Meetings

Brain Research

The fourth visiting seminar of the International Brain Research Organization (IBRO/UNESCO) was held in Santiago, Chile, 22 November–7 December 1966. The visiting team members were from the United States and Europe; brain scientists from Argentina, Brazil, Chile, Ecuador, Peru, Uruguay, and Venezuela attended.

William J. Adelman, Jr. (University of Maryland School of Medicine) presented information relating to the study of the isolated giant axon of the squid. Brain researchers could view the roles that basic electrophysiological techniques, findings, and theories have in providing a cellular or membrane foundation for modern neurophysiology. Recent techniques in internal perfusion and voltage clamping of the isolated giant axon were stressed. Studies involving specificity of the axon membrane for periodic table Group 1A alkaline metal ions were reviewed. Some of the techniques and results were demonstrated on *Dosidicus gigas* axons at the Laboratory of Cell Physiology of the Faculty of Sciences, University of Chile in Montemar, Chile, in collaboration with Eduardo Rojas.

J. M. Affanni (Buenos Aires) described the effects on the brain of total section of the olfactory peduncles. He studied some of the phenomena occurring in the olfactory bulbs when they are separated from the brain. He found that after the section there is a quantitative change in brain rhythms; an increase in the total wakefulness time occurs, and there is a considerable decrease of the total "rapid eye movement phase" time. In the olfactory bulbs Affanni found a great increase of both the amplitude and duration of the olfactory-induced waves.

L. A. Aranda (Santiago) discussed and compared two different, long-lasting effects on the central nervous system of the cockroach: "equilibrium" and "leg position learning." In leg position learning, the training takes minutes, while the effects last for hours. One ganglion was enough to show the phenomenon. In equilibrium learning both the training period and the duration of the effects last for days; several ganglia seem to be necessary for the phenomenon. These two long-lasting processes seem to be closely correlated with changes in the electrophysiological activity of the central nervous system. A nervous pathway impermeable (or closed) to a simple presynaptic volley became permeable (or open) during the process of learning. But this electrophysiological modification is different in the two learning processes. During equilibrium a simple presynaptic volley evokes an all or none postsynaptic response after a short and fixed delay. On the other hand, in leg position learning this postsynaptic response is characterized by a train of spikes of variable duration; the onset of this discharge has a long and variable delay. It was concluded that these two types of learning represent two successive phases of memory storage.

W. Buño, Jr., and E. García Austt (Montevideo, Uruguay) reported on changes in acoustic nerve potentials and cochlear microphonics during acoustic habituation, distraction, and conditioning in awake free guinea pigs. These changes were thought to be mediated through the olivo-cochlear bundle, because all prereceptorial mechanisms were eliminated and no changes could be found in animals with sectioned olivo-cochlear bundles. Experiments were performed in guinea pigs with stimulation and section of the bundle. Responses were averaged with a CAT computer and simultaneous recordings of the acoustic nerve potentials and cochlear microphonics were made. Changes in both amplitudes during stimulation of the olivo-cochlear bundle were not only dependent on parameters of trains of electrical pulses, but also on intensity of acoustic stimulus and on the position of stimulating electrodes in the floor of the fourth ventricle.

M. Canessa-Fischer (Chile) presented evidence that the intracellular perfusion of giant axons of the Chilean squid renders the active transport of sodium inoperative, even though its bioelectric properties remain unaltered. The preparation offers the opportunity to investigate the metabolic pathways of the cell membrane which make it able to pump sodium against its electrochemical gradient in the resting state and after the conduction of nerve impulse. Enzymic studies with membrane fragments isolated from the sheath of squid axons indicated that the cation-activated-adenosine triphosphatase activity of these particles (transport-ATPase) was also markedly dependent on the nature of the anion. Parallel studies combining biochemical and physiological experimentation may lead to an understanding of the active transport of sodium across the nerve membrane.

J. M. Fuster (Los Angeles, California) reported on the electrical activity of single neurons of limbic brain regions as recorded with microelectrodes in the unanesthetized monkey. Characteristic changes in the frequency of cell discharges are induced in the amygdala and hippocampus by visual stimuli used by the animals as discriminanda in instrumental behavior for reward and in stress conditions. Autocorrelation analysis of spike discharge patterns reveals periodicities in the activity of some limbic neurons. Fuster also presented some results of a survey of intracellularly recorded activity in neurons of the lateral geniculate body and the striate cortex of the rabbit. Study of synaptic activity of these neurons in reactions to retinal stimulation emphasizes the importance of reciprocal inhibition at all levels of the visual pathway, probably an essential factor in central representation of contrast.

E. García Austt (Montevideo, Uruguay) described the electrical activity recorded from different brain structures in the albino rat while awake and during slow, paradoxical sleep. During alertness and paradoxical sleep a 6-per-second regular rhythm was observed in the caudal aspect of the neocortex and in many subcortical structures. Visual evoked responses recorded on the cortex were elicited by means of a microlamp fixed on the skull, and averaged with a CAT computer. Responses were similar during alertness and paradoxical sleep. However, in both circumstances they underwent progressive changes.

K. F. Killam (Palo Alto, California) presented data from experiments examining electroencephalographic correlates during the acquisition, stabilization, and

modification by drugs of two visual discrimination tasks in the cat. The cats were conditioned to obtain milk by pressing translucent panels upon which were projected identical geometric forms varying in total light flux or different geometric forms having the same light intensity. Changes were seen in evoked response patterns and the stability of estimates of time series derived from electroencephalograms during conditioning and under the effects of pharmacological agents. These findings were discussed in terms of the functional organization of the central nervous system. In addition, the role of computer technology in pharmacological research with special emphasis on neuropharmacology was discussed. Examples of actual research findings were demonstrated using a LINC computer.

J. V. Luco (Santiago, Chile) presented evidence of reinnervation of the smooth muscle of the nictitating membrane by the central root of the vagal nodose ganglion. The contraction during stimulation of the vagal trunk was abolished by small doses of atropine, potentiated by prostigmine, and unaffected by *d*-tubocurarine. From these observations it was concluded that the chemical transmitter of the afferent vagal fibers is probably acetylcholine. Luco also reported that the replacement of the normal adrenergic innervation by cholinergic reinnervation results in a significant increase of the specific cholinesterase in the smooth muscle of the nictitating membrane. He concluded that a given biochemical structure and its preservation in the postneural element is due to an influence played by the nervous system and that this influence is dependent on the biochemical features of the innervating neuron; in this case an adrenergic or a cholinergic nerve terminal. Another trophic effect was also discussed. Adrenergic reinnervation of striated muscle leads to significant decrease of the fibrillation due to previous denervation.

H. R. Maturana (Santiago, Chile) discussed a new way of treating the problem of color coding in the retina that he and his co-workers, Uribe and Frenck, have recently developed. This method indicates that the chromatic opponent characteristics of the receptive fields of the retinal ganglion cells do not characterize the spatial distribution of the visual stimulus but that, on the contrary, they are an intrinsic feature of the color-coding systems in which all geometric implications are suppressed. Accordingly, this feature makes impossible a unique correlation between the output of these cells and the visual stimulus, a condition which would apply particularly to midget ganglion cells. Maturana thinks that color cannot under any circumstance be coded in the output of any single ganglion cell, but that since the midget ganglion cells can be classed (anatomically) into three groups which differ in the chromatic preference of their central cone, color has to be coded in the relative activity of these three classes of cells. He showed how these relative activities can be deduced, and how the Grassman laws would be satisfied by such a system. He based his argument on the known anatomy and neurophysiology of the retina and on psychophysical experiments derived from the Land phenomenon.

Averaging techniques, using the LINC in data processing, in analysis of LGN cell discharges of the rat to patterned visual stimuli were discussed by V. Montero (Madison, Wisconsin). Two basically different groups of units were found. One group comprises those units whose responses to stationary stimuli were consistent with the responses to moving stimuli. In fact, the former responses allow one to predict the latter ones. Variations in spatial distribution within the receptive field of excitatory and inhibitory components, both to the "on" and "off" of the light, originate subtypes of units. In the concentric type of arrangement the periphery of the receptive field could be antagonistic and inhibitory to the center response; or a peripheral effect may be undetectable. A less frequent type of unit presents an elongated receptive field with opposing reactions to the light in each extreme. Another type reacts only with inhibition of spontaneous activity when light falls in the field. The second group comprises those cells to which the temporo-spatial sequence of the stimulus is an important factor. These units discharge briefly to the "on" and "off" of the light anywhere in the receptive field. The responses to a moving stimulus brighter or darker than the background are indistinguishable. These responses could be symmetrical to any direction of the movement or asymmetrical (directional units). In the last type of cells a facilitatory process was found to take place with the preferred direction of the stimulus, and conversely, an inhibitory one with the opposite direction.

S. M. Ornstein (St. Louis, Missouri) demonstrated a technique wherein the LINC computer is used to assist in mapping sensory response areas in the cortex. Evoked potentials of the auditory cortex of the cat were used for purposes of demonstration. However, the technique has also been used with human subjects during the course of neurosurgery to delineate areas of high response to external stimuli.

R. Piezzi (Mendoza, Argentina) discussed the nerve endings in the adrenal gland of the toad, *Bufo arenarum* Hensel. There is convincing morphological evidence of two types of synaptic nerve endings in the adrenal chromaffin tissue, which can be classified as adrenergic and cholinergic endings. There are special types of microtubules in the adrenal nerve endings. Most of them look similar to those described previously by other authors, but there is another type of microtubule which presents a central granular condensation about 30 Å in diameter. The microtubular content may be a structural component of the microtubule or it may be the morphological expression of endotubular flux of an electron dense material.

C. E. Rocha-Miranda (Rio de Janeiro, Brazil) spoke on the advantages of primitive mammals, for example, marsupials, for the study of the organization of the motor system. The talk was illustrated by his work on the common opossum (*D. aurita* and *D. virginiana*), comprising an analysis of the gamma loop in these animals, the distribution of lumbar and sacral dermatomes, a stereotaxic atlas of the diencephalon of the opossum, and the results of recordings at the dorsal thalamus and stimulation of motor cortex.

E. L. Rodríguez-Echandia (Mendoza, Argentina) presented an electron microscopic study of the cochlear innervation in the cat. The fine structural characteristics of the afferent and efferent nerve fibers, the recepto-neural junctions and the cochlear "neuro-neural synapses" were described. Evidence was presented of the existence of granulated vesicles (aminergic type of vesicles) in the cochlear efferents. This finding provides a morphological basis for the identification of afferent and efferent nerve fibers in the organ of Corti.

E. Rojas (Viña del Mar, Chile), who works with internally and externally perfused giant axons of squid and measures steady state membrane conductance by means of the voltage-clamp

procedure, presented evidence that the membrane conductance measured in the presence of potassium as the only internal and external cation is independent of ionic concentration from 550 m*M* to 100 m*M*, thus supporting the notion that the membrane has negative charges in the so-called potassium channel. Similar results were obtained with sodium as the only internal and external cation. The steady state conductance ratio, G_K to G_{Na}, was shown to be equal to 8 for concentrations of 550 m*M*.

J. E. Rose (Madison, Wisconsin) discussed the discharge characteristics of single auditory nerve fibers of the squirrel monkey. In a response to a tone of low frequency the discharges of a fiber are spaced at intervals which group around integral multiples of the period of the stimulating tone regardless of the frequency or intensity of an effective stimulus.

R. Santolaya (Mendoza, Argentina) examined the neurons in the gigantocellular nucleus of the medulla oblongata of the rat with electron microscopy. Three types of synaptic complexes were described: axodendritic, axosomatic and axoaxonic. Some axosomatic synapses exhibit the *en passant* modality. The amount and varieties of synapses in the neurons studied lead one to conclude that important temporospatial phenomena will occur in their mechanism of stimulation.

W. V. Slack (Madison, Wisconsin) discussed the use of the Laboratory Instrument Computer (LINC) to interview patients directly regarding their medical symptoms. A program dealing with the symptoms of allergy (presently being researched at the University of Wisconsin) was translated into Spanish and used to interview two patients from the University of Chile Hospitals. In addition, the use of the LINC to interview physicians directly regarding their findings on patient examination was described and demonstrated.

B. Weiss (Rochester, New York) gave two formal lectures and two sets of demonstrations devoted to the experimental analysis of behavior. The first lecture and set of demonstrations outlined the principles of behavior and their applications to investigations of the behavioral effects of drugs. The second lecture discussed the application of digital computers to the experimental analysis of behavior. The second set of demonstrations employed the LINC and an actual experiment with pigeons.

Its aim was to show how a computer might be programmed and interfaced for behavioral studies.

I. C. Whitfield (Birmingham, England) discussed the mechanisms in the auditory pathway concerned with the treatment of steady-state and time-dependent stimuli. The auditory cortex appears to be relatively unessential to the recognition of steady tones, whereas it is essential for the discrimination of temporal sound patterns. This is linked to the observation that in the cat, many neurones in the primary auditory cortex either do not respond to tonal stimuli at all, do so insecurely, or else respond indiscriminately to a very wide range of such stimuli. Many of these neurones respond, on the other hand, to changes of frequency and furthermore are responsive only when the change is in a particular direction.

Whitfield also discussed the effects of electrical stimulation of some centrifugal pathways in the auditory system on the thresholds of single neurones in the cochlear nucleus and described both increases and decreases in excitability produced by such stimulation. Some examples of the pharmacology of the centrifugal process were given in the form of a demonstration.

C. N. Woolsey (Madison, Wisconsin) presented new experimental data on the relations of the visual field to visual areas I and II of the cerebral cortex of the cat. This study extended the original work of Talbot and Marshall and of Talbot on the visual system of the cat by defining, for each cortical point examined in VI and VII, that portion of the visual field related to it. In general, cortical points related to central vision are activated from smaller field areas than points related to peripheral vision, and the fields for points in VII are larger than those for points in VI for the same parts of the visual field. The importance in single unit, visual cortical studies of considering where the cell is situated within the cortical localization pattern was emphasized.

C. N. Woolsey also read two lectures which had been prepared for delivery by E. V. Evarts (Bethesda, Maryland), who unfortunately was unable to attend. The first of these dealt with unit activity in the pyramidal tract during conditioned hand movement in the monkey. The second was concerned with the question of whether movements or muscles are represented in the cortex. The results of these studies on the activity of the pyramidal tract dur-

ing learned behavior gave an exciting view of what may be accomplished in the performing animal with the unit recording method.

In addition to the papers described above, the following presentations were made: H. Adrian and W. Lifschitz (Santiago), "Functional organization of the auditory system"; O. Gutiérrez (Santiago), "Chromatic information and retina"; M. Palestini (Santiago), "Neurophysiology of sleep"; Teresa Pinto (Santiago), "Cortical functions in instrumental learning"; and A. Rojas (Santiago), "Functional organization of the visual cortex of the rat."

An important aspect of the seminar was a course on the use of the LINC computer in biological research offered by J. E. Rose (Madison, Wisconsin) and demonstrations with a LINC which was taken to Chile for the seminar from Washington University, St. Louis (C. Molnar).

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Cancer Dissemination

The slow progress in clinical chemotherapy of malignancies, based largely on the lack of specificity of present drugs and the overlapping characteristics of tumor and normal tissues, prompted the convening of a meeting on cancer dissemination. It was felt that the invasiveness of tumor cells, leading to metastatic growth, might offer an opportunity for selective chemotherapy since this process does not occur with normal tissue. The meeting, held at the Istituto di Ricerche Farmacologiche "Mario Negri," Milan, Italy, 23 June 1967, was sponsored by the International Union against Cancer (UICC); Silvio Garattini, director of the "Istituto "Mario Negri" and chairman of the Committee on Experimental Chemotherapy of the UICC, was the organizer. A working party was attended by about 50 cancer scientists from 12 countries.

Under the topic of in vitro tests available for studying tumor cells, J. A. For-