

Chemical phrenology of the hypothalamus: another illusion?

George Fink

Handbook of the Hypothalamus. Edited by Peter J. Morgane and Jaak Panksepp. Vol. 1 *Anatomy of the Hypothalamus*, pp.756, ISBN 0-8247-6834-5; Vol. 2 *Physiology of the Hypothalamus*, pp.688, ISBN 0-8247-6881-7. (Dekker: 1979-1980.) \$145 per volume.

"It is quite curious that psychologists, after so many years of seeing the remainder of the brain only as an appendage of the hypothalamus, suddenly now see each complex behaviour as being 'generated' by a particular chemical pathway", writes Peter Morgane, one of the editors of the *Handbook of the Hypothalamus*, in a swingeing attack on the concept of brain centres and the new chemical phrenology. However, neither the introductory chapter in Vol. 1 by Morgane nor the other chapters on anatomy provide a realistic alternative. We are still far from a perfect understanding of the precise anatomy of the hypothalamus, but even if we were approaching this goal, would we be any closer to the "functional truth"? Thus, for example, although the intrinsic and extrinsic connections of the cerebellum are almost perfectly understood — certainly better than those of the hypothalamus — we are still not able to state precisely how the cerebellum controls movement.

Several of the chapters in Vol. 1 are too long, and dwell tediously on detail which is neither new, exciting nor especially relevant to current research on hypothalamic structure or function. The development of the hypothalamus, for example, is the subject of a scholarly contribution by Keyser, in which emphasis is placed on classical embryological issues such as the relationship between the sulcus limitans and the hypothalamic sulcus, but, surprisingly, no mention is made of either the development of specific neurotransmitter systems or of the critical periods of development related, say, to sexual differentiation of the brain. In a 110-page chapter, Ambach and Palkovits give the most detailed and beautifully illustrated description of the vasculature of the hypothalamus that, I think, has been published in the present century, but do not include, for example, either quantitative data on the density of capillaries relative to perikarya or a discussion of endothelial-glial-neuronal relationships.

The chapters on the neural connections

● Volumes 3A and 3B of the *Handbook of the Hypothalamus*, dealing with behavioural studies, have been published recently and will be reviewed in *Nature* at a later date.

● The paperback edition of *Wholeness and the Implicate Order* by David Bohm (reviewed in *Nature* 291, 435) is published today in the United Kingdom by Routledge & Kegan Paul, price £3.95.

of the hypothalamus by Palkovits and Zaborsky, and on the medial hypothalamus by Renaud, do, however, contain useful information presented in handbook style. Millhouse's beautifully illustrated and thorough account of Golgi anatomy also provides a useful starting point for the workers who will eventually settle down to unravel definitively the intrinsic connections and cyto-architecture of the hypothalamus. Parent's contribution on monoaminergic and cholinergic neurons will be especially valuable to those doing research on fish, amphibia and reptiles, and Sutin and McBride re-examine hypothalamic limbic-brain-stem connections mainly with horseradish peroxidase and electrophysiological techniques. The editors have also included a "cyto-architectonic atlas of the hypothalamus", but this might have been more useful had the coronal sections been related to stereotaxic co-ordinates and had the descriptions of cells been more quantitative and detailed.

Vol. 2 on physiology starts with a competent chapter by McKelvy and associates on the biosynthesis of peptides, which also bravely tackles the interesting story of why and how several respected workers were led to think for a time that thyrotropin releasing hormone was synthesized extra-ribosomally. This chapter might have been even better had McKelvy not included the rushed catalogue, at the end, of facts about non-peptide transmitters. Knigge and his colleagues then detail the distribution of some of the peptide-containing perikarya, display some fascinating scanning electronmicrographs of the third ventricle and continue their polemic on the importance of the tanocytes in transporting substances from the third ventricle to the hypophysial portal vessels. One major and at least two minor errors of scholarship detract from the standard of this chapter. The major error occurs in Table 3 (p.77), which implies that vasopressin and oxytocin are selectively located in the supraoptic and paraventricular nuclei, respectively; the minor errors are that it was Brown-Grant, in the early 1960s, who developed the idea of selective thyroxine uptake by the median eminence and this should have been acknowledged in Fig. 49 (perhaps the most important diagram in this chapter), and Popa and Fielding did not work at Oxford (p.102).

Then follow standard, but nonetheless sound, accounts of the hypothalamic regulatory hormones (by Vale and associates) and the neurotransmitter (classical, non-peptide) regulation of anterior pituitary function (by Kordon and associates). De Wied and Witter describe in detail the way in which oligopeptides affect behaviour, mainly in animals and under

strictly defined experimental conditions. These authors probably over-reach themselves in areas of physiology as shown, for example, by the confused statement on the relevance of protein synthesis to the action of luteinizing hormone releasing hormone (p.361). Spector throws a timely challenge at the Bernard-Cannon concept of homeostasis ("Every living organism, from birth to death, is in a state of non-equilibrium"), and then explores the involvement of the hypothalamus in the immune response and cancer in the context of his (Spector's) theory of the "fluctuating central state". Spector's review of the experimental evidence is especially important since several recent clinical studies suggest that the mental state, by way of a neuro-endocrine mechanism, may either predispose the individual to and/or affect the course of systemic disease. A succinct chapter by Frohman on the control of metabolism by the hypothalamus concludes with the mid-1970s view (not that it has been replaced by any better view) of anorexia nervosa and obesity. Frohman's chapter is complemented by Oomura's account of the effects of metabolites on neuronal activity measured by single and multiple unit recording.

Overall, the standard of this work is quite variable and in some technical respects, such as the reproduction of micrographs and electronmicrographs, is uniformly poor. Too many of the chapters are written as standard reviews, and some are only slightly modified versions of accounts published in the many other books on the hypothalamus that have recently appeared. The work could have been made much more valuable had an attempt been made to tabulate data relevant to current research. For example, there are no comprehensive tables showing quantitative data on the distribution of transmitters and the enzymes that synthesize or metabolize non-peptide transmitters, the distribution of the various types of neurons, or the electrophysiological characteristics of neurons in various nuclei. To obtain these facts, the reader must wade through a lengthy text and often look up references cited by the authors — the point of a "handbook" is to reduce this laborious task to a minimum.

However, although these volumes are less than a handbook should be, the novel treatment of some of the data, together with the extensive bibliography (mostly up to 1977-1979), probably makes it reasonable for the aspiring or practising chemical phrenologist to recommend the work to the nearest main library. □

George Fink is Director of the MRC Brain Metabolism Unit, University Department of Pharmacology, Edinburgh.