

In: Neuro-Psychopharmacology. Proc. 1st International Congress of Neuro-Psycho-pharmacology, Rome, Sept. 1958.
Ed. by: P.B. Bradley, 1959, p. 441-446.

EEG AND BEHAVIORAL EFFECTS OF PSYCHOPHARMACOLOGIC AGENTS*

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Recent studies have presented data supporting a neurophysiologic-adaptive view of the convulsive therapy process^{4, 15}. This hypothesis holds that the clinical efficacy of repeated induced convulsions is dependent upon the induction of a persistent alteration in cerebral function, which provides the milieu for changes in the subject's interaction with the environment. In these studies the best index of neurophysiologic change has been those aspects of cerebral function reflected by δ activity in the electroencephalogram⁸⁻¹⁰.

The efficacy of newer psychopharmaceuticals in altering psychotic behavior patterns led to the suggestion of a similar hypothesis for the mode of action of these agents⁴, and to studies of the relationship and specificity of altered behavioral patterns to neurophysiologic change as reflected in electroencephalography. This report summarizes some of the experimental data observed in on-going tests of this hypothesis.

SUBJECTS AND METHODS

We have studied consecutive patients, suffering from depressive psychoses, agitated and excited schizophrenic states and severe psychoneurotic disorders, referred for physiodynamic therapies (convulsive, psychotropic drug, insulin coma) in a voluntary, open-ward, psychiatric hospital. Serial electroencephalograms were taken prior to,

* Aided, in part, by grants M-927 and MY-2092, National Institute of Mental Health, National Institutes of Health, U.S.P.H.S., and Bristol, Wyeth and Smith, Kline and French Laboratories.

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during and after the course of therapy. In addition, at various stages of the treatment program acute experimental studies were done. As both convulsive and chlorpromazine therapies elicit varying degrees of EEG slow wave activity, these acute observations have been made in two groups of subjects: those without slow wave activity, and those with diffuse slow wave (HSD, LSD) or burst and slow wave (BSD) activity¹⁸.

Observations have been made in the EEG laboratory. Following a routine bipolar EEG recording, an unstructured psychiatric interview was tape-recorded. Under continuous EEG recording, medication was administered intravenously at a set rate until EEG or behavioral effects were observed. Following the injection the interview was repeated and recorded. Periods of EEG recording and interview recording were alternated for the duration of the drug activity.

Behavioral evaluations have been based both on clinical descriptions by the participants (subject, physician and technician) and analyses of changes in language patterns^{12, 14}. Electroencephalograms were measured for shifts in dominant frequencies, and changes in voltage, modulation, and per cent time of α , β and δ frequency bands.

The psychopharmacologic agents were administered orally for extended periods in clinical trials, and intravenously in the acute experimental trials (Table I). Dosage for each compound varied, but in each instance sufficient medication has been given to achieve clinical behavioral effects.

TABLE I
PSYCHOPHARMACOLOGIC AGENTS STUDIED
(Oral and intravenous)

Chlorpromazine	Amobarbital	Atropine **
Promazine	Thiopental **	Diethazine **
Trifluorpromazine		LSD-25 ^b
Perphenazine	Amphetamine	Win-2299 ^c **
Reserpine *	Methamphetamine	JB-318 ^d **
		JB-336 ^e **
Iproniazid	Meprobamate *	
Deanol ^a **		Benactyzine

^a Dimethylaminoethanol¹⁷.

^b Lysergic acid diethylamide.

^c 2-Diethylaminoethyl cyclopentyl (2-thienyl) glycolate¹⁶.

^d N-Ethyl-3-piperidyl benzilate¹.

^e N-Methyl-3-piperidyl benzilate¹.

* Oral only.

** Intravenous only.

OBSERVATIONS

(a) *Electroencephalographic*

Four broad types of EEG patterns may be identified according to the characteristics of frequency shift and synchronization⁴:

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- 1) Increase in slow wave activity and in synchrony;
- 2) Increase in synchrony without frequency shift;
- 3) Increase in fast wave activity and in synchrony;
- 4) Desynchronization and frequency irregularity.

Examples of each are seen in Figs. 1-4.

During convulsive therapy, an increase in slow wave activity and synchrony is manifest⁸. With drug administration similar changes in frequency spectrum and in synchrony can be observed. Such changes include an augmentation of the slow wave activity⁸ or a marked decrease in such activity with desynchronization of frequencies⁵.

Of the psychopharmaceuticals tested in acute experiments an increase in synchrony with or without an increase in slow wave activity has been observed for chlorpromazine, promazine, and trifluorpromazine. Barbiturates regularly induce an increase in fast activity with an increase in synchrony, while amphetamine and

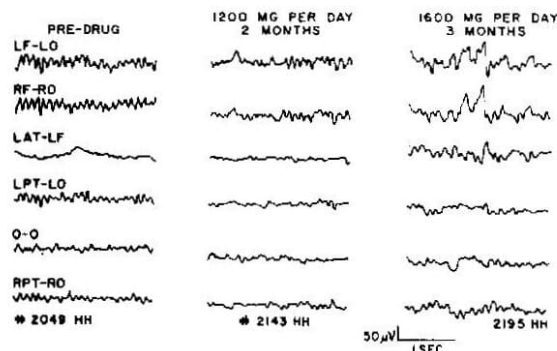


Fig. 1. Chlorpromazine, oral (male, age 15).

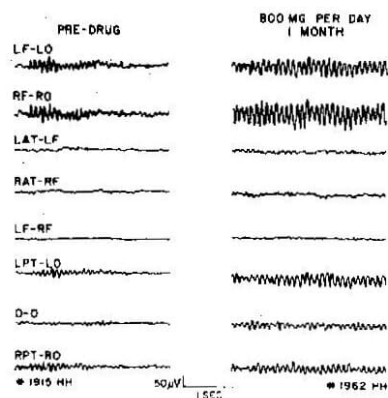


Fig. 2. Chlorpromazine, oral (female, age 34).

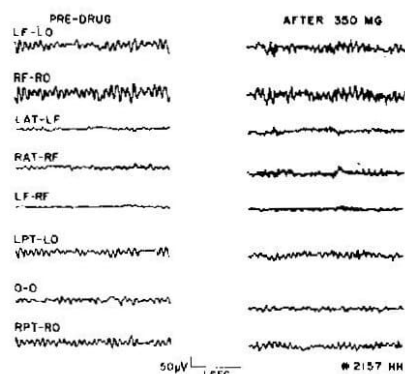


Fig. 3. Amobarbital, intravenous (male, age 31).

methamphetamine increase fast activity without increased synchrony. Desynchronization of frequencies is prominent after diethazine, LSD-25, Win-2299, JB-318, JB-336, and benactyzine.

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In subjects with post-convulsive δ activity, acute administration of chlorpromazine, promazine, trifluorpromazine, amobarbital and pentothal increased the per

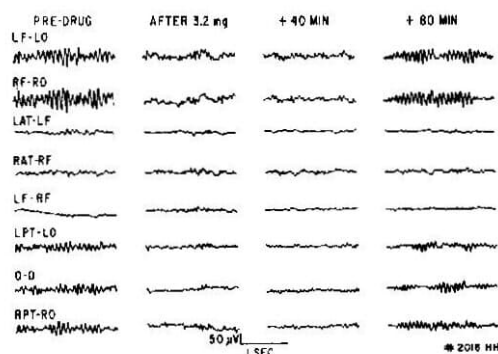


Fig. 4. Win-2299, intravenous (female, age 41).

cent time and voltage of slow wave activity. Decrease in voltage and per cent time of slow wave activity is seen with LSD-25, benactyzine, Win-2299, JB-318, JB-336 and diethazine^{5,6}.

Similar electrographic patterns are noted in chronic oral administration of these compounds. Chlorpromazine, promazine, high doses of reserpine and occasionally perphenazine elicit increased synchronization and a shift of frequencies to the δ range. Increased synchronization without frequency shift is occasionally observed with iproniazid. Increased high voltage fast activity is observed with meprobamate and barbiturates. Oral administration of LSD-25 and benactyzine induces EEG desynchronization with an increase in fast frequencies.

(b) Behavioral

Initial studies of convulsive therapy noted that behavioral change was dependent upon the development of synchronous slow wave activity⁸. Prominent among the associated behavioral effects were sedation, tranquillization and euphoria in agitated, depressed subjects, and a decrease in somatization, paranoid ideation, hallucinations and delusions in schizophrenic and excited subjects. Increasing agitation, paranoid ideation and panic were observed in less than 10% of the subjects.

Similar behavioral relationships were prominent with these psychopharmacologic agents. In acute experiments, administration of chlorpromazine, promazine and trifluorpromazine was associated with increasing sedation, drowsiness, denial and euphoria, decreasing agitation, panic, excitement and delusional and hallucinatory activity, and minimization and displacement of symptoms. Sedation, euphoria, denial and minimization were similarly associated with amobarbital.

Administration of amphetamine and methamphetamine resulted in behavioral alerting, hypomania, excitement, and increased motor activity. Similar increased alerting, excitement, tension and panic were observed after benactyzine. In addition to these patterns, illusory sensations and hallucinatory, delusional and paranoid ideation were observed with diethazine, LSD-25, Win-2299, JB-318, and JB-336.

Equally prominent with the behavioral changes were alterations in patterns of language. Previous studies of convulsive therapy had indicated that specific syntactic language patterns (as in the use of the third person mode, past and future tense, displacement, minimization, denial, clichés, and cryptic remarks) increased with increasing neurophysiologic change¹⁴. These language patterns were further exaggerated by intravenous amobarbital^{14,15}. In the present studies, chlorpromazine, trifluorpromazine and iproniazid increased these language patterns. Diethazine, LSD-25, Win-2299, and benactyzine decreased and reversed these language patterns, increasing the use of the present tense, first person mode, and somatization⁷.

(c) Relation of behavioral and electrographic observations

The electrographic patterns were consistently altered concurrently with behavioral changes both in the acute and chronic administration studies. Tranquillization, euphoria, sedation and minimization of symptoms were commonly associated with increased EEG synchronization and shift of frequencies to the delta range. Agitation, tension, panic, excitement, illusions and hallucinations were associated with a desynchronization of frequencies.

Similar patterns were demonstrated in subjects with prior δ activity. Agents that tended to synchronize frequencies, as chlorpromazine and barbiturates, augmented the per cent time δ activity and enhanced clinical patterns, while agents that desynchronized frequencies, as diethane, LSD-25 and benactyzine, minimized the clinical effects ascribed to repeated convulsions⁵⁻⁷.

DISCUSSION

These observations are consistent with the neurophysiologic-adaptive hypothesis of the mode of action of the newer psychopharmaceuticals⁴. This hypothesis states that the clinical efficacy of psychotropic drugs is dependent upon the induction of a persistent alteration in cerebral function which provides the milieu for changes in the subjects' interaction with the environment. The variety of neurophysiologic patterns induced by these agents is in contrast to the limited patterns resulting from convulsive therapy and thus provides amplification of the original hypothesis. It is evident from these studies that the type of neurophysiologic alteration induced, as reflected in EEG synchrony and frequency patterns, is related to specific types of behavioral adaptation. With increasing synchrony and a shift to the δ frequency spectrum, tranquillization, sedation and decreased agitation become prominent, while desynchronization and a shift to β frequencies are associated with excitement, illusions and delusional ideation.

These studies are also consistent with numerous reports of the neurophysiologic effects of these compounds^{2,3,11,13,19,21}, and specifically support and amplify those of WIKLER who concluded, in his studies of morphine and mescaline, that "regardless of the nature of the drug administered, shifts in the pattern of the electroencephalogram in the direction of desynchronization occurred in association with anxiety, hallucinations, fantasies, illusions or tremors, and in the direction of synchronization with euphoria, relaxation or drowsiness"²⁰.

This hypothesis, and the electrographic measure of neurophysiologic change, lends itself to application in the assay of new psychotropic drugs⁴, the rational

application of pharmacotherapy⁷, and as a basis for further experimental study of neurophysiologic-behavioral relationships in psychiatry.

ACKNOWLEDGEMENT

We are grateful for the cooperation of the following laboratories who made supplies of the various psychopharmaceuticals freely available: Ciba Pharmaceutical Prods. (reserpine), Lakeside Laboratories (JB-318, 336), Eli Lilly & Co. (amobarbital), Merck, Sharpe & Dohme (benactyzine), Riker Laboratories (deanol), Roche Laboratories (iproniazid), Sandoz Pharmaceuticals (LSD-25), Schering Corp. (perphenazine), Smith, Kline & French Laboratories (chlorpromazine, diethazine), E. R. Squibb & Sons (trifluorpromazine), Winthrop Laboratories (Win-2299), Wyeth Laboratories (promazine, meprobamate).

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CHEMICAL ASPECTS OF PSILOCYBIN, THE PSYCHOTROPIC PRINCIPLE FROM THE MEXICAN FUNGUS, *PSILOCYBE MEXICANA* HEIM

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Since the pre-Columbian era, the Indians of Mexico have made the eating of certain fungi a part of their religious rites; tribal soothsayers ate such fungi to acquire clairvoyance. An American ethnologist, R. GORDON WASSON, and his wife, made several expeditions into remote regions of Mexico between 1953 and 1955. They studied the