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Dr. Monnier's excellent review presents a vivid picture of neurophysiologic techniques in the study of drug effects. From monosynaptic and polysynaptic to organismic patterns the methods of study appear rich in promise. One phase of these studies, that of cortical EEG analysis, has been of considerable interest to our laboratory. Changes in EEG patterns induced by pharmacologic agents are generally considered to be poorly related to changes in clinical behavior. Yet, from the extensive experience with anesthetics, alcohol, sedatives and convulsants, and the theoretical views ascribing to brain function a central role in conscious behavior we would expect that psychotropic drugs may also have significant electrographic - behavioral relations. The difficulties in such studies lie in inter-species differences in physiologic response, the range of inter-individual and intra-individual variability in both neurophysiologic and behavioral parameters, and the wide variety of events which must be measured to obtain a reasonable image of mammalian interactive behavior. A further difficulty has been a lack of reasonable theoretic models of brain function-behavioral interrelations. Recent suggestions, however, may be helpful, including the synaptic models of Marrazzi (1) amongst others; the brain stem models of Magoun, as elaborated by Himwich (2); and the general neurophysiologic-adaptive views of Wikler (3), Weinstein (4) and our laboratory (5).

In 1954, Wikler (6) stated that drugs that alter human behavior in the direction of EEG desynchronization are associated with behavioral excitement, alertness, illusory sensations, and hallucinations; while drugs which induce EEG synchronization, with or without increased slowing, are associated with sedation, tranquillization and decreased excitement. In our studies in psychiatric patients, this hypothesis has been substantiated. The following compounds administered in physiologic dosage ranges have been shown to decrease synchronization of the EEG: mescaline, LSD-25, amphetamine; anticholinergics as diethazine, benactyzine, JB-318, JB-336; and local anesthetics as cocaine, procaine, and lidocaine. The following agents increase synchronization of the EEG: barbiturates, chlorpromazine and similar phenothiazines, meprobamate, and anesthetics as ether, chloroform, *etc.* In addition, various compounds without significant clinical behavioral effects have been studied, including phenyltoloxamine, WY-3149 and deanol - and these have inconsistent or indefinable EEG effects.

In these studies we have observed, however, that the continuum of synchronization-desynchronization is an oversimplified generalization. In our present view, two other EEG pattern changes have assumed considerable prominence. One is a shift of dominant frequencies either to the slow (theta or delta) or the fast (beta) ranges; and the second, the presence of such figures as burts, spikes or spindling. These latter two patterns were significant in

describing the EEG behavioral relations of imipramine (7). Examples of these paterns may be found in publications from this laboratory and elsewhere (8, 9, 10, 11).

It is our impression, therefore, that further EEG analyses of new compounds in man is indeed warranted. We would suggest that the number of quantification procedures be extended to include, in addition to frequency analysis, the techniques of topographic analysis, chronologic analysis - and these techniques may be augmented by computer techniques of summating evoked potentials.

In studies of drug effects, not only is it important to define neurophysiologic parameters, but the behavioral parameters are equally significant. The equation of change in rates of animal pole-climbing, bar pressing or jiggle-cage movement with human excitation and tranquillization is inaccurate and inappropriate. There is no evidence that such tasks in experimental animals are related to changes in human interaction of significance to physicians and psychologists. Indeed, if one impression dominates the session today, it is that the behaviors studied by pharmacologists are not the behaviors of interest to the clinicians. Further study of the relations between the laboratory tasks highlighted today and human behavioral measures are needed. In this regard multivariate pattern analyses of behavior and the newer applied psycholinguistic techniques may be helpful in defining the changes in human behavior patterns.

In conclusions, I wish to reenforce Dr. Monnier's review, and indicate that increased attention to EEG analyses may be profitable in understanding the mode of action and the significant differences and similarities in psychopharmacologic agents.

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