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Mr. Gerald Piel, Editor
Scientific American, Inc.
415 Madison Avenue
New York, New York 10017

copy

Dear Mr. Piel,

I should like to suggest two topics for your consideration for reports in *Scientific American* -- the effects of seizures (convulsive therapy) on mood and behavior in man, and developments of quantitative electroencephalography in the study of psychoactive drugs. These topics are quite singular but there are peripheral relationships which makes their review complementary. Both are timely for educational and social reasons.

Convulsive therapy: This treatment is based on the observation that repeated seizures at daily intervals elicits long-term effects on mood, thought processes and affects in man. It is effective in alleviating severe depression and mania, and was developed as a treatment made in the 1930's, concurrent with studies of daily coma (insulin coma) and leucotomy (psychosurgery). Their concurrent development has led to some confusion that these treatments are equivalent, and the same name, "shock therapy" is erroneously applied to all. Many view their mechanisms of action as the same. During the past few decades, however, insulin coma has been replaced by drug therapy, and leucotomy (psychosurgery) has found a limited niche in the treatment of a small, well defined group of mentally ill. Repeated seizures, in contrast, are used more widely, and in comparison with other therapies for depression, exhibit better therapeutic results.

While it is customary to say that we know little of the mode of action of these therapies, the opposite is true. The neurophysiology of the seizure and cerebral sequelae of repeated seizures have been defined. The parameters of the seizure induction, the effects of different electrode placements, and the effects on performance tests and memory have been studied. While less is known of the biochemical effects, there is much that is relevant to the modern

biogenic amine hypotheses, and some unique studies of cholinergic mechanisms are particularly contributory to our understanding of the role of neurohumors in brain function. Indeed, it is fair to say that we know as much about the biochemical aspects of seizures as we do about antidepressants and sedatives.

From a basic science point of view, the ECT process contributes to our understanding of seizures (epilepsy), the role of cerebral hemispheres in behavior and particularly, memory; and such psychologic mechanisms as the role of personality in depression and changes in task performance with changes in brain function.

From an educational point of view, a presentation of the ECT data may alleviate misconceptions about 'shock therapy' and provide independent information to allow the reconsideration of laws restricting seizure therapies now in force in California and under consideration elsewhere.

Some of the recent physiologic, biochemical, and psychologic (memory) data were brought together by the NIMH in a conference, published in mid-1974 entitled, "Psychobiology of Convulsive Therapy", edited by myself, Seymour Kety, James McGaugh and Thomas Williams (V. H. Winston, Washington, 1974).

2. Quantitative Electroencephalography: The measurement of the electrical activity of the brain has been a subject of interest for more than four decades. During the past 15 years, the development of sophisticated quantification methods based on digital computer programs and an understanding of the requirements for controlled experimentation has defined applications in psychopharmacology which are of general academic interest. Psychoactive drugs, hallucinogens, and drugs of abuse have defined effects on brain function in the alert subject. These effects are drug specific, that is, each compound has a defined signature which is used to classify the compound. When new compounds are assayed, EEG classification provides a prediction of their clinical application before human trials are undertaken.

The techniques are sufficiently well developed to assess dose response curves and to measure bioavailability and neurophysiologic equivalence of compounds. Lately, the EEG methods have been compared with blood level measurements to study the pharmacokinetics of drugs affecting the brain.

Quantitative EEG has been used to develop automatic sleep classification scoring systems. Parallel with these systems, is the development of automatic drug classification systems.

The methods have been applied to problems outside psychopharmacology. In our understanding of the ECT process, the methods have shown that electrode placement and hemispheric localization are contributory to clinical effects. The methods have been used in studies of drugs of abuse, particularly in the role of THC-delta-9 in cannabis, and in examining the reactions between heroin and methadone and their interactions with narcotic antagonists. Some students have assessed the effects of hypnosis, zen, and transcendental meditation using these methods with some success.

From an educational point of view, a discussion of quantitative EEG analysis would be of interest to psychopharmacologists, neurophysiologists, psychologists, and drug abuse specialists.

I commend both topics to your consideration. In part, this letter is occasioned by discussions with Dr. Alfred M. Freedman of the New York Medical College, who has been a firm supporter of these programs for many years. Should it be useful, I can supply the usual literature and suggest the names of scientists who are active in both research areas.

Thank you for your consideration.

Sincerely yours,

Max Fink, M. D.
Professor of Psychiatry

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