Biology of Affective Disorders

The Psychobiology of Depression. JOSEPH MENDELS, Ed. Spectrum, New York, 1975 (distributor, Halsted [Wiley], New York). xiv, 176 pp., illus. $15.

The study of functional abnormalities of the central nervous system (CNS) that may underlie depressive syndromes has been hampered by poor access to functional CNS tissues in both normal and depressed subjects. In investigations of the role of amines in affective disorders various research strategies have been developed to provide indirect evidence concerning CNS biology. Such strategies, together with recent findings on depressive populations, are detailed in this volume.

One strategy has been the examination of cerebrospinal fluid (CSF) for evidence of altered turnover rates of monoamines. Post and Goodwin report low accumulations of acidic metabolites of dopamine and serotonin when transport of the metabolites from the CSF was blocked by probenecid. Moreover, accumulation of serotonin metabolites remained low during remission both in patients taking antidepressants and in those in the drug-free state.

A second strategy is to approach functional CNS neurotransmission by examining abnormalities of basal or provoked neuroendocrine secretion. It has recently become appreciated that the release and inhibition of neuroendocrine secretion are modulated by known neurotransmitter systems. Testing dopamine receptor sensitivity, Frazer found growth hormone responses following administration of apomorphine to be compromised in 21 percent of depressives. Sachar found lower growth hormone responses following induction of hypoglycemia and lower basal concentrations of luteinizing hormone in a group of postmenopausal depressed women than in controls matched for age and sex. Furthermore, he reports elevated plasma cortisol concentrations in depressives. These findings may be consistent with low central norepinephrine function, since norepinephrine elevates basal concentrations of luteinizing hormone in postmenopausal women, facilitates the growth hormone response to hypoglycemia, and may exert a tonic inhibitory influence on corticotropin-releasing factor, which, through adrenocorticotropic hormone, controls cortisol release.

A third strategy, the study of behavioral effects of agents of known pharmacologic mechanism, is represented by the work of Davis and Janowsky. Previously mania has been studied in relation to presumed excess of catecholamine function. Davis reports that much of manic symptomatology can be relieved temporarily by a centrally acting cholinesterase inhibitor, physostigmine. Such observations, together with previous work, suggest that two or more neurotransmitter systems modulate critical balance within the CNS and that disruption of this balance may result in affective symptomatology. Catecholamine predominance may result in mania. Increasing the cholinergic tone of the system, as by administration of physostigmine, has an effect similar to the presumed restoration of balance and relief of symptoms that follow catecholamine blockade.

A fourth strategy is to seek evidence from peripheral tissues of alterations in enzyme activity and electrolytes. Such work is reported in this volume by Murphy and Costa and by Mendels and Frazer. Platelet monoamine oxidase activity was found to be significantly reduced in a group of depressives who had a history of manic episodes. An increase in red blood sodium following administration of lithium occurred only in patients whose depression was alleviated by the lithium. Whether abnormalities in electrolyte transport are related to neurotransmitter abnormalities in these diseases or are a nonspecific concomitant of depressive illness is not clearly understood.

A critical question concerning the biological processes leading to depression is raised by Tsuang on genetic grounds. He points to evidence of genetic clustering of depressed patients into "bipolar," unipolar "depressive spectrum," and unipolar "pure depressive disease" groups. Implied by such studies is the probability that the different clusters of patients have different biological abnormalities underlying specific disease processes as well as common biological abnormalities as a result of a common final pathway to depressive symptoms. In all probability, the study of depression is the study of several different disease processes, and psychiatric investigations of depression will be confounded until the processes can be distinguished from one another.

Murphy and Costa's grouping of depressed patients into bipolar and nonbipolar groups according to platelet monoamine oxidase activity is a step in the right direction. The Feighner criteria for unipolar primary depressive illness used by Post and Goodwin and by Sachar may group together depressives who are in fact heterogeneous, as suggested previously by work of Beckmann and Goodwin showing differential response to two tricyclic antidepressants following two different norepinephrine metabolite excretion patterns.

Baldessarini, in his overview of amine hypotheses of affective disorders in this volume, laments that there is not yet universal agreement about how to categorize such disorders. Carroll, in the final chapter, offers a potential way out of the diagnostic impasse. He suggests moving beyond the study of one or two biological variables to a multivariate design. By the study of electrolytes, CSF amine metabolite accumulation, neuroendocrine hormone release, specific pharmacologic response, and genetics of transmission in the same patient we may be able to build a profile of both common and differing biological variables within subgroups of patients. It is only when profile clusters of subgroups of depressed patients can be described that meaningful statements concerning the underlying biology of depressive diseases can be made. While it would be hoped that the diseases might be identifiable clinically by history or by symptomatology, accurate diagnosis of subtype may, as Maas suggests, depend ultimately upon a laboratory test specific for the underlying disorder.

This volume is an excellent introduction to current psychobiological thinking for students of neuroscience. Though generally supportive of the amine hypotheses of affective disorders, it poses questions concerning, for example, the relationship of ion transport changes to such hypotheses. It challenges investigators more clearly to define and distinguish depressive disorders and points the way toward greater progress.

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Overview of Mesoamerica

Middle America. A Cultural History of Heartland and Frontiers. MARY W. HELMS. Prentice-Hall, Englewood Cliffs, N.J., 1975. xvi, 368 pp., illus. $11.50.

Although intended primarily as a textbook for introductory courses in the cultures and culture history of Middle America, this volume should attract a wider readership including anthropologists and other scholars interested in that region. It is, I believe, the first work since Eric Wolf's *Sons of the Shaking Earth*, published in 1959, to attempt to cover the entire sequence of Middle American cultural development from the time of the earliest aboriginal inhabitants up to the present day. Indeed, the present book is even more ambitious than Wolf's since Helms, unlike Wolf, does not restrict herself to the zone of the Indian high civilizations of Mexico

and Guatemala (the anthropologists' Mesoamerica) but includes treatment of northern Mexico and lower Central America as well. This wider coverage follows from the author's intention (similar to Wolf's) to provide more than a mere summary of facts by ordering the material according to some organizing principle of wider theoretical interest. The framework chosen is the contrast between and interaction of "heartland" and "frontier" regions because the latter, while relatively neglected in previous research, "are an integral part of the region as a whole and necessary components in the consideration of its cultural development." The point is well taken, yet the very breadth of geographical and temporal treatment the framework demands presents a dilemma—given the length of the book and the audience for which it is primarily intended—which Helms does not resolve in a fully satisfactory manner.

Each of the three major sections of the book (dealing with the evolution of the Prehispanic cultures, the colonial period, and the era of the modern nation states, respectively) is written in an agreeable and concise style. References (appearing where they ought in a work of this sort—as footnotes) are numerous, complete, and as current as may reasonably be expected. An annotated reading list, organized by chapter, appears at the end of the book. The maps and charts are adequate, granted the page size, with the only serious omission being the failure to include any dealing with climatic zones. In the same way, the photographs are relevant and well integrated with the text, although they are not always as crisply reproduced as one might wish. Helms has, moreover, an excellent command of the material and of current theory. Thus, for example, in the section dealing with the aboriginal societies (the subject most familar to the reviewer) she includes recent work on the urban nature of Mesoamerican elite centers (though not always using the newest population estimates), on irrigation, on the nature of the Maya subsistence base, and on the role of trade in the Mesoamerican Late Classic and Early Postclassic; these and related topics are presented in terms of a moderate cultural ecological approach.

There are, nevertheless, some unfortunate omissions. Mesoamerican prehistorians will be somewhat taken aback by a treatment that ignores possible highland priority for various of the traits once lumped as "Olmec," treats La Venta as more significant than San Lorenzo, deals with Cuicuilco in an aside, and despite its critical significance for the emergence of Classic Maya culture completely omits the Izapan culture—or style—of the Guatemalan highlands. In similar fashion, the treatment of the 19th century omits both the Mexican-American war and the American filibustering expeditions into Central America. Failure to discuss these topics lets slip particularly apt illustrations of the problem of control of the frontier from the heartland, presumably a major integrating theme of the book. Another, more minor, example might be the failure to mention that recent intensification of the hunting of sea turtles for sale to export firms along the Miskito coast may well seriously deplete the local subsistence base; here too one could note the disruptive effect on a local economy of external penetration.

The problem, clearly, is that with so many topics to cover treatment must often be not only concise but actually sparse. The usual way out of this difficulty has been to follow precisely the course Helms has rejected—to cover the Prehispanic and European periods separately. This procedure is commonly reflected in course organization and is perhaps justified by the severe cultural disruption of the Spanish conquest. Although Helms's discussions of both periods are quite good (remarkable, considering their length; either could well stand alone as part of a series of case studies), one wonders just how to fit the book as a whole into the academic scheme without costly supplemental readings. It is unfortunate that such solutions as elaborating the heartland-frontier theme into a major theoretical synthesis or expanding the treatment of folk continuities with preconquest conditions were evidently also rejected owing to considerations of length. Ironically, Helms's very attempt to be all-inclusive and her refusal to follow a traditional, "easy" approach may so limit her audience as to cause the neglect of a generally well written and interesting book.

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The H-2 System

Biology of the Mouse Histocompatibility-2 Complex. Principles of Immunogenetics Applied to a Single System. JAN KLEIN. Springer-Verlag, New York, 1975. xii, 620 pp., illus. $39.80.

The mouse histocompatibility-2 (H-2) complex is a cluster of genetic loci that controls histocompatibility antigens. In addition, it governs a variety of traits of immunological importance, such as susceptibility to tumor viruses, immune responsiveness, mixed lymphocyte reactivity, and concentrations of serum protein, complement, and even cyclic adenosine monophosphate. The striking similarity of the mouse H-2 complex to the human HL-A system suggests that the two have a common evolutionary background. The remarkable polymorphism of the H-2 complex and its unusually high immune responsiveness to histocompatibility antigens have led to interesting hypotheses about its biological significance, such as the immune surveillance theory of Burnet. A few years ago the possibility was raised that histocompatibility antigens are themselves involved in the recognition of foreign antigens and thus in the control of the level of immune responsiveness. It is now known that the response is governed by the distinct *Ir* locus that is located within the H-2 complex. Altogether it appears that the study of the H-2 complex is still in a rather early stage. Entirely new phenomena governed by the complex may await discovery and important similarities between it and other genetic loci may appear.

In spite of the importance of the H-2 system, the literature on it is usually complicated and hard to comprehend because of complex technical details and a somewhat confusing terminology. Many immunologists, mammalian geneticists, and cell and membrane biologists have long felt a need for a clear and systematic account of the subject. This requirement is met excellently by Klein's book. The author illuminates every seemingly esoteric aspect of the subject by defining phenomena in simple, lucid language, and the organization is clear and systematic.

About two-thirds of the volume is devoted to the peripheral region of the complex. The author first introduces the serology and histocompatibility, then presents the relevant genetics, and ends with a description of the current state of biochemical investigation. Each section includes a brief section on methodology as a key to understanding the experimental evidence. The last third of the book deals with the biology of central regions of the H-2 complex, a subject that is developing rapidly. Much current work is described, ample references are provided, and all the chapters have helpful tables and figures. The first part of the volume contains a history of research on the entire H-2 system, each section contains a summary of the historical background, and an appendix presents a chronology of the work in the field. This historical perspective is thought-provoking.

Its grand scale, considerable depth, and clear, systematic outline make this book an excellent summary that should be useful to both beginners and experts in the field, as well as to interested outsiders.

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