest collaterals was greatest in 40-day olds and adults, with both groups having longer collaterals than intact or 4-day cats. Number of collaterals was greatest in the 40-day cats followed by 4-day, intact and adult. Number of axon collateral branch points was greatest in intact followed by 40-day, 4-day and adult. Apical dendritic spines were counted as an indicator of extent of synaptic contacts. Highest counts were from intact, followed by 4-day, 40-day and adult. That axonal proliferation occurs in denervated immature cortex (4-day, 40-day) is indicated by length and number of axon collaterals but it is counterindicated by the observations that these same axons branch less and that there are fewer synaptic contacts. Data from adults take an intermediate position between immature and intact cortex. It seems that growth potential in denervated immature cortex is expressed as apparent proliferation of pyramidal cell axon collaterals, but such changes likely contribute little to intracortical reorganization since terminal branches and synaptic contacts are actually fewer than in intact cortex. (Supported by USPHS NIH Grant NDS 04119).

13.28 PRE AND POST JUNCTIONAL LOCALIZATION OF ACETYLCHOLINESTERASE BY QUANTITATIVE E.M. AUTORADIOGRAPHY. Miriam M. Salpeter and Andrew W. Rogers*. Cornell University, Ithaca, New York 14850.

Radioactive diisopropylfluorophosphate (DFP) has been applied in a specific incubation sequence to determine the total number of AchE molecules at motor endplates (Rogers et al., J. Cell Biol. 41:665, 1969) as well as its submicroscopic distribution (Salpeter, J. Cell Biol. 42:122, 1969). Electron microscope analyses determined that in the mouse sternomastoid muscle the AchE is distributed over the entire zone of the junctional membranes. The resolution of the E.M. autoradiographic method is, however, inadequate to determine directly whether the enzyme is restricted to the post junctional membrane or is also present on the axonal membrane. An indirect method was, therefore, employed to "resolve" this question.

One type of endplate in the external ocular muscle has large regions entirely devoid of post junctional folding. Each of this type endplate was divided into 2 synaptic zones -- one with and one without post junctional folding. χ^2 tests established that the relative proportions of developed grains in the 2 zones was significantly different from that of either the post junctional or the axonal membrane individually, but was not significantly different from that of the axonal plus post junctional membranes combined.

Results are compatible with a uniform distribution of AchE on both pre and post synaptic membranes (at $\sim$3200 sites/μ^2) but could also fit other models which will be discussed.

*Permanent Address: MRC Neuroendocrinology Unit, Oxford, England.

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13.29 THE ORGANIZATION OF THALAMIC NUCLEI AND THEIR EFFERENT PATHWAYS IN THE NURSE SHARK, GINGLYMOSTOMA CIRRATUM (BONNATERRE). D.M. Schroeder and Sven O.E. Ebbesson. Dept. Neurosurgery, Univ. of Virginia, Med. Sch., Charlottesville, Va. 22901 and Lerner Marine Lab., Bimini, Bahamas.

The present experiments deal with the structural characterization of thalamic nuclei with Nissl and Golgi methods as well as the determination of efferent connections of the various neuronal aggregates with the aid of modified Nauta and Fink-Heimer techniques. The Nissl and Golgi sections demonstrated that cytoarchitecturally the dorsal thalamus can be subdivided into various nuclear groups although their boundaries are often vague. Small electrolytic lesions were placed in the various cell groups of the diencephalon in 25 nurse sharks. The findings indicate that not only do select thalamic areas project to specific nuclear aggregates within the telencephalon, but all of these projections are unique in that they are almost completely crossed.

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13.30 NEURONAL GROUPS AND FIBER PATTERNS IN CEREBELLAR TISSUE CULTURES. Fredrick J. Seil. Dept. Neurology, Stanford U., Vet. Admin. Div., Palo Alto, Calif. 94304.

Parasagittally oriented explants derived from newborn mouse cerebellum reveal arrangements consisting of structured cortical and nuclear groups, with organized bundles of fibers coursing between them. The cortex is stratified, with recognizable granule and Purkinje cell layers. Purkinje cell axons converge toward cerebellar nucleus neurons, and individual axons can in some preparations be traced to termination near the dendrites of deep nuclear neurons. The deep nuclear neurons from lateral cerebellar explants are arranged in a roughly linear pattern several cell layers thick, and are usually surrounded by numerous fibers. These nuclei are located superior to easily identifiable ependymal cysts. At the level of or inferior to these cysts another nuclear group is usually recognizable, which contains large multipolar neurons and occasionally giant neurons which have the configuration characteristics of giant neurons of the Deiters nucleus. A fiber bundle typically courses between the deep cerebellar and the vestibular nuclei. Vestibular nucleus neuron axons can be traced to virtually all areas of the explant. They frequently make some contribution to a band of fibers which lies in the outer margin of the cerebellar cortex and follows the cortical curve. This band frequently contains numerous myelinated fibers, and is most dense at the anterior and posterior edges of the cortex, where it receives contributions from Purkinje cell axons. In the thinner portion of this band, over the convexity of the cortex, some of its recognizable components appear to be Purkinje cell axon collaterals, as they travel for short distances to terminate either freely or in the dendritic fields of other Purkinje cells. The overall architecture of the cerebellar cultures is reminiscent of that of the animal at the time of explantation.

13.31 POSTNATAL CHANGES IN THE ARRANGEMENT OF NEUROFILAMENTS AND MICROTUBULES IN CLARKE'S NUCLEUS IN THE KITTEN. Diane E. Smith*
(SPON: A. R. Morrison). Dept. of Anat., Jefferson Med. Col., Thomas Jefferson Univ., Philadelphia, Pa. 19107.

Light microscope investigations indicate postnatal changes occur in the lumbosacral spinal cord of the kitten which parallel similar alterations occurring peripherally and in higher centers. In addition to supporting these findings, preliminary investigations at the ultrastructural level show postnatal alterations and rearrangements occurring among the cellular organelles. Newborn to twelve-week kittens were perfused with a paraformaldehyde-gluteraldehyde solution and processed for examination with the electron microscope. At birth, the perikaryon contains many neurofilaments and a few scattered groups of microtubules. The converse is true in the dendrites which are filled with microtubules, the neurofilaments being scarce. By three weeks, microtubules and neurofilaments are present in equal proportion in the perikaryon and distinctive filament "packets" are seen in the dendrites. The parallel-row arrangement of "packets" appears stabilized by nine weeks. The migration of filaments into the dendritic processes to the accompaniment of the postnatal growth of these cells is compatible with the theory that neurofilaments play a supportive role. However, the postnatal shifts in location and arrangement of neurofilaments and microtubules also suggest these elements might function in additional capacities than the obvious one of structural support.

13.32 ROLE OF THE GROWTH CONE AND CELL JUNCTIONS IN VENTRAL-ROOT FORMATION. Henry J. Wehman and Barbara A. Plantholt*. Res. Dept., Rosewood State Hosp., and Dept. Pediatrics, Univ. of Maryland, Baltimore, 21201.

Electron-microscopic studies were made of the ventral root of the spinal cord in fetal rats at 10 through 15 days of gestation. Special attention was paid to the presence of growth cones and cell-cell junctional specializations. Ventral-root axons first leave the spinal cord, penetrating through its basal lamina, on day 12. The axon tips begin to make contact with peripheral cells on day 12, and they make increasing contacts through day 15. The peripheral cells are identified as primitive Schwann cells. Growth cones are present at the tips of free-growing axons in the form of vacuole-filled varicosities. It is not known whether these vacuoles are derived from the axonal cell membrane (i.e., through pinocytosis) or from smooth endoplasmic reticulum (Tennyson, J.C.B. 44: 62, 1970). The growth-cone structure persists through day 15, when the axons are extensively covered by Schwann cells. By this time, however, the varicosities also contain mitochondria and 880-A° dense-core vesicles. Such profiles suggest a transitional stage between growth cones and synaptosomes. Junctional specializations, 150-A° plaques, are found between axons and Schwann cells. They are found only at the lateral edge of the axon. Serial sections have failed to reveal any junctional specialization at the distal edge of an axon. The above observations are interpreted partially in terms of the classical contact-guidance model originally proposed by Paul Weiss (J.E.Z. 68: 393, 1934).
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14.3 NEUROSCIENCE FOR MEDICAL STUDENTS. Louise H. Marshall. National Research Council, Washington, D. C. 20418.

A survey of U. S. medical school catalogues for 1969-1970 reveals that prospective physicians are exposed to a wide variety of interdisciplinary experience in the broad area of neuroscience. As shown by course descriptions, the variety ranges from zero exposure to completely integrated courses offering brain and behavior in the same breath, so to speak. In addition, the opportunity to participate in research in some aspect of neuroscience varies from nonexistent to elective status as a full semester credit. Current trends seem to indicate that the recently established medical schools are now taking the lead from the older prestigious schools in putting together multidisciplinary, integrated programs in this area. What are the graduate schools doing along these lines?

15.5 MECHANISM OF ACTION OF L-DOPA IN PARKINSON'S DISEASE. Kenneth G. Lloyd* and Oleh Hornykiewicz. Dept. of Pharmacology, Univ. of Toronto and Clarke Institute of Psychiatry, Toronto, Ont., Canada.

The mechanism of L-DOPA's beneficial effect in Parkinson's Disease (P.D.) has been attributed either to (a) enzymatic formation of dopamine (DA) in the striatum, (b) non-enzymatic decarboxylation to DA, or (c) direct action of L-DOPA or unknown metabolite or condensation product. To decide which of these possibilities exhibit the greatest experimental validity, we have studied the distribution of DOPA and some of its metabolites in discrete brain areas in L-DOPA treated and "untreated" Parkinsonian patients (P.p.). L-DOPA decarboxylase (DD), catechol-O-methyl-transferase (COMT), and monoamine oxidase (MAO) were estimated radiometrically, DOPA, O-methyl-DOPA, DA and homovanillic acid (HVA) by fluorimetric procedures. The concentrations of DA in the caudate and putamen, and those of HVA, DOPA and O-methyl-DOPA in the above and other brain areas were significantly greater in the L-DOPA-treated group than in the "untreated" P.p.; the striatal HVA in L-DOPA treated cases was even higher than in controls. In contrast, the severity of clinical symptoms and the decrease in brain DD were similar in both groups of P.p. indicating equal involvement of the nigro-striatal system. In all P.p. examined there remained sufficient DD, COMT and MAO to account for the DA, HVA and O-methyl-DOPA found in the L-DOPA treated brains. In addition we have found that not only L-DOPA but also its D-isomer are subjected to non-enzymatic decarboxylation in vitro; however, in vivo D-DOPA has no pharmacological activity attributable to catecholamines. Thus, non-enzymatic decarboxylation as a possible mechanism of L-DOPA's in vivo effects is most improbable. Our studies lend direct experimental support to the hypothesis that the beneficial action of L-DOPA in P.D. is exerted mainly via enzymatic formation of DA, preferentially in the caudate and putamen. (Supported by Clarke Inst. and Eaton Labs., Norwich, N.Y.)

15.6 FUNCTIONAL ZONES IN THE CAT VENTROLATERAL THALAMUS. P.L. Strick* (SPON: J.M. Sprague). Dept. of Anat., School of Medicine, Phila., Pa. 19104.

Two adjacent zones can be distinguished in the cat ventrolateral thalamus on the basis of their cyto- and myeloarchitecture. The first zone borders the internal medullary lamina. It is sparsely myelinated and its cells appear homogeneous in size and distribution. Focal stimulation here evokes contractions of proximal somatic musculature and lesions cause terminal degeneration in particular regions of area 6 of the motor cortex. The second zone borders the ventrobasal complex. It is more densely myelinated and is characterized by relatively large cells arranged in clusters surrounded by smaller cells. Stimulation in this zone evokes contractions of more distal somatic musculature and lesions cause terminal degeneration in particular regions of cortical area 4. This organization of the ventrolateral thalamus corresponds to that found in the cerebellum and motor cortex where there are also distinct zones for control of proximal and distal musculature.

Efferents from both ventrolateral thalamic zones diverge markedly in their projection to the motor cortex, a pattern that contrasts to the point to point cortical projection of the ventrobasal complex. Thus, a small lesion in the ventrolateral thalamus produces sparse degeneration over a relatively wide area of motor cortex, while a comparable lesion in the ventrobasal complex produces dense degeneration focused in a small area of somatic sensory cortex (SI). Supported (in part) by USPHS grant 5 T01 GM00281.

Session 16

No Contributed Papers

Session 17

17.1 THE RECEPTIVE FIELD CHARACTERISTICS OF PRINCIPAL AND ASSOCIATION CELLS IN THE RAT LATERAL GENICULATE NUCLEUS. William R. Mead* and Mary Emily Bussey* (SPON: Constantine Trahiotis). Dept. of Psychol., Univ. of Ill., Champaign, Ill. 61820.

Significant progress has recently been made in delineating the neural interconnections which underlie complex information processing in the retina, but little is known about the mechanisms of any but the simple center-surround receptive fields (RFs) of cells in more centrally located nuclei. With respect to this problem, the rat offers a potentially useful visual system. In rat directionally selective movement detecting cells are found earliest in the lateral geniculate nucleus (LGN), and the retinal ganglion cells all possess quite simple RFs. Since a large amount of work has been done in rat LGN on differentiating the principal cells which send their axons to the visual cortex (P cells) and the association cells whose axons terminate within the LGN (I cells), it should be possible to determine the roles of P and I cells in the production of directional sensitivity in this nucleus. RF data were obtained from over 100 rat LGN cells, of which approximately 20% were I cells. Directionally selective RFs were found in P cells, and the other simpler center-surround and diffuse RFs were found for both P and I cells. These data will be discussed within the context of the Barlow and Levick model of directional sensitivity and models of thalamic inhibitory interneuron activity.

17.2 ELECTROPHYSIOLOGICAL CORRELATES OF FLICKER PERCEPTION IN THE CAT. Arthur S. Schwartz. Div. Neurobiology, Barrow Neurol. Inst., Phoenix, Az., 85013.

Previous work in the cat suggested that flicker discrimination and the critical flicker frequency threshold (CFF) were a function of the interaction of two separate neural mechanisms, one including the geniculostriate pathway and the posterior thalamus (Visual System I), and the other including the tectal region (Visual System II). Evidence from lesion and electrophysiological recording experiments in chronically implanted cats is presented here which supports the notion that System I mediates perception of high flicker rates while both systems may be involved in discriminating low rates. Twenty-two cats were trained to discriminate between a steady and a flickering light, with flux held constant. Thresholds were determined by increasing the flicker rate until no discrimination was apparent. Subtotal lesions in System II resulted in increased CFFs in 9, no change in 3, and decreases in 2 animals. Subtotal lesions in System I uniformly decreased the CFF. Seven of these cats had been implanted earlier for electrical recordings of the EEG under conditions identical to those during the CFF determination, except that much higher frequencies were also presented. Photic following limits, defined as the highest frequency which appeared in the power spectra of the EEGs and which represented a fundamental or harmonic of the flicker frequency, were then determined for the relevant Visual Systems. The data showed that the photic following limits were higher in the geniculo-striate pathway of System I than in the superior colliculus of System II, while the limits observed in the latter corresponded more closely to the pre-operative CFFs than those in the former. The results support the above characterization of the two Systems, and suggest that lesions in one system may enhance the role of the other system in mediating flicker perception.

17.3 SUPERIOR COLLICULUS: INTERACTIONS OF CORTICAL AND RETINAL PROJECTIONS ON SINGLE NEURONS IN THE CAT. James T. McIlwain and Howard L. Fields. Brown Univ., Providence, R. I. 02912 and Boston City Hospital, Boston, Mass. 02118.[1]

Visually responsive units in the superior colliculus of the midpontine-pretrigeminal cat are driven by electrical stimulation of optic tract and visual cortex (area 18). A synchronous volley over either input elicits excitation followed by prolonged inhibition of the neuron. When cortical and tract stimuli are paired at intervals of 3-15 msec, the excitatory effects summate on superior colliculus neurons. At longer shock separations, either input inhibits the response to the other. The collicular response to tract stimulation often consists of an early spike followed by a late burst of spikes. When this response is preceded by cortical shock or by another tract shock, at an appropriate interval, the late burst is inhibited and the early spike little affected. The cortical area most effective for exciting a collicular unit is also that area producing the strongest inhibition.

[1]These experiments were performed in the Division of Neuropsychiatry, Walter Reed Army Institute of Research, Walter Reed Army Medical Center, Washington, D. C.

17.4 LINE ORIENTATION DISCRIMINATION DEFICITS FOLLOWING PARTIAL ABLATION OF THE GENICULO-CORTICAL SYSTEM IN CATS. Mark A. Berkley. Dept. Psych., Fla. State Univ., Tallahassee, Fla. 32306.

Cats were trained to discriminate between a vertical (V) and a horizontal (H) line. Lines of intermediate orientations were presented in subsequent training and the ability of the animals to discriminate these orientations from V or H was determined. All cats learned the initial task (V vs H) rapidly. Discrimination of the intermediate orientations from V or H was initially poor but improved considerably with practice. Partial ablation of the neocortex of the geniculo-cortical system produced little deficit in the V vs H discrimination task but did produce a significant reduction in performance on the intermediate orientation discrimination task. The degree of the deficit appeared to be correlated with a) the size of the lesion and b) the portion of the cortical visual projection field damaged. The ablations almost always included that portion of cortex receiving input from the central visual fields. The results are interpreted as indicating a poorer capacity to discriminate line orientation in the peripheral visual fields when compared to the capacity to make such discrimination in the central visual fields.

17.5 INTERACTION BETWEEN THE VISUAL CORTEX AND SUPERIOR COLLICULUS OF THE CAT DURING LEARNING. Bonnie J. Shubart. Dept. Anat., Cornell Univ. Medical College, N.Y., N.Y. 10021.

Following optic chiasm section and monocular learning of a two choice dark-light discrimination in a continuous-type Y-maze, cats were subjected to unilateral removal of the entire occipital-temporal neocortex. After this procedure, although there was complete retention through the eye contralateral to the cortical lesion, there was no retention of the dark-light discrimination through the eye ipsilateral to the cortical lesion. In addition, the cat was unable to relearn the problem through this latter eye. Next, the superior colliculus contralateral to the cortical lesion was removed, after which the cats were able to relearn the discrimination through the eye ipsilateral to the cortical lesion. This study seems to confirm and extend the findings of previous investigators, who measured visual half-field deficits, that there is return of visual responses in the previously hemianopic field following removal of the superior colliculus contralateral to the neocortical lesion. The initial loss of learning capacity through the eye ipsilateral to the cortical lesion may result from a depression of function of the superior colliculus ipsilateral to the cortical lesion by means of inhibition from the opposite colliculus via the commissure of the superior colliculus.

17.6 LATE INTRACELLULAR EVOKED RESPONSE. Ronald A. Cyrulnik* and Rafael Elul (SPON: J.D. FRENCH) BRI and Dept. Anat., Univ. Calif., Los Angeles, 90024.

The intracellular evoked response to photic flash has been investigated in the visual cortex of unanesthetized cats. Many cells display a complex response, containing both an early depolarizing component (15-30 msec latency), and a late biphasic hyperpolarizing-depolarizing response (50-100 msec latency). Other cells exhibit the late depolarization alone. It thus appears that the early and late responses cannot be due to the same afferents. To further investigate this question we have averaged successive responses from the same neuron, and compared them with the averaged gross evoked response recorded simultaneously in proximity to the microelectrode. The early component has the same polarity in gross and unitary responses, whereas polarity of the late components is reversed on the surface. These results suggest that the different components arise in different cortical layers. In cells where both early and late responses are present, they most likely involve activity in different synaptic loci on the cell surface; because of the reversal of its polarity, the late component probably involves synapses close to the surface. It is known that callosal afferents terminate close to surface of the cortex, and the late component may thus possibly be due to efferents from neurons in the contralateral visual area, activated there by the early component of the response. At this stage it is however not possible to exclude the possibility of late efferent impulses from the lateral geniculate, or from non-specific systems. An additional possible mechanism of the late response may be through a local cortical circuit involving interneurons. The cells exhibiting only the late component may then act as interneurons, re-exciting the cells receiving the primary afferents.

17.7 A DORSOMEDIAL VISUAL AREA ADJOINING V II IN THE OWL MONKEY (AOTUS TRIVIRGATUS). John M. Allman*, Jon H. Kaas*, F. M. Miezin*, (SPON: C. N. Woolsey). Lab. of Neurophysiology, U. Wis., Madison, Wis. 53706.

The visuotopic organization of the extrastriate visual cortex adjoining V II in the owl monkey has been mapped by determining receptive fields of single neurons and small clusters of neurons with microelectrodes. Our data indicate that more than one extrastriate visual area adjoins V II in the owl monkey. One of these visual areas has been mapped in detail in 122 penetrations in 13 owl monkeys. This visual area adjoins approximately 1/5 of the rostral border of V II and is located on the dorsal surface and medial wall of the occipital lobe. This dorsomedial visual area (DM) corresponds to a heavily myelinated region histologically distinct from surrounding cortex. DM is a strip of cortex approximately 8 mm in mediolateral extent with the rostrocaudal dimension varying from 4 mm laterally to 3 mm medially. The approximate surface area is 26 mm^2. The vertical meridian is represented along the rostral border of DM, and the center of gaze is represented near the caudal tip of the sylvian sulcus. The contralateral upper visual quadrant is represented in the lateral part of DM and the lower quadrant is represented in the medial part. Receptive field size ranged from 5^o in diameter near the center of the gaze to 27^o in the temporal periphery of the visual field. (Supported by NIH Grants NS 06225 and NS 05326.)

17.8 RESPONSES OF MONKEY LGN CELLS TO LUMINANCE AND COLOR FIGURES. D. Max Snodderly, Jr., Russell L. De Valois, William E. Yund* and Norva K. Hepler*. Dept. Psych., U.C., Berkeley, Calif. 94720.

Single neurons in the lateral geniculate nucleus (LGN) of the macaque monkey respond to both color and luminance figures, provided the size and position of the stimulus is carefully controlled. We have employed lines of different width, color, and luminance to explore how LGN cells respond to stimuli that drive cortical neurons. Both spectrally opponent and non-opponent cells respond vigorously to achromatic or colored lines when they differ in brightness from the background. In addition, spectrally opponent cells are very responsive to larger colored lines when they are matched in brightness to the background. Further processing in the visual system presumably will be necessary to sort out the difference between small luminance stimuli and larger colored ones.

17.9 COLOUR AND CONTOUR DETECTION BY CELLS REPRESENTING THE FOVEA IN MONKEY STRIATE CORTEX. John Boles. Psychology Depart., University of Western Ontario, London 72, Ontario, Canada.

Receptive fields (RF) of single cells were studied with emphasis on two things, electrode placement in the striate cortex getting input from the fovea (confirmed by ophthalmoscopy and histology), and use of projected monochromatic stimuli and adapting lights. Cynomolgus macaques were unanesthetized, painlessly immobilized, and held by a special headplate.

Among the 44 cells examined so far are simple, complex, and lower hypercomplex types (Hubel & Wiesel, J. Physiol., '68,195). However, some units, binocularly influenced and without direction sensitivity, responded in some way--usually opposite to that elicited from the small RF center--to large stimuli and room lights. Full RF sizes are not definite, but central regions, whether excitatory or inhibitory, seldom exceeded $1/2^{o}$, typically being $1/5^{o}$ on the longest side.

Overall about 25% of the units clearly responded selectively to wavelength; most increased firing to bars of 640 or 606 nm but not to 580 nm or shorter. The excitation to 640 and 606 nm was cancelled by a 520 nm spot superimposed on the RF of either eye, but not by the red bar going in one eye and the green spot in the other. The 520 nm spot might initiate inhibition somewhere else in the striate or more distally, but not on these binocular units. A few other cells were excited maximally by 442 nm, less by 470 nm, and not at all by longer wavelengths. Monochromatic adapting lights failed to alter color selective responses very much.

Three cells fired to either a black or a white bar end (certain size), whether flashed on (good response) or moved over (better) the identical RF position. Such contour excitation could result from the "on" response of excitatory LGN units and the "off" firing of inhibitory LGN cells.

17.10 FUNCTIONAL PROPERTIES OF NEURONS IN THE STRIATE CORTEX OF THE MACAQUE MONKEY SUBSERVING THE FOVEAL REGION OF THE RETINA. G.F.Poggio, R.J.W. Mansfield* and A.M.Sillito*, The Johns Hopkins University, Baltimore,Md.

Spatial and chromatic properties of foveal cortical neurons were studied in unanesthetized paralyzed monkeys, artificially ventilated and maintained in pain free conditions. Unitary activity was recorded extracellularly and the retina stimulated with moving or flashing patterns of white and monochromatic light under conditions of low photopic adaptation. Most foveal neurons respond to stimulation of one eye only and are best activated with small patterns (0.1-0.2 degrees at the eye) moving within or in and out of a retinal region of similar size. Spatial orientation and direction of motion of small stimuli are not critical and flashes may also evoke a response. For some neurons the receptive field is limited to this small activating region, for others the receptive field is larger and spatially organized to include symmetrical or asymmetrical surround regions. For the latter neurons the response to stimuli larger than the activating field is highly dependent on the size, shape and orientation of the stimulus. No responses are obtained by stimulation of the surround regions alone. To investigate chromatic properties the action spectrum of single neurons was determined by measuring the light energy necessary for an optimal spatial pattern to produce the same criterion response at various wavelengths. Some neurons have broad band action spectra which match the behaviorally determined photopic spectral sensitivity of the macaque, and others broad band spectra with maximal sensitivity shifted toward one end of the spectrum. A few neurons exibit narrow band chromatic selectivity and fewer still an opponent spectral organization. (Supported in part by USPHS Grant 5 PO1 NSO 6828).

17.11 PATTERN EVOKED RESPONSES FROM PRIMARY AND ASSOCIATION AREAS IN MAN. Earle G. Wallingford, Jr.* and Donnell J. Creel. Neuropsychology, Duke Univ., Durham, N.C. 27706, and Neuropsychology, VA Hospital, Kansas City, Mo. 64128.

Summed electrical responses evoked by pattern stimuli were recorded from the scalp over primary visual (area 17) and association (areas 18 & 19) cortices in male and female college students. Striped, rectangular, checked and L-shaped patterns were used to determine which stimuli were associated with the highest amplitudes of evoked responses at electrode position O2, and at a point 3cm laterad to O2 (both the ipsilateral ear and the contralateral ear as a reference were tested). In agreement with most published data, a checked pattern with checks subtending 15' of an arc evoked a larger response than most other patterns. However, it was also found, and at both lead placements, that an L-shaped pattern of 15' widths, with arms extending one degree, evoked as large a response as the optimal checked pattern. The effectiveness of both these patterns to evoke large amplitude components in the 100-200 msec range recorded from areas 17, 18 & 19 is probably a reflection of populations of cortical cells with their receptive fields responsive to edges, angles and slits. Also, the negative component at a peak delay of 60-80 msec, which was identifiable in most responses recorded from O2, was absent or dramatically attenuated when recording from the point 3cm more laterad to O2. The negative component at 60-80 msec probably represents a volume response of geniculo-striate projection fibers coursing to area 17, and is therefore missing when recording at the more lateral placement over visual areas 18 & 19, both of which lack the well defined projection systems.

Session 18

18.1 A COMMON ERROR IN THE MEASUREMENT OF BRAIN DOPAMINE FOLLOWING L-DOPA. J.C. de la Torre* and William O. Boggan* (Spon: D.X. Freedman). Departments of Neurosurgery and Psychiatry, Pritzker Sch. Med., Chicago, Ill. 60637.

Increases in the content of brain dopamine (DA) following acute administration of L-dopa may be misleading as far as the endogenous neuronal concentration of this amine are concerned. Histochemical fluorescence studies show an increase in fluorescence in both the brain capillary lumen and endothelial cells following intraperitoneal injections of L-dopa in rats. The fluorescence seen in the lumen may be circulatory DA thought to occur as a result of extracerebral decarboxylation of L-dopa while the endothelial cell fluorescence is probably due to rapid decarboxylation of L-dopa to DA within these cells. The fluorescence of the other brain tissue remains unchanged. Furthermore, biochemical assays of DA show that 15-30 min after L-dopa administration, DA in brain increases $2\frac{1}{2}$ times from its control levels. However, intracardiac saline perfusion performed 15 and 30 min following L-dopa reduces this increase by 50 and 40%, respectively. Perfusion also decreases the fluorescence in the lumen. The remainder of the DA is trapped in the capillary endothelial cells where it is shielded from the perfusion. These data suggest that values of central DA after L-dopa as measured following homogenization of brain tissue are inflated due to inclusion (a) of circulating DA in the capillary lumen and (b) of the trapped DA in endothelial cells.

18.2 TOPICAL PHARMACOLOGY OF MONOAMINE-SENSITIVE STRUCTURES IN THE RAT BRAIN. D. Bieger*, L. Larochelle* and O. Hornykiewicz. Clarke Institute of Psychiatry and Dept. of Pharmacology, Univ. of Toronto, Ontario, Canada.

By means of close-arterial injections of L-DOPA and other dopamine-like drugs in the brain, it was shown that central dopaminergic mechanisms are engaged in the control of the activity of the branchial musculature (floor of the mouth). In order to localize the brain structures involved, we examined the effects of intracerebral stereotaxic microinjections of putative neurotransmitters on branchial muscles' EMG in urethane-anesthetised rats. The drugs were injected in a volume of maximally 2 µl through glass micropipettes (tip: 50-100 microns); a latency of no longer than 2 minutes was taken as critical for the specificity of the site of action. So far three major reactive loci have been detected: (a) Most sensitive to dopamine (30 µg), but not serotonin, proved the ventro-medial part of the rostral striatum; (b) the lateral part of the anterior hypothalamic area reacted very sensitively to serotonin (13 µg), but not to dopamine; (c) the dorso-medial area of the rostral thalamus responded to apomorphine (50 µg), but not to dopamine or serotonin; since in this area the direct cholinomimetic ethylarecaidine (4 µg) also proved effective, the effect of apomorphine in the thalamus was probably mediated through cholinergic receptors. In contrast, in the rostral striatum apomorphine had a dopamine-like action. These observations indicate that, among the brain structures involved in the control of branchial muscle activity, the striatal mechanisms react specifically to dopamine and other dopaminergic drugs. This model is now being used for studying the pharmacological characteristics of brain dopamine receptors. (Supported by Clarke Institute of Psychiatry and MRC of Canada.)

18.3 HYPOTHALAMIC AND MEDIAN EMINENCE CATECHOLAMINES AND THYROID FUNCTION. Gregory M. Brown and Oleh Hornykiewicz. Clarke Institute of Psychiatry and Dept. of Psychiatry, University of Toronto.

A central dopaminergic mechanism has been postulated in the control of anterior pituitary (AP) secretion. In the present study dopamine (DA), norepinephrine (NE) and homovanillic acid (HVA) were determined chemically in the hypothalamus and median eminence (ME) of control and thyroxine treated rats in order to determine whether a central catecholamine mechanism may be involved in thyroid regulation. Tissue components pooled from groups of 31 to 45 animals were the ME (2.56 $\pm$ S.E. 0.21 mg, N=6), the anterior and middle hypothalamus (AMH, 12.9 $\pm$ 0.7 mg, N=6) and the posterior hypothalamus (PH, 3.21 $\pm$ 0.42 mg, N=6). HVA was not measurable in any tissue component from either control or thyroxine treated animals. As expected, a high concentration of DA was found in the ME (2.20 $\pm$ 0.32 µg/g, N=5). However, observations of Bjorklund et al (Brain Res., 17, 1, 1970) and Iwata and Ishii (Neuroendocr., 5, 140, 1970) were confirmed that ME NE concentration (4.52 $\pm$ 0.94 µg/g, N=6) is significantly higher than that of DA. Lower concentrations of both NE and DA were found in the AMH (NE, 1.94 µg/g; DA, 0.54 µg/g) and the PH (NE, 3.26 µg/g; DA, 0.98 µg/g). In the thyroxine treated animals PBI was elevated over that of control animals (10.1 vs 4.5 µg/g, $P \leq 0.01$). Following thyroxine treatment a significant lowering of DA was found in the AMH (0.37 $\pm$ 0.02 µg/g, N=5, $P \leq 0.025$) with no significant difference in NE. No alterations in catecholamine concentration were found in either the ME or PH. These findings (1) indicate that ME NE is present in higher concentrations than DA suggesting that this catecholamine may also be important in AP regulation, (2) suggest that there may be a hypothalamic DA mechanism involved in the regulation of TSH secretion.

18.4 CATECHOL-O-METHYL TRANSFERASE: REDUCTION BY CHRONIC L-DOPA THERAPY. James L. Weiss*, Cal K. Cohn* and Thomas N. Chase. Laboratory of Clinical Science, National Institute of Mental Health, Bethesda, Maryland 20014.

Red blood cell catechol-O-methyl transferase (COMT) activity was assayed in 17 parkinsonian patients. Assay (J. Pharm. Exp. Therap. 176:650, 1971) involved incubation of red blood cell (RBC) hemolysate with norepinephrine and C^{14}-S-adenosyl methionine and measuring the radioactivity of isoamyl alcohol-extracted C^{14}-normetanephrine. Control patients had received no treatment for at least 2 weeks prior to study. The treatment group had received therapeutic doses of L-dopa for 1-20 months. RBC COMT activity in controls did not differ from levels found in normals. COMT activity was 40% lower in L-dopa-treated patients ($p < 0.05$). An i.v. dose of L-dopa administered to 3 previously untreated patients resulted in no measurable differences in COMT levels. Six of the untreated patients were begun on therapeutic doses of L-dopa and followed over a 4-16 week period. There was a significant reduction in COMT activity by the third week of therapy. The activities of 2 other methyl transferases, histamine N-methyl transferase and a methanol-forming enzyme, did not differ from those found in normals or untreated parkinsonians. *In vitro* preincubation with L-dopa did not significantly alter COMT activity. Dialysis experiments excluded the presence of an easily dialyzable inhibitor. The tendency for L-dopa dosage requirement to decrease over weeks to months has been observed previously. Reduced RBC COMT activity in L-dopa-treated patients, if representative of COMT activity in other tissues, may have relevance to this phenomenon, reflecting decreased availability of the transmethylation pathway for catecholamine catabolism.

18.5 FURTHER STUDIES ON CATECHOLAMINE (CA) BIOSYNTHESIS IN MOUSE NEUROBLASTOMA TUMORS AND IN CULTURED MOUSE NEUROBLASTOMA CELLS. B. Anagnoste*, L. S. Freedman*, M. Goldstein and J. Broome*. Depts. of Psychiatry & Pathology, N.Y.U. Med. Ctr., New York, N.Y. 10016.

CA synthesizing and metabolizing enzymes were found to be present in mouse C-1300 neuroblastoma tumors and in cultured cell lines of mouse neuroblastoma. The activities of CA synthesizing enzymes vary in different cell lines. Treatment with 6-hydroxydopamine (6-OH-DA) causes a regression of the tumors (Pharmacologist, 12, 382, 1970) which is noticeable only two to three weeks after tumor implantation. In subsequent days the treatment loses its effectiveness and the tumor increases in size. Treatment with 5-bromodeoxyuridine (BrdU) causes a marked regression in tumor growth. Dopamine-β-hydroxylase (DβH) activity in the serum of neuroblastoma mice is significantly higher than in the serum of the control mice. In BrdU treated mice the decrease in tumor size is concomitant with the decrease in serum DβH activity. The dopa decarboxylase (DDC) activity in the tumor obtained from BrdU treated mice is significantly higher than in the untreated controls. Mouse neuroblastoma cells from a non-clonal line and from two clonal lines were inoculated into AJ mice. The DDC activity was higher in the tumors derived from the non-clonal line as compared with the activity in the tumors derived from the clonal lines. The DβH activity was higher in the tumors obtained from one clonal line. These findings might be due to genetic heterogeneity of the clones or to differences in regulation of enzyme activities. (Supported by USPHS Grants MH-02717 and MH-44929).

18.6 MULTIPLE FORMS OF RAT BRAIN TYROSINE HYDROXYLASE. Ronald T. Kuczenski and Arnold J. Mandell. Dept.Psychiat., Sch.Med., UCSD, La Jolla, Calif. 92037

Rat brain tyrosine hydroxylase (TH) has been isolated as a soluble and a particulate enzyme depending on the specific region of the brain selected. Homogenization of brain tissue in hypotonic media, or in isotonic sucrose followed by lysis of the particulate material yields 90% of midbrain TH activity in the 100,000xg supernatant, independent of ionic strength or the presence of a wide range of monovalent and divalent ions. On the other hand, depending on the homogenization and/or lysis medium, up to 70% of caudate TH activity can be recovered, bound to a distinct membrane fraction, as isolated on discontinuous sucrose gradients. The membrane bound TH activity sediments as the nerve ending particle ghosts using the Whittaker fractionation technique, and is separable from monoamine oxidase activity. The TH membrane binding is reversible, and the extent of binding depends on ionic strength and the presence of specific monovalent and divalent ions.

While the midbrain and both the caudate soluble and particulate enzymes exhibit identical Km's for tyrosine, the caudate particulate enzyme exhibits a significantly decreased Km for the synthetic cofactor, $DMPH_4$, and an increased affinity for norepinephrine over the soluble enzymes from both midbrain and caudate. In addition, the mucopolysaccharide-induced activation of soluble hypothalamic TH which we have previously reported (J. Neurochem., submitted) is also observed for midbrain and caudate soluble TH, and alters the kinetic properties of the soluble enzymes to resemble the effect of membrane binding of caudate tyrosine hydroxylase. The alteration in Km for cofactor and feedback inhibitor by membrane binding of TH may represent a potential regulatory mechanism in the biosynthesis of NE and DA.

18.7 COMPENSATORY CHANGES IN BRAIN TYROSINE HYDROXYLASE ACTIVITY FOLLOWING CHRONIC ALTERATIONS IN CENTRAL NORADRENERGIC TRANSMISSION. David S. Segal and Arnold J. Mandell, M.D. Dept. Psychiat., Sch. Med., UCSD, La Jolla, 92037

The specific activity of midbrain tyrosine hydroxylase was determined in rats following chronic alteration in central adrenergic transmission manipulated either by pharmacological behavioral or physiological procedures.

The conditions associated with a reduction in the level of central catecholaminergic activity (produced by chronic reserpine treatment, thyroidectomy or environmental deprivation) resulted in a significant increase in the specific activity of midbrain tyrosine hydroxylase. Conversely, conditions which are associated with a facilitated central adrenergic activity (produced by chronic treatment with imipramine, monoamine oxidase inhibitors or amphetamine) led to a decrease in the specific activity of midbrain tyrosine hydroxylase activity.

These results indicate that compensatory changes in the amount and/or activity of tyrosine hydroxylase may result from prolonged alteration in functional catecholamine levels.

In addition, these results suggest that those neuropharmacological models explaining psychotropic drug action based on their acute effects on uptake and release of neurotransmitters (e.g. imipramine's increase in functionally active central catecholamines by blocking re-uptake inactivation) might not be relevent. That is such drugs when given chronically (as they are used clinically in man) lead to significant and long lasting compensatory changes in neurotransmitter biosynthetic enzymes that in turn produce an opposite final state (e.g. a decrease in catecholamine synthesizing enzyme following chronic imipramine).

18.8 ADDICTIVE DRUG EFFECTS ON THE ACTIVITY OF SEPTAL SYNAPTOSOMAL SEROTONIN BIOSYNTHETIC ENZYMES. Suzanne Knapp* and Arnold J. Mandell, M.D. Dept.Psychiat., Sch.Med., UCSD, La Jolla, California 92037

Isotopic assays of tryptophan hydroxylase and 5-hydroxytryptophan decarboxylase activity were carried out using a number of regions and subcellular fractions (characterized by EM and marker enzymes) of rat brain as the enzyme source and various enzymatic methods (including a comparison of the results of coupling the hydroxylase with exogenous decarboxylase using ^{14}C-carboxy labeled tryptophan and the tritiated water release method using suitably ^{3}H-ring labeled tryptophan in determinations of hydroxylase activity). The activity of these enzymes was studied following the acute and chronic administration of various drugs including morphine and amphetamine as well as physiological manipulations such as cold. Septal particulate enzymes, acting in concert, respond with significant increases in activity within an hour after receiving these agents whereas enzymes in other regions and subcellular fractions (for example, midbrain soluble enzyme) responded either not at all or only after long delays and chronic drug treatment. The physical state of the coupled septal enzymes is important in that hypotonic shock reduces their conjoint activity which can be recovered under conditions maximizing membrane binding, such as centrifugation and resuspension in 0.32M sucrose. Whether these reversible, drug-induced, short-latency changes in septal synaptosomal enzyme activity are due to increases in levels of either the hydroxylase, decarboxylase or both--or a drug-induced change in their physical state comparable to the amphetamine-induced effects we have reported for striate tyrosine hydroxylase is currently being explored using enzyme inhibitors, inhibitors of protein synthesis, and in vitro studies of the effect of alteration of physical state on the activity of these enzymes individually and as a functional pair.

18.9 NEUROAMINE METABOLISM IN THE CENTRAL NERVOUS SYSTEM. Michael J. Walsh. Department of Pharmacology, Bowman Gray School of Medicine, Wake Forest University, Winston Salem, N. C. 27103

The metabolism of labelled biogenic amines in the central nervous system has been shown to exhibit time dependent changes. Furthermore, possible differences in the central metabolism of exogenous norepinephrine (NE) compared with endogenously formed NE have been observed after injection of neuroamines into the brain. In these studies the metabolic fate of C^{14}-NE and C^{14}-dopamine (DA) was examined in rat brain at various time intervals (15-90 min.) after intraventricular injection. There was a gradual decline in the concentration of NE and normetanephrine (NM) over this period. However, the proportion of NM to NE remaining in brain was relatively constant (30-40%). At early time periods (<60 min.), the deaminated catechol compounds were the primary deaminated NE catabolites found in brain. At later times, the O-methylated deaminated products of NE were predominant. The proportion of catechol acid to glycol metabolites was constant and practically equivalent. In contrast, the O-methylated glycol exceeded acid formation by about 5:1. The glycol metabolites occurred primarily as the sulfate conjugates in brain. When NE metabolites were examined after DA administration, NM exceeded NE formation and O-methylated acid formation was the major route of metabolism. Temporal variations in biogenic amine metabolic pathways may reflect differences in neuronal pools and may afford a means of in vivo estimation of the substrate specificity of biogenic aldehydes for the dehydrogenase and the reductase enzymes. (Supported in part by NIH General Research Grant RR-054-04)

18.10 CELL-FREE STUDIES ON CATECHOLAMINE-STIMULATED ADENYL CYCLASE FROM RAT CEREBRAL CORTEX. Kern von Hungen* and Sidney Roberts. Dept. of Biol. Chem. and Brain Research Institute, UCLA School of Medicine, Los Angeles, Calif. 90024

Adenyl cyclase activity, determined by the conversion of [8-^{14}C]ATP to cyclic 3',5'-AMP, was studied in subcellular fractions from rat cerebral cortex. The catecholamines, norepinephrine and dopamine, at concentrations of .01-.05 mM produced significant stimulation of adenyl cyclase activity in the crude mitochondrial fraction which contained synaptosomes. This fraction exhibited the highest specific activity of adenyl cyclase. Stimulation by norepinephrine increased up to a concentration of about 1.0 mM, while dopamine stimulation was less dose dependent. Epinephrine and isoproterenol also produced stimulation. Histamine and serotonin, which stimulate adenyl cyclase activity in brain slices were ineffective, as were acetylcholine and GABA. In contrast to studies with brain slices, investigations of adenyl cyclase activity in cell-free preparations should be free from artefacts caused by precursor pools, membrane permeability and other influences on substrate availability. The data support the view that diverse receptors exist in brain for stimulation of adenyl cyclase activity by different biogenic amines. [Aided by a Contract between the ONR (No. N00014-69-A-0200-4008) and UCLA and a research grant from the USPHS (No. NS-07869)].

18.11 THE EFFECTS OF PRENATAL INJECTIONS OF D-AMPHETAMINE SULFATE ON ACTIVITY AND ON CATECHOLAMINES IN THE BRAINS OF YOUNG MICE. Lawrence D. Middaugh*, L. Ann Blackwell*, and John W. Zemp. Departments of Biochemistry and Psychiatric Research, Medical University of South Carolina, Charleston, S. C. 29401.

Pregnant C57BL/6J mice were injected daily with 5 mg/kg of D-amphetamine sulfate (DAMS) during the last six days of pregnancy. Two types of control mothers were used; untreated controls (UC) received no treatment, and saline controls (SC) received daily injections of saline. The offspring of the control and experimental mothers were either kept with their natural mother or cross-fostered to test for possible maternal behavioral effects. The activity level of the young mice has been tested using two activity measurements at intervals from days 12-75. The amount of dopamine (DA) and norepinephrine (NE) in the brain of control and experimental animals was assayed by a modified Anton and Sayre procedure at intervals from day 0-75. Prenatal injections of DAMS decreased the amount of NE on the day of birth, but the level returned towards normal by day 3. NE and DA increased after day 21 to twice the UC values at day 30. Activity at day 30, measured by both jiggle platform and open field behavior, was higher than controls. After day 30, both activity and catecholamine levels decreased to levels below normal at day 60 and again increased towards control values at day 75. At days 30 and 60, the catecholamine and activity levels of the offspring of SC fell between the two other groups. Cross-fostered mice were similar to those reared by their natural mother. Prenatal treatment with DAMS appeared, therefore, to produce long-lasting effects in young mice. (Supported by NIMH Grant 17455 and NIH GRS Grant RR5420).

18.12 PREFERENTIAL PROTECTION OF MONOAMINES IN THE BRAIN: BIOCHEMICAL AND BEHAVIORAL EFFECTS. Dell L. Rhodes* and Larry L. Butcher. Dept. Psych., UCLA, L.A. 90024

The protection regimens of Carlsson (J Pharm Pharmac 19:783, 1967) and Carlsson and Lindqvist (Eur J Pharm 2:187, 1967) were used to prevent reserpine-induced depletion of central stores of either the catecholamines (CA) or 5-HT of mice. Animals which received 5-HTP 30 min before and 90 and 210 min after reserpine had normal brain levels of 5-HT 24 hrs later, but CA levels dropped to 47% (DA) and 18% (NE) of normal. L-DOPA administration prevented depletion of the CA while 5-HT content dropped to 63% normal. Pre-reserpine injection of tetrabenazine (TBZ) maintained DA and 5-HT levels at 77%, with NE dropping to 58%. Thus, although "protection" was only partial in this regimen, the DA/5-HT ratio was identical to that of control mice. Control injections of DOPA, 5-HTP, or TBZ did not significantly change monoamine levels measured 24 hrs later. The behavioral effects of these regimens were assessed using mice trained to press a lever on a food-reinforced fixed-ratio 30 schedule. Animals given reserpine alone and those subjected to the 5-HTP protection regimen showed severe depression of lever-pressing which outlasted the gross behavioral sedation resulting from these regimens. DOPA protection lowered response rates in some animals, but responding showed pre-drug patterning and the rates recovered rapidly. Mice protected with TBZ and those receiving control injections of DOPA, 5-HTP, or saline showed no change in their fixed-ratio behavior. We conclude that (1) the CA are necessary for fixed-ratio behavior, but (2) the ratio of brain monoamine levels is a more important correlate of performance than individual monoamine levels alone. (This research was supported by University of California Grant No. 2637.)

18.13 DECREASES IN REWARDING BUT NOT AVERSIVE BRAIN STIMULATION FOLLOWING ALPHA-METHYL-P-TYROSINE. Barrett R. Cooper* and Ronald M. Paolino. Dept. Pharmacol. & Toxicol., Purdue Univ., Lafayette, Ind. 47907

The hypothesized role of norepinephrine (NE) as a synaptic transmitter in the reward system has been based, in part, on decreased measures of rewarding electrical brain stimulation (ESB) following administration of alpha-methyl-p-tyrosine (aMT), an inhibitor of catecholamine synthesis. However, aMT has also been reported to decrease food reinforced lever pressing, motor activity, and rotorod performance, as well as avoidance and escape responding motivated by footshock. The purpose of this experiment was to assess the specificity of aMT effects on behavior motivated by positively and negatively reinforcing ESB as compared with the apparant general depressant effects noted with conventional peripheral reinforcers - eg - food, footshock. Twenty-four rats were implanted with single bipolar stimulating electrodes aimed at either forebrain (FB), lateral hypothalamic (LH), midline hypothalamic (MH) or dorsal tegmental (DT) structures. Rate free measures of rewarding and aversive properties of 0.3 ma and 0.5 ma of ESB were obtained using a modified shuttle box apparatus. An increase in stimulation current resulted in an increase in both the rewarding (FB and LH placements) and aversive (MH and DT placements) aspects of ESB. Oral administration of 200 mg/kg and 600 mg/kg of aMT produced dose related decreases in the rewarding aspects of ESB. No effects of the drug were seen on negatively reinforced behavior. The data are interpreted as indicating a specific effect of aMT on a central catecholaminergic reward mechanism activated by ESB.

Session 19

19.1 NEUROANATOMICAL CORRELATES OF TIME RECONSTRUCTION IN THE RAT. Robert W. Thatcher. Dept. Anat., Albert Einstein Coll. Med., Bronx, N.Y.

Two groups of rats were classically conditioned to two different frequencies of a visual flicker CS (3.3hz & 8.2hz). Later, while subjects (Ss) were bar pressing for food a 5.8hz test flicker was presented and response suppression noted to occur. EEG recorded from 5 different brain regions (midline thal., medial lat. thal., visual cortex, post. lat. thal., & mesencephal. retic. formation) was subjected to a power density spectral analysis. The mean proportion of power at CS frequencies (±.25hz) was computed for both groups of rats during consecutive 20 sec. epochs time locked to the onset of the test flicker. The spectral analysis revealed statistically significant increases in power at 3.3hz (±.25) in Ss conditioned at 3.3hz. Statistically significant increases in power were also found at 8.2hz (±.25) and at 4.1hz (±.25) in Ss conditioned at 8.2hz. Four separate experiments were conducted each with a different duration CS (40 sec., 60 sec., 80 sec., & 120 sec.). The results showed that significant increases in power at CS frequencies occurred consistently near the time footshock would be expected to occur. As CS duration was lengthened enhanced power at CS frequencies became anatomically more extensive and spatio-temporally more complex. Greater anatomical differentiation of CS frequency activity also occurred as a function of CS duration. The results were interpreted as representing the action of a system involved in reconstructing the CS-UCS interval. This process is necessary for predicting time of occurrence of footshock.

19.2 ELECTROENCEPHALOGRAPHIC CORRELATES AND PREDICTORS OF PERFORMANCE DURING LEARNING AND MEMORY IN THE MONKEY. Samuel L. Moise, Jr.* and Anatol Costin. Dept. Anat., Sch. Med., UCLA, L.A. 90024.

This research is an attempt to assess in detail the involvement of different brain sites during complex information processing in the monkey. Three Macaca nemestrina with chronic implanted electrodes in amygdala, hippocampus, hypothalamus, lateral geniculate body, thalamus, septum, and optic cortex were trained on color discrimination, matching to sample, and delayed matching from sample tasks. All selection of parameters, recording, and evaluation of behavioral data (including latencies) was performed by computer control. Patterns in the EEG were assessed by means of power density spectral analysis, including autospectra, coherence and discriminant functions derived from these variables. Rapid decision making by the primates necessitated the use of .5 sec EEG epochs averaged over 20-40 trials for analysis. Differences in spectral values were evaluated by nonparametric statistical tests. In all tasks the hippocampus and lateral geniculate body showed intimate involvement in the processing of information terminating in correct and incorrect responses. Their autospectra showed predictive differences in degree of involvement for trials resulting in correct and incorrect responses during receipt of information (stimulus onset) and during recall (prior to response). Most of these changes were in the frequency bands 3, 4, 5, 6-7, and 8-12 Hz. Fewer changes were seen in the bands from 13 to 24 Hz. Coherence measurements (the linear relationship between two recordings at a given frequency) indicated that hippocampus and lateral geniculate body were involved in low level but significant linear relationships with each other and with various other structures. This shared activity varied with correct and incorrect responses. (Supported by USPHS GF02 MH 44,369-01A1 PS; GM 16058; and RR-3.

19.3 UNIT ACTIVITY IN THE FRONTAL GRANULAR CORTEX OF THE MONKEY IN A CLASSICAL DELAYED RESPONSE TASK. Joaquin M. Fuster. Department of Psychiatry and Brain Research Institute, School of Medicine, University of California, Los Angeles, Calif. 90024.

Single-cell spike potentials were recorded in prefrontal cortical areas of rhesus monkeys during performance of a delayed response test. Visual cues were used and delay intervals of up to one minute were interposed between cue and response. Units in the region of the sulcus principalis and also in other regions of granular frontal cortex show distinct changes of firing frequency in the course of delayed response trials. For a given unit these changes are relatively consistent and reproducible from trial to trial. Using the inter-trial spontaneous firing rate as the baseline of reference, most units (about 65 % of those investigated) are seen to increase their firing during presentation of the test-cue or during the delay that follows. About one-third of the units activated at presentation of the cue also show transient reactions of lesser magnitude to both auditory and visual stimuli not related to the task. A substantial number of units display sustained high rates of discharge throughout the delay. The changes of neuron activity observed in delayed response behavior are tentatively interpreted as manifestations of a role of the prefrontal cortex in the attentive processes subserving the acquisition of sensory information and its retention in short-term memory storage.

19.4 CORTICAL STEADY POTENTIAL CORRELATES OF TRANSIENT MEMORY IN MONKEYS. Steven C. Rosen* and John S. Stamm, Psychol. Dept., SUNY at Stony Brook, Stony Brook, New York 11790.

Monkeys with chronically implanted Ag-AgCl nonpolarizable electrodes in dorsolateral prefrontal, precentral, and occipital cortex were trained on a two-choice delayed response (DR) task. In a previous report (Electroenceph. clin. Neurophysiol., 27: 684, 1969) we described the occurrence of a surface negative steady potential (SP) shift from prefrontal cortex which reached maximum negativity (20-50 μV) at the start of the delay period. In the present experiment the significance of this SP shift was further examined by systematic variation of the cue, delay, and intertrial interval (ITI) parameters of the DR task. Computer analyses of transcortical DC recordings indicated that: (1) The magnitude of the SP shift was not correlated with variation in duration of either: the cue (.06 to 8 secs), the delay period (2 to 20 secs), or the ITI (8 to 40 secs). (2) However, the magnitude of the prefrontal shift was significantly correlated with the level of correct performance, with r's of .54 to .76 in four monkeys. Corresponding correlations of SP shifts from precentral or occipital cortex were insignificant. (3) SP shifts from occipital cortex were positively correlated with duration of cue presentation. (4) Precentral SP shifts of 1-3 sec duration were related to motor responses. These results permit delineation of a surface negative component of the prefrontal SP shift in relation to the mnemonic processes required for the DR task. The occurrence of this shift at the start of the delay period supports the interpretation that prefrontal cortex functions specifically during the formation of transient spatial memories.

19.5 SPEECH AND SHORT TERM VERBAL MEMORY ALTERATIONS WITH HUMAN VENTROLATERAL THALAMIC STIMULATION. George Ojemann and Arthur Ward, Jr., Neurological Surgery Department, University of Washington, Seattle, Washington 98105.

Effects of electrical stimulation in the human ventrolateral thalamus (VL) on a standard test of object naming and short term verbal memory are reviewed. These studies occurred during stereotaxic procedures for treatment of dyskinesias in 25 right-handed patients. All stimulations were at current levels below the threshold for sensation. Disturbance of object naming was evoked from left VL, but not right. Within left VL changes in object naming of the anomic and perseverative types were evoked only from a discrete area in medial central VL. This area was contiguous anteriorly and posteriorly with the areas where similar changes were evoked in right-handed subjects in a previous study of thalamic stimulation and object naming (Ojemann et al., Brain 91:99, 1968). Taken together, these studies outline a discrete localization of speech function in left lateral thalamus including pulvinar, and medial central VL. Short term verbal memory was measured by an adaptation of the technique of Peterson and Peterson (J. Exp. Psych. 58:193, 1959) in the same 25 patients. Stimulation in left VL, at current levels less than those altering object naming, disturbed recall performance when stimulation occurred at the time of recall. The same stimulation of the same left VL sites, when applied at the time of presentation of material to be recalled significantly improved recall performance over control levels. Stimulation during the distraction period, during both presentation and recall periods on the same trial, or of right thalamic sites during any part of the test did not alter performance over control levels. Left VL thalamus is apparently involved in short term verbal memory, determining what enters or leaves it at any given moment. This function overlaps, but is not so discretely localized in left VL as is speech.

19.6 OPERANT CONTROL OF LAMBDA WAVE PRODUCTION IN NORMAL AND PARALYZED CATS. Paul School* and Vernon Rowland. Depts. of Psychology and Psychiatry, Case Western Reserve Univ., Cleveland, Ohio 44106.

Lambda waves from chronically implanted cats were electronically discriminated and controlled the delivery of rewarding electrical stimulation to the median forebrain bundle in two contingencies, "go" and "no-go". The "go" contingency, a fixed ratio schedule, was signalled by a 60 H_z auditory stimulus; the "no-go" contingency by a 2.5 kHz tone which required lambda waves be withheld for up to six seconds for each reinforcement. Subjects were trained to each contingency separately and then placed on a combined schedule. Lambda waves and associated saccades were clearly more frequent with the "go" than with the "no-go" contingency despite approximately equal rates of reinforcement. Discriminated lambda production was then elicited on the same schedules in total darkness and with complete flaxedil paralysis. The capacity of the cat to produce or withhold lambda activity in order to maximize reinforcement in the absence of retinal input or muscular activity establishes that the lambda generating mechanism can be effectively coupled with central motivational mechanisms as well as with the previously demonstrated more reflexive adjustments triggered by peripheral inputs (visual, vestibular, etc.)

19.7 Long-term observations of patterns of self-stimulation. George Koob* and Zoltan Annau. Dept. of Environ. Med., Johns Hopkins Univ., Baltimore, Maryland 21205

Rats with chronically implanted electrodes in the lateral hypothalamic and septal areas were allowed ad lib access to self-stimulation in a three-lever Skinner box. For some rats, with a posterior lateral hypothalamic electrode, one lever provided access to self-stimulation on a CR schedule while two other levers provided food pellets and one drop of water also on a CR schedule. For other rats, each lever activated a different electrode, one septal, one anterior lateral hypothalamic and one posterior hypothalamic electrode. Both groups of animals started with a typical period of self-stimulation alternating on all electrodes that lasted about 12 hours. Following this period, the animals displayed characteristic periodic behavior that consisted of bursts of self-stimulation followed by eating and drinking, and a rest period. The periodicity of the three electrode animals appeared very similar to that of the single electrode animals except the activities alternated between the three brain stimulation levers and then were followed by rest periods. Our results indicate that given long periods of free access to self-stimulation behavior, animals display behavior patterns characteristic of normal drives such as hunger and thirst. These results seem to confirm previous work that activation of rewarding brain circuits is regulated by normal drive mechanisms.

19.8 BEHAVIORAL STUDIES OF ANALGESIA RESULTING FROM ELECTRICAL STIMULATION OF THE BRAIN. David J. Mayer*, Huda Akil*, and John C. Liebeskind. Dept. of Psychology, UCLA, Los Angeles, California 90024.

Complete analgesia to even intense peripheral pain resulted from pulsed electrical stimulation of discrete brainstem regions in 22 of 54 rats. These animals were totally unresponsive to strong shock, pinch, burning or cold although they appeared normally responsive to visual, auditory and tactile stimuli. In fact several were hyper-responsive to light touch while unresponsive to pain. During stimulation many animals locomoted normally and some would, for example, grasp and consume a food pellet or explore a novel object. No analgesic animal showed either motoric or electrographic seizure activity but seizures were seen in several non-analgesic animals. The peripheral field of analgesia included the entire body in a few animals but more commonly was restricted to one or two limbs and/or the tail. Analgesia outlasted brain stimulation by as much as 45 min. Electrodes supporting analgesia were primarily in ventral, posterior mesencephalic central gray, ventral tegmentum, and dorsomedial thalamus. All but one analgesic placement supported self-stimulation. However, a number of self-stimulation sites failed to produce analgesia. Thus, while neural systems underlying analgesia and reward may be partially overlapping, they appear not to be identical. One animal with an analgesic, non-rewarding placement did self-stimulate reliably in the presence of pain. This behavior was presumably reinforced by pain reduction. From this experiment and the observations described above we conclude that brain stimulation can reduce or abolish not only the observable manifestations of the pain response but also the perceived aversiveness of noxious stimuli.

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19.9 PAIN SUPPRESSING EFFECTS OF REWARDING BRAIN STIMULATION. Mitchel D. Rose* & C. R. Gallistel. Dept. of Psychol., Univ. of Penn., Phila., Pa. 19104.

A possible association between the neural substrates of rewarding electrical self-stimulation of the brain and focally induced electrical analgesia was investigated in 4 sets of experiments on the rat. Electrodes implanted along the medial forebrain bundle (MFB) were screened for both self-stimulation and stimulation-induced analgesia. Analgesia was operationally defined by changes in two types of responses to noxious footshock: decrease in unconditioned responses (flinch, vocalization and agitation) and increase in latency in two-way escape. Self-stimulation was measured by barpressing. Almost all electrodes produced either both self-stimulation and analgesia or neither. Further, a relatively high threshold for one effect predicted a relatively high threshold for the other, on electrodes which produced both effects. In the third set of experiments, electrical analgesia was found to have a pain-suppressing aftereffect comparable in duration to the post-stimulation enhancement of performance in self-stimulation (the priming effect). The aftereffect of rewarding-analgesic stimulation can both increase running speed (for self-stimulation in a runway) or decrease running speed (in escape from footshock). This finding eliminates the possibility that the analgesia aftereffect is an artifact of response suppression. Finally, the refractory period of neurons underlying analgesia was assessed by the pulse pair technique, with speed of escape as the dependent variable. The refractory period was similar to that previously found for the drive (or priming) set of neurons in self-stimulation (0.8 - 1.2 msec), and was dissimilar to the value for the reward fibers (0.6 msec). The results of the four experiments indicate that electrical analgesia and the drive effect of self-stimulation are mediated by a common set of fibers in the MFB.

19.10 COMPARISONS OF SUBSTANTIA NIGRA AND CAUDATE NUCLEUS LESIONS ON THREE LEARNING MEASURES IN RATS. Judson C. Mitcham* and Roger K. Thomas. Dept. Psychol., U.Ga., Athens 30601.

Owing to the known anatomical and dopaminergic relationships between the substantia nigra and the caudate nucleus, possible functional similarities were studied in one-way active avoidance learning followed by learning to inhibit the acquired active avoidance response. Additional groups were trained in an active two-way avoidance learning task. Non-operated and operated controls, which did not differ, were significantly better in performance than the lesion groups on all measures. The caudate lesion group was better than the nigral lesion group on one-way active avoidance but the lesion groups were statistically equivalent on the other tasks. The data suggested considerable functional similarity bewteen these structures as well as some differences. Results will be considered in terms of several categories of behavioral deficits that have been associated with caudate nucleus damage and the possible role of dopamine in such deficits will be discussed.

19.11 TIME FACTORS IN RECOVERY OF FUNCTION FOLLOWING FRONTAL LOBE LESIONS IN THE RAT. Geoffrey A. Patrissi* and Donald G. Stein. Dept. of Psychology, Clark University, Worcester, Massachusetts. 01610.

The following study was designed to investigate the minimum period of time required for functional reorganization following 2-stage lesions in the CNS. The frontal cortex was chosen for suction removal because bilateral, 1-stage surgery produces highly characteristic behavioral syndromes. The 45 albino rats were randomly assigned to the following lesion groups: sham operates, 1-stage removal (1-S), 2-stage (2-S) 30 day interlesion interval (ILI); 2-S, 20-day ILI; and 2-S; 10-day ILI. On the acquisition of a spatial alternation task in a T-maze, the sham, 2-S 30 and 2-S 20 day groups did not significantly differ from each other. However, the 2-S 10 day and 1-S groups were markedly impaired. Also, there was a significant difference between the 2-S 10 and 1-S groups with the latter being most impaired. The results suggest that reorganization of brain function occurs in the temporal interval between 2-stage lesions. This reorganization can be differentially affected by contralateral destruction at various times after initial surgery. The finding suggests compensation of function is gradual and could result from the establishment of alternate systems in other areas of the CNS using the remaining contralateral structure as a template.

19.12 RETENTION OF THE SECOND OF TWO PRE-OPERATIVELY LEARNED BRIGHTNESS DISCRIMINATIONS FOLLOWING POSTERIOR NEODECORTICATION IN THE ALBINO RAT. Lois O. Stratton. Dept. Psych., LSUNO, New Orleans, 70122.

Three groups of albino rats learned both simultaneous and successive brightness discriminations in a T-maze apparatus. Groups I and II received posterior neocortical ablations after learning, and Group III Ss were ablated prior to learning the problems. Group I Ss were tested for retention of both problems in their original order and Group II Ss relearned the SU problem first. Zero or negative savings were found for the first post-operative problems, but significant savings were obtained for the second problems. Scores for acquisition Group III were significantly poorer than acquisition and retention scores of Groups I and II. The data suggests that the relevant cortical receptor area is necessary for gaining access to the memory engram, but that memory itself is not stored in neocortical sensory areas. In this study, access to the engram was regained by relearning the first of two post-operative problems so that memory of the second problem was demonstrated. Learning differences between operates and normals suggest that sensory, motivational or attention losses also occur following posterior ablation of albino rats.

Session 20

20.1 BIDIRECTIONAL AXOPLASMIC FLOW IN FROG SCIATIC NERVE IN VITRO. Lester M. Partlow, C. David Ross* and David B. McDougal*. Dept. of Pharmacology, School of Medicine, Washington Univ., St. Louis, Mo. 63110

Branchless segments of sciatic nerve lying between the hip and knee were ligated and removed from Rana pipiens. These were incubated in frog Ringer's at 4° or 22° C for up to 48 hours. Nerves were then frozen in liquid N_2, freeze-dried, cleaned and cut into ½-2 mm pieces. Redistribution of enzymes along the nerve was studied as an indicator of axoplasmic flow. No gradient in enzyme activity was detected in these 25 mm segments before incubation at 22° C or after incubation at 4° C. The distribution of the soluble enzymes glucose-6-phosphate dehydrogenase, 6-phosphogluconate dehydrogenase and α-glycerophosphate dehydrogenase did not change in short-term experiments at 22° C. Two mitochondrial enzymes, hexokinase(HK) and glutamate dehydrogenase(GDH), and cholinesterase(ChE) accumulated in the 1.5 mm above the distal tie and below the proximal tie. The data suggest that only a fraction of each enzyme is available for flow: HK-9%, GDH=12% and ChE=25%. Rates of flow were calculated on this basis. The rate of flow away from the cell body was 13 mm/day for HK and 22 mm/day for GDH; the rate toward the cell body was 6 mm/day for HK and 8 mm/day for GDH. ChE accumulated at rates of 70 mm/day(distal) and 17 mm/day(proximal). Flow of ChE was not altered by incubation in buffered 110 mM KCl with glucose, indicating that axoplasmic flow continues in depolarized nerve at the same rate. The distribution of choline acetylase activity changes with time, but is hard to quantitate, as it does not accumulate in the 1.5 mm adjacent to the ties. Accumulation of HK, GDH and ChAc below the proximal tie was linear through 48 hours, indicating continuing viability. This preparation seems promising because movement of several different enzyme markers can be accurately quantitated in vitro and the effects of known and potential inhibitors can be easily assessed. NIH grants 2-TO1-NB05221 and 1-RO1-NB06800.

20.2 RAPID AXONAL TRANSPORT OF GLYCOPROTEINS LABELED WITH ^{3}H-FUCOSE IN THE GOLDFISH OPTIC SYSTEM. David S. Forman, Bruce S. McEwen, and Bernice Grafstein. Rockefeller Univ., and Cornell Univ. Med. Coll., New York, N.Y. 10021.

^{3}H-Fucose injected into the goldfish eye labels glycoproteins which are rapidly transported to the optic tectum. In large "pond" goldfish at 20.5°C the glycoproteins are transported at a rate of 60-70 mm/day, the same rate as rapidly transported proteins labeled with radioactive amino acids. Whereas amino acids also label a larger wave of slowly transported proteins which move 0.5 mm/day, there is no detectable slow component labeled with ^{3}H-fucose. Inhibition of retinal protein synthesis with acetoxycycloheximide reduces the amount of fucose-labeled glycoprotein arriving in the tectum to 15-20% of control values. Most of the fucose-labeled transported glycoproteins are membrane-bound. After acid hydrolysis, more than 90% of the incorporated radioactivity can be recovered as fucose. A small amount of acid-soluble radioactivity is also rapidly transported. These results are similar to those obtained with ^{3}H-glucosamine (Forman, McEwen, and Grafstein, Brain Res. 1971, 28, 119-130).

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20.3 TRANSPORT OF RADIOACTIVE PROTEIN FROM EYE TO VISUAL CORTEX. Bernice Grafstein and Robert Laureno*. Dept. Physiol., Cornell Univ. Med. Coll., New York, N.Y. 10021.

Radioactive amino acids or sugars injected into the mouse eye label proteins which are transported in the optic axons to the lateral geniculate body and superior colliculus. After a few hours, labeled protein also appears in the striate cortex. With a number of different precursors, including tritiated proline, glucosamine, and fucose, and at a number of different times after the injection, the amount of labeled protein in the colliculus was consistently about 3 times that in the geniculate. This ratio presumably reflects the relative numbers of optic axons ending in colliculus and geniculate. If similar optic axons were responsible for the radioactivity in the cortex, the amount of labeled material in the cortex would also be expected to show a constant ratio to that in the geniculate. This was found not to be the case, suggesting that the label appearing in the cortex was not conveyed by fibers going directly from eye to cortex.

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20.4 AXONAL TRANSPORT IN OPTIC NERVES OF MICE LACKING VISUAL RECEPTORS. Marion Murray and Bernice Grafstein. Dept. Anat., Univ. of Chicago, Chicago, Ill. 60637 and Dept. Physiol., Cornell Univ. Med. Coll., New York, N.Y. 10021.

After injection of tritiated proline or leucine into the mouse eye, the rate of axonal transport in the optic nerve was determined from the time course of appearance of labeled protein in the superior colliculus. Two rates of transport could be distinguished, which in normal mice averaged about 80 mm per day and 3 mm per day respectively. In mutant mice with hereditary degeneration of the visual receptor cells (C57BL/6j rd le) the fast transport rate was the same as normal, but the slow rate was only about half normal. Since the level of electrical activity in the optic nerves of the mutants would be substantially less than normal if not completely absent, these results suggest that the rate of fast transport is uninfluenced by physiological activity. On the other hand, the reduced rate of slow transport might be due to the decreased activity, but at least 2 other possibilities cannot be excluded: the reduced rate might be a) a direct consequence of the genetic defect or b) an indirect consequence of the fact that the overall level of amino acid incorporation in the retinal ganglion cells of the mutants was only about 65% of normal.

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20.5 A RAPID QUANTITATIVE METHOD FOR ASSESSING THE EFFECT OF DRUGS UPON AXOPLASMIC TRANSPORT: STUDIES WITH ANTIMITOTIC AGENTS. Anne L. Cahill*, James C. Paulson*, and William O. McClure, Department of Biochemistry, University of Illinois, Urbana, Illinois 61801.

Tritiated l-leucine injected into the eyes of rats is incorporated by ganglion cells into proteins, some of which are then carried to the brain by fast axoplasmic flow. Addition of drugs to the injected solution may result in a decrease in transported radioactivity. With appropriate controls, this decrease can serve as a rapid means of screening for drugs which affect axoplasmic transport. The method can be quantitated by using the contralateral eye as a control. We have studied the anti-transport activity of several compounds which inhibit mitosis, probably by interacting with microtubules which make up the mitotic spindle. All these agents depress transport, using doses which do not reduce the incorporation of leucine into proteins of the retina. Dose-response curves indicate that, in order of decreasing efficacy as anti-transport agents, vincristine$\gtrsim$vinblastine>>colcemid$\gtrsim$colchicine>griseofulvin. These relationships are similar, but not identical, to those reported for anti-mitotic activity in the rat. The ordering is very different from that observed when studying antimitotic activity in Pectinaria oöcytes. It is probable that some common element, such as the system of microtubules, relates the antimitotic and anti-transport activities of these compounds. Quantitative comparisons further suggest that other effects, such as cellular permeability, may complicate interpretation of the results.
This research was supported by the National Institutes of Health, the Illinois Department of Mental Health, and the Research Board of the University of Illinois.

20.6 AXOPLASMIC TRANSPORT OF AChE, LDH AND MAO IN MAMMALIAN NERVE FIBERS. M. A., Khan*, N. Ranish and S. Ochs, Department of Physiology, Indiana University Medical Center, Indianapolis, Indiana, 46202.

A well defined fast transport of material in nerve fibers at a rate close to 400 mm/day was shown by a crest of labeled proteins in the cat sciatic nerve after uptake and incorporation of ^{3}H-leucine injected near the nerve cell bodies, L7 dorsal root ganglion or ventral horn region of the cord (Ochs and Ranish, J. Neurobiol. 1; 247, 1969). Another method of studying axonal transport is the accumulation of materials proximal to a nerve ligation or cut, either of labeled materials or of materials normally present in nerve fibers. A study using this method was made of the enzyme AChE in the particulate fraction, LDH in the soluble component of axoplasm and MAO, a marker for mitochondria. Accumulation of these enzymes in a 5 mm segment of cat sciatic nerve proximal to a ligature was linear over a period of 24 h. The sample was subjected to homogenization and centrifugation. Analysis was made of the nuclear free supernatant or after further centrifugation, of the mitochondrial fraction for MAO, of the small particulate fraction for AChE and the high speed supernatant for LDH. Double ligations were made in nerves at an average distance between the ligations of 83.5 mm. The accumulation of AChE proximal to the distal ligation continued in a linear fashion for about 4.3 h and then remained at a constant level for times up to more than 20 h. This indicated an exhaustion of a fraction of AChE in the nerve segment moving at a rate within a 95% confidence interval of 380 to 578 mm/day. The soluble enzyme LDH did not show a leveling off nor did MAO, indicating that these two substances are carried down the fibers by the slow axoplasmic transport system.

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20.7 AMINO ACID TRANSPORT IN VITRO BY RAT BRAIN SYNAPTOSOMES. N. A. Peterson* and E. Raghupathy* (SPON: C. M. McKean). Brain-Behavior Research Center, Sonoma State Hospital, Eldridge, California 95431.

The transport of labeled amino acids in vitro by synaptosomal fractions, one possible rate-limiting step in synaptosomal protein synthesis, was studied. The fractions were prepared from rat brains on ficoll density gradients as described by Kurokawa et al. (Biochem. J., 97, 833, 1965) and, after incubation with labeled amino acids, were collected and washed on millipore filters. The fractions rapidly concentrated a number of amino acids. The concentration of leu in the fractions reached maximum within 5 min of incubation, and declined progressively following the initial period of influx. The uptake of leu obeyed typical saturation kinetics (V_m=2 x 10^{-4} µM/0.25 mg protein/3 min; K_m=15 + 6 µM) and was inhibited by tyr, ileu, leu, val, his and phe. The inhibition by phe was of the competitive type (K_i=9 µM). The uptake was not influenced by pro, arg and lys. Leu influx was not dependent on the presence of Na^+ or K^+ in the incubation mixture. Ouabain (2 mM) inhibited this influx only if the fractions were preincubated with the inhibitor in the presence of both Na^+ and K^+, and the effect of ouabain was antagonized by high $[K^+]$. In agreement with other reports, the incorporation of labeled amino acid into protein was dependent on Na^+ and K^+ concentrations of the incubation medium and was significantly greater in fractions from immature rats than in the fractions from adult rats. In contrast, the rates of leu influx into fractions from brains of 8-day old and adult rats were not different. The results indicate that Na^+-independent active transport of leu takes place across the synaptosomal membrane and further suggest that the incorporation of amino acid into protein by the fractions may involve a second transport mechanism which is dependent on the concentrations of Na^+ and K^+.

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20.8 NEURAL REGULATION OF MUSCLE GANGLIOSIDE BIOSYNTHESIS. Stephen R. Max. Department of Neurology, University of Maryland School of Medicine, Baltimore, Md. 21201.

We have recently reported that denervation of skeletal muscle results in a marked increase in the content of the major sialoglycolipid of muscle, N-acetylneuraminylgalactosylglucosylceramide (GM3) (Max, Nelson and Brady, J. Neurochem., 1970). Studies utilizing N-acetyl-^{3}H-D-mannosamine, a specific precursor of the sialic acid moiety of gangliosides, indicated that GM3 is synthesized de novo in response to denervation. It was considered possible that the increased ganglioside synthesis is related to the hypersensitivity to acetylcholine of denervated muscle. In this report, we present the results of the determination of the ganglioside levels in muscles undergoing atrophy due to disuse, rather than denervation. Disuse atrophy of rat gastrocnemius muscle was produced by the skeletal fixation technique of Solandt et al. (J. Neurophysiol., 1943). After 8 days following the production of disuse, the gastrocnemius muscles were removed, weighed, and analyzed for ganglioside content. In this period immobilized muscles lost about 40% of their mass, while denervated muscles lost about 30%. There was no increase in the GM3 content of disused muscles, compared with contralateral control muscles, which is in contrast to the increased GM3 content and synthesis observed in denervated muscle. We conclude that the augmented ganglioside biosynthesis in denervation is specifically related to deprivation of the muscle of its innervation, and not to disuse. Thus the motor nerve exerts a regulatory influence on ganglioside biosynthesis in skeletal muscle.

20.9 DEPENDENCE OF SYMPATHETIC REINNERVATION OF THE RAT IRIS IN ORGAN CULTURE ON NERVE GROWTH FACTOR. S.D. Silberstein*, D.G. Johnson*, I. Hanbauer* and I.J. Kopin. NIMH, Bethesda, Md. 20014.

Reinnervation of sympathetically denervated rat iris by superior cervical ganglia (SCG) has been shown to occur in vitro. Irides and SCG from adult male Sprague-Dawley rats have been grown in organ culture in a chemically defined medium (BGJ_B). Return of ^{3}H-norepinephrine uptake by irides incubated in contact with ganglia was associated with the reappearance of nerve fibers containing catecholamines. Exogenous nerve growth factor (NGF) appeared to enhance the rate and extent of reinnervation and apparently was required to be present early in culture (one to two days). Specific antibody to NGF further reduced the reinnervation. Endogenous NGF, measured by immunoassay, was present in both fresh iris and ganglia. After 24 hours in culture NGF was markedly decreased in cultured organs, but was recovered in the culture medium. Preincubation of an iris for 24 hours alone, before adding a ganglia, decreased the reinnervation measured after six days of culture. Preincubation in the presence of exogenous NGF returned the innervation to control levels. These results suggest that endogenous NGF is important in sympathetic reinnervation.

20.10 ^{45}Ca and ^{40}Ca UPTAKE AND EXCHANGE IN LEG NERVES OF "LIBINIA EMARGINATA". C. Paul Bianchi. Department of Pharmacology, School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania 19104.

Preliminary studies of ^{45}Ca uptake and washout by leg nerves of "Libinia Emarginata" showed that nerves equilibrated for 200 minutes or 10 minutes in ^{45}Ca sea water containing 44 mM Ca underwent 100% exchangeability of tissue calcium and that the exchange was complete in 10 min. The half-time for washout of the fast component of ^{45}Ca was 1 minute for nerves pre-soaked in ^{45}Ca sea water for 10 minutes or 200 minutes. The slow component has a half-time of washout of 3.5', for nerves washed out for 10' with collection intervals taken every minute, when the collection interval was increased to five minutes and the total washout period increased to 35 minutes the half-time of washout was increased to 15 minutes. The increase in half-time at the longer washout intervals was attributed to back flux. The tissue calcium and ^{45}Ca uptake after 30 minutes was studied at 44 mM Ca_o, 22 mM Ca_o, 11 mM Ca_o, and 1.0 mM Ca_o. The exchangeability varied from 100% at 44 mM Ca_o to 60% at 22 mM Ca_o, 50% at 11 mM Ca_o and 46% at 1.0 mM Ca_o. The slow component of ^{45}Ca exchange was essentially constant from 1.0 mM Ca_o to 22 mM Ca_o and only slightly increased at 44 mM Ca_o. After correction for calcium uptake into the interstitial space as measured by the sucrose space (0.165 ml/gm wet weight nerve), the calcium bound to fast exchangeable binding sites only became evident at Ca_o concentrations of 11.0 mM or greater. (This was supported by USPHS NS-03321.)

20.11 ROLE OF ADENOSINE TRIPHOSPHATE AND CERTAIN CATIONS IN MEMBRANE FUNCTION OF NORMAL AND MUTANT PARAMECIUM AURELIA. John Nurnberger and Jorgen Fex, Center for Neural Sciences, Ind. U., Bloomington 47401.

The effect of adenosine triphosphate (ATP) on several behavioral and electrophysiological responses of Paramecium aurelia was tested. Paramecia change the movements of their cilia when they are introduced into solutions containing concentrations of Na^+, K^+, or Ca^{++} that are significantly different from those of their adaptation solutions (Dryl, Anim. Behav., 11, 393, 1963). Intracellular recordings were made from paramecia exposed to different concentrations of these cations with and without ATP. Ciliary activity was recorded with a Bolex movie camera. The methods of Kung (Z. vergl. Physiologie, 71, 142, 1971) were used to produce genetic mutants with altered responses to cationic stimuli; their responses to ATP were also tested. The relationships between ATP and Ca^{++}, K^+, and Na^+ were explored, and conclusions drawn regarding their interaction in the membrane.

20.12 ARE CILIATED NEURONS FUNCTIONAL? David A. Goodman and Chester L. Richards* Newport Neuroscience Center and Univ. Calif. Irvine, Irvine, Calif. 92664

Recent work on the amphibian receptors and central nervous system reveals hitherto unsuspected similarities between certain neurons and ciliated epithelial cells. Morphologically some ciliated neurons have been identified as receptors. Other ciliated neurons found throughout the central nervous system are of unknown function. These are of interest because they are numerous. Also neurons on stimulation can be induced to extrude cilia from the basal bodies. These cilia exit from the cell's dendritic pole. From this data, we have formulated two hypotheses which are currently under investigation. The first hypothesis assumes that the subcellular machinery of the ciliated epithelial cell is resident and active in the neuron. We may expect that mechanical as well as electrical oscillations should be observed in neurons. The second hypothesis stresses the possibility that properties of neurons in the aggregate can be predicted from functional interactions of assembled ciliated epithelial cells. To test these hypotheses, optical techniques for remote sensing of cell function might be employed. These include double-pulse holography to examine cell membrane movement and stroboscopic technique for the study of the effects of "neurotropic" drugs on ciliated epithelium. Results of model experiments are discussed with reference to periodicity of function and "metachronism" in neurons and neuron aggregates.

20.13 POSTWEANING GROWTH OF CHOROID PLEXUSES AND A REGIONALLY SPECIFIC EFFECT OF A LOW SODIUM AND POTASSIUM DIET. W. B. Quay. Dept. Zool., University of California, Berkeley, Ca. 94720.

Choroid plexuses (c.p.) of the brain's ventricles are believed to be sites of partial origin and control of cerebrospinal fluid (c-s.f.). Although it is often assumed that these structures are physiologically equivalent in the four ventricles, metabolic evidence suggests that this may not be true (Quay, W. B., Brain Res. 2: 378, 1966). The present study was based on the hypothesis that particular choroid plexuses may differ in their involvement in regulation of electrolyte composition of c-s.f. and consequently in their response to low or high dietary levels of particular salts. The results support at least the latter part of this hypothesis and favor the concept of regional differences in the choroid plexuses. Choroid plexuses from ventricles I and II (c.p. I+II), III (c.p. III) and IV (c.p. IV) of untreated male rats 3, 4, 5, 7, 9 and 25 weeks of age show: increases in mean dry weights of 216.0% for c.p. IV, 88.8% for c.p. I+II, and 39.3% for c.p. III; different percent water contents for the three c.p. regions and their decline with age. A study of the effects of control, high NaCl, high KCl and low Na and K diets for 7-8 weeks on female rats started at 28-32 days of age shows a selective and significant ($P<0.001$) stimulation of c.p. IV by the low Na and K diet (c.p. IV dry wgt. $\times 10^3$/brain dry wgt. = control - 108.2±3.5, high NaCl - 108.1±4.6, high KCl - 107.0±3.3, low Na and K - 124.0±2.6). A similar experiment with male rats, and with a pair-fed control group matching the low Na and K group, shows the same effect and provides microscopic preparations for quantitative analysis of the effect's tissue basis. (Supported by USPHS-NIH research grants NS-06296 and HD-04103.)

Session 21

21.1 EFFECT OF PROBE-PENETRATION LESIONS ON SLEEP-AWAKE BEHAVIOR IN PIGEONS

Samuel M. Church* and Irving J. Goodman
Department of Psychology & Psychiatry, West Virginia University
Morgantown, West Virginia 26505

Pigeons were chronically implanted for monitoring EEG, EOG, and EMG activity. Unilateral probes (1.0 mm diameter), initially designed for chemical stimulation, were lowered in 1 mm steps into forebrain areas. Penetration into parolfactory, septal, and adjacent striatal areas produced a transitory state of somnolence lasting 4-7 days. In a second group of pigeons, bilateral probes (0.6 mm diameter) were lowered in 1 mm steps into forebrain areas. Penetration into ventral thalamic sites produced a chronic state of somnolence. Areas involved included the ansa lenticularis, ventrolateral thalamic nucleus, nucleus subrotundus, posteroventral nucleus, and nucleus intercalatus, thalami. Behaviorally, pigeons in both groups exhibited little spontaneous activity, but were capable of normal movements and postures if aroused (handling, noise, etc.). Somnolent pigeons stood or sat quietly with fluffed feathers, puffed chest, beak tucked, and eyes closed throughout the day. Electrographically EOG and EMG activity was decreased, and the EEG exhibited high voltage slow waves characteristic of sleep; however, REM activity was also recorded. A twenty-four hour period of behavioral and electrographic activity showed that 46% of the time was spent in sleep, in a control pigeon, while as much as 75% of the time was spent in sleep in an experimental bird. In both conditions, REM sleep accounted for approximately 3% of total sleep time. The basal forebrain of pigeons appears to play a significant role in maintaining wakefulness.

21.2 Responses of Diencephalic Neurons to Olfactory Bulb Stimulation, Odor, and Arousal.

B.R. Komisaruk and C. Beyer.
Institute of Animal Behavior, Rutgers University, Newark, N.J. 07102.

Neuron populations in the lateral hypothalamus, medial thalamus, and dorsal periventricular diencephalic region along the projection pathways of the medial forebrain bundle and stria medullaris-inferior thalamic peduncle, were activated by electrical stimulation of the olfactory bulb in urethane-anesthetized rats. Fifty-seven percent of these neuron populations were also activated by xylene vapors. The median response latency of hypothalamic neurons to single pulses was 10 msec (range: 4-16 msec) and that of thalamic neurons was 14 msec (range: 4-21 msec). Stimulus trains activated neuron populations at substantially longer latencies as well as at these short latencies. The most common types of response were excitation, and excitation followed by inhibition followed by re-excitation. Responses were usually recorded ipsilaterally to the stimulation site, but were also obtained contralaterally. They were blocked by transection of the lateral olfactory tract. The neuronal responses to olfactory bulb stimulation and xylene, even very short latency responses, were strongly modified in relation to arousal level, as monitored by the cortical EEG.

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21.3 EYE MOVEMENTS AND LATERAL GENICULATE NUCLEUS SPIKES IN SLEEPING AND AWAKE CATS FOLLOWING UNI- AND BILATERAL LABYRINTHECTOMY AND CEREBELLECTOMY. John B. Munson and Ron A. Waldorf☆. Department of Physiology, College of Medicine, University of Florida, Gainesville, Florida 32601.

The role of the labyrinthine apparatus and the cerebellum in producing sleep rapid eye movements and LGN spikes was assessed by performing staged labyrinthectomies and cerebellectomies in cats with chronically implanted electrodes. Following unilateral labyrinthectomy (produced by irrigating with alcohol and streptomycin through the round window) nystagmus toward the intact side occurred accompanied by LGN spikes coincident with the initiation of the slow component. This subsided in the drowsy animal but often reoccurred during fast-wave sleep. Eye movements and LGN spikes during fast-wave sleep were otherwise normal. Following compensation, the surviving labyrinth was likewise destroyed. Nystagmus reappeared (fast component toward side of first lesion:Bechterev's nystagmus) again accompanied by LGN spikes with the initiation of the slow component. Eye movements during slow- and fast-wave sleep were as above. The LGN spikes of late slow-wave and of fast-wave sleep were again apparently normal. Suction lesions of the cerebellum destroying vermis, anterior lobe and fastigial nuclei were then produced. Eye movements during fast-wave sleep and LGN spikes in the awake and sleeping cat or following reserpine administration were apparently normal in all respects. (Certain of these findings confirm data reported by Pompeiano and by Baldissera.)

Lesions of the medial and descending vestibular nuclei prevent the appearance of fast-wave sleep rapid eye movements and LGN spikes (Pompeiano, Arch. ital. Biol. 1965, 1966). Principal input to these nuclei is from the labyrinths and cerebellum (Brodal, Pompeiano and Walberg, "The Vestibular Nuclei..." 1962). Since labyrinthectomy and cerebellectomy affect neither of these phasic events, the events are not the result of vestibular nuclear gating of activity from those structures. (NSF GB-7622)

21.4 MOVEMENT DISORDERS INDUCED IN SLEEP BY COMBINED CEREBELLAR-SPINAL CORD LESIONS IN CATS. Adrian R. Morrison and Robert M. Bowker,*Department of Animal Biology, School of Veterinary Medicine, University of Penna.,Phila.

Control of tone and movement varies in sleep. Synchronized sleep (SS) is characterized by quiescence and by reduced muscle tone. In paradoxical sleep (PS) there is generalized muscle atonia, but also periodic muscle twitches occur. Cats implanted with electrodes for monitoring brainwaves (EEG), muscle activity (EMG),and eye movements were studied following sequential cerebellar vermal and spinal cord lesions to examine the inhibitory roles of these structures in sleep. As noted previously (Henley & Morrison, 1971), cerebellar lesions alone released extensor jerks of neck and limbs during SS but did not appear to affect PS. Major recovery followed in 2 weeks. Interruption of ascending inhibitory fibers by postbrachial cord transection at T8 alone released forelimb and neck extensor tone tonically during SS and PS except during bursts of rapid eye movements in PS as reported earlier (Morrison & Bowker, 1971). Effects of transection were largely compensated for within 1 week although a residual increase in extensor tone persisted in SS. Results of combined lesions were as follows: (1) Cerebellar lesions following cord transection in 3 cats failed to release the compensated effects of prior cord damage but produced jerks in SS. Compensation followed. (2) Following recovery from cerebellar damage in 1 cat, cord transection released forelimb extensor jerks and also produced signs similar to those observed with transection alone. Compensation followed in 2 weeks. However, one cat with superficial medial vestibular nuclear damage as well exhibited permanent release of antigravity tone and extensor jerks in SS. The results indicate an intriguing complexity in the interaction of motor control systems during sleep. Supported by NIH Grants NS 08377 and FR 5464.

21.5 OPERANT CONDITIONING OF LATERAL GENICULATE SPIKES IN OWL MONKEYS. LaNelle Linnstaedter* and Adrian A. Perachio. Yerkes Regional Primate Research Center, Emory University, Atlanta, 30322.

Eye movements (EMs) and monophasic spikes in the lateral geniculate nucleus (LGSs) are highly correlated during wakefulness. An attempt was made to determine if this correlation could be altered by operantly conditioning LGSs to occur without EMs. Owl monkeys were chronically implanted with electrodes to monitor EOG, EMG of cervical muscles and activity in the lateral geniculate nucleus, striate and frontal cortices. The EOG was used as the operant for a DRO schedule for EMs. LGSs were used as the operant for an FR5 schedule. The animals were trained, using a liquid reinforcer, to fixate their eyes to maintain a DRO 6-s schedule for EMs. Any EM greater than 50 μv within 30 ms reset the DRO. Subsequently, the Ss were also required to produce five (FR5) LGSs (at least 75 μv amplitude, rise time of 30 ms, duration of approximately 100 ms). Counts of EMs and LGSs were summed for each training session of four hours for four consecutive days. Comparisons were made between the concurrent DRO and FR5 schedules and a DRO-only control condition. The total number of EMs was not significantly different for the two conditions. However, a significantly greater number of LGSs was made under the DRO+FR5 condition. Results confirm the hypothesis that LGS can be operantly controlled. The relationship between EMs and LGSs during wakefulness can be altered using this conditioning procedure. Since EMs and LGSs also occur during sleep, the impact of this training procedure on subsequent sleep will be discussed.

21.6 RELATIONSHIPS BETWEEN FIRING RATE AND FIRING PATTERN OF CEREBELLAR PURKINJE CELLS. Robert W. McCarley* and J. Allan Hobson. Dept. Psychiatry, Harv. Med. Sch., Boston 02115.

Firing pattern of neurons during waking (W), synchronized sleep (S), and desynchronized sleep (D) has sometimes been assumed to change independently of alterations in the mean firing rate, but this hypothesis has not been rigorously tested. We investigated the relationship between firing rate and firing pattern in simple spike trains recorded extracellularly from 39 cerebellar Purkinje cells during natural W, S and D in 7 unrestrained, unanaesthetized cats. Least squares techniques were used to construct separate linear regression equations for W, S and D relating $\log_{10}$ mean interspike interval duration (the independent variable) to $\log_{10}$ of the 4 dependent variables measuring various aspects of histogram form: variance, 3rd moment, 4th moment and percent intervals at the mode. An analysis of covariance showed no statistically significant differences in slope or elevation of the regression lines among the behavioral states. This indicates that units firing at the same mean rate, regardless of behavioral state, will tend to have the same histogram form; this aspect of firing pattern is a function of firing rate, and behavioral state is not important except insofar as mean rate is altered. Autocorrelation analysis demonstrated a tendency toward rhythmic firing with period duration near the modal interval. The effects of temporal ordering of firings were separated from the production of many intervals near the mode by use of convolutions of the sample histogram. A high degree of rhythmicity was associated with a high firing rate, and a low degree of rhythmicity was associated with a low firing rate, suggesting that this aspect of firing pattern, like that of histogram characteristics, was also a function of firing rate.

21.7 NEURONAL ACTIVITY OF THE PONTINE BRAIN STEM DURING SLEEP AND WAKING. J. Allan Hobson. Dept. Psychiatry, Harv. Med. Sch., Boston 02115.

The theory that the phases of sleep are controlled by centers in the pontine brain stem rests heavily on evidence from lesion studies. This report presents complementary physiological evidence for an active central role of brain stem neurons in the control of the desynchronized phase of sleep. Chronic extracellular microelectrode recordings were made from 69 neurons in the pontine brain stem of 4 male cats. The recording site of each unit was anatomically localized by histological study of sagittal sections. By spike form and amplitude criteria, many of these units appear to be giant cell somata intrinsic to the paramedian reticular formation. The mean discharge rate of each neuron was determined by computer analysis of tape recorded segments in waking (W), synchronized sleep (S), and desynchronized sleep (D). 34 neurons in the gigantocellular tegmental field (FTG) showed a high degree of selectivity of firing in D. 10 FTG neurons did not discharge at all in W and 6 of these and one other were silent in S. To quantify this property, we calculated geometric means and the ratios of the means in D over those in W or S. FTG neurons had a D/S ratio of 50:1, and a D/W ratio of 100:1. These ratios are more than 5 times higher than those in other tegmental fields (13 neurons) and more than 10 times higher than those of the pontine grey (8 neurons) and the pontine reticular nucleus (14 neurons). The ratios are 25 to 30 times higher than corresponding values computed from our own previously collected data on cerebral cortex and cerebellar neurons. The marked selectivity of firing of FTG neurons in D and the large differential values attained by them in D are compatible with their playing an active and central role in the production of rate changes elsewhere in the nervous system during desynchronized sleep.

21.8 ACTIVITY OF SINGLE RAPHE NEURONS DURING SLEEP AND WAKEFULNESS. Dennis J. McGinty and Ronald M. Harper*. VA Hospital, Sepulveda, Calif. 91343, Depts. of Psych. and Anat., UCLA, Los Angeles 90024.

Brain serotonin (5HT) is thought to be released at the terminals of neurons whose soma are localized in the raphe nuclei of the brain stem. The functional role of 5HT release may be studied by determining the behavioral correlates of activity in raphe neurons. Thus, single neurons of the dorsal raphe nucleus, recorded through moveable chronically-implanted fine wires (62μ), were studied in behaving cats during wakefulness (W), slow wave sleep (SWS), and paradoxical sleep (PS), and in relation to spiking activity of the lateral geniculate nucleus (ponto-geniculo-occipital: PGO spikes) associated with PS. Raphe neurons were characterized by a slow rhythmic pattern of firing (.5-3 spikes/sec), as observed in anesthetized rats by Aghajanian and his collaborators, and antidromic responsiveness to stimulation of 5HT terminal areas in the forebrain. There was a 10-50% decrease in firing rate from W to SWS. Many raphe neurons were greatly slowed or completely silent during PS. Cessation of firing during PS has not been reported for other brain neurons. Many raphe neurons decellerated or stopped a few seconds before the occurrence of isolated PGO spikes during SWS and, in addition, complete cessation of firing during PS was correlated with bursts of PGO spikes. Slowing of raphe neurons was the earliest physiological change preceding PS, while recovery of firing was earliest sign of the end of PS. The slowing of 5HT neurons during PS may constitute an underlying mechanism of this state. In agreement with Dement's report that 5HT-depleted cats show PGO spikes during waking, these data also suggest that slowing of 5HT release results in the occurrence of PGO spikes.

21.9 Excitability changes in visual cortical neurons in natural transitions of sleep and waking

T. Kasamatsu and W. Ross Adey
Space Biology Laboratory, Department of Anatomy, UCLA

Spontaneous and evoked unit activity was studied in the visual cortex of unrestrained cats. Tungsten microelectrodes were driven by a hydraulic device. The region studied was at AP-2.0 to -6.0 mm, ML 1.0 -5.0 mm in the stereotaxic coordination. Steel wire electrodes were implanted in the sensorimotor cortex and the lateral geniculate body. Recording conditions were classified into three states: resting arousal (RA), sleep with the slow cortical EEG (light sleep, LS) and sleep with the fast cortical EEG (deep sleep, DS or REM).

Ninety units were recorded from six chronic cats. Two types of cortical units were encountered. The majority tended to fire most rapidly in DS and least in LS with intermediate values in RA. The minority with extremely slow firing rates (< 1 spike/10 sec) showed a tendency to fire in LS by contrast with other states including DS. The latter remained silent in DS in spite of occurrence of phasic activity in the background.

In fast units the firing probability in response to stimulation of the lateral geniculate body shifted as LS → RA → DS with increasing sensitivity. By contrast slow units typically showed an opposite trend. It was noted in the latter that there was much less tendency for evoked unit activity in response to geniculate stimulation.

There were also different response latencies to geniculate stimulation in these two types of units. The high frequency units showed shorter latency than the extremely slow frequency ones, in cases where the latter were responsive.

21.10 CHANGES IN INHIBITORY EVENTS ELICITED IN CORTICAL PRECENTRAL UNITS OF BEHAVING MONKEY DURING SLEEP AND WAKING.

M. Steriade, M. Deschênes*, P. Wyzinski* and J.Y. Hallé*. Lab. Neurophysiol., Dept. Physiol., Sch. Med., Univ. Laval, Québec, Canada.

Alterations in recurrent and afferent inhibition during wakefulness and behavioral sleep with EEG slowing have been studied by extracellular recordings in chronically implanted Macaca mulatta sitting in a primate chair. Testing stimuli were applied to the pes pedunculi, the ventrolateral (VL) thalamic nucleus, and to the homotopic points of the contralateral precentral area. The degree of inhibition was estimated from spontaneous firing of single units and from the amplitude of slow waves reflecting hyperpolarization in a pool of neurons. As compared with drowsiness and deepened stages of synchronized sleep, waking was associated with depression in all the components of inhibitory sequences following antidromic invasion or afferent stimulation: decrease in amplitude of the slow positive wave, simultaneous with restoration of spontaneous unit discharges, and erasure of subsequent rhythmic clustered firing (rebound) superimposed on slow negative, depolarizing waves. In most (especially pyramidal tract) neurons, the reduced efficiency of inhibition during waking could be related with an increase in the over-all amount of discharge. In other cells, driven by VL or callosal volleys, increased inhibition was obvious during the onset of sleep in spite of only minor changes in spontaneous EEG waves and no differences in the mean rate of unit discharge. Some evidence for strong excitation overwhelming inhibition and depression of inhibitory interneuronal apparatus on arousal are presented. (Supported by MRC, through grant MA-3689).

Session 22

22.1 QUANTITATIVE ANALYSIS OF MECHANORECEPTOR DISCHARGE PATTERNS IN RESPONSE TO CHANGES IN MUSCLE LENGTH. John T. Murphy, Edward J. Davison, Frank Johnson*, Hon C. Kwan* and William A. Mackay*. Depts. Physiol. and Elect. Eng., U. of Toronto, Toronto, Can.

The activities of functionally single stretch receptor units of the frog gastrocnemius muscle were monitored by recording from fine filaments of peripheral nerve near its junction with the muscle. The muscle was initially set at physiological length. Displacement and tension transducers were placed in series with the muscle near its tendon and feedback-controlled longitudinal displacement was applied to the muscle. The vibration noise level of the preparation and recording apparatus was less than 0.2μ. The muscle was displaced in accordance with input ramps of various slopes, and plateaus of various amplitudes and durations. Receptor firing patterns and outputs of the tension and displacement transducers were analyzed and correlated on-line with a general purpose computer. Results were in general agreement with the qualitative findings of Katz (J. Physiol. 111:261) and provided additional insight into receptor behavior. The displacement thresholds for receptor firing were in the range of 5-10μ, and firing rates had an almost linear relationship to static displacement over a range of 10-20 x these threshold values. With greater displacements response saturation occurred. In contrast a marked power law relationship was observed between velocity of displacement and receptor firing. The second time-derivative of displacement was signalled by oscillations in receptor firing; when a static displacement was resumed, this oscillation quickly dampened to an appropriate new steady level of firing. A predictive model incorporating time-varying non-linear differential equations was developed which satisfies the observed transduction of externally applied displacement into neural activity by the receptor.
Supported by grants from the Medical Research Council of Canada.

22.2 ON STRUCTURAL CORRELATES OF CODING MECHANISMS IN MUSCLE SPINDLES. Ulf L. Karlsson*, Elizabeth G. Bendeich* and William M. Hooker*. (SPON: R. Llinás) Dent. Res. Lab. and Dept. Anat., Coll. Dent. and Med., Univ. Iowa, Iowa City, Iowa 52240.

Frog muscle spindles are simpler versions of their mammalian equivalents. They are accessible for electrical and 3-D ultrastructural investigations. Experiments were conducted on the assumption that physiological stimuli cause differential structural deformation that is reflected by the known dynamic and static electrical responses of the spindle system. -Quantitative electron microscopy was applied to serial sections of physiologically stretched and relaxed spindles. They consist of innervated muscle fiber groups enclosed by inner and outer capsules. With stretch the inner capsule decreased in diameter around the sensory zone. -The intrafusal muscle cell is organized into three zones (compact-reticular-compact), the reticular zone typified by relative lack of contractile material and the presence of radial cell processes. The reticular zone appeared more stretchable than the compact zones. -The afferent nerve terminates as chains of bulbs and links along the muscle axis with some bulbs contacting the muscle in all three zones. Differential deformation of bulbs occurred with stretch in reticular and compact zones together with decreased diameter and better parallel alignment of links. -The nerve chains are embedded in extracellular filaments, particularly in the reticular zone. From a randomized organization the filaments aligned with stretch into a periodic pattern. -Since differential effects were observed in nerve bulbs, contractile material and extracellular material, it was concluded that the intrafusal unit undergoes differential deformation. Although the observed changes are responsible for the net static response the differential deformation should reflect unequal forces during stretch which may represent the dynamic part of the response.

22.3 SOME FUNCTIONAL PROPERTIES OF STATIC AND DYNAMIC FUSIMOTOR INNERVATION OF CAT SOLEUS MUSCLE SPINDLES. Russell Durkovic* and James B. Preston. Dept. Physiology, Upstate Med. Ctr., S.U.N.Y., Syracuse, N.Y. 13210.

Single soleus IA afferent fibers were isolated from dorsal root filaments and placed on recording electrodes. Single static and dynamic fusimotor neurons, modulating the soleus IA fiber activity were isolated from the distal cut end of ventral root filaments and placed on stimulating electrodes. The tendon of the isolated soleus muscle was attached to a muscle puller and the tension and length of the muscle were continuously monitored.

Discharge frequency recorded from single soleus IA afferents was depressed below control levels following the termination of stimulation of single static fusimotor axons, but not following termination of single dynamic fusimotor stimulation. The post-stimulus depression was usually greater on the phasic discharge during ramp stretch of the muscle than on the tonic component of the afferent discharge at the end of stretch. This difference can be explained, at least in part, by the brief time course of post-stimulus depression. In some experiments interaction between static and dynamic fusimotor effects on the same muscle spindle afferent was studied. The results demonstrated little or no interaction between static and dynamic effects. These findings are consistent with Matthews' and Boyd's proposals that static and dynamic fusimotor axons innervate different intrafusal fibers. (Supported in part by USPHS Grant NS-02957 and USPHS postdoctoral fellowship to R.D. #1 F2 NB 24,501)

22.4 EFFECTS ON MUSCLE SPINDLES OF DISUSE AND INCREASED USE OF THE CROSS MUSCLE. Alfred Maier* and Earl Eldred. Dept. Anat., Sch. Med., UCLA, L.A. 90024.

Histological and electrophysiological studies were made on hindlimb muscles of adult cats to determine what effect disuse and increased use might have on muscle spindles. Atrophy was induced by immobilizing one leg in a plaster cast, the other leg being free. In terminal observations after 4 to 6 weeks of fixation, the discharge from populations of primary and secondary spindle afferents in the two medial gastrocnemii was monitored from the otherwise denervated legs. Ventral roots were cut. It was found that the background activity and the mean response to stretch were elevated on the experimental side as compared to the control muscle. Measurements on serial histological cross-sections showed the spindle capsules to be dilated and the mean area of the intrafusal (IF) as well as extrafusal fibers (EF) to be reduced in the atrophied muscle. Moderate hypertrophy of the medial gastrocnemius was achieved through functional isolation of this muscle by selective denervation and tenectomy of the other calf muscles. When two weeks later comparison was made of discharge levels there was again suggestion of increased activity on the operated side. Histological measurements failed to reveal any difference in spindle structure, although the mean cross-sectional area of EF fibers did show a small increase. It is concluded that in disuse atrophy, morphological changes in IF fibers occur paralleling those in EF fibers, and due to this change or other causes, spindle sensitivity is altered.

22.5 MEASUREMENT OF THE % OF DISCHARGE OF A MOTONEURON POOL BY MEANS OF MONOSYNAPTIC REFLEX, EMG AND TWITCH TENSION. H.P. Clamann* and E. Henneman, Dept. of Physiology, Harvard Medical School, Boston, Mass.

In order to determine the thresholds of individual motoneurons in terms of the % discharge of the entire pool, three methods of measuring % output were devised. (1) Brief, maximal shocks were applied to the medial gastrocnemius (M.G.) nerve in a decerebrate cat, eliciting an antidromic volley in the axons of all M.G. motoneurons and a dromic volley in all of its IA fibers. The monosynaptic reflex evoked by the dromic volley was recorded in the proximal half of the divided L7 or S1 ventral root; the antidromic volley was recorded with equal gain in the distal half of the same ventral root. The antidromic response was a measure of 100% discharge of the M.G. pool, with which the reflex was compared to give % of maximal discharge. (2) A wick electrode covering a large surface area of the M.G. muscle was used to record the E.M.G. The polyphasic potential was full-wave rectified and integrated with respect to time. Percent of maximal discharge was estimated by comparing EMGs recorded during monosynaptic reflexes with those obtained during maximal "direct" twitch responses of the muscle. (3) Twitch tension, measured directly with a transducer was recorded after PTP and compared with that produced by a maximal motor volley in the M.G. nerve. All three methods gave reliable measurements of % discharge of a motoneuron pool.

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22.6 RANKING OF MOTOR UNITS IN THE MEDIAL GASTROCNEMIUS MUSCLE ACCORDING TO REFLEX THRESHOLD, SUSCEPTIBILITY TO INHIBITION AND SPEED OF CONTRACTION. E. Henneman and J. D. Gillies*. Dept. of Physiology, Harvard Medical School, Boston, Mass.

Monosynaptic reflexes were recorded simultaneously from individual medial gastrocnemius (M.G.) axons in ventral root filaments and from the entire population of responding M.G. fibers in an adjacent root. A gated electronic integrator produced the time integral of the population response, which was varied between 0 and 100% by means of post-tetanic potentiation (P.T.P.) and by controlling the intensity of the shock applied to the muscle nerve. Individual motoneurons always discharged when the population response exceeded a certain percentage of maximum and never discharged below a slightly lower level. This "threshold" was constant for a given cell, but varied from 1 to 100% for different motoneurons, indicating a rank-order for all the motor units in the M.G. pool. Threshold was not altered by addition of inhibitory inputs from various sources, indicating a similar rank-order for susceptibility to inhibition. When the twitch tensions of the M.G. muscle were recorded myographically during the decline in P.T.P., their rise-time increased progressively as tension declined. This indicates a rank-order of contraction speeds for motor units corresponding to that for thresholds and susceptibility to inhibition.

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22.7 MECHANICAL EVIDENCE FOR A SINGLE POPULATION OF FAST CONTRACTILE ELEMENTS IN EXTRAOCULAR MUSCLE. N. H. Barmack and B. G. Rence* Lab. Neurophysiol., Good Samaritan Hosp. & Med. Center, Portland, Oregon 97210.

The isometric responses of the lateral rectus muscle to stimulation of the VIth nerve and to direct stimulation of the muscle were recorded in order to answer two questions: Was there some parameter of tension development in extraocular muscle which would lend functional meaning to the high rates of discharge of extraocular motoneurons? Could two populations of contractile elements, slow and fast, be demonstrated in response to indirect and direct stimulation at different frequencies? Tension and rate of tension development increased with increasing tetanic stimulation from 50/sec to 250/sec where the tension response was maximal. However, the rate at which tension was developed kept increasing with stimulus frequency up to 625/sec. Double pulse stimulation caused no interaction between the isometric responses until the interpulse interval was shortened to less than 25 msec. There was no evidence for any interaction between isometric responses when either two pulses or a train of pulses was delivered at a frequency which should have produced fusion in putative "slow fibers". Furthermore, the contraction time and decay time of single isometric responses decreased with increasing stimulus intensity. These two facts were taken as evidence against the possible existence of two classes of contractile elements in extraocular muscle. Since the interaction between isometric responses at double pulse intervals of less than 25 msec was identical for indirect and direct stimulation, it was concluded that this interaction was due primarily to the contractile mechanism of the extraocular muscle fibers and not neuromuscular transmission at the motor end plates.

22.8 BEHAVIOR OF ABDUCENS MOTONEURONS DURING VESTIBULARLY INDUCED EYE MOVEMENTS. Alexander A. Skavenski* and David A. Robinson. Dept. Biomed. Eng., Johns Hopkins Univ., Balto., Md., 21205.

It is well known that the primary afferents from the semicircular canals relay to the vestibular nuclei a frequency coded signal proportional to head velocity not acceleration. These reports, coupled with the finding that extraocular muscle motoneurons discharge at rates that depend primarily on the position of the eye in the orbit, necessitate the hypothesis that a neural network which converts velocity to position information (by integration) must exist in the neural pathway of the vestibulo-ocular reflex. Evidence for this hypothesis was obtained by recording from isolated motoneurons in the abducens nuclei of alert, intact and behaving rhesus monkeys while rotating them at various sinusoidal frequencies or at different constant velocities in a horizontal plane. Discharge rates of the motoneurons during the slow phase of vestibular nystagmus were related only to the position and velocity of the eye and for each neuron this relation was identical to that found for visually driven smooth pursuit eye movements: a finding that indicates that vestibularly driven eye movements are not served by a unique subset of motoneurons but do share the same final common path with visually guided movements. Discharge patterns of abducens motoneurons were shifted in phase from head velocity during sinusoidal rotation by amounts predictable only if a neural integrator lay in the path of the vestibulo-ocular reflex. This integrator function can probably be ascribed to the system of extra-medial longitudinal fasciculus collaterals described and studied by Lorente de Nó and others.

22.9 LOSS OF OPTOKINETIC AFTER-NYSTAGMUS AFTER BILATERAL LABYRINTHECTOMY. Bernard Cohen and Takuya Uemura*. Department of Neurology, Mount Sinai School of Medicine, New York, N.Y. 10029.

Optokinetic after-nystagmus (OKAN) is nystagmus which follows optokinetic nystagmus (OKN). It is rarely induced in humans but it is prominent in monkeys when they are placed in darkness after OKN. In the first phase of OKAN the direction of the beats is the same as that of the preceding OKN. OKAN lasts for approximately 60 seconds regardless of the period of preceding OKN, and the maximum velocity of the slow phases declines linearly during this period of time. Secondary phases of OKAN in the reversed direction may follow at the end of the first phase. OKAN is a sensitive index of disease of the oculomotor system and is reduced by lesions of the pontine or mesencephalic reticular formation. The purpose of this note is to report that after unilateral labyrinthectomy there was a marked diminution in OKAN to both sides, ipsilateral > than contralateral. Furthermore after bilateral labyrinthectomy OKAN was permanently abolished. One animal with normal OKAN in both directions before labyrinthectomy had no return of OKAN for 18 months after bilateral labyrinthine destruction. Despite this OKN of normal amplitude with slow phases of high velocity was readily induced. Central pathways for OKAN are not clear, but it is generally assumed to be predominantly a visual-oculomotor reflex. The present data suggest that the vestibular system may also play an important role in mediating or supporting this reflex.

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22.10 PUPILLARY CONSTRICTION AND UNIT ACTIVITY. Kyozo Watanabe* (SPON: J.M. Fuster). Max-Planck Institut für Psychiatrie, München, Germany.

Unit activity from the region of the lateral oculomotor nucleus in curarized cats was found to be related to pupillary constriction. Firing rate increased following a light stimulus eliciting decrease of diameter of the pupil. The latency of the unit frequency increase was approximately 140 msec. In some units, the increase of firing rate also preceded spontaneous pupillary constriction. Averaged unit frequency indicated that there was a gradual decrease of firing after termination of the light stimulus. This decrease was sometimes accompanied by oscilation. The described unit activity is considered in terms of stimulus duration, intensity, and amount of pupillary constriction.

22.11 SENSORY-MOTOR FUNCTION AFTER DORSAL COLUMN LESIONS IN MACAQUES.
Charles J. Vierck, Jr., Jack E. Maniscalco* and Alexander A. Manning*.
Dept. Neuroscience and Cntr. Neurobiological Scs., Univ. Fla. Col. Med., Gainesville, 32601.

Previous experiments specifically studying sensory capabilities after dorsal column lesion have generally failed to obtain marked and enduring deficits. On the other hand, evaluation of lesioned monkeys with the neurological exam has demonstrated striking impairments. In view of this discrepancy and the integral relationship of the lemniscal and corticospinal systems, Macaca speciosa monkeys were tested on several motor tasks to see if proprioceptive deficits would be apparent with active movement. The lesions were high cervical, and both forelimbs and hindlimbs were tested on three types of task: (a) ability to place the limb at different points in space without visual guidance, (b) ability to make rapid alternating movements and (c) ability to grasp small objects. The major difficulties in movement were seen at the distal extremities, and forelimb deficits were more profound and enduring than those of the hindlimb. Ability to pick up small objects was marginally impaired for the feet, and severely disrupted for the hands. Slight deficits in speed of gross movements were observed for the arms but not the legs. Facility in placing the forelimb without visual control was severely affected, but the deficit was related primarily to a lack of manual dexterity and not to a difficulty in orienting the arm. The hindlimbs showed only transient difficulties with this task.

22.12 PROPRIOCEPTIVE INFLUENCES ON INFERIOR OLIVARY CELLS DURING PHASIC REFLEX MOVEMENT IN CATS. M. A. Clendenin[1], A. J. Szumski, and J. Astruc.
Medical College of Va.-Va. Commonwealth Univ., Richmond, Va. 23219.

The origin of the climbing fiber system from the inferior olive, and its precise synaptic relation with the cerebellar Purkinje cells which represent the efferent pathway from the cerebellar cortex, suggests that the spino-olivo-cerebellar pathway may contribute to the mechanism of a phasic reflex movement. The right hindlimb was denervated except for the posterior tibial nerve. Intracellular recordings of inferior olivary cells were obtained using glass capillary electrodes in non-anesthesized decerebrate cats during spontaneous clonus of the right gastrocnemius-soleus muscle (GS). Inferior olivary cells were identified as responding to proprioceptive input from the GS muscle by their activation to electrical stimulation and manual stretch of the GS tendon. Simultaneous records of the inferior olivary cell and the GS myogram and EMG were obtained. Impaled inferior olivary cells were iontophoretically injected with Fast Green dye and identified histologically by Nissl counterstaining. Impaled inferior olivary cells activated during spontaneous clonus were recorded firing during the contraction phase of the reflex. These results suggest a supraspinal influence on phasic reflex movement via the climbing fiber system based on the established inhibitory output of the Purkinje cells and the spinal inhibitory influence of the Golgi tendon organs during the contraction phase of the phasic reflex. The inhibitory supraspinal influence combines with the spinal inhibitory influence to inactiviate the contraction phase of the phasic reflex.

[1](Supported by a Social Rehab. Services-Amer. Physical Therapy Assn. Doctoral Fellowship in Anatomy).

22.13 CEREBRAL CORTICAL CONTROL OF JAW REFLEXES IN THE SQUIRREL MONKEY (SAIMIRI SCIUREUS). Michael H. Chase * (SPON: D. Maxwell). Departments of Anatomy and Physiology, UCLA School of Medicine, Los Angeles and the Veterans Administration Hospital, Sepulveda, California, USA 90024.

The induction of somatic motor activity by cerebral cortical stimulation in the primate has been examined traditionally in the absence of an analysis of accompanying motor inhibition. As the contraction of a muscle group is almost invariably coupled with some decrease in the tone of its antagonist, investigations into the cerebral control of motor activity might equally well have been performed through an investigation of induced inhibition in appropriate flexor antagonists. Based upon these considerations, an examination of the influence of motor cortex upon the excitability of antagonistic jaw reflexes in the unanesthetized, restrained squirrel monkey was deemed desirable. Extensor activity (jaw closing) was monitored along the masseter nerve and was induced by stimulation of the mesencephalic V^{th} nucleus. Flexor activity (jaw opening) was recorded from the nerve to the anterior belly of the digastric muscle and was induced by stimulation of the inferior dental nerve. Cortical sites were stimulated with a train of 4 pulses (400 cps). The period between cortical stimulation and the induction of either test reflex was 10 msec. Two adjacent sites on the dorsolateral cortex were found to inhibit extensor activity and to facilitate flexor discharge. These two sites were distinguished on the basis of the cortical stimulating threshold (mamps) necessary to modulate reflex activity. The conclusion was reached that there are two separate and functionally distinct somatotopic areas on the dosolateral cerebral cortex which influence reflex activity and that these areas are organized to provide primarily for extensor inhibition and flexor facilitation. Supported by Grant MH 10083 and the Sepulveda Veterans Administration.

Session 23

23.1 Kinetics of Acetylcholine Receptor Production and Incorporation Into Membranes of Developing Muscle Fibers. H. Criss Hartzell* and Douglas M. Fambrough. Dept. Biol., Johns Hopkins U. and Dept. Embryol., Carnegie Inst., Baltimore, Md.

Using electrophysiological and quantitative autoradiographic techniques, we have studied the kinetics of Acetylcholine (ACh) receptor production and incorporation into membranes of developing muscle fibers. We have studied these relationships in vertebrate skeletal muscle grown in tissue culture since the chemosensitivity of these cells to ACh varies during myogenesis and in response to innervation and denervation. These studies were performed by utilizing α-Bungarotoxin (BGT), which we have confirmed irreversibly blocks the depolarizing effects of ACh iontophoretically applied to muscle cells, presumably by combining with the ACh receptor. Thus, we blocked the ACh receptors with BGT (ACh sensitivity less than 0.01 mV/nC) and then monitored the reappearance of ACh sensitivity after washout of free BGT. Although some heterogeneity existed among cells in each culture, thirty minutes after BGT washout the ACh sensitivity had increased from 0.01 mV/nC to about 0.5 mV/nC. The appearance of new ACh receptors, detected by autoradiography of cultures incubated in ^{125}I-BGT at various times after BGT washout, paralleled the increase in ACh sensitivity. The rate of reappearance of ACh sensitivity was greatly depressed by complete inhibition of protein synthesis by cycloheximide and, to a slightly greater extent, by inhibition of ATP synthesis with dinitrophenol and iodoacetate. Likewise, the incorporation of new receptors into the membrane as measured autoradiographically requires both protein and ATP synthesis. Utilizing this data, we have correlated the level of ACh sensitivity with the corresponding density of ACh receptors in the membrane.

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23.2 SYNAPTIC TRANSMISSION BETWEEN NEURONS AND MUSCLE FIBERS IN CELL CULTURES DERIVED FROM CHICK EMBRYOS. G. D. Fischbach. NIH, Bethesda, Md. 20014

Neuromuscular transmission was studied in muscle cultures derived from dissociated myoblasts to which dissociated spinal cord cells were added. Connective tissue cells were reduced in number by adding the drug cytosine arabinoside 10^{-5}M for 2 days after plating the muscle. Less than 5% of the muscle fibers were innervated. A few of the fibers were innervated at more than one point. Both small (less than 3 mV) and large synaptic potentials occur in the absence of nerve stimulation. The small potentials are true miniature endplate potentials (mepps) because they occur at random intervals, increase in frequency with graded presynaptic depolarization and increase in osmotic pressure and persist in the presence of 10^{-6} g/ml of tetrodotoxin (TTX). The mean mepp frequency and amplitude ranged between .01/s and 2/s and 0.3 and 1.5 mV respectively in different cells. Large potentials probably reflect impulse activity in innervating neurons: they are more regular in pattern, are abolished by 10^{-6} g/ml TTX and can often be elicited by focal stimulation of nearby neurons. Amplitude histograms of series of endplate potentials (epps) evoked by extracellular or intracellular stimulation of nearby neurons indicate that transmitter release is quantal. Estimates of mean quantum content varied between 0.5 and 15.0. The amplitude and quantum content of evoked epps are reduced by lowering the Ca++ or raising the Mg++ concentration in the bath. The size of spontaneous and evoked potentials vary directly with muscle membrane potential, and they reverse in polarity when the membrane is depolarized to about -10 mV. Curare (10^{-7} g/ml) reversibly reduced epp amplitude in every case studied but cholinesterase inhibitors have little or no effect. Thus, in major outline, synaptic interaction between initially dissociated cells is similar to adult neuromuscular transmission. One striking difference is that, in three cases, evidence for direct electrical coupling between spinal cord and muscle cells has been obtained.

23.3 ACh SENSITIVITY OF NON-INNERVATED AND INNERVATED MYOTUBES IN CELL CULTURES
S. Cohen* and G. Fischbach. NIH, Bethesda, Md. 20014

The response to iontophoretically applied Acetylcholine (ACh) of muscle fibers that developed from dissociated myoblasts alone or with added spinal cord cells has been studied. Elimination of most of the connective tissue cells in the culture by addition 2-3 days after plating of cytosine arabinoside (ara C) 10^{-5}M for 24-48 hours permitted precise localization of the ACh pipette and direct visualization of long lengths of single muscle cells and neurons. Brief pulses of ACh produced a transient increase in membrane conductance and decrease in potential. The potential change reversed in polarity when the membrane was depolarized to -10 to 0 mV. The response was rapidly and reversibly blocked by steady (iontophoretic) application of ACh, by low doses (bath applied) of curare (10^{-7} g/ml) and higher doses of atropine (10^{-4} g/ml). Uninnervated muscle fibers were sensitive over their entire length including the thin ends, but the distribution of sensitivity was clearly not uniform. In several cells one or more sharp peaks (3-10x background) were evident. After the addition of dissociated spinal cord cells a small percentage (under the culture conditions employed) became innervated as evidenced by spontaneous and evoked synaptic potentials. Sharp peaks of increased sensitivity were detected in innervated fibers near nerve endings. However, unlike adult innervated muscle, the sensitivity tested as long as 3 weeks after addition of neurons remained high over the remainder of the fiber. Consideration of the relative peaks in innervated fibers as evidence of trophic influence of nerve on muscle is complicated by the occurrence of similar peaks in uninnervated fibers.

23.4 ACETYLCHOLINE RESPONSES IN NEUROBLASTOMA CELL CULTURES: BLOCKING EFFECTS OF ATROPINE VERSUS TUBOCURARINE.
J. Peacock*, P. G. Nelson, J. Minna*, and M. Nirenberg. NIH, Bethesda, Md. 20014

Intracellular microelectrode recordings from mouse neuroblastoma (C 1300) cells in tissue culture (clone N18) showed depolarizing (D) and hyperpolarizing (H) responses to microiontophoretic pulses of extracellularly applied acetylcholine (ACh). D-responses occasionally were large enough to trigger action potentials but usually the sensitivity was less than 10 mV/nanocoulomb of applied ACh. Relatively prolonged (0.5 to 1.0 sec) pulses of ACh were required to elicit the H-response which ranged from about 4 to 30 mV in amplitude. Pure D, pure H, and combined D-H responses were seen in different cells, a finding which suggested independent regulation of response types. Rarely was more than one kind of response observed in a given cell. The incidence of pure H-responses was increased by shifting cultures of non-dividing cells maintained in Dulbecco's Modified Eagle's Medium and 10^{-5} or 10^{-6}M aminopterin to Ham's F-12 medium which permitted cell division to resume in several days. As concomitants of H-response activity, reversal potentials of about -80 mV were found. Microiontophoresis of atropine produced complete and reversible H-response blockage whereas tubocurarine had only a slight inhibitory effect. In some but not all cases D-responses were selectively blocked by tubocurarine.

23.5 SYNAPTIC TRANSMISSION IN THE CHICK CILIARY GANGLION DURING EMBRYOGENESIS. G. Pilar and Lynn Landmesser*. Dept. Physiol., U. of Utah, and Regulatory Biology, U. of Conn., Storrs, Conn. 06268.

The development of synaptic transmission was studied in the two cell populations of the isolated ciliary ganglion with electrophysiological and histological methods from Stage 29 until hatching. Degree of transmission was quantified by comparing amplitudes of extracellulary recorded postsynaptic responses to maximal pre- and postganglionic stimulation. Transmission begins at Stage 32 and is 100% in both cell groups by Stage 36. In electronmicroscopic (E.M.) observations of Stage 36 ganglia, while most cells were in contact with bundles of unmyelinated axons, there were few specialized junctions with synaptic vesicles. Fibers innervating ciliary cells were from the beginning distinguishable from those innervating choroid cells: they had lower thresholds and conducted more rapidly. Transmission in both cell groups was entirely chemical until Stage 41 when electrical transmission first appeared in the ciliary group. Its onset and increase in magnitude was correlated with increased presynaptic conduction velocity and myelinization. At Stage 41, the fine initial contacts on ciliary cells have fused to form neurotubule containing calyces that as yet contain few synaptic vesicles. Stage 41 intracellular records from ganglion cells show subthreshold electric coupling potentials (CPs) and after 2-3 msec synaptic delay, chemical postsynaptic potentials (PSPs) with prolonged decay times that are further prolonged by anticholinesterases. By Stage 43, PSP decay times are greatly shortened and insensitive to anticholinesterases, the CP suprathreshold, and the synaptic delay decreased. E.M. observations now show ciliary cells with vesicle-filled calyces and myelinated somas. Such clear physiological changes with time in two homogeneous populations allow one to correlate ultrastructure with the development of synaptic transmission. It is further concluded that each cell population is specified by Stage 32 when presynaptic fibers first make contact, and that they are selectively innervated with no initial random connections.

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23.6 THE EFFECTS OF HIGH [Ca^{++}] ON THE ACTIVITY OF NEURONS OF THE ISOLATED SPINAL CORD OF THE FROG. G. E. Dambach* and S. D. Erulkar, Dept. Pharm. School of Medicine, University of Pennsylvania, Phila., Pa. 19104

The effects of high (5 or 10 mM) and normal (1.0 mM) calcium Ringer solutions on the activity of frog spinal neurons were compared. Upon elevation of the Ringer calcium concentration, ventral root potentials elicited by dorsal root (DR) or lateral column (LC) stimulation, showed an initial reduction in latency; this was accompanied by attenuation of longer latency responses and a progressive decline in the total response. This effect developed to a steady state within one hour. Activity returned to control levels over a similar time course with a transient phase of enhanced activity when the calcium concentration was returned to normal. Intracellular recording from motoneurons showed normal antidromic activation in high calcium Ringer solutions, however, supramaximal stimulation of DR, LC and intracellular depolarizing current elicited only single spike responses in contrast to multiple spike activation by these modes in normal Ringer solution. DR stimulation, in normal Ringer solution, elicited an EPSP monosynaptically, followed by multiple spike activity at longer latencies; in high calcium Ringer solution, the EPSP amplitude was increased and generated a single spike. Spontaneous synaptic potential frequency was increased and frequent bursts of spontaneous potentials were observed in high calcium Ringer solutions. The bursting activity was attenuated by addition of TTX (10^{-6} g/ml). It appears that a high calcium Ringer solution enhances both the spontaneous and elicited release of transmitter but may attenuate excitability of frog spinal neurons. Supported by NS 02941, NS 02400, and NS 09752.

23.7 l-GLUTAMATE: POSSIBLE EXCITATORY TRANSMITTER IN CNS OF LAMPREY. Burgess N. Christensen*. (SPON: F. F. Ebner). Div. Bio-Med Scs., Sect. Neurosciences, Brown Univ., Providence, R. I. 02912.

Iontophoretically applied l-glutamate depolarized the giant interneurons of the lamprey (Petromyzon marinus) in the isolated spinal cord, confirming the observation of Martin, Wickelgren, and Beranek (J. Physiol. 207:653, 1970). In this preparation, small depolarizing and hyperpolarizing post synaptic potentials (PSPs) occur in the absence of any external stimulation. The PSPs are blocked by tetrodotoxin (TTX-10^{-7}gm/ml) and by high concentrations of magnesium (22mM). The frequency of these potentials increases on addition of tetraethylammonium chloride (TEA-2mM). Because of the effects of TTX, magnesium, and TEA it is assumed that these PSPs are not caused by spontaneous release of transmitter but rather by spontaneous action potentials in presynaptic elements. In the present experiments the null potential for the l-glutamate effect was compared with the reversal potential of the excitatory PSPs. The cell is depolarized by passing current through an intracellular electrode and l-glutamate is applied at different levels of membrane potential. As the cell is depolarized there is a rapid increase in the conductance of sodium and potassium which is reflected in a decrease in membrane resistance. This decrease in resistance makes difficult the determination of the reversal potential for the l-glutamate effect. The membrane potential at which no response to l-glutamate is seen (null potential) is used as an estimate of the reversal potential. Addition of TTX and TEA to the bathing fluid decreases the conductance of sodium and potassium making possible a more accurate estimate of the null potential. The null potential for the l-glutamate effect ranged from 36 to 55 millivolts inside negative, while the reversal potential for the excitatory transmitter ranged from 38 to 54 millivolts inside negative. These experiments suggest that l-glutamate is an excitatory transmitter in the spinal cord of the lamprey.

23.8 EFFECTS OF STRYCHNINE, BICUCULLINE AND PICROTOXIN ON LABYRINTHINE-EVOKED INHIBITION IN NECK MOTONEURONS OF THE CAT. Leslie P. Felpel* (SPON: Victor J. Wilson). The Rockefeller University, New York, N.Y. 10021

The disynaptic inhibitory pathway from labyrinth to neck motoneurons, relaying in the medial vestibular nucleus (Wilson & Yoshida, 1969), was investigated pharmacologically in pentobarbital-anesthetized cats. Intracellular recordings were made from cervical (C3) dorsal rami (DR) motoneurons following electrical stimulation of the labyrinth before and after intravenous injections of drugs. Before strychnine, disynaptic IPSPs were evoked in 85% (n=69) of DR cells. Occasionally depolarizing current had to be passed through the recording electrode in order to reveal the IPSP. Following strychnine (0.15-0.3 mg/kg), disynaptic IPSPs were evoked from 15% (n=38) of DR cells. With higher doses (0.45-0.6 mg/kg), no disynaptic IPSPs were seen (n=12) even though depolarizing current (5 x 10^{-8}A) was passed. In a limited number of cells, intracellular recording was maintained during injection. Disynaptic IPSPs were diminished by strychnine even though any resting potential changes were in a depolarizing direction. Disynaptic excitatory postsynaptic potentials (EPSPs) from the labyrinth were usually present before and after strychnine. Low threshold N_1 potentials were recorded in the vestibular nuclei after strychnine. No significant difference was noted between the percentage of cells receiving disynaptic IPSPs before (92%,n=13) or after (85%, n=28) bicuculline (0.2-0.4 mg/kg). Similarly, no significant difference was noted before (95%, n=27) or after (100% , n=16) picrotoxin (1-6 mg/kg). Intracellular recordings were maintained for several cells during picrotoxin injection and in no case was the IPSP blocked. These results do not identify the inhibitory transmitter in this pathway but do suggest that glycine is a more likely candidate than GABA. (Supported by Grants # NS 02619, NS 05463 and Special Fellowship 2 F11 NS 02108-02, NINDS).

23.9 TRANSMISSION AT SYNAPSES OF ELECTRORECEPTORS. M. V. L. Bennett. Albert Einstein College of Medicine, N. Y., N. Y. 10461.

Electroreceptors, found in various fish, are lateral line receptors specialized for detection of electric fields. A potential difference across the skin acts on epidermal receptor cells that transmit to afferent nerve fibers. Threshold is as low as a few μV in marine fish and is 10-100 times higher in fresh water fish. Fibers from tonic electroreceptors are tonically active in the absence of stimulation, apparently due to spontaneous release of transmitter. Nerve discharge is accelerated or decelerated by stimuli of appropriate sign. In tonic receptors of teleosts, stimuli act directly on presynaptic secretory membrane of receptor cells to modulate spontaneous release; depolarization increases release. In elasmobranchs stimuli modulate tonic electrically excitable activity of receptor cells, and thereby indirectly modulate tonic transmitter release. Evidence for these modes of operation is still partially indirect, but involves intracellular recording from receptor cells and nerve fibers of various receptors. Recent data are summarized in my papers now in press in Ann. N.Y. Acad. Sci. (Conference on Orientation: Sensory Basis) and Fish Physiology, Vol. 5 (edited by W. S. Hoar and D. J. Randall, Academic Press). A. B. Steinbach and I are attempting to identify the transmitter. There is some evidence for glutaminergic transmission (J. Gen. Physiol., in press). Properties of transmission in electroreceptors appear relevant to synapses of mechano-receptors of the acoustico-lateralis system and perhaps to other receptor synapses as well.

23.10 ANTIDROMIC INHIBITION: A POSSIBLE NEURAL MECHANISM TO ACCOUNT FOR PERIPHERAL INTERACTIONS BETWEEN TASTE STIMULI. R.A. Bernard. Dept. Physiol., Mich. State Univ., East Lansing, Mich. 48823

A peripheral taste fiber sends branches to more than one tongue papilla, forming a sensory unit, the afferent analog of a motor unit. In addition, a single taste papilla receives connections from more than one parent fiber, indicating an overlap between sensory units. Individual fibers may respond to more than one taste quality and, in the cat, the majority of fibers responds maximally to only one quality, with the quality varying among fibers. With whole-tongue stimulation the response of cat taste fibers was depressed or enhanced by cross-adaptation to contrasting taste stimuli, depending on the sensitivity of the fiber and the quality of the adapting stimulus. A simple convergence from many papillae to a single afferent fiber would not explain these results, which suggest that peripheral interactions occur between taste fibers. Rapuzzi & Casella (J. Neurophysiol. 28: 154, 1965) have shown that action potentials are antidromically conducted from a stimulated to a non-stimulated papilla in the frog. The axon reflex is an analogous mechanism that has been proposed to account for the flare surrounding a skin wound in mammals. A similar mechanism utilizing antidromic conduction along the collateral branches of overlapping sensory units is proposed to account for the interactions observed in cat taste fibers. Overlapping taste sensory units would have an inhibitory effect upon each other, either directly or through the receptors. Cross-adaptation would depress or enhance the response of a sensory unit depending on the distribution and number of overlapping units with similar or different sensitivities. (Supported in part by NIH NS-09168.)

23.11 EFFECTS OF CARBOXYLATE MODIFICATION ON FROG NEUROMUSCULAR TRANSMISSION. S. Stuesse,* N. Katz,* and C. Edwards. Dept. Biol. Sci., SUNYA, Albany, New York 12203.

The compound N-ethoxycarbonyl-2-ethoxyl-1,2-dihydroquinoline (EEDQ), which modifies carboxyl groups (Belleau et. al., J. Am. Chem. Soc., 90:823, 1968), inhibits activation of both -adrenergic and muscarinic receptors (Martel, J. Pharmacol., 166:44, 1969; Chang, et. al., Pharm. Res. Comm., 2:63, 1970). The extracellular moving electrode technique of Fatt (J. Physiol., 111:408, 1950) has been used to measure the effect of EEDQ on acetylcholine (ACh) depolarization in frog sartorius muscle. At 2 x 10^{-4}M, EEDQ reversibly decreased the ACh response. The membrane depolarization produced by KCl was unaffected by EEDQ. Intracellular recordings from the sartorius nerve-muscle preparation showed an increase in quantal content (indicative of a presynaptic effect) and a decrease in quantal size (indicative of a postsynaptic effect). Membrane resting potential and membrane resistance were largely unaffected by chemical treatment. These results, suggesting that carboxylate groups may be at or near the postjunctional receptor site, are in agreement with previous findings from this laboratory (Edwards et.al., J. Memb. Biol., 2:119, 1970). Supported by Grants # NB 07681 and # NS 02376.

23.12 FALSE NEUROCHEMICAL TRANSMITTERS IN THE CNS. Ross J. Baldessarini. Neuropharmacology Lab., Psychiatry Res. Labs., Mass. Gen. Hosp. and Harvard Med. Sch., Boston 02114.

Norepinephrine, tyramine, octopamine and metaraminol were accumulated by nerve endings in homogenates of rat brain much more vigorously than phenethylamine or amphetamine. Km values were 0.5, 3 and 6 µM for D,L-norepinephrine, p-tyramine and octopamine, respectively, using whole brain, and uptake was more vigorous in striatal tissues than in the cortex. Uptake was dependent on temperature, glucose, and Na^+ and was inhibited by desmethylimipramine, cocaine, ouabain, CN^- and dinitrophenol, or pre-treatment with reserpine or 6-OH-dopamine. The amines migrated with nerve endings during sucrose gradient ultracentrifugation and were released by membrane disrupting procedures which break synaptosomes. The presence of a ß-OH group led to protection of the amines from monoamine oxidase. Labelled octopamine and metaraminol were released from coronal slices of brain much better than tyramine or amphetamine by electrical stimulation or high [K^+]. Striatal tissue, however, appeared to release the non-ß-hydroxylated amines, dopamine or tyramine relatively well. Several amines led to increased rates of efflux of [^{3}H] norepinephrine from nerve endings and unlabelled L-norepinephrine similarly increased efflux of [^{3}H] octopamine or metaraminol. Thus, hydroxylated aromatic amines may accumulate in central nerve endings, compete with physiological neurotransmitters and act as false neurotransmitters in certain circumstances which may facilitate the formation of aromatic amines or impair their destruction.

Session 24

24.1 THE ELECTROENCEPHALOGRAM DURING VOLUNTARY BREATH HOLDING IN MAN. Robert Lansing, Peter Crown* and John Thomas*. Dept. Psychol. Univ. Arizona, Tucson 85721.

Breath holding to breaking point, a classical maneuver for rapidly increasing ventilatory drive and the associated sensations of "need to breathe", was performed repeatedly by 12 normal adults. Occipital and central EEG recordings were obtained simultaneously with end-tidal CO_2, air flow rate, and in some subjects key signals indicating degrees of discomfort. These key signals and flow rate measures of glottal closing supported Agostoni's division of the breath holding period into two parts; before and after involuntary respiratory movements occur (J.Appl.Physiol. 1966,123:30). We assumed that P_aCO_2 increases linearly during the whole period of apnea. We found little evidence of electrocortical "activation" corresponding to these physiological and subjective changes during breath holding. Brief periods of alpha blocking occurred in the last 20 seconds before breaking point but these were highly variable from trial to trial. Slow potentials (SP) during breath holding were studied with D.C. recordings from non-polarizing electrodes at the mastoid and vertex. Within 10 sec after apnea vertex positive SP shifts began, increased to from 100-500 uV, and declined to original levels within 30 sec after breathing resumed. Several characteristics including their polarity and magnitude make it unlikely that this SP is a "contingent negative variation. When 8% CO_2 is rebreathed at breaking point breathing movements may occur without restoring normal $PaCO_2$. We performed this experiment in several subjects and found the positive shift remains even though respiratory movements occur. Hyperventilation and rebreathing in the absence of breath holding produce negative and positive SPs respectively. We believe the breath holding SP is related increased $PaCO_2$, although the physiological basis of this phenomenon is not known.

24.2 ELECTROCORTICAL WAVES ASSOCIATED WITH DYSKINETIC MOVEMENTS PRODUCED BY LESIONS OF THE CAUDATE NUCLEUS IN CATS. Samuel L. Liles. Louisiana State University Medical School, New Orleans, La. 70112.

A previous study showed that experimental lesions which damaged exclusively the anteroventral area of the caudate could induce a permanent behavioral change in which the animals exhibited dyskinetic movements (Science 164:195, 1969). Larger lesions causing more diffuse destruction of the caudate did not produce these symptoms. In the present study, intact adult cats were submitted to an initial surgical procedure in which electrodes were permanently implanted over various cerebral cortical areas and in certain muscles of the forelimbs. The animals recovered and control observations and recordings were made for 2-4 weeks. In a second surgical procedure, electrolytic lesions were placed unilaterally in the anteroventral caudate area. Although a variety of abnormal movements were noted after placement of the lesions, the major dyskinetic symptom consisted of slow hyperextension and dorsiflexion movements of the toes and paw of the forelimb contralateral to the lesion. With the animal lying quietly on the floor of the test cage and observed covertly, the movements occurred at intervals of a few seconds to two minutes, and were frequently accompanied by coarser movements which thrusted the limb off the floor for several seconds. These dyskinetic movements were associated with specific changes in electrocortical activity in the contralateral motor cortex (ipsilateral to the lesion), in which a burst of slow waves of variable duration (1-2 sec) preceded each dyskinetic movement. The slow-wave burst ceased shortly (<250 msec) before each movement began, so that electrocortical activity was desynchronized during the dyskinetic movement (indicated by EMG traces). These data suggest that anteroventral caudate lesions which induce dyskinetic movements cause a significant disruption or imbalance of subcortical influences which control motor cortex function (Supported by USPHS, NIH Grant NS08907)

24.3 COMPUTER-ANALYSIS OF 40 Hz EEG IN NORMAL AND MBI CHILDREN. Daniel E. Sheer and Lyllian Hix.* Dept. Psychol., University of Houston, Houston, Texas 77004.

Two groups of male children, ten each, were matched on age and I.Q. One was at normal grade level; the other, scholastically placed as minimally brain-injured, had no hard neurological signs and no primary sensory or motor deficits. The children were given a series of fifteen Verbal-Visual (VV) and fifteen Verbal-Auditory (VA) programmed tasks. There were significant differences between the two groups on both series of tasks. EEG's were recorded under baseline conditions and continuously during the presentation and solution of the tasks. Control of overlapping muscle artifact, particularly in the 40 Hz range, is critical in the analysis of scalp-recorded EEG during behavioral situations. Control of muscle was automatically accomplished by (1) controlling bursts through the blanking of pre-set amplitude levels of the first derivative of the raw EEG; and (2) statistically controlling finer muscle artifact through covariance analysis with an independent measure of muscle. Power spectral functions of the EEG from occipital leads gave significant differences between the two groups. The norm children showed a substantial rise in the 40 Hz band during the VV tasks as compared with VA tasks and baseline conditions. They were clearly different with little overlap from the MBI children, who showed no changes in EEG during task situations as compared with baseline. The 40 Hz will be discussed as a "consolidation rhythm" for short-term store.

24.4 VARIABILITY OF THE EEG IN RELATION TO REACTION TIME IN NORMAL CHILDREN Walter W. Surwillo. Dept. Psychiat., Univ. Louisville Sch. Med., Louisville 40202.

In pursuit of the factors associated with the slower and more variable reactions of young children, the variability in duration of consecutive half waves of the EEG recorded during performance of a reaction-time task was investigated. The study was based on a model which views the EEG as a series of timing or gating pulses, with increased variability in time of occurrence of the pulses resulting in decreased rates at which information may be processed. It was hypothesized that high EEG variability would be reflected in and associated with longer reaction time. EEGs were recorded from scalp leads over P_3- O_1 and P_4-O_2 in a group of 36 boys, aged 5-17 years. Variability in duration of the half waves ($\sigma_{\frac{1}{2}D}$) recorded in the reaction interval for each trial of an auditory reaction-time task was determined. The correlation between mean reaction time and mean $\sigma_{\frac{1}{2}D}$ from P_3-O_1 for the group tested was equal to +0.59. Reaction time and age had a correlation of -0.894 and this value dropped to -0.837 when $\sigma_{\frac{1}{2}D}$ was partialled out. Although EEG variability could account for about 12% of the variance shared by reaction time and age in the sample tested, the prime factor or factors involved in the remarkably slow reactions of young children still remain obscure.

24.5 OBSERVATIONS ON FREQUENCY CHANGES AND ON SYNCHRONIZATION OF THETA WAVES.
Clara Torda,Mt.Sinai School of Medicine, New York,N.Y.,10029.

Theta activity of hippocampal origin of frequencies from 11 to 1 cycles/second have been shown to result from afferent impulses that reach the hippocampus via septohippocampal fibers(reviewed by Stumpf, International Review of Neurobiology, 8,77,1965). The afferents generate theta activity through somatodendritic interactions of hippocampal cortical pyramidal cells at cost of some loss of bioelectricity. The synchronization of the output seems to depend on a pacemaker located in the medial nucleus of the septum. The frequency of the output seems to depend on both the frequency of afferent stimuli, and the nature of cholinergic synaptic transmission at the pyramidal cells of the hippocampus.-Theta activity was recorded through extracellular microelectrodes (near pyramidal cells of hippocampal cortex,or efferent fibers).The afferent neurons were stimulated either electrically or chemically (microinjections of norepinephrine(NE)).The hippocampal concentrations of serotonin(SE) and acetylcholine(ACH) were increased through microinjections, and were decreased through administration of specific inhibitors of SE or ACH synthesis.- Through selective changes in the relative concentrations of the three biogenic amines (SE,NE,ACH) theta activities of different frequencies could be produced. The frequency increased with local increase of the available acetylcholine.Serotonin in increasing concentrations decreased the frequency of theta output, probably through serotonin-concentration-dependent inhibition of cholinergic transmission. Stimulation of afferent neurons increased the frequency of theta activity. Synchronization could be induced by both: 1) the presence of an intact medial nucleus of the septum, and 2) changes of the relative concentrations of the three biogenic amines.-- The results support the assumption (Torda) that during deep sleep (1-2 cycles/second EEG activity) and paradoxical sleep (2-11 cycles/second EEG waves) the synchronized EEG waves depend, in part, on serotonin regulation of transmission of cholinergic synapses.

24.6 A COMMON NEURONAL PATTERN IN SEIZURES

EMIL C. ZUCKERMANN, M.D., DIVISION OF NEUROLOGY

YALE UNIVERSITY SCHOOL OF MEDICINE, NEW HAVEN, CONNECTICUT

Extracellular microelectrodes were used to analyze the behavior of neuronal populations during seizure activity in chronic awake cats. The structures investigated were the dorsal hippocampus, a typical laminar neuronal organization, and the reticular formation of the brain stem, a non laminar neuronal organization. Seizure activity was induced by electrical stimulation in close vicinity to the recording microelectrodes, by increasing K^+ concentration in the CSF and by increasing the plasma concentration of urea. The seizures induced in this way had quite different clinical and electrical patterns as seen with macroelectrodes. However, microelectrodes reveal a common pattern at the cellular level: a) In some of the focal neurones, paroxysmal depolarization shifts develop, with or without spike inactivation; b) A large number of surrounding neurones are activated; their asynchronous and sustained discharges apparently generate the depolarization shifts. The results suggest the build up during any epileptic activity of local abnormal reverberating neuronal chains.

24.7 THE FASTIGIAL PRESSOR RESPONSE: SIMILARITY TO CARDIOVASCULAR ADJUSTMENT TO POSTURE. Nobutaka Doba* and Donald J. Reis.
Dept. Neurol., Cornell Univ. Med. College, New York, N.Y. 10021.

In cat, electrical stimulation of the fastigial nucleus evokes tachycardia and an elevation of systemic blood pressure. To establish the functional significance of this cerebellar-brainstem reflex, the fastigial pressor response (FPR), its cardiovascular characteristics were analyzed. In cats anesthetized with chloralose and paralyzed with gallamine, regional blood flow was measured with electromagnetic flow meters, cardiac output by a thermal dilution method and cardiac contractility with a strain gauge sutured to the right ventricle. The contribution of sympathetic and parasympathetic components of the FPR were evaluated by selective denervation or pharmacological blockade. The FPR is characterized peripherally by a sympathetically mediated decrease in femoral, axillary, renal and mesenteric arterial flow. Common carotid flow increases suggesting increased cerebral blood flow with suspension of autoregulation. Central venous pressure showed only slight elevation. There are increases in peak systolic pressure with increased dp/dt in both ventricles and some augmentation in right ventricular contractility reduced by stellectomy. Tachycardia is mediated both by sympathetic excitation and vagal inhibition. Changes in cardiac output are minimal. Phentolamine and propranolol both attenuate the FPR indicating alpha- and beta-sympathetic components. During the FPR there is inhibition of the baroreceptor reflex. On the basis of the pattern of cardiovascular changes, the FPR appears to simulate the reflex cardiovascular changes associated with the maintenance of upright posture. The essentiality of the fastigial nucleus in postural regulation adds support to this view. (Supported by NIH grants.)

24.8 SPLANCHNIC REPRESENTATION IN THE FASTIGIAL NUCLEUS OF THE CEREBELLUM. Charles H. Hockman. Brain Res. Lab., Dept. of Pharmacology, Univ. of Toronto, Toronto, Ontario, Canada.

Recent findings from this laboratory indicate that the fastigial nucleus of the cerebellum (FN) exerts pronounced influences on autonomic effector mechanisms. Since baroceptor afferents have been shown to project to this region, it seemed logical to assume that other viscera might also be so represented. In adult cats, either anesthetized or encéphale isolé preparations, the FN was explored with stainless steel microelectrodes while single shocks (0.25 to 0.5 msec) were delivered at 4 sec intervals to the central cut-end of the right splanchnic nerve. Splanchnic stimulation evoked large responses from the ipsilateral FN with latencies between 10 and 16 msec. These potentials were processed on an averaging-computer and examined on a storage oscilloscope for variability. In earlier work, we had shown that reflex vagal bradycardia could be inhibited by electrical stimulation of the FN, and that baroceptor afferents projected to this same circumscribed region. It should also be pointed out that potentials evoked either by baroceptor or splanchnic nerve stimulation are extremely sensitive to anesthetics such as ether and sodium pentobarbital. It now appears that the FN, which can mediate changes in systemic blood pressure, heart rate and rhythm, also receives visceral information via splanchnic afferents. Evidence from several laboratories would suggest that the cerebellum is capable of exerting influences on autonomic function which might be deemed preparatory or anticipatory in nature. Such findings have also led to the suggestion that the cerebellum "may play a role in the integration of affective behavior and the autonomic reactions accompanying such behavior." (Supported by grants from the Ontario Alcoholism and Drug Addiction Res. Fdn., and the Medical Research Council of Canada.)

24.9 FOCAL REFLEX MYOCLONUS. Richard F. Mayer and Granger G. Sutton*. Dept. Neurol., Sch. Med., U. Md., Baltimore, 21201

Patients, who have myoclonus initiated by afferent stimuli or movement, have been studied but little attention has been given to spinal reflexes. The present report describes a detailed study of reflex activity in a patient with reflex myoclonus limited to the right side of the body. Physiological studies of electrically induced monosynaptic H reflexes, antidromic F responses and long-loop C reflexes were made. Studies of the cerebral evoked responses (CER), which are greatly enlarged in this disorder and electroencephalograms (EEG) were also performed. Stimulation of the median nerve in the digits or at the wrist elicited a small polyphasic response (250-800 μV) in the thenar muscles with a latency of 50-55 msec. This response represents an electrically evoked myoclonic response and is maximum in the right hand muscles where the myoclonus is most prominent; it is transmitted in rapidly conducting afferent and efferent fibers, and is a polysynaptic long-loop reflex, which is augmented by repetitive stimulation. Excitability cycles of this C reflex, studied with pairs of threshold stimuli, show facilitation to 175% at 40-80 msec, which persists for 500 msec. and is followed by inhibition with recovery by 1 second. Although the excitability of spinal motoneurons was increased as judged by the recovery cycles of the H reflex, this alone does not account for the myoclonic jerks. The type of myoclonus in this patient with the associated C reflex and changes in EEG and CER may result from an increase in the excitability of cortical motoneurons secondary to release from thalamic nuclei or from thalamo-cortical or cerebello-cortical connections.

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24.10 CEREBELLAR ACTIVITY IN EMOTIONAL BEHAVIOR. Robert G. Heath. Dept. Psychiat. & Neurol., Sch. Med., Tulane University, New Orleans, La. 70112.

Data for this report were obtained from extensive studies in 20 rhesus monkeys, including 5 raised in isolation, and in 2 patients with temporal lobe epilepsy. All subjects were prepared with electrodes implanted for long-term study into the following brain structures: septal region, caudate nucleus, hippocampus, amygdala, hypothalamus, posterior ventral lateral thalamus, cerebellum, mesencephalic reticular formation, and over several cortical sites. Procedures that were used which demonstrated significant correlations between cerebellar activity and emotional expression included: (1) evoked potential studies to demonstrate direct functional relationships with sites in pathways for emotional expression, and substantiation of this finding by introduction of mirror foci in monkeys; (2) EEG recordings during alterations in emotion and in levels of awareness induced by administration of euphorizing drugs, psychotomimetics, and narcotics; (3) EEG recordings from deep and surface brain regions of the patients during specially arranged pleasurable events, viz., sexual activation; (5) EEG recordings from isolation-raised monkeys showing pathological emotional expression, and from the two patients during episodes of psychotic behavior. From this wide range of studies, data will be presented to demonstrate that deep cerebellar nuclei are integral parts, both anatomically and functionally, of the pathways for emotional expression.

24.11 THE ASSOCIATION OF CEREBRAL AMINE DEFECTS AND ABNORMAL VISUAL EVOKED RESPONSES IN PHENYLKETONURIA. Charles M. McKean, Marilyn M. Marcus* and Edward W. P. Schafer*. Brain-Behavior Research Center, Sonoma State Hospital, Eldridge, California 95431.

On the basis of findings in the brains of hyperphenylalaninemic animals, in addition to findings in the blood and urine of PKU patients, it has been postulated that a reversible disturbance of amine metabolism exists in the PKU brain, which may be implicated in the associated behavioral maldevelopment. We have sought to determine whether such a cerebral metabolic defect is present and, if so, whether its reversal can produce functional improvement in previously untreated phenylketonurics. In autopsied PKU brains the amine precursors tryptophan and tyrosine are 45% and 48%, respectively, of non-PKU levels with comparable reductions in serotonin, dopamine, and noradrenalin. To study amine metabolism in vivo we blocked the active efflux of homovanillic and 5-hydroxyindoleacetic acids from the cerebrospinal fluid compartment with probenecid in 3 adolescent PKU patients, before and after blood phenylalanine (phe) was reduced to normal by dietary treatment. Under these conditions the rate of accumulation of the acid metabolites of dopamine and serotonin doubled following normalization of phe concentrations. These data indicate that there is a cerebral disturbance in serotonin and catecholamine metabolism in PKU, which may be reversed by lowering blood phe concentrations. They suggest, further, that substrate deficiency, produced by competitive interference with amino acid transport into brain, may be contributory to the amine defects. Following the apparent increase in rates of cerebral amine synthesis, definitive improvements were observed in the abnormal Visual Evoked Responses, which suggested faster CNS conduction and increased capacity of the visual system to discriminate pattern from flash stimuli.

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Session 25

25.1 NEW EVIDENCE CONCERNING REFRACTORY PERIOD IN SELF-STIMULATION NEURONS. Mary C. Wetzel. Dept. Psychol., Univ. of Ariz., Tucson, Ariz. 85721.

J. A. Deutsch (J. comp. physiol. Psychol., 1964, 58, 1-9) and others have reported, for the rat, sharply reduced self-stimulation rates for brief intrapair pulse intervals (IPIs). The effect has been attributed to a neuronal refractory period of approximately 1 msec. An attempted replication, using cats instead of rats, failed to reproduce the previous findings. The IPI test range investigated was from 0.2 to 1.3 msec. There were two principal results. First, for some electrodes there was no reduction in rate for brief IPIs. Second, while other electrodes did yield a reduction, the minimum rate fell at approximately 0.5 msec, thus failing to confirm the generality of the 1 msec estimate. Conclusions were that: 1) the demonstration of refractoriness may be obscured by other neuronal mechanisms, 2) rate variations for brief IPIs are dependent upon electrode locus, and 3) measurement may be affected by brain size or a species difference.

25.2 BEHAVIORAL TYPES OF NEURONS IN HIPPOCAMPAL FORMATION OF RAT. James B. Ranck Jr. Department of Physiology, University of Michigan, Ann Arbor, Michigan. 48104.

Action potentials from single neurons in all parts of hippocampal formation have been recorded in unrestrained rats. Firing of single neurons correlates well with overt behavior and over 90% of all neurons encountered fall into one of the following types.

a) Neurons which fire up to 60/sec when a regular theta rhythm appears in the slow waves---during voluntary behavior. The most rapidly firing neurons seen---almost always greater than 10/sec. Increase rate in paradoxical sleep (P.S.). About 10% of neurons in all parts.

b) Most neurons in entorhinal cortex, parasubiculum and presubiculum fire when the rat orients to a specific object (for instance food, or things associated with food). Completely off almost all the time. Most rapid firing in P.S.

c) In CA1 and fascia dentata some neurons only fire at the end of an orienting movement to a specific object. Completely off most of the time and in P.S.

d) Most neurons in CA3 and some neurons in CA1 fire most rapidly during a specific well learned or consummatory behavior (for instance eating). Off or no change in P.S.

e) Most neurons in CA1 fire during voluntary behavior toward a specific goal (for instance food). Completely off most of the time and in P.S.

f) Most neurons in fascia dentata fire during some aspects of approach of a specific thing or exploration in the usual vicinity of this thing. Completely off most of the time and in P.S.

g) Most neurons in subiculum increase firing rate during any movement.

(Supported by NSF Grant GB26184)

25.3 ELECTROMICTURITION IN MAN AND ANIMALS. Blaine S. Nashold, Jr. and Harry Friedman*. Dept. of Surg., Div. of Neurosurg., Duke Univ. Med. Center, Durham, N. C. 27706

Attempts to empty the bladder of paraplegic patients by electrical stimulation have not been successful enough for clinical use. Electrodes have been implanted either on the efferent nerves to the bladder or directly on the wall of the bladder to excite the muscle. Electrical stimulation of this kind will partially contract the bladder with varying degrees of urine expressed. Recently we have shown that the bladder of paraplegic animals can be contracted with micturition occurring if the stimulation is within the micturition center of the sacral spinal cord for periods up to 6 months. It was found that two factors controlled the micturition responses. One was the localization of the stimulating electrodes in the central gray of the conus medullaris, plus the specific control of the electrical parameters of stimulation. Cystometric and EMG studies in animals have shown that contractions of the bladder with simultaneous relaxation of the sphincter does occur with central stimulation of the isolated spinal cord.

Four paraplegic patients have undergone electrode implantation in the conus medullaris. Stimulation by an RF stimulator and receiver has produced adequate bladder emptying in 3 of the patients plus autonomic responses, both regional and generalized. The autonomic responses produced by direct spinal cord stimulation can be controlled by selection of the parameters of the electrical stimulus. The autonomic function of the conus medullaris will be discussed.

25.4 TOPOGRAPHY OF LONG-LATENCY SOMATOSENSORY RESPONSES IN THE HUMAN BRAIN: A REEXAMINATION. Merlin W. Donald* (SPON: W. R. Goff). Neuropsychology Laboratory, V. A. Hospital, West Haven, Ct. 06516.

In our studies of scalp-recorded somatic evoked responses (SER) during human performance we have observed that there is considerable spontaneous fluctuation of late component amplitude, independently of the amplitude of early components. We have studied this phenomenon in five subjects. They were required to perform vigilance tasks and sensory discrimination tasks for two to three hours each session and asked to return a minimum of 5-10 sessions. We continuously monitored their somatic evoked responses (SER) to wrist shock during these periods at 16 different electrode locations. Small Ns were used for averaging (usually 16) to maximize the sensitivity of the SER to short term cortical excitability changes. All subjects showed large (up to 500%) within and across-session fluctuations in late component amplitude, especially after the third or fourth session, when they had become habituated to the experimental situation. In fact, late positive waves 200 and 300 msec after the stimulus, which peak at or near the vertex, sometimes virtually disappeared from the averaged responses. This spontaneous "suppression" occurred periodically despite the fact that the subjects were still alert and performing, and in the absence of any diminution of the early components or peripheral nerve response. Suppression of the late vertex components revealed somatic late components over the contralateral hand area which were normally obscured by the much larger vertex late components. We have worked out the detailed topography of these components, as well as their interaction with other types of cortical sensory responses.

25.5 EFFECTS OF EARLY WEANING AND DIFFERENTIAL HOUSING ON EMOTIONAL REACTIVITY AND BRAIN BIOCHEMISTRY IN THE RAT. S. Michael Plaut* and Jimmie M. Davis. Galesburg State Research Hospital, Galesburg, Illinois 61401.

In maternal deprivation studies, it is necessary to determine whether effects on pups are related to nutritional factors, to nonnutritional aspects of parental care, or to the absence of adults per se. Litters of CAW:CFE(SD)spf rats were deprived of mothers at age 15 days (deprivation), or left with mothers (control), some of which had their nipples cauterized to prevent suckling (cauterization). Half the litters had been reared from birth in the presence of a virgin female (aunt), which was never taken from the litter. Each of the six groups contained 10-12 litters. At 21 days of age, half the pups in each litter were tested for whole-brain levels of eight free amino acids, and other pups were housed alone, or in peer groups, to be tested five weeks later. Pups from deprivation and cauterization groups had lower body and brain weights and reduced levels of aspartic acid with respect to controls, but a deprivation-related decrease in threonine was attenuated in pups left with cauterized mothers. Rearing and housing conditions affected reaction-to-handling test scores at age 56 days, individually housed rats showing higher incidence of startle and vocalization, while rearing with aunts increased resistance to being picked up. Rearing with aunts and group housing increased 56-day-old brain weights in control, but not deprivation or cauterization offspring. The brain tissue is currently being analyzed for water and protein content and levels of protein and free amino acids. Combined data emphasize the importance of considering nutritional and social aspects of the adult-litter relationship, as well as the nature of the postweaning environment, in studying the effects of maternal deprivation on any given index of development.

25.6 EFFECT OF NEONATAL SPLIT-BRAIN SURGERY ON SHOCK THRESHOLDS AND AVOIDANCE LEARNING IN RATS. Jeri A. Sechzer. Dept. of Psychiatry, Cornell Med. Coll., White Plains, NY 10605

Split-brain surgery was performed on 22 Sprague Dawley and 6 Long-Evans rats within 8 hours of birth. They were raised in the laboratory and weaned under the same conditions as untreated control rats. At 120 days all animals were housed individually. Shock threshold levels were determined in milliamperes (ma.) in ascending, descending and random order. Shock threshold levels were found to be significantly lower in the neonatal split-brain group. "Y" maze learning, on the other hand, was significantly prolonged. Many neonatal split-brain rats never reached an 8 out of 10 criterion. Comparison with shock threshold levels and subsequent avoidance learning in adult commissurotomized rats emphasizes the importance of age of separation of the hemispheres in evaluating the development of interhemispheric interrelations.

25.7 CLINICAL RECONSTRUCTION OF NATAL MEMORY AND NEUROBEHAVIORAL RESEARCH. Virginia Johnson, Private Practice, 1516 Westwood Boulevard, Los Angeles, California 90024.

In terms of current research, certain statements relative to neonatal learning and conditioning seem acceptable: (1) neonates can be conditioned; (2) there may be a "critical developmental period" when such learning is more significant, or qualitatively different, than during later periods; (3) this conditioning is assumed to be significant for later patterns of behavior, and therefore functions as "memory" even in the absence of conscious awareness or cognitive recall. Valid research evidence of specificity relating early conditioning to later behavior has been difficult to obtain, but in an experimental clinical program based upon a technique of experiential recall a number of subject incidentally reported neonatal experiences. The preliminary procedure involved the administration of methylphenidate in high dosage; however, interviews conducted with these subjects after the drug was discontinued elicited natal recall sequences which reflected early prior conditioning affecting known patterns of later behavior and frequently specific with respect to psychopathological symptoms. This suggests that not only may neonatal experience "imprint" permanent memory traces, but that such early conditioning is indeed significant for later behavior patterns, is accessible to certain recall techniques, and is subject to reinforcement and feedback processes. These findings appear significant in connection with neurobehavioral research and memory process, especially with respect to psychopathology; and with certain effects of the drug related to memory stimulation and recall which may represent an as yet incompletely explored aspect of certain neuropharmaceuticals.

25.8 ESCAPE TRAINING IN PARAMECIA. Thomas E. Hanzel* and William B. Rucker* (SPON: W. L. Byrne). Department of Psychology, Mankato State College, Mankato, Minnesota, 56001.

Single paramecia were sucked into a capillary tube and allowed to escape back into a drop of their own culture medium. Consistent with earlier reports by French (J. of Exp. Psych. 26: 609, 1940), and by Hanzel and Rucker (revised for Comm. Beh. Biol., 1971), escape speed increased reliably over trials. Linear trend was highly significant ($p < 0.005$). Neither variations in intertrial interval (massed or 1-min), variations in the inner diameter of the tube (0.45 or 0.63 mm), nor the interaction between these two factors affected escape speed.

A measure of general activity was taken just before and just after escape training. Activity was found to be greater after training (contrary to French), but there was no significant interaction between increase in activity and the rate of increase in escape speed. These results and previous work lend support to the hypothesis that single celled animals are capable of demonstrating changes in behavior which in higher animals would be described as learning.

25.9 ALTERATION OF BLOOD PRESSURE FOLLOWING INSTRUMENTAL CONDITIONING IN RATS. S. N. Dutta* and S. N. Pradhan. Dept. of Pharmacol., Howard Univ. Col. of Med., Washington, D. C. 20001

Conditioning technique has been used in numerous studies in an attempt to modify cardiovascular responses. The purpose of this study was to determine the direction of acquisition of conditioned changes of systolic blood pressure in conscious rats by using a signal (CS) that has been paired with a noxious (electric shock) stimulus (US), and extinction of such learned response. Further, attempts have been made to modify systolic blood pressure of a group of hypertensive (experimentally induced) rats by similar conditioning procedure. Sixteen naive male rats of Wister-derived Walter Reed strain and weighing from 200 to 550 g were used as Ss. The CS was 2100 cps tone delivered from an audio oscillator. The US was an electrical shock delivered by a AEL electronic stimulator to stainless steel electrodes implanted subcutaneously near the root of the tail. The systolic blood pressure was measured indirectly by the tail-cuff method and recorded on a Physiograph. Experimental hypertension was produced in Ss by unilateral nephrectomy, postoperative DOCA injections and salt loading. Hypertensive Ss with a sustained systolic blood pressure above 150 mm Hg were subjected to instrumental conditioning. The majority of the normotensive Ss were capable of raising the blood pressure (6-16 mm Hg) consistently in response to CS. Subjects exposed to CS alone showed no change in the blood pressure. Extinction of conditioned response was observed almost immediately after US was discontinued. One of the four hypertensive Ss showed lowering of blood pressure to conditioning procedure and the rest indicated rise of blood pressure. (Supported by USPHS, NIH grant GM MH 17824).

25.10 ANALYSIS OF EMOTIONAL HYPERGLYCEMIA IN MONKEYS. Benjamin H. Natelson*, Peter E. Stokes*, and Gerard P. Smith. Bourne Behav. Res. Lab., Dept. Psychiatry, New York Hosp.-Cornell Med. Ctr., Westchester Division, White Plains, and Dept. Neurology, Albert Einstein College of Med., New York.

Emotional hyperglycemia was elicited by tail shock in 5 rhesus monkeys adapted to chronic restraint in primate chairs. Mean peak change of plasma glucose during the hour of tail shock (10 sec of every 30 sec) was +55.4 mg% (range: +17 to +96 mg%, n=5). Similarly vivid emotional behavior as determined by a behavioral rating scale measuring bodily movement, pupillary dilatation and vocalization was elicited by electrical stimulation of anterior hypothalamus (A 15.0-11.5, L 2.0-3.0, H +0.5 to +5.0; 5 monkeys) and of posterior hypothalamus (A 10.0, L 2.0, H +3.0 to +4.0; 2 monkeys). Plasma glucose increased markedly during the hour of stimulation (30 sec of every 60 sec). Mean peak change was +63.7 mg% (range: +17 to +121 mg%, n=25). Pentobarbital anesthesia markedly reduced the hyperglycemia elicited by hypothalamic stimulation (mean reduction = 74.6%). Emotional hyperglycemia was dependent on epinephrine secretion because it was markedly reduced in 1 monkey maintained on cortisone after bilateral adrenalectomy. Emotional hyperglycemia was not associated with an increase in plasma insulin concentration in 5 of 5 stimulation experiments in 2 monkeys. These data suggest that Cannon's interpretation of the biological significance of emotional hyperglycemia must be revised. Since the hyperglycemia was not accompanied by increased insulin, hyperglycemia must serve the metabolic demands of the activated and insulin independent neural systems which underlie emotional behavior, not the metabolic demands of the insulin dependent peripheral muscles.

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25.11 EEG ALPHA PATTERNS ASSOCIATED WITH NEUROPROCESSING DYSFUNCTION IN CHILDREN. Juan de Dios Pozo-Olano. Division of Biological Sciences University of Georgia, Athens, Georgia 30601.

EEG recordings were taken in a group of children aged 8-10, some clinically normal, others dyslexic. Time-locked sequences of averaged alpha activity were computer-processed as spatio-temporal contour maps. A description of the morphological characteristics, and of the spatio-temporal configuration of the average alpha rhythm (a new concept introduced by Remond) in posterior cerebral regions, was made for each child. Neural mechanisms underlying dyslexic process -dysfunction in neuroprocessing- are associated with certain EEG activity. This appears to be true for the spontaneous rhythms, as well as for the sensory evoked potentials. Our studies -using computer data reduction and digital quantification of EEGs- permit us to observe the dissimilarity between the average alpha rhythms of normal and dyslexic children. The alpha activity of the latter is unstable and irregular, with a very poor chrono-topographic organization for the ensemble of cerebral regions covered by the electrode montage. Presentation of average alpha rhythm as potential gradients has permitted observation of the lack of electric equipotentiality between the hemispheres in dyslexic children, possibly denoting physiological impairment of interhemispheric communication. Calculation of the alpha potential field (as delimited by the montage) confirms the absence of harmony in the distribution of alpha currents at the scalp surface.

25.12 THE NEUROPSYCHOLOGY OF PSYCHOSIS AND SOMATIC TREATMENT. I. F. Small, M.D. and J. G. Small, M.D.* Department of Psychiatry, Indiana University Medical Center, Indianapolis, Ind. 46202

Observations with extensive neuropsychological testing of psychotic patients before and after somatic therapy are described in this paper. Complete test results were obtained in 45 patients when drug free during acute psychotic episodes and again after treatment with either phenothiazines, lithium or unilateral electroconvulsive treatment. Results of the test battery prior to somatic treatment generally did not suggest diffuse or localized central nervous system impairment. With few exceptions test scores were within non-brain damaged values despite the presence of severe psychotic symptoms with apparent disruption of mentation, perception and cognitive functions. Performance on the test battery remained within normal ranges after somatic treatment without impairment in tests of dominant, non-dominant or bilateral hemispheric functions, even in the patients receiving convulsive treatment on the right or left side of the head. There were improved retest scores on some battery items which varied according to treatment modality and diagnosis. There was no indication of preferential influences upon uni- or bilateral hemispheric functions.

This investigation established that extensive neuropsychological investigations of psychotic patients were feasible and that clinical disturbances resembling organic disruptions of brain function were not associated with neuropsychological indications of brain damage. Further somatic therapies known to alter and interfere with certain CNS functions did not impair neuropsychological test performance. Moreover differential patterns of test scores and changes with treatment discriminated between the three kinds of somatic therapy and clinical diagnosis.

25.13 CEREBRAL TRAINING AS A REHABILITATIVE MODALITY. Ernst Schmidhofer. Director, Cerebral Training Institute, Columbus, Ohio. 43228

Cerebral Training had its beginnings in 1944. It is a very highly structured, massively standardized regimen, that makes use of neurophysiologic principles instead of psychiatric concepts--cerebral mechanisms rather than mental dynamisms. It is a nonmedicinal, controlled, methodic, organized, sustained training program which concerns itself with the systematic and orderly cultivation of continuing and progressive self-potentiated, self-development. Aside from the Curriculum Course at the Cerebral Training Institute, there are others being conducted for both patients and staff in 3 of Ohio's correctional institutions. It is estimated that upward of 8000 persons have been exposed to this method. Heterogeneous diseases and disorders may be worked with concomitantly. Large groups of 100 to 150 or more may be dealt with concurrently. Nonprofessionals may be trained to become effective instructuors. A lengthy history is not required. Insight is unnecessary. Ventilation is excluded. Each trainee participates actively in his own recovery by studying the 30 training manuals he receives, and by practicing the various principles between class instruction periods. The method may be used indefinitely after the formal course of training has ended. Perhaps the greatest asset is the prevention of recurrence of medical afflictions and of offending acts. This method can be made up literally into the form of a package program and delivered as such. In many cases symptom relief begins to appear in one to 3 weeks. In one study of a group of 100 alcoholics, 64% were reported as being abstinate 12 to 18 months later. Hard core heroin addicts are also responding favorably.

26.3 MOTOR CONTROL OF THE ABDOMEN IN FLYING AND FLIGHTLESS LOCUSTS. Jeffrey M. Camhi and Maija Hinkle*. Section of Neurobiology and Behavior, Cornell, Ithaca, N.Y. 14850.

By recording motorneuron activity in the locust abdomen during flightless and simulated flight conditions, we can correlate single unit activity with specific behaviors. During flight, wind angle changes evoke yaw-correcting lateral deflections of the abdomen, while wind velocity fluctuations induce vertical abdominal deflections, probably used in pitch control. This wind information is monitored by the facial wind receptor hairs. Temporarily flightless locusts show no abdomen responses to the same wind angle and velocity changes, suggesting that during flight the nervous system switches from a condition of unresponsiveness to one of responsiveness to wind sense inputs. All fifteen motorneurons in the nerves of the first abdominal segment are driven by the central neuronal flight motor, which also controls the wing beat. During flight, the abdominal motor spikes occur in bursts synchronous with the motor bursts to the wing downstroke muscles. This activity stiffens and raises the abdomen into flight posture. Sensory inputs containing wind angle and velocity information superimpose upon this on-going rhythmic activity commands which alter the number of spikes/burst, but not the burst frequency or phase. In the absence of flight motor activity, wind inputs are inadequate by themselves to drive the motorneurons. Therefore, the state of responsiveness to wind inputs is determined by the state of activation of the central flight motor. During flightless intervals, about half of the motorneurons are driven by another, much slower, central neuronal oscillator, that controlling ventillatory pumping. In flight, these same units can be driven by the flight motor alone, or by both central oscillators, summating their separate excitatory inputs. Thus by employing three different signals (two central and one sensory) of varying strengths, individual motorneurons can engage in a variety of stereotyped behaviors.

26.4 CYCLING ACTIVITY IN ARTIFICIAL NERVE NETS. Photios A. Anninos* (SPON: R. ELUL) Dept. Anat. and BRI, Univ. Calif., Los Angeles, Calif. 90024.

Artificial nerve nets constructed of discrete populations of 200-1000 "neurons" have been studied in computer simulation. Assumptions on mode of operation of these nets were: (i)each neuron fires at times which are integral multiples of the synaptic delay τ, i.e. neurons fire at discrete intervals, (ii)firing produces an appropriate PSP after τ, (iii)all neurons have identical refractory period and (iv)temporal summation occurs without decrement, but only for a period less than one synaptic delay. Overall structure of the nets was specified by a number of statistical parameters: fraction of inhibitory neurons in the population, average number of connections to each cell, threshold for cell firing, and coupling coefficient between cells. These parameters do not determine the detailed "microscopic" structure, which is initially established on random basis, but maintained fixed thereafter. The nets received a steady input through a number of "afferents". The level of this input was constant throughout.

For the range of the parameters considered in this study, neural nets are capable of supporting self-maintaining activity in the form of cycling modes, characterized by a fixed period. The period of cycling in these conditions was found to be dependent upon the statistical parameters of the net and upon stimulus characteristics, rather than on the detailed "microscopic" structure of the net. Nets with different "microscopic" structure cycled at identical or closely similar periods in response to the same steady input. These results suggest that (i) non-structured nerve nets may respond to specific stimuli and (ii) such reverberating activity might serve as a carrier of short-term memory.

26.5 DEVELOPMENT OF ORGANOTYPIC BIOELECTRIC ACTIVITIES IN CULTURED REAGGREGATES OF RODENT CNS CELLS AFTER COMPLETE DISSOCIATION. Stanley M. Crain and Murray B. Bornstein. Depts. of Physiology and Neurology, Albert Einstein Coll. Med. and Rose F. Kennedy Center, Bronx, New York 10461.

Explants (ca. 1 mm^3) of fetal mammalian CNS tissues develop organotypic synaptically mediated repetitive-spike or slow-wave discharges during maturation in culture (Crain, Internat. Rev. Neurobiol. 9, 1966). Similar microelectrode recordings have now been made on small clusters of neurons after reaggregation in vitro of trypsin-dissociated cells obtained from 13- to 14-day fetal mouse spinal cord and brainstem (morphologic aspects: Bornstein and Model, this issue). After 2 to 4 weeks in vitro, complex repetitive spike discharges have been recorded, spontaneously as well as in response to electric stimuli, from dozens of discrete neuronal clusters which had become attached to the collagen-coated coverglass over an area of about 1 cm^2, and which appeared to be connected to one another via complex neuritic bridges. Larger clusters containing more than 20 cells also showed characteristic negative slow-waves in association with the spike barrages. The amplitudes of these potentials and the duration and complexity of the discharge sequences were greatly enhanced after introduction of strychnine (10 μg/ml). Furthermore, the spontaneous and evoked activities in the clusters were often clearly synchronized even between neurons separated by distances greater than 3 mm (with variable latencies reflecting conduction and synaptic delays). Completely dissociated mammalian CNS neurons can, therefore, not only form synaptic connections after reaggregation in culture, but they can organize into functional synaptic networks with complex properties suggesting involvement of inhibitory as well as excitatory mechanisms. (Supported by NINDS grants NS-06545 and NS-06735 and Kennedy Scholar awards.)

27.5 AN INFORMATION THEORY ANALYSIS OF THE AUDITORY LOCALIZATION OF A LATERAL SOUND SOURCE. Terence W. Barrett. Dept. Physiol. & Biophysics, Univ. Tenn. Med. Units, Memphis, Tenn. 38103

To account for interaural information used in locating a lateral sound in space, the one-dimensional wave mechanics equation: $\Delta f.\Delta t = c$, where Δf is signal bandwidth, Δt is signal duration and c is a constant, is extended to two dimensions. To satisfy Laplace's equation, the input from one ear to the contralateral cerebral hemisphere may be considered a simple harmonic function: e^{z}, where z is a complex number referencing both the binaural and interaural information content of the signal.

The ability to auditory locate a lateral sound necessitates an extra degree of freedom in information space to register the input from the ipsilateral hemisphere. This second input is the conjugate harmonic function of the first. Thus the summated input to one cerebral hemisphere remains a simple harmonic function of the natural logarithmic kind but of a second degree. The dynamic equilibrium properties expressed in an uncertainty condition give an explanation for the time-intensity trading relations which occur in locating a sound in lateral space.

27.6 NEURONAL CODING OF COMPLEX LOW FREQUENCY STIMULI AT SUBCORTICAL AUDITORY SITES IN CAT BRAIN. James L. Walker* and Edward S. Halas. Dept. of Psychology, University of North Dakota, Grand Forks, N.D. 58201.

Multiple unit electrophysiological techniques were used to record from the dorsal cochlear nucleus and inferior colliculus of six cat brains during ipsilateral, contralateral and bilateral aural stimulation. Standard electrophysiological techniques were employed to implant gross macroelectrodes at each anatomical site. Stimuli consisted of the spoken integers "one" through "ten" presented by three male and three female voices. The stimuli were recorded once onto a tape loop and then relayed directly to ear phones placed in the external auditory meatus. The multiple unit discharge frequency was directly recorded onto an analog tape recorder, converted from analog to digital, and punched into IBM cards (Halas, et al., Physiology & Behavior, in press). The results indicated the following: different spoken integers produced different and unique patterns of multiple unit discharge; male and female voices produced similar pattern configurations for identical stimuli; a high degree of similarity in neuronal response was observed between cats and, the same word produced highly similar patterns of neuronal discharge at both the dorsal cochlear nucleus and the inferior colliculus. The multiple unit frequency discharges seem to reflect an important frequency coding mechanism of the central nervous system observable only at subthalamic levels. (Supported by NSF Grant GB-7265 and NIMH Grand MH-11150).

27.7 CODING OF SPECIES-SPECIFIC VOCALIZATION IN THE AUDITORY CORTEX OF AWAKE SQUIRREL MONKEYS. Z. Wollberg*, and J. D. Newman. NIH, Bethesda, Md.20014

This study is concerned with the processing of complex sounds by neurons in the superior temporal cortex of squirrel monkeys. Special attention is being paid to sounds used by this species in intra-specific communication to determine which acoustic features of these sounds serve as cues for distinguishing between the various elements of the communication repertoire. Awake monkeys are presented with tape recordings of this species' vocalizations while recording extracellularly from single neurons. From a total of 213 neurons studied in this brain region more than 80 percent respond to vocalizations. These neurons can be categorized according to their response selectivity and the temporal complexity of their discharge patterns. At one extreme are cells which respond to one or only a few call types with simple discharge patterns. At the other extreme are cells which respond to most of the vocalizations with temporally complex discharge patterns. Using an electronic switch, selected portions of a given vocalization can be electronically removed and the effects on the responsiveness of the neuron tested. In some cases, this technique has permitted determining which portions of a vocalization are necessary to produce a given neuronal discharge pattern. Also, using this method, we have evidence which suggests that the nature of a neuron's response can be a result of the interaction between different parts of a given vocalization.

27.8 AUDITORY EVOKED POTENTIALS DURING SPEECH PERCEPTION. Charles C. Wood*, William R. Goff, and Ruth S. Day*. Neuropsychology Laboratory, V. A. Hospital, West Haven, Ct. 06516.

Auditory perception experiments in normal and brain-damaged subjects have suggested that the neural mechanisms required for the perception of speech are lateralized in one cerebral hemisphere, usually the left. This interpretation is consistent with clinical analyses of language disorders following brain damage, and may be related to anatomical differences between left and right temporal lobes. The present experiment provides direct neurophysiological evidence that a unilateral neural mechanism is specialized for the perception of speech. Neural responses evoked by the same binaural speech signal were recorded from ten right-handed subjects during two auditory identification tasks. One task required identification of acoustic parameters which are important for distinguishing between voiced stop consonants (direction and extent of second and third formant transitions), while the other task required identification of an acoustic parameter which provides no linguistic information at the phoneme level in English (fundamental frequency). In the time interval between stimulus onset and subjects' identification responses, evoked potentials during the two tasks were significantly different over the left hemisphere but identical over the right hemisphere. These results indicate that different neural events occur in the left hemisphere during analysis of linguistic versus nonlinguistic parameters of the same acoustic signal.