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