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PATTERNS OF ORGANIZATION IN THE NERVOUS SYSTEM AND THEIR DEVELOPMENT: NOTES ON A SYMPOSIUM

John B. Bateman

European Research Office
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13. ABSTRACT
General impressions and report on selected papers in neurobiology. Based on the Sixth International Meeting of Neurobiologists held at St. Catherine's College, Oxford, 18 - 21 September 1972. Abstracts of papers and a list of participants are appended.

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PATTERNS OF ORGANIZATION IN THE NERVOUS SYSTEM AND THEIR DEVELOPMENT:

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CONTENTS

NOTES

The Sixth International Meeting of Neurobiologists

The International Meetings of Neurobiologists have been held approximately triennially starting at Groningen, The Netherlands in 1955. At the last meeting in Sandefjord, Norway, in accordance with custom, the venue of the 1972 meeting was selected and Professor C.G. Phillips, F.R.S. and Professor D. Whitteridge, F.R.S. of the University Laboratory of Physiology, Oxford, were asked to make plans and implement them. With the aid of an Organizing Committee of eight this was done, and the meeting duly took place at St. Catherine's College, Oxford.

Such a gathering of some 140 neurobiologists could only be brought about with considerable financial backing, acknowledged in the program reproduced here in Annex A, and including a grant from the European Research Office (number DA-ERO-591-72-G0017). In return for the ERO grant, the organizers will furnish a critical report of the proceedings which will be made available to interested U.S. Army neural scientists.

The international character of the meeting can be seen from the breakdown of nationalities represented, the names of the individual members being reproduced in Annex B:

Australia	2	Hungary	2
Belgium	2	Italy	4
Canada	1	Netherlands	4
Denmark	2	Norway	9
Finland	1	Sweden	9
France	6	Switzerland	3
Germany	4	UK (excluding 34 from Oxford)	39
Greece	1		
		USA	15

Total: 104 (138 including Oxford)

Since a technical report is forthcoming under the terms of the ERO grant, the present notes will be limited to generalities except for two topics which may be of special relevance to the Army program. The meeting was attended by the present writer because of the unavailability of a suitably qualified neurophysiologist from Walter Reed Army Institute of Research or Dr. Ralph Sonnenschein of ONRL.

Comment

One of the purposes of this series of international meetings is to expose to free discussion among experts different facets of neurobiology. In Stockholm in 1966, for example, the subject was "Inhibitory Neuronal Mechanisms;" in Norway in 1969,"Excitatory Synaptic Mechanisms;" and this year in Oxford, "Patterns of Organization in the Nervous System and their Development." In enlarging upon the 1972 title the organizers stated that

> "instead of concentrating on the properties of single cells and relatively simple networks, we shall try to see how we could advance our undertaking of the structure and function of the more elaborate neuronal organizations on which depend such higher abilities as stimulus generalization and pattern recognition, combination of simple movements into sequences of movements and skilled performances..., especially of the processes whereby the necessary neuronal connections are established during the growth and development of the individual."

A glance at the program (Annex A) will suggest that these aims were pursued by imposing deliberate limitations on subject matter: to a large extent the discussion of the establishment of necessary neuronal connections was confined to 13 papers on visual mechanisms and seven on afferent motor and somatosensory projection and processing in the cerebral cortex. At the peripheral end, four had to do with nerve-muscle interactions; and several dealt with synaptic development within the cortex in its functional and architectonic aspects.

The meeting went off very well, with much lively discussion dominated and illuminated by the comments of Sir John Eccles, a genial spirit - in both the insular and the continental senses of the word - who in his informal attire put one in mind of a sort of scientific Picasso. All the same, if there were any new points of view of general significance, they were hard to discern among the mass of experimental details.

It would have been desirable to devote a final session to generalities, real or imagined, or, lacking either, to relate the various contributions to each other within some sort of conceptual framework. Time was in fact reserved for a general discussion but it permitted only very brief summary and prognostic statements: Creuzfeldt and Whitteridge on visual pathways, Mountcastle on synaptic pathways - scholarly, witty and systematic in their respective styles, but failing either to reveal a large elegant structure on the one hand or to confine the diverse materials within a nutshell on the other.

The formal papers and some of the remarks made left me with one or two lay impressions concerning the present state of affairs:

(1) Electrical transmission in the cerebral cortex: Never actually demonstrated; but Eccles remarked that we are committed to the idea that all communication in the central nervous system is by nerve impulse, adding poetically that we must listen as the nerve cells speak their language. The words are said in the midst of loud noise, and the message can only be delivered if there are many lines in parallel: Eccles questions the existence of inoperative synapses. MacKay of the University of Keele said that if detection of coincidences is necessary, as multiple pathways would seem to imply, the number of synapses should be proportional to the square of the number of neurones. These considerations might be expected to lead away from the prevalent emphasis on evoked potentials following sensori-motor stimuli. More intimate microphysiological studies of the cortex are needed in order to understand the intrinsic nature of cortical activity and to define - as V.B. Mountcastle of Johns Hopkins expressed it - the cortical "operon" that responds to an input.

(2) Cortical involvement in "simple" processes: Mountcastle remarked upon the demonstrated activity of the entire nervous system during training for simple tasks. As a relief from evoked potentials and ultrastructure, the meeting was given a simple demonstration, with human subjects, of the access of muscle afferents to consciousness. The sensations accompanying reflex flexion of the arm brought about by 100 Hz vibration of the biceps were registered by instructing the blindfolded subject to "track" the movement by flexing or extending the other arm. The tracking arm failed to follow the vibrated arm, with an error of

10 - 40 degrees in the elbow angle. The observation is compatible with the opinion that vibratory excitation of spindle primary endings produces a stretch reflex; the evidence provided by the tracking arm shows that the subject felt that the biceps had been stretched. Indeed, when the reflex flexion was prevented mechanically, the tracking arm was extended.

In the second demonstration, with Professor G.S. Brindley very appropriately serving as subject, the whole hand was paralysed anoxically by occluding the circulation at the wrist with a sphygmomanometer cuff. Brindley, who with P.A. Merton has doubted the role of muscle afferents in kinesthesia, was able to detect passive movements of the fingers. The sensation could arise only from the muscles attached to the finger joints, which are situated in the forearm above the occlusion.

(3) Role of excitation and experience in development and regeneration: The long recognized importance of excitation in establishing correct functional relationships (cf. ref. 1) was stressed in several papers, both in connection with the innervation of muscle (v. infra) and in the development of binocular vision; the latter has important practical implications, as D. Whitteridge said, in the common treatment of squint and other visual defects by prolonged occlusion. To be sure, these are not new ideas, but they often entered into the discussion and some new experimental evidence was presented.

(4) Chemical mechanisms and techniques: Given the strongly electrophysiological orientation of the meeting, it is not surprising that while the evident importance of chemical recognition of a neural target by a developing neurone (cf. ref. 2) received frequent lip service, there were no contributions to an understanding of a kind of chemical specificity quite as extraordinary, in its way, as that of the immune reaction. There was in fact one paper (v. infra) in which modern physicochemical techniques were essential to the investigation. There was another in which the migration of injected radioactive aminoacids was used in tracing the development of neuronal pathways and in identifying the target area in the amphibian retino-tectal connection, but this did nothing to illuminate the chemical nature of the target-directed tropism. It was also clear that a chemical mediator must be involved in confining the sensitivity of the muscle fiber to acetyl choline to the end plate region, a condition that changes to one of disseminated

hypersensitivity upon denervation. Chemicals must enable the growing nerve fiber to recognize the correct muscle, or must inhibit innervation of the wrong muscle, as well as playing some part in determining the physiological performance characteristics of the innervated muscle. Yet, strangely, there was neither experimental evidence nor informed speculation as to the nature of these substances. The nerve growth factor was totally ignored, as was the work of Hydèn - critically reviewed some years ago by one of the participants, S.W. Kuffler - and the well-known experiments of Kerkut on centripetal axonal transport of small molecules.

Trophic Interactions of Nerve and Muscle

Presenting work done in part in Katz's laboratory (1) and later in his own laboratory in Oslo, Lømo showed that development of hypersensitivity in single fibers of the rat soleus muscle can be prevented by direct stimulation for several days. A second consequence of stimulation is that the fiber acquires contractile properties characteristic of one innervated by a fast nerve. Lømo also reported success in obtaining a doubly innervated fiber. This was done by transplanting the fibular nerve on to the soleus muscle and then placing anaesthetic "cuffs" around the sciatic, rendering it silent though still intact.

Vrbová similarly had adopted the hypothesis that denervation hypersensitivity is due to inactivity. In a short paper (4) she had tested it by examining hypersensitivity in neonatal rats prior to the development of end-plates, arguing that these muscles should not fibrillate and so should develop enhanced denervation hypersensitivity. This was found to be the case for the excised denervated soleus muscle when compared to that of an adult animal. In the same paper the results were described of bilaterally denervating rat soleus muscles, stimulating one side, and then comparing sensitivities to acetyl choline after excision. The stimulated muscles were much less sensitive than the others.

A rather surprising insight into a possible mechanism of denervation hypersensitivity was provided by autoradiographic observations which showed that cell division, accompanied by phagocytic invasion, occurred in the denervated muscle. Cytotoxic drugs which inhibit cell division brought the ACh sensitivity back to normal values. Vrbová speculated that the phagocytes increase the accessibility of the fiber membrane to ACh.

The third paper in this area was that of R.F. Mark, adequately summarized in the abstract (Annex A). The points made there were illustrated and supported by experiments in which nerves to extensor and flexor muscles were switched and the tendons reversed. It was also shown that in the salamander limb (the muscle fibers of which have polyneuronal innervation) the spinal nerve territories of the limb were unaltered by reinnervation - a fact explained by a scheme of competitive synaptic repression inaugurated by recognition between neurone and target site and emission of an appropriate signal.

These papers were of special interest to our office in connection with recent work on the neural control of muscle regeneration, a proposal for further investigation in Buller's laboratory at Bristol being currently under consideration.

Neuroglial Involvement in Synaptic Remodelling

The interest of W.E. Watson's paper lay, for me, largely in the fact that alone among the speakers at the symposium he uses very modern physical techniques for examination of single cells isolated from the brain after various physiological and physicochemical manipulations of the nervous system. These methods included determination of cell dry mass by interference microscopy, nuclear and nucleolar nucleic acid by ultraviolet absorption microspectrography, and metabolic activity by radiouridine uptake.

In his early published work between 1965 and 1969 Watson (5-8; cf. Prestige, ref. 10) had demonstrated the retrograde movement of radioactivity associated with labelled aminoacids along a muscle nerve in the rat. He had also shown that hypoglossal axotomy or neuromuscular blockade produced by botulinum toxin caused transient increases in the total and the nucleolar nucleic acid content of neurones isolated from the hypoglossal nucleus. Similar changes of nucleic acid content were produced when the hypoglossal nerve, implanted "passively" in the ipsilateral sternomastoid muscle with intact innervation, was "activated" by cutting the spinal accessory nerve. Thus transfer of information, presumably by a chemical messenger, seemed established. Other experiments (9) demonstrated that the dendritic tree of hypoglossal neurones in the rat medulla retracts following hypoglossal nerve transection or injection of botulinum toxin.

Watson's more recent work, published in part in the form of abstracts (11-14) and presented at Oxford, shows that information about presynaptic or postsynaptic events is passed also to the cells of the neuroglia, thus bringing new insight to the vexed question of neuroglial function. For example, increase of the ambient potassium concentration by ventricular perfusion leads to a transient increase of the dry mass and nucleolar RNA of astrocytes, as determined by isolation of single cells. On the other hand, ependymal cells, in these and later experiments, remained unchanged. More striking results followed other stresses such as prolonged dehydration of the animal, axotomy, botulinum toxin, and "activation" of the transplanted hypoglossal nerve in the manner already described. These changes take the form of what Watson calls, in axonological terminology, a "biphasic" increase of astrocytic dry mass and nucleolar RNA - meaning two successive transient increases, with normal values intervening. The first hump is attributed to changes in the noradrenergic presynaptic boutons, and the second to re-expansion of the retracted dendritic tree. The same sequence of events was seen in cells prepared from the paraventricular nucleus after injection of 6-hydroxydopamine into the left lateral ventricle.

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ANNEX A

SIXTH INTERNATIONAL MEETING
OF NEUROBIOLOGISTS

Patterns of Organization in the Nervous System
and Their Development

St. Catherine s College, Oxford

18-21 September 1972

ORGANIZING COMMITTEE

G. Gordon
C.G. Phillips
T.P.S. Powell
D. Whitteridge

University Laboratory of Physiology
Parks Road, Oxford, OX1 3PT
England

Monday 18 September 1972

9.15 a.m. INTRODUCTION: D. Whitteridge

9.30 a.m. SESSION I (Chairman: R. Granit) Stockholm

The nature of the nervous control of some muscle properties

T. Lømo ✓ Oslo, Inst. of Neurophysiol

A number of properties of mammalian skeletal muscles may be influenced by experimental procedures such as denervation, cross-innervation, tenotomy, immobilization and electrical stimulation of the muscle. Properties susceptible to one or more of these procedures include contraction speed, chemosensitivity, enzyme activity and the inability of the normal muscle to accept innervation by a foreign nerve. The mechanisms behind these changes are not clear. They may be related to variations in nerve or muscle activity or to some influence of the nerve independent of impulse activity.

Recent findings indicate that in the rat the control of ACh sensitivity depends on muscle activity since supersensitivity in the denervated muscle can be prevented by direct stimulation of the muscle (Lømo & Rosenthal, 1972). Current work is aimed at investigating whether muscle activity is the determining factor in the control of other properties of the muscle.

Reference: Lømo T. & Rosenthal Jean (1972) J. Physiol. 221, 493-513.

Distribution of chemosensitivity along the muscle fibre and its control

G. Vrbová ✓ Birmingham

In adult mammalian muscle fibres only a small area is sensitive to the transmitter. This region is in close proximity to the motor nerve terminals. In newborn animals this area is relatively insensitive to depolarising drugs and gradually the high sensitivity of the adult endplate develops. When the motor nerve was crushed in newborn kittens the high sensitivity of this area failed to develop. Activity of the motor nerve in adult animals increased the chemosensitivity of the synaptic area, whereas inactivity reduced it. It is suggested that the nerve terminal, or its Schwann cell, releases a chemical that induces and maintains the high chemosensitivity of the postsynaptic membrane.

wrong Ach

It was also found that the inherent chemosensitivity of the muscle fibre outside the endplate region, apparent in newborn animals and in denervated muscles, can be suppressed by direct electrical stimulation. Thus in a normal muscle, chemosensitivity is being reduced by the activity of the muscle itself, while the nerve terminal maintains the synaptic area chemosensitive.

Recognition and repression of regenerating nerve terminals by striated muscle

R.F. Mark ✓ Clayton

Regeneration of mixed motor nerves to fish fin or eye muscles or to salamander limbs may restore good co-ordinated movement to a mechanically complicated muscular system. The mechanism in each case is the same. Muscles become functionally reinnervated by the correct set of motoneurones but the anatomical innervation may not give this appearance at all. Foreign nerve fibres may form terminals in muscles but synaptic transmission is blocked by a competitive process depending upon the presence of terminals from the original, developmentally correct, nerve in the muscle. Repressed foreign synapses appear ultrastructurally normal and are retained for many months. Thus whether or not a muscle will accept innervation and permit transmission depends upon a trophic interaction between the muscle and the applicant nerve terminal. The nature of the interaction differs according to whether or not the muscle is already in possession of a well matched innervation.

Limb movements in salamanders: myotypical modulation or selective neuromuscular connections

G. Székely ✓ Pers

In salamanders the majority of limb muscles receive innervation from each of the three limb-moving segments of the spinal cord. Simultaneous recordings from 8 limb muscles of freely moving salamanders disclose extensive overlaps in the activity of antagonistic muscle groups, and this pattern of activity is maintained after complete deafferentation of the limb. Muscle activity recorded from limbs innervated by a single segment or part of a segment indicate that each arbitrary small part of the limb-moving section of the spinal cord delivers a rhythmic output to the limb. Myograms recorded from synchronously moving normal and grafted limbs showed that the homologous pairs of muscles did not contract simultaneously, and neuromuscular reconnections were not selectively made in the grafted limb.

2.30 p.m. SESSION II (Chairman: S.W. Kuffler) Boston

Some associated changes in nerve cells and glia

W.E. Watson ✓ R

Hypertrophy and hyperplasia of astrocytes measured quantitatively accompany changes of synaptic connection in the brain of the adult rat, whether caused by primary presynaptic or postsynaptic events. The changes accompany loss and restoration of synaptic contact. Similar increases are found around neurons during enhanced natural stimulation: they do not correlate with the metabolic changes in the postsynaptic neuron so far measured.

Hyperplasia of oligodendroglia near nerve cells accompanies dendritic growth, and the formation of new synapses in the brain of the adult rat. These changes will be counted in relation to the possible involvement of glia in synaptic remodelling.

Ultrastructural evidence for reinnervation of deafferented postsynaptic sites in the brain of the adult rat

G. Raisman ✓ (

A quantitative analysis of synapses in the neuropil of the septal nuclei in the adult rat shows that the various types of synapses are present in constant proportions in the normal animal. A sequential analysis of the changes at intervals for the first few months after complete destruction of specific afferent pathways such as the fimbria shows that deafferented postsynaptic sites are reinnervated. Although the synapses formed by this process are of an abnormal type, the reaction follows a rigidly determined pattern. It results in a remarkably precise restoration of the proportions of the various synaptic types present in the intact animal.

Physiological and anatomical factors determining the ~~receptive field of single~~ cells

P.D. Wall ✓ L

The receptive field of any cell must depend on both the anatomy of fibres ending on the cell and on the physiological consequences of activity in those fibres. Examples will be described of spinal cord cells whose receptive fields show the nature of this interaction. In particular it will be shown that certain types of afferent ending are extremely ineffective in influencing the cell following natural stimuli, while others affect the cell with a very high safety factor.

Specificity of connections within the retino-tectal system and in the hippocampal formation

W.M. Cowan

St. Louis

Recent studies of the development of the retino-tectal projection in the chick indicate that the retina becomes axially polarized during the second day of incubation and that the retino-topic projection on the tectum cannot be determined simply by the temporal sequence in which the retinal fibres enter the tectum, but rather by some chemo-affinity mechanism of the type first suggested by Sperry. Temporal factors may, however, be critical in determining the final distribution of synaptic sites between competing groups of afferent fibres, as recent autoradiographic studies of the commissural and association connections of the hippocampus have shown. Thus, the formation of specific patterns of connections may depend on two distinct mechanisms: a matching of chemospecificities between the afferent fibres and their target neurons and, in the case of fibres which share the same chemospecific markers, by the time of arrival of fibres at their target sites.

Tuesday 19 September 1972

9.15 a.m. SESSION III (Chairman: D. Whitteridge) Oxford

The development of the retinotectal projection in Xenopus and its relationship to the mode of growth of the retina and the tectum

R.M. Gaze

London

The retina in Xenopus grows concentrically by adding rings of cells at the ciliary margins. This process involves all three retinal layers and continues until after metamorphosis. The tectum, on the other hand, does not grow concentrically; it grows from front to back and from lateral to medial. During larval life retinal fibres establish an ordered projection across the 'tectum' from as early as stage 43-44. Thereafter the retina, the tectum and the retinotectal projection all grow while maintaining the general retinotopic organization of the map.

Consideration of the mode of growth of the retina and of the tectum and correlation of these with the mode of spread of the electro-physiologically-mapped retinotectal projection during development, leads us to believe that the growth of this system involves a continuous shift of retinotectal relationships at the level of the individual fibres and cells, while preserving the overall order of the whole projection.

The formation of central visual connections in amphibia

M.J. Keating

London

The integration of information from binocular visual space requires the convergence of information from the two eyes at common neural areas. In anuran amphibia this is achieved by commissural fibres linking selectively the direct monocular inputs from the binocular field to the two optic tecta. The role of visual function and particularly that of binocular visual function in the development and maintenance of these connections will be discussed. The susceptibility of the nervous system to disruption of normal binocular function is related to the developmental stage. Parallels between the development of the amphibian and mammalian binocular visual systems will be considered.

Development of synapses in cerebral cortex

B. Cragg

Clayton

Synapses have been counted on full depth scans of visual cortex during the period of their formation. The depth distributions change with age. Counts of cell bodies allow the average number of synapses associated with one neurone to be calculated. The rise in this number, and also the times of appearance of some of the extrinsic connections of visual cortex, can be correlated with aspects of maturing visual function.

Development of spinal sensory pathways in the kitten

S.A. Anderson

Surface potentials evoked in the cerebral cortex via different parts of the spinal cord have been studied in kittens at various ages, 1-120 days, after lesions of the cord at C3-C5. Electrical and tactile stimulation of the skin evoked prominent cortical potentials via at least three different spinal pathways. In addition to the dorsal column and the spino-cervico-lemniscal pathways activated from ipsilateral spinal afferents another pathway was found to ascend in the ventral quadrant. This pathway was excited by contralateral spinal afferents. Large cortical surface potentials were also elicited by tactile stimulation of the skin after a hemisection contralateral to the stimulus and a transection of the dorsal column and the dorsal part of the lateral funiculus on the stimulated side. This finding may indicate the existence of a fourth tactile pathway located laterally in the cord. The size of the surface potentials evoked via this pathway and via the ventral pathway diminished with increasing age of the animal.

2.30 p.m. SESSION IV (Chairman: D. Albe-Fessard)

Effects of deprivation on the development of the cat visual cortex

T.N. Wiesel

We reported a few years ago that the highly specialized neurons in the cat's visual cortex can establish their proper connections even in the absence of normal visual experience. This finding has been questioned by Barlow and Pettigrew after a 'more careful' look at cortical neurons in normal and deprived kittens at various stages of development. We therefore decided to re-examine the problem. Our main findings were in agreement with previous results; the visual cortex of visually inexperienced animals contained cells specific in their response to oriented stationary or moving lines, to the direction of movement and to binocular stimuli. Furthermore, cells responding to the same orientation were grouped together in a columnar fashion just as in the normal adult cat. Before the age of 4 weeks both normal and binocularly deprived kittens also had cells with no clear orientation specificity. The presence of such non-specific cells in older deprived animals could be a reflection of either an arrest in the maturation or a degenerative process.

Experience-dependent development of binocular specificity in the geniculo-striate system of the kitten

H.B. Barlow & J. Pettigrew

Single neurones were studied in the primary visual cortex of young kittens during the period defined by Hubel and Wiesel to be critical for the "disruption of cortical connections". Response curves for the orientation and binocular disparity of moving targets were sharply tuned only when the kitten had had patterned visual experience. In a number of cases, a single isolated neurone studied for a period of hours revealed changes in response specificity which were similar to the changes known to occur in the neural population as a result of visual experience during the critical period. By appropriate stimulation we have produced changes in the ocular dominance of a single cell, or in its preferred stimulus orientation or binocular disparity.

Strategies of adaptive modification in the kitten's visual cortex

C. Blakemore

Genetic information cannot specify completely the coding properties of every sensory neurone, although it may provide strong predispositions in their development. The environment certainly lends a hand in shaping the response characteristics of cells in the cat's visual cortex.

The degree of binocularity is altered by monocular deprivation or squint; orientational preference is modified by selective visual experience. A very short period of monocular eye closure or exposure to only one orientation, during a "critical period" of 4-12 weeks, leads to a loss of binocular cells or changes in their preferred orientations to match the environment.

It will be argued that these fast environmental modifications are adaptive since the loss of binocularity can preclude the establishment of conflicting retinotopic maps from the two eyes and the changes in orientation selectivity ensure that these sensory neurones are optimally matched to environmental features.

The organization of visual cortex in the Siamese cat

D.H. Hubel

In the Siamese cat a group of optic nerve fibres from the temporal retina cross in the chiasm, and terminate in the part of the lateral geniculate (in layer A_1) that the corresponding fibres from the ipsilateral eye would normally have occupied. Each hemisphere thus receives an abnormal input from parts of the ipsilateral field of vision. Our object was to determine the fate of this projection when it reaches the visual cortex. Recordings show that a region of cortex on either side of the 17-18 border is given over to a systematic double representation of about 20° of the ipsilateral visual field. In addition, some geniculate cells receiving abnormal input project to the cortex together with axons of cells in the layers directly above and below, just as occurs in normal cats. In the cortex the result is a bizarre mixture of cells, some driven from one visual field, some from the othe , and even occasional cells influenced from two entirely sepa ate regions in the two half fields. Presumably in normal cats there is a tendency for axons of neighbouring geniculate cells in adjacent layers to travel together, and also a tendency for an orderly cortical topographical representation. Normally these mechanisms do not compete, but in the Siamese cat they are brought into conflict.

Wednesday 20 September 1972

9.15 a.m. SESSION V (Chairman: L. Weiskrantz)

The organization of monkey visual cortical areas

S.M. Zeki

Judged by behavioural and psychophysical studies, the rhesus monkey possesses a highly developed visual system. Correspondingly, the amount of neocortex devoted to vision is very large and reveals several subdivisions and an elaborate organization in terms of both ipsilateral and interhemispheric connections. The visual fields are represented over and over again in these areas. Some of them, such as areas 17, 18 and 19 show a more detailed topography than others such as the fourth visual areas, the posterior bank of the superior temporal sulcus and the subdivisions of the inferior temporal cortex where the topography appears to be much blurred. All have complex interhemispheric connections with some differences in laminar distribution. Electrophysiological studies reveal that this elaborately organized cortex does, in the monkey, what the much more simply organized subcortical centres do in other species such as the frog, rabbit and squirrel. But it does it in a more versatile and sophisticated manner because of its very great wealth in cells, which allow a larger number of different and alternative interconnections.

Connections and functions of non-striate visual areas in primates

A. Cowey

The visual field is represented topographically in striate cortex (V.I), the central 8 degrees appearing on the lateral surface. Cells in this region project in topographic form to two further visual areas (V.II and V.III), which are largely hidden in the posterior bank of the lunate sulcus and the superior bank of the inferior occipital sulcus. V.I also projects in a much less clearly topographic form to the inferior bank of the superior temporal sulcus. From V.II and V.III there are projections to the pre-lunate and inferior occipital gyri, and from there to the inferotemporal cortex where all topographic relations cease. These anatomical findings will be related to the behavioural effects of removing each of these areas, and to electrophysiological studies of single neurones in non-striate visual areas. The non-striate regions are also compared in rhesus and squirrel monkeys.

Stimulus specificities and receptive field organization of simple striate neurons

P.O. Bishop, B. Dreher & G.H. Henry

The receptive field organization of simple striate neurons can be conceived in terms of excitatory and inhibitory subregions. Excitation is always stimulus specific but inhibition is non stimulus specific. Excitatory subregions always have mixed excitatory and inhibitory properties depending upon the stimulus complex but inhibitory subregions may respond inhibitorily whatever the stimulus. Though the basic stimulus parameter is a change in light intensity, for excitation to occur the change must have specific spatial and temporal characteristics: certain subregions must be stimulated simultaneously (spatial summation) and, for maximal discharge, the regions of spatial summation must be stimulated in the correct sequence (ordinal stimulation). Spatial summation underlies orientation specificity and ordinal stimulation provides the basis for the two motion selectivities, namely radial and direction selectivity. Radial selectivity refers to motion along a particular line through the discharge centre of the receptive field and direction selectivity to the two possible motions along this line.

The centrifugal pathway running to the pigeon retina

A.L. Holden

Single unit records were taken from the isthmo-optic nucleus of the pigeon. Centrifugal cells have small receptive fields, and respond briskly to small spot stimulation and to moving stimuli. A regular topographical organization is found within the nucleus, fully confirming the anatomical study of McGill, Powell & Cowan (1966) J.Anat. 100 5-33.

Centrifugal control of the avian retina

F.A. Miles

Visual properties of cells in the retina and isthmo-optic nucleus (ION) were studied after excluding any centrifugal influence by severing the isthmo-optic tract (IOT). Electrical stimulation of IOT could enhance retinal responses, usually by suppressing inhibitory mechanisms, more rarely by facilitating excitatory ones. Reversible cold block of IOT had no clear-cut effects on the visual responses of either retinal or centrifugal neurones to a variety of moving stimuli; however, the customary weak retinal firing to large spots of light turned on in the receptive field was augmented after the recent passage of a dark edge moving forwards through the visual field (– a stimulus known to activate most centrifugal neurones), an effect abolished by cooling IOT. It is suggested that this centrifugal effect may aid the bird's normal visual search in shadowed areas; further support for this idea comes from behavioural observations on birds with lesions of ION.

Thursday 21 September 1972

9.15 a.m. SESSION VI (Chairman: V.B. Mountcastle)

Organization of connections in the sensory and motor areas of the neocortex

T.P.S. Powell

Recent observations on the ultrastructure of normal material of the sensory and motor areas of the neocortex will be summarized to provide a basis for considering the results of light and electron microscopic studies of experimental material. The differential termination in these areas of afferent fibres from other cortical and subcortical sites will be described, together with the results of an experimental investigation of the intracortical connections of the visual cortex in which the laminar origin, course and termination of certain of these connections has been determined. There are marked similarities between the areas studied, both in their structure and in the details of termination of the different afferent pathways. These findings will be correlated with those made in studies of cytoarchitecture, on Golgi-impregnated material and in electrophysiological experiments. Certain conjectures will be examined about the number and type of neurons which may form a basic unit of organization at many levels of the sensory pathways, of the presence of a columnar organization in subcortical as well as cortical structures, and of the distribution of laminated structures.

Organization of the muscle afferent input to the cerebral cortex examined with natural stimulation

I. Rosén

The functional organization of the cuneo-thalamo-cortical projection of forelimb muscle afferents in cat will be reviewed in the light of recent experiments with natural stimulation of muscle receptors.

1. Collaterals of primary and secondary muscle spindle afferents and of tendon organ afferents ascend in the dorsal funiculus to the level of the dorsal column nuclei.

2. Three groups of cuneo-cerebellar neurones were identified, each activated by one of these three types of afferents. Cuneo-thalamic relay cells, however, received their input only from muscle spindle afferents.

3. Complex patterns of inhibitory and excitatory convergence were encountered among the group I activated cuneo-cerebellar neurones. The group I activated cuneo-thalamic neurones received only excitatory input from usually one muscle.

4. With natural stimulation in awake cats group I activated cells in cortical area 3a showed a higher degree of spatial specificity than could be anticipated from results of nerve stimulation.

The role of muscle afferents in the afferent projection to the motor cortex will be discussed.

The organization of the low threshold afferent input from joints and from the skin of the hind limb to the postsigmoid gyrus of the cat's cerebral cortex

F.J. Clark, S. Landgren & H. Silfvenius

The cerebral cortex cytoarchitectonically defined as area 3 is characterized by the reception of fast afferent paths from large muscle spindle afferents and it has been assumed to play a role in motor control. The present report contributes further information concerning the input from low threshold joint and low threshold cutaneous afferents to areas 1-3 of the cat's cerebral cortex. Chloralose anaesthesia and graded electrical stimulation of dissected contralateral elbow, knee joint, cutaneous, and muscle nerves was used. Afferent volleys were monitored and cortical evoked potentials were recorded from the postsigmoid gyrus. Low threshold joint and cutaneous afferents projected to two separate sets of loci: one in area 3 overlapping the projections from muscle afferents, and one further caudally in or close to area 1 and 2. Systematic spinal transsections were used to reveal the course of the afferent path to the cortical loci.

A ventral spinal pathway projecting to the first somatosensory area of the monkey

U. Norrsell

After transection of the dorsal funiculi somatotopically distributed short latency potentials can still be evoked in the first somatosensory area from below the level of the lesion in the monkey as in the carnivora. Surface evoked potential experiments have indicated, however, that in the monkey, in contrast to the carnivora the major spinal pathway responsible for this residual projection is one located in the ventral quadrant contralateral to the efferent input. Microelectrode experiments have shown that units in the post central gyrus can be activated by light tactile stimuli from below a dorsal hemisection of the spinal cord made at the C_4 level.

Some aspects of information processing in somatic sensory cortex

G. Werner

The response of individual neurons within somatic sensory area I of unanesthetized macaques to moving tactile stimuli was recorded with extracellular microelectrodes. The data indicate that the pyramidal cell population of this cortical area contains neurons which generate different firing patterns in response to stimuli moving across their cutaneous receptive fields in different directions. This class of neurons for which cutaneous stimulus movement is a "trigger feature" is preferentially located in lamina III, where it constitutes 50% of the neurons examined, and to a lesser extent also in lamina V.

Directionally selective responses were not displayed by first order afferents supplying the low threshold mechanoreceptors in the hairy skin, nor did the majority of neurons in lamina IV exhibit directional response preferences. The close proximity of these latter neurons to the specific thalamocortical input suggests that directional selectivity of neurons above and below lamina IV results from intracortical synaptic interactions.

Arguments will be presented to support the idea that stimulus feature detection by somatosensory cortical neurons, as well as the laminar differences in their spontaneous activity, can be attributed to a re-grouping of afferent terminations in the transition from lamina IV to more superficial and deeper cortical laminae. This is thought to enable the replication of certain arrays of peripheral sensory units in the form of the sequential ordering of synaptic terminations along the pyramidal cell dendrites.

2.30 p.m. SESSION VII (Chairman: J.C. Eccles)

The organization of the descending pathways and the visual control of different classes of movements in the monkey

H. G. J. M. Kuypers

The organization of the descending pathways in monkeys (Lawrence & Kuypers, 1968) will be reviewed. These findings combined with the distribution of cortical fibres in brain stem (Kuypers & Lawrence, 1968) and spinal cord (Kuypers, 1962) suggest that each hemisphere controls individual arm, hand and finger movements contralaterally but mainly proximal and complex arm movements ipsilaterally. This is supported by findings in eight split-brain monkeys (Brinkman & Kuypers, Science, 1972) which findings will be discussed. In order to begin to clarify the role of the cortico-cortical connections (Kuypers et al, Exp. Neurol., 1965) in visual guidance of movements, in four rhesus monkeys (Haaxma & Kuypers, in press) one occipital lobe was removed. These animals could visually steer individual arm, hand and finger movements bilaterally. However, after additional transection of the telencephalic, thalamic and collicular commissures, visual steering of individual hand and finger movements contralateral to the lobectomy was severely impaired. With film.

The origin of the cortical projections to the dorsal column nuclei of the cat

G. Gordon

Muscle afferents and kinesthesia

G.M. Goodwin, P.B.C. Matthews & D.I. McCloskey

For the last decade muscle afferents have usually been considered to be denied access to consciousness. Recent experiments contradicting this view will be described, and in part, demonstrated. This raises the problem as to how fusimotor induced discharges in spindle firing are prevented from being interpreted by the sensorium as due to muscle stretch. The major findings have already been briefly published (Goodwin, McCloskey & Matthews, 1972a, b).

References: Goodwin, G.M., McCloskey, D.I. & Matthews, P.B.C. (1972a); Science, N.Y. 175, 1382-1384. (1972b); Brain Res. 37, 326-329.

Cortico-cortical connections between areas 3a and 4 in the baboon

P. Andersen & C.G. Phillips

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