Book Reviews

A Somatic Therapy in Psychiatry

Psychobiology of Convulsive Therapy. Papers from a conference, San Juan, Puerto Rico, Apr. 1972. MAX FINK, SEYMOUR KETY, JAMES MCGAUGH, and THOMAS A. WILLIAMS, Eds. Winston, Washington, D.C., 1974 (distributor, Halsted [Wiley], New York). xii, 312 pp., illus. $11.95.

Convulsive therapy is one of the oldest somatic therapies still used in clinical psychiatry. Electroconvulsive therapy (ECT) is one of the most effective treatments known for severe depressive illness. It is also acknowledged to be effective treatment for acute mania and some acute variants of schizophrenia, particularly catatonia. Though most psychiatric clinicians are capable of providing safe and effective ECT, there has been little understanding of the mechanisms involved. This book, a comprehensive review of the current investigational and theoretical aspects of convulsive therapy, goes far toward providing a rational basis for its use.

The clinical application of convulsive therapy in reasonably standardized form is well accepted in practice and in the literature. The indications for its use mentioned above are widely followed. In most centers, patients are treated approximately 6 to 12 times at 48-hour intervals with electrical stimuli delivered through bilaterally placed electrodes. When ECT is used in conjunction with rapidly acting barbiturate anesthesia, muscle relaxant, and atropine administered by an anesthesiologist, major complications are rare. There are very few contraindications to treatment, mortality risk is probably on the order of 0.1 percent, and efficacy is well documented.

Amnesia, the most commonly studied concomitant of treatment, is addressed in the book both as an undesired side effect of therapy and as an experimental key to the understanding of mechanisms of memory. Clinically, memory impairment correlates with intensity of stimulus (or concentration of chemical or inhalant convulsant) but not with the cerebral seizure per se, which is the primary correlate to therapeutic efficacy. In an effort to minimize the side effect, unilateral electrical stimulation of the nondominant hemisphere has been used to induce seizures. D'Elia's paper reviews this work and documents that anterograde and retrograde amnesia and posttreatment confusion are less with unilateral treatment. A paper by I. Small discusses the use of the inhalant convulsant flurothyl, another alternative means of induction, which also seems to produce less amnestic effect than bilateral ECT. Cherkin capitalizes on the high lipid solubility of flurothyl to study and document factors in amnesia that are independent of specific neuroanatomic pathways of electrical conduction.

McGaugh's and Zornetzer's discussions of amnesia in infrahuman species suggest that electroconvulsive shock (ECS) interferes with consolidation or storage of memory. Zornetzer provides descriptive neurophysiologic data on electroencephalographic correlates of memory disruption in rats. These data indicate that brain seizures are neither necessary nor sufficient for the production of amnesia, reinforcing the belief that memory disturbance is a side effect rather than a primary therapeutic factor.

Dunn *et al.* discuss amnesia in relation to impaired protein synthesis at synaptic sites. Most important clinically is their suggestion that ECS may produce small amounts of protein degradation and membrane damage, one of the rare indications that minute brain damage may result from treatment. Essman, in studies of ECS effects on mouse forebrain, shows that decreased synaptic RNA is associated with an increase in turnover time and in concentration of 5-hydroxytryptamine (5-HT). Interestingly, exogenous 5-HT not only seems to reduce the rate of amino acid incorporation into proteins at nerve endings, but also, when administered intracerebrally in mice, can produce a retrograde amnesia similar to that produced by ECS.

Possible mechanisms of the therapeutic action of ECT are clarified in this book. For example, Kety's summary of the effects of ECS on biogenic amines indicates that its mode of action is similar to that of antidepressant drugs. A decrease in norepinephrine and an increase in its metabolites after an acute ECS have been reported. There is further evidence of an increase in norepinephrine after a series of ECS, suggesting that there is a cumulative overall increase in norepinephrine synthesis and turnover during a course of treatment.

Some of these changes in the metabolism of indoleamines and catecholamines persist for some time after the last induced seizure. Kety suggests, therefore, that repeated ECS may induce a metabolic change (increased amine turnover) that contributes to the clinical efficacy of the therapy. This conclusion is indeed tentative, but it represents a conceptual leap from the old attempts at psychologic explanation of ECT to the level of psychobiologic integration of pathophysiology, neurophysiology, and biochemistry.

This book will be read with interest by anyone involved in the study of memory function and it should be read by all clinicians who administer convulsive therapy. It is regrettable that two years must pass between a symposium and its publication in book form. We must hope that the authors will soon present an updated account of the evolution of their ideas.

THOMAS D. HURWITZ
Department of Psychiatry, Dartmouth Medical School, Hanover, New Hampshire

Neurotransmitter

Serotonin—New Vistas. E. COSTA, G. L. GESSA, and MERTON SANDLER, Eds. In two volumes. Histochemistry and Pharmacology. xvi, 330 pp., illus. $19.75. Biochemistry and Behavioral and Clinical Studies. xviii, 428 pp., illus. $19.75. Raven, New York, 1974. Advances in Biochemical Psychopharmacology, vols. 10 and 11.

One of the rewards attending a novel scientific discovery is the opportunity to watch the progress of the research it stimulates. It has been just 25 years since pure serotonin, 5-hy-

droxytryptamine, appeared on the scene, and 22 years since its chemical synthesis and competitive distribution by two American drug firms made it widely available to researchers. These two volumes are the fifth (at least) and the most recent collection of papers representing the efforts of many scientists caught in serotonin's web. They contain 82 separate contributions describing various aspects of the biochemistry, physiology, pharmacology, anatomical distribution, and behavioral implications of serotonin.

Although it is only one of a growing number of chemical neurotransmitter substances in the central nervous system (CNS), serotonin has been particularly provocative, enticing neuroscientists to follow its trail in the naive hope of finding simple answers to some questions about CNS function. Despite enormous effort and very considerable progress, the questions have become more complex as more information has been acquired.

What is the function of serotonergic tracts and of tracts utilizing other neurotransmitters such as acetylcholine, norepinephrine, and dopamine? How is behavior modified by interactions of various neural pathways that utilize different neurotransmitters? What is the mechanism of action of hallucinogenic substances, many of which (for example, LSD, bufotenin) are structurally closely related to serotonin? Is physical dependence on drugs (such as morphine) connected with serotonergic pathways? Is there a simple relationship between a disordered metabolism of serotonin (methylation, deamination, turnover) and human behavioral disorders such as depression and schizophrenia?

These two volumes show that scientists engaged in this work are aware of these larger questions but have not yet acquired sufficient information to attack them. Rather, they are concerned with smaller questions that *can* be answered, in the expectation that the smaller answers obtained will shed light on the larger questions of function. These smaller questions mainly concern regulation of concentration and turnover of serotonin in the CNS.

Regulation, which determines how much neurotransmitter reaches the receptor site on the postsynaptic membrane, involves consideration of at least five processes: biosynthesis, breakdown, storage, and release from and reuptake into the nerve endings. With the exception of release, each of these processes receives some consideration in these volumes. Particular attention is given to biosynthesis (activity of the rate-limiting enzyme, tryptophan hydroxylase, is affected by availability of substrate, hormones, feedback inhibition by intermediary and final products, and feedback regulation through neuronal loops), breakdown (multiple forms of monoamine oxidase), and further metabolism (methylation and acetylation).

Much of our progress comes through the discovery of drugs that not only have a selective action on a particular neurotransmitter system, but also preferentially affect only one of the five or six regulatory processes. The newest drugs are the neurotoxic agents 5,6- and 5,7-dihydroxytryptamine, which are useful not only for mapping serotonergic tracts but because their effects force us to a higher level of sophistication in considering the function of such tracts. For example, these agents and *p*-chlorophenylalanine (an inhibitor of tryptophan hydroxylase) lower brain serotonin concentrations, but the enzyme inhibitor produces no obvious changes in behavior, whereas the neurotoxic agents cause bizarre behavioral effects.

One of the assets of a comprehensive review of current studies is that it suggests, by its omissions, kinds of research that are needed. For example, these volumes do not report on: (i) studies of release mechanisms; (ii) development of a peripheral model, perhaps the myenteric plexus, that will play the role that the neuromuscular junction does for cholinergic mechanisms; (iii) determination of which behavioral effect (rapid eye movement sleep, temperature, sexual activity, memory, affective disorders) is most significant for determining selectivity of antiserotonin agents; (iv) studies of the relation of serotonin synthesis in the perikaryon to that in the nerve ending and of the role of axonal transport; (v) studies of storage forms other than synaptic vesicles, whose existence is indicated by new biochemical, morphological, and pharmacological data (for example, the presence of a special compartment for newly synthesized transmitter, the presence of reserpine-resistant stores, the electron microscope evidence for "tubular reticulum-like structures," and the presence of soluble high-affinity binding proteins in nerve ending cytoplasm).

Costa, Gessa, and Sandler have performed a great service in compiling such a comprehensive discussion of the present state of serotonin research and the current hypotheses invoked to explain complex observations. These hypotheses are no longer very simple, but even a touch of insight often requires an enormous number of very small steps.

MAURICE M. RAPPORT
HADASSAH TAMIR
Division of Neuroscience, New York State Psychiatric Institute, and *Department of Biochemistry, Columbia University College of Physicians and Surgeons, New York City*

Eastern Biota

Ecology and Biogeography in India. M. S. MANI, Ed. Junk, The Hague, 1973. xx, 774 pp., illus. + maps. Dfl. 190. Monographiae Biologicae, vol. 23.

That the biogeographical and geomorphological evolution of the Indian subregion or subcontinent should be considered in an integrated fashion is the purpose of this work edited by M. S. Mani. Mani, whose distinguished work in entomology, particularly on the insect fauna of high altitudes, has been known to the reviewer for over 20 years, has performed a most valuable task in putting together this monumental work. Taking advantage of new information from plate tectonics and continental drift, weather and climatic patterns, and recent revisions in botany and zoology, he and his co-workers have assembled a thorough synthesis of present-day biogeographical evidence.

One of the important points the editor makes is that nothing is static in biogeography. Perhaps this is one of the difficulties of the subject which prompt him to say that "field ecology and biogeographical researches in India often seem to have been looked upon with considerable misgivings as belonging to the realm of speculation." It is true that in the halcyon days of speculative biogeography floating islands, land bridges, and mountain range gaps were created and made to appear and disappear, like conjurors' rabbits, at the whim of biologists. Today patterns are studied with new geomorphological and climatological evidence in mind, and biogeography is becoming bedded in a firm body of documented evidence.

The evolution of distributional patterns of animals and plants, subject as they are to a complex web of circumstances, has indeed tended to confuse