COMPARATIVE NEUROCHEMISTRY

Edited by D. RICHTER

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Proceedings of the Fifth International Neurochemical Symposium

Edited by

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PREFACE

AT the time when the International Neurochemical Symposia were started there were few books on the subject, and one of the main aims of the Organizing Committee was therefore to produce a small series of books on aspects of neurochemistry which had not previously been adequately reviewed. The Symposia held at Oxford (1954), Aarhus (1956), Strasbourg (1958) and Varenna (1960) led to the publication of four books entitled: *Biochemistry of the Developing Nervous System* (*Ed.* H. WAELSCH); *Metabolism of the Nervous System* (*Ed.* D. RICHTER); *Chemical Pathology of the Nervous System* (*Ed.* J. FOLCH-PI); and *Regional Neurochemistry* (*Ed.* S. S. KETY and J. ELKES).

The subject of the Fifth Symposium held at St. Wolfgang, Austria, in 1962, was *Comparative Neurochemistry*, which deals with variation in neurochemical mechanisms in different animal species. There have been a number of observations on differences in chemical composition and enzyme distribution in different species, and there are some striking species differences in the actions of drugs; but little attempt has hitherto been made to integrate the data derived from comparative studies in different disciplines, or to assess their significance in relation to our understanding of nervous mechanisms in the higher animals, including man. Comparative neurochemistry was chosen by the Organizing Committee as the topic for the Fifth Symposium for this reason, and also because it appears to be one of the most promising growing points in neurochemistry at the present time.

As in the previous Symposia, the participants were limited to a relatively small group of active investigators, with research workers from a number of different fields including this time a number of zoologists. In the invitation of participants consideration was also given to the growing importance of comparative neurochemistry in relation to pharmacological and pesticide research. The meetings at St. Wolfgang were characterized once again by lively interdisciplinary discussion, some of which is reflected in the chapters of this book.

It is a pleasure to thank our hosts, and particularly Herr MATTHIAS HÖDLMOSER, Mayor of St. Wolfgang and Landtagspräsident of Oberösterreich, for their generous hospitality. We are indebted also to our Austrian colleagues, Professor F. BRÜCKE and Dr. H. LECHNER, for the local administrative arrangements which contributed so greatly to the success of the meeting.

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FIFTH INTERNATIONAL NEUROCHEMICAL SYMPOSIUM

ST. WOLFGANG, AUSTRIA, 1962

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SECTION I

FUNCTIONAL ORGANIZATION IN DIFFERENT SPECIES

THE INTER-RELATION OF SECRETORY AND NERVOUS FUNCTION IN THE CENTRAL NERVOUS SYSTEM OF LOWER ANIMALS

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DURING the past decade evidence has accumulated indicating that, in addition to the role of coordination of response by connecting receptors with effectors, parts of the central nervous system serve an endocrine function by producing and releasing into the blood stream a number of different hormones concerned with development, water balance, colour change and other activities (HELLER and CLARK, 1962). These findings must be of especial interest to neurochemists, for they demonstrate a greater chemical heterogeneity of the central nervous system than had hitherto been supposed.

It is now customary to employ the term neurosecretion to denote a particular function of the central nervous system which is carried out by nerve cells which possess features associated with glandular activity in addition to ordinary neuronal characteristics (BERN, 1962). DE ROBERTIS (1962) and others have suggested, however, that care should be taken in the assessment of neurosecretory function by structural criteria alone. For instance, HAGADORN and NISHIOKA (1961) have shown that approximately 5 per cent of the neurons of the leech brain can be classified as neurosecretory by ordinary staining reactions; however, with the electron microscope no neuron has yet been encountered in the leech which is completely devoid of granules that resemble the elementary neurosecretory inclusions found in known neurosecretory systems (e.g. sinus gland, neurohypophysis). This difficulty of defining neurosecretion on the basis of structure alone was foreseen many years ago, and it was suggested that their relationship to the blood system was a fundamental feature of neurosecretory neurons (KNOWLES, 1954). Certainly most neurosecretory fibres do not appear to innervate any end organ but terminate blindly at the wall of a blood sinus (PALAY, 1955; KNOWLES, 1962): There are, however, instances of neurosecretory fibres which permeate endocrine tissues and suggestions have been made that these may release transmitter substances which affect the normal activity of such endocrine tissue. On the present evidence it would seem imprudent to attempt a precise definition of the term neurosecretion, yet we can recognize certain neurons in the central nervous systems of many species which do not innervate any muscle or exocrine gland or other neurons, and which contain considerable amounts of stainable secretory material; the relationship between these elements and the rest of the nervous system will be considered in this brief review of the evolution of the central nervous system.

Some objection to the use of the term neurosecretion has been based on the grounds that secretion is a characteristic of all nerve cells, as indeed of cells in general. This is undeniable, but BERN (1962) and others (HELLER and CLARK, 1962) have demonstrated that certain elements of the central nervous system are specialized for an endocrine activity, whereas others may secrete in pursuance of their normal neuronal function. It is pertinent to enquire at a symposium of comparative neurochemistry whether an apparent simplicity of organization of the nervous system as observed in the lower animals is likely to be accompanied by a corresponding biochemical simplicity. We may perhaps find some answer to this question in a survey of the evolution of the nervous system in the more elementary animals. There are in fact indications that a chemical heterogeneity may be of especial importance in the primitive invertebrate central nervous systems and that, during the course of evolution, an anatomical complexity of neuronal pathways and synaptic connections may have replaced pathways which depended on chemical differentiation for their specificity (HORRIDGE, 1961).

THE EVOLUTION OF THE CENTRAL NERVOUS SYSTEM

Coelenterates

The simplest nervous system is that which consists of a net of neurons in which every neuron appears to be equivalent to every other, and to be connected by synapses or fusions with any other neurons with which it comes into contact. Such a system is found in the polyp type of sea-anemone, and all known types of their rapid behaviour can be paralleled in a model by changing the parameters of probability of transmission, density of connexions and so forth, in a randomly connected net (HORRIDGE, 1957).

The next grade of complexity is found where there are two overlying nerve nets covering much of the animal. For example the polyps of the soft coral *Heteroxenia* continually beat out of phase, and it can be shown by cutting them in pieces that each arm of the polyp apparently contains a spontaneously active nervous centre. Yet stimulation of any part of the colony causes all polyps to become immobile, and HORRIDGE (1956) has shown that this is due to an inhibitory nerve net which runs to all the pacemakers of the colony.

An aggregation of neurons to form ganglia or nuclei is an essential characteristic of a central nervous system, and this we find in the jellyfish type of coelenterate. A number of separate ganglia are arranged symmetrically at invervals along the margin of the bell in relation to simple sense organs which are able to detect gravity and light. These ganglia feed motor impulses into a nerve net, the so-called giant fibre net, which co-ordinates the symmetrical beat of the muscles over the whole bell. It is interesting to note that in certain species of jellyfish, e.g. *Cyanea*, two distinct efferent pathways run from a ganglion at the periphery of the bell—one modulates the frequency of the pacemaker in the giant fibre net, the other runs only locally to muscles of the bell and brings about an asymmetrical component of the beat.

An evolution of complexity of the nervous system of coelenterates appears to have proceeded from a single non-ganglionic network of neurons conducting diffusely, through a stage in which there are two networks physiologically distinct, to simple ganglia each of which integrates several types of sensory excitation. Such an evolution is dependent on some form of differentiation or specification whereby distinct pathways of conduction can be kept separate from one another. This too is a fundamental characteristic of higher nervous systems and it is pertinent to enquire the nature of this specification at this very early stage of evolution seen in the coelenterates. HORRIDGE (1961) has drawn attention to two possibilities which he terms "anatomically addressed systems" and "chemically addressed systems", respectively. An anatomically addressed system is one in which structural relationships between a neuron and others which it excites can be clearly and regularly discerned. A chemically addressed system might consist of an intermingled mass of neurons in which no clear anatomical relationships can be discerned and yet in which different neurons produce different transmitter substances and in which a differential sensitivity of efferent neurons to these transmitter substances would permit specification of pathways of stimulation.

It is interesting to note that the more elementary nervous systems (e.g. coelenterates, platyhelminthes, annelids) are characterized by profuse ramifications of dendrite and axon aborizations which may vary in form from specimen to specimen, to which the name neuropile has been given, whereas in higher forms (e.g. vertebrates) more precise relationships between individual neurons can often be discerned. Many attempts have been made to determine anatomically distinct patterns or "circuit diagrams" in invertebrate nervous systems, but consistent specific contacts have been found only in a few instances of axon–axon synapses of giant fibres to motor fibres (YOUNG, 1939; JOHNSON, 1924; HORRIDGE, 1959) where there is a widespread but clear anatomical addressing to motor neurons of a particular class. More characteristic however of invertebrate nervous systems is the neuropile. As we proceed from coelenterates through the worms to the arthropods individual neurons can be recognized both physiologically (WIERSMA, 1958) or anatomically (SMITH, 1957) more numerously and more clearly, yet the interesting activity in invertebrate nervous systems seems to take place in the neuropile, where the pattern of branching frequently resembles that of primitive nerve nets in which the neurons appear to be non-addressed. In the ganglia of the jellyfish nervous system, neuropile is abundant, a fact which, as HORRIDGE (1961) has pointed out is more compatible with a chemically addressed rather than an anatomically addressed system.

Platyhelminthes

Different grades of complexity in the evolution of a central nervous system can be seen within the phylum Platyhelminthes. The marine forms belonging to the class Acoela have nerve nets which are similar in form to those which are found in coelenterates; some concentration in the neighbourhood of sense organs can sometimes be observed (Fig. 1a).

Within the class Tricladida a further concentration of nervous tissue to form ganglia is observed (Fig. 1b), with a corresponding reduction in the form of the nerve net. As yet no neurosecretory cells have been detected in triclads, but it has been shown that a water-soluble factor derived from a brain extract will affect regeneration of excised eyespots (STEPHAN-DUBOIS and LENDER, 1956; TÖRÖK, 1958). TURNER (1946) has reported neurosecretory cells in the brain of a polyclad. In polyclads the sensory input from a variety of receptors (statocysts, eyes, chemo-receptors) is related by clearly defined central nervous systems of some complexity (Fig. 1c).

Annelids

The evolution of metameric segmentation in the phylum Annelida which makes possible more complex movements by independent muscles, was accompanied by a concentration of neurons to form paired ganglia in each segment. At the anterior end of the body some degree of cephalization is apparent in the evolution of supra-oesophageal ganglia which receive sensory input from various sense organs on the head (Fig. 2), and a pair of sub-oesphageal ganglia. The influence of these two centres on the remainder of the nervous system appears to differ; for instance removal of the brain (supra-oesophageal ganglia) from a nereid worm or a leech brings about increased motor activity, but after the sub-oesophageal ganglia have been removed nereids are nearly motionless. The brain then appears to be a sensory centre and it normally has an inhibitory or restraining control over the motor centres in the sub-oesophageal ganglia.

Neuropile predominates in the brain and in the ventral ganglia of annelids (Figs. 2 and 3). Anatomical junctions are difficult to distinguish

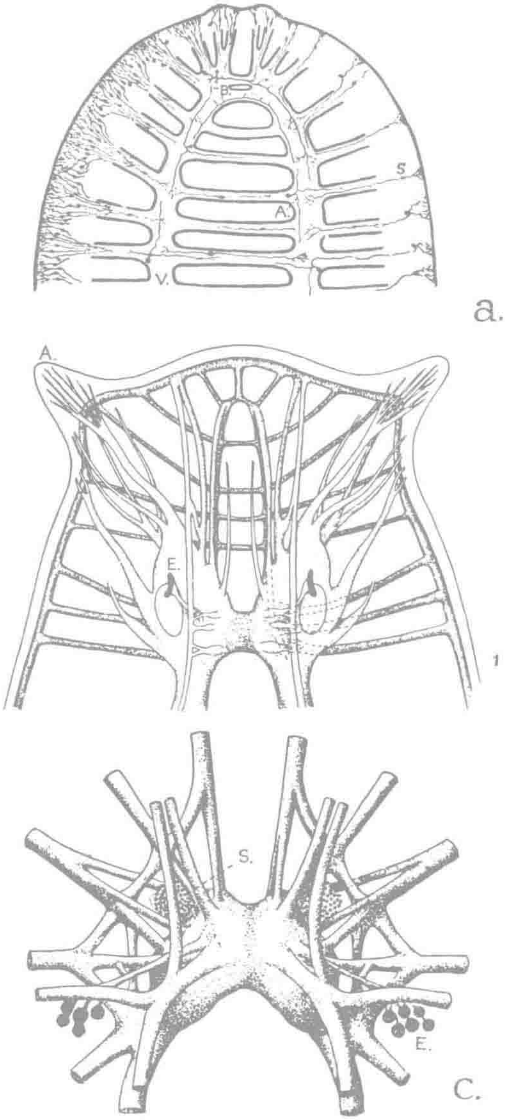

FIG. 1. The evolution of the brain within the phylum Platyhelminthes.

a. Anterior end of *Bdelloura candida* (after HANSTROM, 1926). B, brain; V, ventral cord; S, sensory cells; A, associative neuron.

b. Brain of *Crenobia alpina* (after MICOLETZKY, 1907). E, eye; A, auricle containing various sensory cells.

c. Brain of *Notoplana atomata* (after HADENZELDT, 1929). S, sensory cels; E, cluster of tentacular eyes.

After HADENFELDT in HYMAN'S *The Invertebrates*, Vol. II, 1951. McGraw-Hill, New York.