

# Book Reviews

## Key Neurotransmitters

**Frontiers in Catecholamine Research.** Proceedings of a symposium, Strasbourg, France, May 1973. EARL USDIN and SOLOMON H. SNYDER, Eds. Pergamon, New York, 1973. xvi, 1220 pp., illus. \$50.

Nowhere else can one find in a single volume such striking evidence of the range and depth of our knowledge about the catecholamines as in this record on the proceedings of the third international catecholamine symposium. The book nicely complements detailed and critical reviews that can be found elsewhere, since it both enables the reader to capture the excitement of new discoveries and challenges him with some of the problems to be solved in the future.

The volume contains 220 articles and is divided into eight sections, the first six of which deal with enzymes of catecholamine synthesis and metabolism, regulation of enzymes, catecholamine receptors, dynamics of the nerve terminal, and catecholamines in the central nervous system. The last two sections, on drugs of abuse and on catecholamines in man, together with the opening address by Alfred Pletscher, illustrate the growing importance to society of fundamental research on the catecholamines. As a whole the book is well produced, although in the desire to publish it as soon as possible after the symposium the standards of editing have been somewhat compromised. The subject index, although it is 30 pages long, is by no means complete. The omission of an author index is inexcusable and causes great inconvenience in a book of this kind. Another frustration is that not infrequently references quoted in the text do not appear in the reference lists.

With this book in front of one, it is quite possible to claim that more is known about the catecholamines than about all the other neurotransmitter substances put together. This does not, of course, mean that the catecholamines are more important than the other transmitters. An imbalance in our knowledge has arisen, largely as a result of key technical advances made in the study of catecholamines during

the last 20 years. Some of these advances have come about by the imaginative application of established chemical or biochemical procedures, such as the oxidation of catecholamines to give fluorescent derivatives and the demonstration that catecholamines are stored within membrane-limited particles in cells. On the other hand, serendipity played a role in one of the most dramatic advances, the introduction of the fluorescence-histochemical method for revealing catecholamines in tissue sections. Eränkö's chance discovery in 1955 that some of the cells of the adrenal medulla exhibited strong fluorescence when the tissue had been fixed in formaldehyde led to the work of Falck and Hillarp and their colleagues that established the conditions necessary for revealing catecholamines in nerve fibers. The importance of this technique extends beyond its great contributions to our knowledge of the particular pathways of catecholamine-containing nerve fibers; it has given visual expression of the incredible complexity of even one part of the nervous system, a complexity we do well to remember each time we are attracted by simple models. The symposium contains many examples of the applications of the original Falck-Hillarp method of fluorescence histochemistry, together with an account of a new method, involving condensation with glyoxylic acid, that gives striking pictures of axons in the central nervous system and that is so sensitive that even the minute amounts of catecholamines in normal nerve trunks are revealed.

In parallel with the development of new techniques to study the catecholamines themselves, another major advance has been in the study of the specific proteins of catecholamine-containing neurons. Work on these proteins, the enzymes of catecholamine biosynthesis and the vesicle proteins, such as chromogranins and chromomembrins, would not have been so easy if they had not also been present in adrenal chromaffin cells. Indeed, all antibodies to these proteins have so far been prepared by use of the adrenal medulla as a source for the antigen. Studies of neuronal proteins have re-

vealed the plasticity of noradrenergic neurons; thus, stressful conditions influence the levels of enzyme activity not only in the cell bodies, but also in the terminal networks. This plasticity is not merely a reflection of the role these enzymes play in the biosynthesis of norepinephrine, for one of the enzymes (dopamine  $\beta$ -hydroxylase) is secreted from the nerve terminals together with norepinephrine. The recognition that the sympathetic neuron is a protein-secreting cell provides both a challenge to the physiologist and a new tool for the study of sympathetic nervous activity. Measuring the amounts of dopamine  $\beta$ -hydroxylase or of chromograinin secreted from tissues has led to the discoveries that  $\alpha$ -adrenergic blocking agents facilitate the impulse-induced release of norepinephrine by exocytosis and that indirectly acting sympathomimetic amines evoke the release of norepinephrine by a mechanism not involving exocytosis. Several chapters deal with the measurement of dopamine  $\beta$ -hydroxylase concentration in the blood plasma of man. These studies show that in any one person the concentration of this enzyme in the blood can indeed reflect sympathetic nervous activity. However, the wide variation in concentrations between individuals makes it difficult to use such measurements for diagnostic purposes. On the other hand, such a variation might be a clue to some unsuspected long-term adaptation of sympathetic nervous activity, differing from person to person.

The preparation of antibodies to neuronal proteins opened up the possibility, first exploited by Hopwood in 1968, of applying the immunofluorescence technique for localizing proteins in tissues. This method is now challenging the procedure for the fluorescent microscopy of the catecholamines themselves in sensitivity and specificity. The elegance of this technique should not lead us to forget that interpretation of the results in terms of the function of the nervous pathway identified depends both upon the purity of the original antigen and upon the assumption that the presence of antigenic sites in an enzyme is always accompanied by the specific catalytic activity. If the latter assumption is valid, then the presence of neurons containing phenylethanolamine *N*-methyl transferase in the hypothalamus means that epinephrine might be a transmitter in this part of the brain.

In marked contrast to the great

progress in our knowledge about the macromolecules present in sympathetic neurons is our almost total ignorance about the nature of the receptors for catecholamines in postsynaptic cells. The development of antagonists that are relatively specific for the different types of adrenergic receptor has provided the biochemist with valuable tools in his search for the elusive receptor molecule—tools which, alas, seem to be little used and poorly understood in a chapter dealing with a substance from heart tissue that binds catechol derivatives.

Possibly the most challenging and exciting area of research covered in this book is that having to do with the functions of catecholamines in the central nervous system. The gateway into this area was opened 20 years ago by Vogt's discoveries that the distribution of norepinephrine between the regions of the brain was not uniform and that centrally acting drugs, such as morphine and reserpine, markedly reduced the concentration of norepinephrine in the brain. Some of the problems raised then still remain. As Vogt aptly puts it, "We know a great deal about correlations between the effects of drugs on behaviour and on brain biochemistry, but the transformation of mere correlations into causal relationships is in its mere infancy." One of the difficulties in deducing causal relationships from studies of the actions of drugs on the central nervous system arises because no drug is entirely specific in action. The widespread use of intracranial injections of 6-hydroxydopamine, for example, as a method of causing damage to central catecholamine-containing neurons may lead to erroneous conclusions because this is a highly reactive substance that could damage other neurons when applied locally in high concentration.

Such pitfalls can be more easily avoided if a truly interdisciplinary approach is used. For example, because it is known that the rate of synthesis of catecholamines from tyrosine increases in stimulated nerves, there has been a tendency to assume that an increased rate of synthesis always reflects an increased impulse flow in the nerves. However, Aghajanian and his colleagues, by a combination of biochemical, histochemical, and electrophysiological methods, have convincingly demonstrated that such an assumption is not valid for the dopaminergic fibers in the nigrostriatal pathway of the rat brain. It was found that upon adminis-

tration of two drugs that lead to an increased rate of dopamine synthesis there is actually a decrease in the impulse flow in this pathway.

Another problem in studies of the role of catecholamines in the brain is that of the measurement of behavior. Not only is it regrettable that different procedures are used in different laboratories, there is also a need for more precise methods of measurement. A procedure introduced by Ungerstedt is a good example of what is required. By measuring the rotational movement of rats that have a lesion in the nigrostriatal dopaminergic tract on one side of the brain, it has been possible to construct dose-response curves for the interaction of drugs with striatal dopamine receptors and so to study one component of the animal's behavior. The striking behavior changes following overactivation of dopamine receptors in rats resemble some aspects of human psychoses, and it is suggested by Davis that amphetamine psychosis, which clinically is difficult to distinguish from schizophrenia, may involve an interaction between amphetamine and dopaminergic neurons. We can hope that a combination of the scientific study of behavior together with the pursuit of interdisciplinary studies on catecholamine-containing neurons in the brain will yield dividends for the understanding and treatment of mental illness. Society will then obtain another benefit, to add to those it has already received for the treatment of circulatory diseases and of Parkinsonism, from the resources it devotes to research on the catecholamines.

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## Forestry and General Ecology

**Genetics of Forest Ecosystems.** KLAUS STERN and LAURENCE ROCHE. Springer-Verlag, New York, 1974. x, 330 pp., illus. \$29.60. Ecological Studies, No. 6.

This book is remarkable for setting a large block of forestry literature into the context of the ecological and evolutionary theory of the 1970's. The first chapter opens with a detailed exposition of niche theory and fitness sets. The literature of forestry has been better known for introspection and chauvinism than for contributing to advances in general biology. Therefore it is almost

beyond belief that a book on forests should be quoting extensively from the work of Hutchinson, Lewontin, Pimentel, Warburton, Pianka, Levins, MacArthur, Waddington, Bradshaw, Haldane, Crow, Kimura, and van den Planck. None of these authors has been concerned specifically with forests, or even with trees (except MacArthur, as a home for warblers), but all have contributed strongly to general biological theory.

Some of the wealth of forestry knowledge is now brought forth both to test the robustness of general theory and to be illuminated by it. This book arranges a marriage and richly endows the partners. The exercise will prove itself if there are intellectual descendants—extended or modified theory, new approaches to forest experimentation and practice.

The book carries a very large bibliography, a source list to guide population biologists and evolutionists to the forestry literature and foresters to general theory. The title of the book is most misleading—there is no useful sense in which an ecosystem has a genetics. There is a useful analogy by which ecosystems may be said to evolve, but genetics is about individuals and populations. It is a description of the relationship between ancestors and descendants. The ecosystem itself has no genetics. Large parts of the book have been translated from the German. For the most part the text reads smoothly and easily, but the misleading title may reflect translation. There are six chapters, the first five concerned with genetics and evolutionary theory and the sixth with the role of man in forest ecosystems. The book ends with a startlingly effective last page, a description of the "present status of a tree species in danger of extinction," *Vateria seychellarum*. The description contains these comments: "Status: critically endangered. Present distribution: three trees survived on Mahé on the Seychelles . . . formerly a common timber tree. . . . Nothing is recorded of its biology. Protective measures already taken: none." It is in such a context that theories of genetic drift, biogeography of islands, niches, and the genetics of adaptation take life.

Klaus Stern died tragically in a bicycle accident before the book was published.

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