EFFECTS OF PSYCHOTROPIC DRUGS ON COMPUTER 'SLEEP PRINTS' IN MAN*

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Investigations have shown that all psychoactive drugs produce qualitative and quantitative changes in the EEG. The EEG alterations depend on the type of drugs given, the dosage, and the route and rate of administration (Itil, 1964). Some psychotropic compounds such as chlordiazepoxide and LSD produce characteristic changes in the EEG, while many others induce no 'drug-specific' alterations per se.

Due to the limitations of the resting EEG, functional electroencephalography (Liberson *et al.*, 1943; Liberson, 1945) using sleep activation was advocated in the early years of EEG and psychopharmacology research (Bente and Itil, 1954). Using hexobarbital and thiopental for EEG activation, it was shown that major neuroleptic drugs produce different alterations than thymoleptics (Goldman, 1960; Itil, 1964). The most significant finding that stemmed from our investigations using thiopental activation was the marked decrease of the length and depth of the postnarcotic sleep stage (Itil, 1961) after major neuroleptic drugs, while after thymoleptic compounds the postnarcotic sleep stage was not changed or was increased (Itil, 1964, 1966).

These drug-induced alterations of the postnarcotic sleep stage, which is similar to natural sleep, stimulated our interest in studying the effect of psychotropic drugs on the all-night sleep EEG. This presentation will be concerned primarily with the methods we have used to evaluate drug effects on all-night sleep and some of our results.

MATERIAL

Investigations were carried out in normal volunteers, chronic schizophrenics, and depressive patients. In general, EEG's were recorded for three consecutive drug-free nights to serve as a baseline, but in some subjects, up to 10 consecutive drug-free nights were investigated to study variability. The effects of single and chronic doses of drugs were determined in single subjects and in groups of patients. In order to classify psychotropic drugs, up to 20 different compounds were given to some subjects at weekly intervals.

This procedure was aimed at reducing individual variability, a factor that must be taken into account when studying drug effects on the sleep EEG. In addition to the classical psychotropic drugs, phenobarbital, dextroamphetamine, Dilantin, and atropine were also included in our investigations.

METHOD

Along with the all-night sleep EEG, muscle potential (EMG), rapid eye movement (REM), and the EKG were simultaneously recorded on paper and analog tape for a duration of $7\frac{1}{2}$ to 8 hours. The anterior vertex to right ear combination was analyzed using an IBM 1710 computer system. In our laboratory, period analysis has been the principal program used for computer analysis of the EEG (Burch *et al.*, 1964). Period analysis includes primary wave baseline cross and first derivative analyses. For both analyses, the per cent time spent in the

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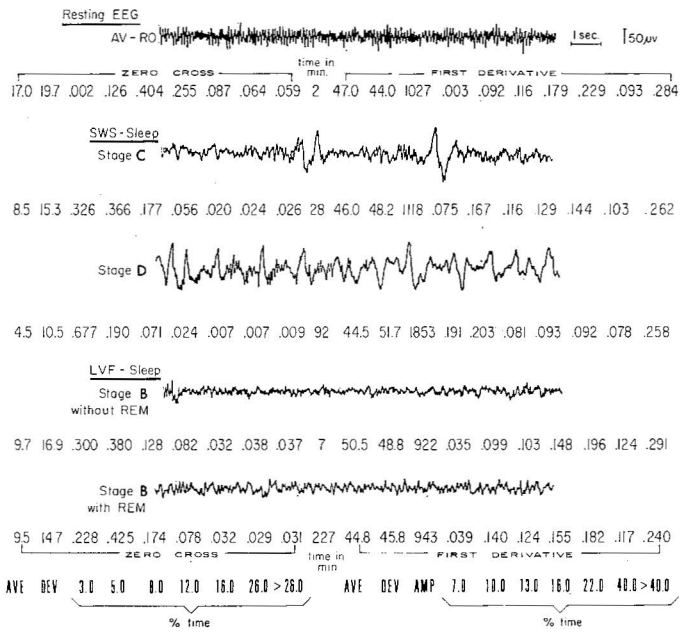

Fig. 1. C. K., 39 years old. Normal volunteer. Visual classification and computer period analysis data of all-night sleep EEG stages.

various frequency bands, the average frequency, and the frequency variability were the measures computed in each EEG sample. In addition, the average absolute amplitude and its deviation were also quantified.

Various methods to classify sleep have been developed in our laboratory in recent years using the period analysis approach (Fink and Shapiro, 1965; Itil *et al.*, 1968*a*, 1969). Our preliminary investigations indicated the study of the drug-induced alterations of the computer 'sleep prints' (Itil and Shapiro, 1969*a*, *b*) to be the most useful of the methods explored (Itil, 1968). Sleep prints were obtained by computer classification of each 30-second or 1-minute EEG sample. Each EEG sample was classified by the computer into one of the nine sleep stages on using a distance function approach on the mean values of the 7 period analysis measurements (3rd through 9th measurements of the zero cross analysis) (Fig. 1). The nine-stage sleep classification includes the five sleep stages of Loomis *et al.* (1936), with four additional intermediate sleep stages (Itil and Shapiro, 1968*b*). The results of the analyses of the all-night sleep EEG and the sleep classification can be obtained in numeric and/or graphic form with the digital computer. The graphic display of the computer-classified all-night sleep EEG demonstrates the profile of the sleep process for the entire night. Since these profiles seem to be characteristic for each person and remain relatively stable under standard conditions, we call them 'sleep prints' (Itil *et al.*, 1968*a*, 1969; Itil and Shapiro, 1969*a*, *b*). The temporal shape of the sleep process was found to be quite similar in the computer and visual classification (Fig. 2). With this method, programs have also been developed to classify sleep not only into nine stages but also into five stages (A-E of Loomis *et al.*, 1936) and three stages (low voltage fast sleep, LVF; slow wave spindle sleep, SWS; and neither, N) (Fig. 3). A high percentage of agreement was established for the computer and visual classifications, particularly using the five-stage classification (Itil *et al.*, 1969). However, we observed that the nine-stage sleep classification was more reliable than the three- or five-stage classifications in determining drug effects on the sleep print; consequently, we have used this in most of our investigations.

In general, we studied the following parameters in each all-night sleep record: (1) The total profile of the sleep EEG (computer sleep print); (2) The length of EEG sleep stages of the

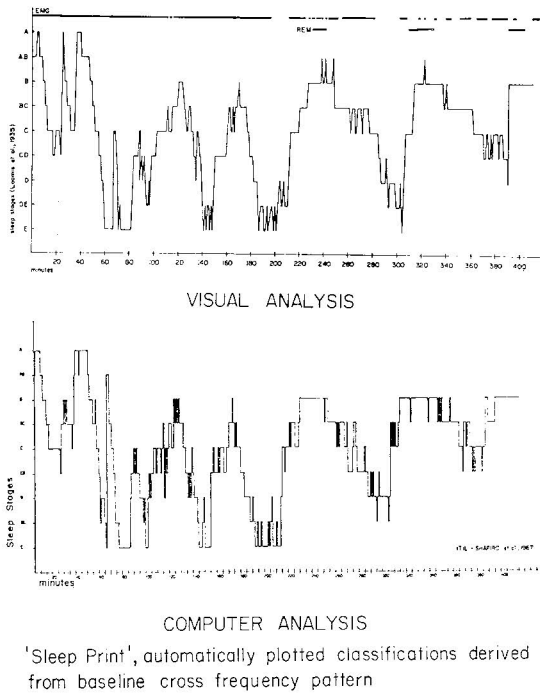

Fig. 2. H. K., 36 years old. Normal volunteer. Visual and computer classification of identical one-minute samples of all-night sleep EEG stages.

three-, five-, and nine-stage computer classifications (Stage B or 1 was determined using only quantitative EEG measurements so that in our computer classification stage B includes 'drowsiness periods' as well as 'REM periods'); (3) The length of the periods of 'paradoxical sleep' (Jouvet *et al.*, 1959) (the length of this stage was determined by EEG, REM and EMG using visual means), also called 'REM periods'; (4) The amount of single REM and REM bursts (counted by visual means); (5) The amount of cycles of the paradoxical sleep periods; and (6) The mean values of the 20 EEG variables of the computer period analysis during the total sleep time and during the total paradoxical sleep time.

RESULTS

If the conditions that affect the sleep process do not change, the temporal shape of the sleep print remains relatively stable over different drug-free nights (Fig. 4).

I. CHANGES IN SLEEP AFTER SINGLE DOSE OF DRUGS

A. Sleep prints

It was found that altering the dosage of a drug produced different effects on the sleep print. After 10 mg of chlorpromazine administered orally, no significant changes were seen (Fig. 5); after 25 mg, the variability of the sleep cycles was increased. After 60 mg of chlorpromazine, the maximum deep sleep cycle shifted from early night to early morning hours; light sleep stages (AB and B) decreased significantly; and the long-lasting B stage (Stage 1 of Dement and Kleitman, 1957) no longer occurred. The study of various 'neuroloptic' phenothiazines in

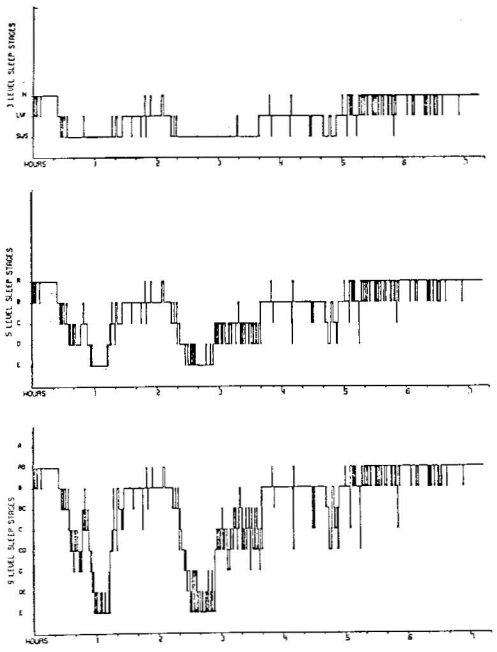

Fig. 3. Sleep prints based on 3, 5 and 9 level of sleep stages (based on computer period analysis of EEG). Automatically plotted classification derived from baseline cross frequency pattern.

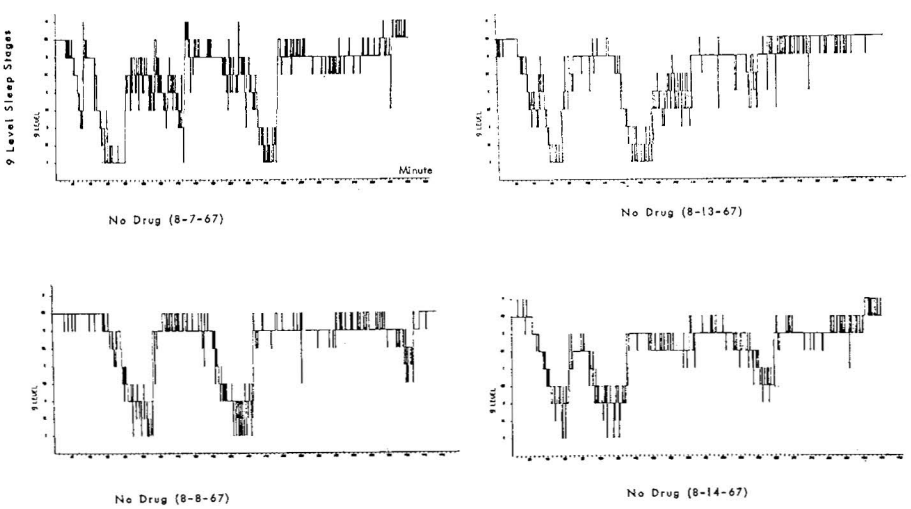

Fig. 4. J. B., age 28. Sleep prints in drug-free nights (based on computer period analysis of EEG).

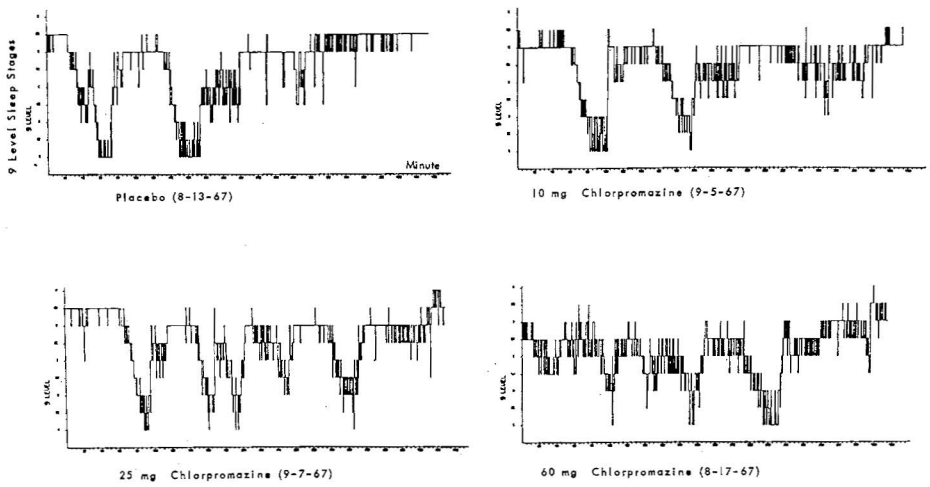

Fig. 5. J. B., age 28. Effect of different doses of chlorpromazine on sleep print (based on computer period analysis of EEG).

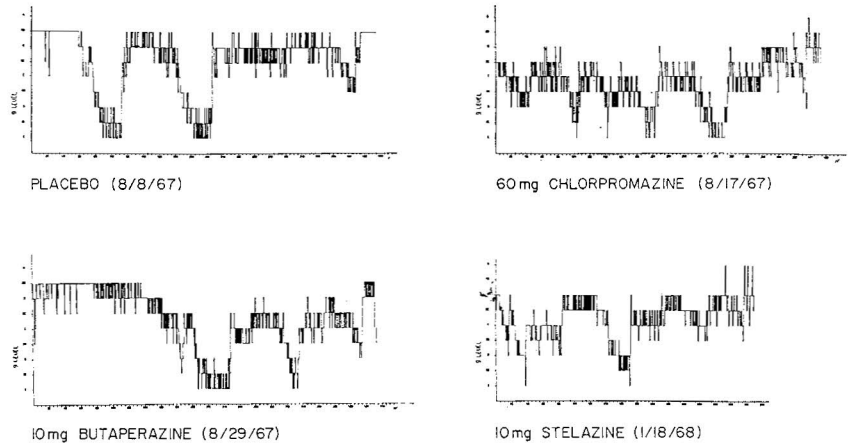

Fig. 6. J. B., 28 years old. Dx: Schizophrenia. Effect of major tranquilizers on sleep print (based on computer period analysis of EEG).

the same subject demonstrated that each drug induced marked alterations in the sleep print even after single doses. The effect of 60 mg of chlorpromazine is much different from that of 10 mg of butaperazine or 10 mg of Stelazine (Fig. 6). The effects of both piperazine phenothiazines are similar with respect to decreasing the deep sleep cycles. Deep sleep periods occurred less frequently after Stelazine than after other drugs or during drug-free nights. While Stelazine and butaperazine affected the sleep prints in somewhat the same manner, their influence on the length of paradoxical sleep and the amount of single and burst REM activity was completely different. Butaperazine markedly decreased the length of paradoxical sleep and the amount of REM in comparison to placebo nights, whereas both increased after Stelazine (Fig. 7). REM activity also significantly decreased after 60 mg of chlorpromazine.

The effects of various hallucinogenic drugs on sleep prints were most characteristic. Ditran,

an anticholinergic hallucinogen, shifted the sleep cycle from the onset to the end of the night's sleep and the length of very deep sleep stage was considerably decreased (Fig. 8). LSD, an indole hallucinogen, markedly inhibited the deep sleep cycles. Cyclazocine*, a narcotic hallucinogen, almost completely blocked the deep sleep EEG activity. Night sleep fluctuated between AB and C stages (1 and 2 of Dement and Kleitman, 1957). Both hallucinogens (LSD and cyclazocine) significantly inhibited the length of the paradoxical sleep stage and the amount of REM bursts and single REMs in comparison to placebo nights (Fig. 9). After Ditran, a slight decrease was seen in the amount of REM bursts.

Two minor tranquilizers, chlordiazepoxide (20 mg) and meprobamate (200 mg), given orally induced relatively slight alterations in the sleep print (Fig. 10). Phenobarbital (250 mg)

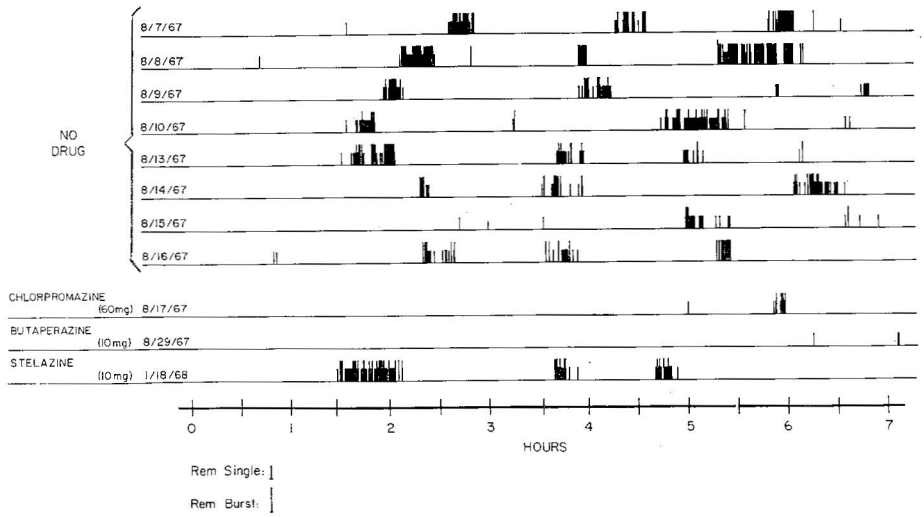

Fig. 7. J. B., 28 years old. Dx: Schizophrenia. Effect of major tranquilizers on 'REM' activity.

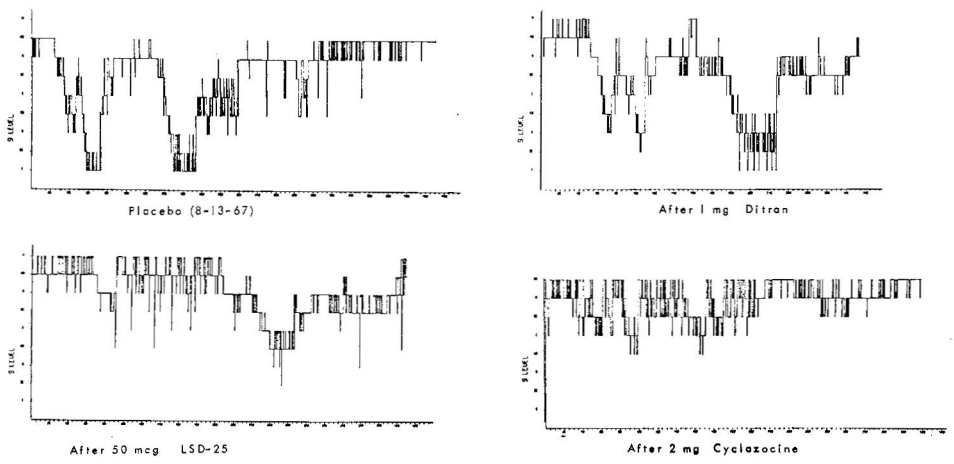

Fig. 8. J. B., age 28. Effect of hallucinogenic drugs on sleep print (based on computer period analysis of EEG).

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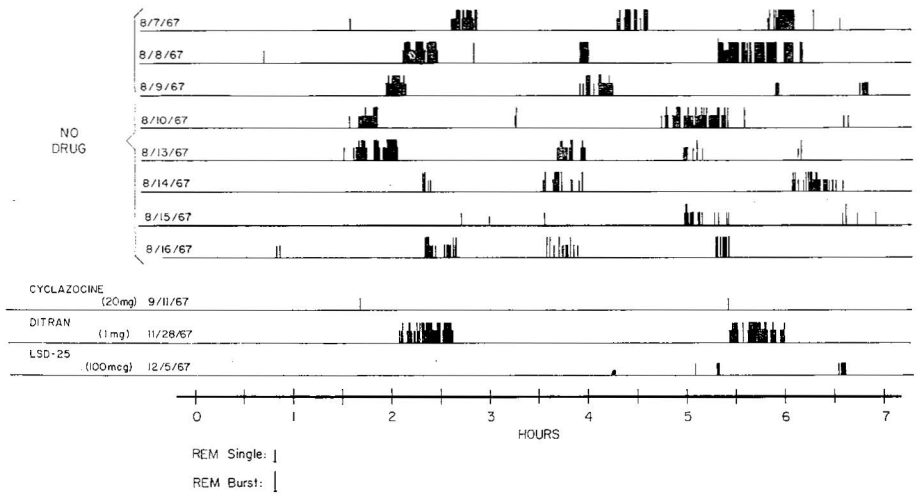

Fig. 9. J. B., 28 years old. Dx: Schizophrenia. Effect of hallucinogenic drugs on 'REM' activity.

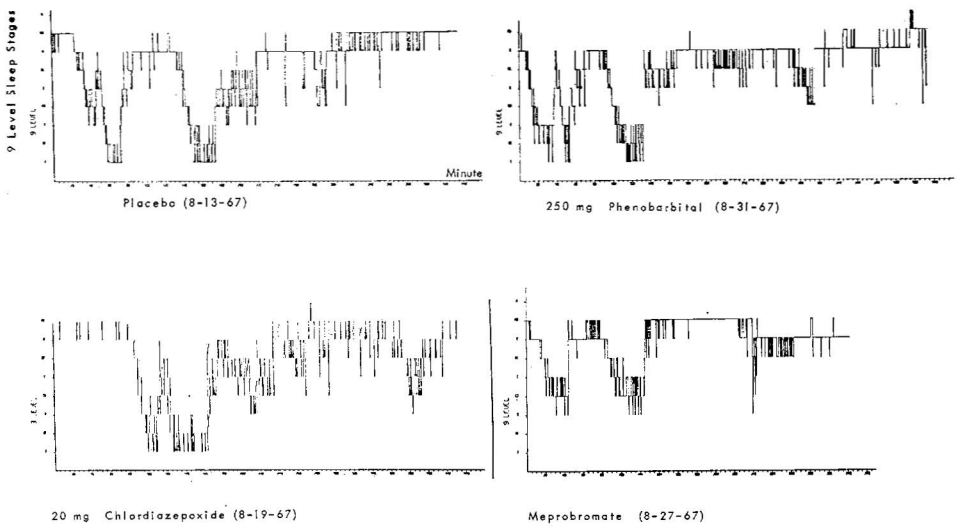

Fig. 10. J. B., age 28. Effect of barbiturate and minor tranquilizers on sleep print (based on computer period analysis of EEG).

produced even fewer changes in the sleep print than the two tranquilizers. After chlordiazepoxide, the variability of sleep stages increased. After meprobamate, very deep sleep periods decreased. The amount of single and burst REM activity did not change significantly after chlordiazepoxide in comparison to placebo nights (Fig. 11); however, the REM cycles were disturbed and there was a significant increase of the length of paradoxical sleep. After meprobamate, no significant changes were observed in any of the REM characteristics. After phenobarbital, a decrease of single REM activity was seen.

B. Length of sleep stages

Statistical analysis (t-test) of the length of sleep stages during drug nights as compared to

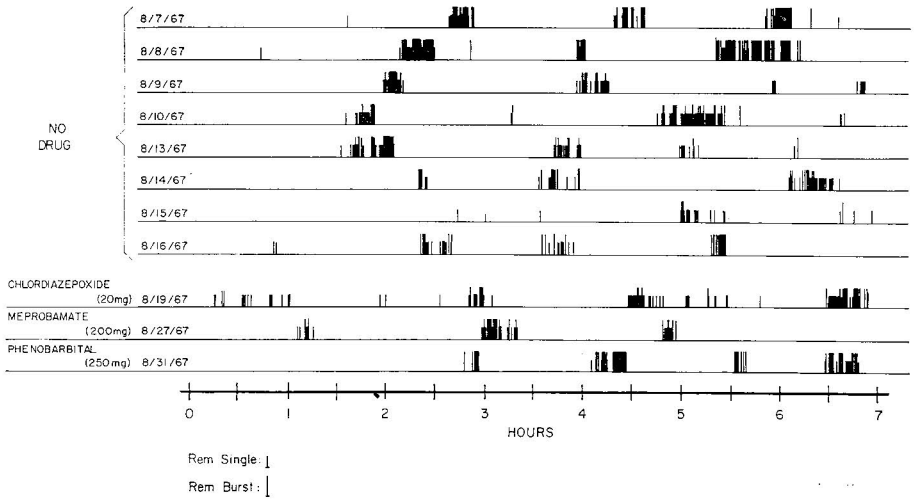

Fig. 11. J. B., 28 years old. Dx: Schizophrenia. Effect of minor tranquilizers and barbiturate on 'REM' activity.

the average length of the stages during eight placebo nights in a subject in whom 8 drug-free sleep recordings and 20 different drug recordings were carried out demonstrated that various psychotropic drugs induced significant changes in the length of EEG sleep stages. Chlorpromazine (60 mg), Phenergan, and Stelazine, all three phenothiazines, significantly decreased the length of light sleep stages (AB) in comparison to placebo nights (Table I). The length of light sleep stages was significantly increased by chlordiazepoxide, meprobamate, butaperazine, cyclazocine, and LSD. Stage B or 1, which included the drowsiness state and REM period, and was classified on the basis of low voltage fast EEG measurements only, decreased significantly after 60 mg chlorpromazine and Phenergan and increased after imipramine, phenobarbital, and 10 mg chlorpromazine. The length of deep sleep stages was increased by Phenergan and chlordiazepoxide, while it was significantly decreased by many other compounds.

C. Paradoxical sleep

The length of paradoxical sleep periods, which were determined by visual inspection and did not include drowsiness periods, was significantly decreased after single doses of 60 mg chlorpromazine, cyclazocine, LSD, and butaperazine. There was a significant increase in comparison to placebo nights after Dilantin, Stelazine, chlordiazepoxide, imipramine, 10 and 25 mg, chlorpromazine and dextroamphetamine. Paradoxical sleep cycles showed a marked decrease after 60 mg chlorpromazine, Phenergan, cyclazocine, LSD, butaperazine, and 10 and 25 mg chlorpromazine (Table I).

D. Single or burst REM activity

The amount of single REM activity which was counted by technicians decreased significantly after single doses of 60 mg chlorpromazine, Phenergan, cyclazocine, LSD, imipramine, butaperazine, and phenobarbital. The amount of single REMs was significantly increased only after Stelazine. REM bursts decreased after 60 mg chlorpromazine, cyclazocine, LSD and butaperazine. None of the drugs increased REM bursts significantly (Table I).

E. EEG computer period analysis measurements

Statistical analysis of the mean values of the EEG computer period analysis measurements

TABLE I

Effect of drugs on sleep stages and on REM
(Drug night vs *8 placebo nights)*

Drug *vs*		Sleep stages																REM			
		9 level									5 level					3 level			Length of periods	Single	Burst	Cycles
		A	A-B	B	B-C	C	C-D	D	D-E	E	A	B	C	D	E	N	LVF	SWS				
Chlorpromazine	60 mg		−	−	++	++						−	++		−	−	−	+	−−	−−	−	−−
Phenergan	50 mg		−−	−−	++	++	++			++	−−	−−	++	+	++	−−	−−	++		−−		−−
Cyclazocine	2 mg		++				−−	−−	−−	−−	++			−−	−−	++		−−	−−	−−	−−	−−
LSD-25	100 mcg	++	++			−	−	−−	−−	−−	++			−−	−−	++		−−	−−	−−	−−	−−
Dilantin	200 mg				++				−	−−	−				−−	−			++			
Stelazine	10 mg		−		++			−−	−−	−−	−			−	−−	−			++	++		
Chlordiazepoxide	20 mg		++					−		++	++			−		++			++			++
Imipramine	25 mg			+	−							+					+		+	−−		
Meprobamate	200 mg		++		−−		−	−−	−−	−−	++		−	−−	−−	++		−−				
Butaperazine	10 mg		+								+					+			−−	−−	−−	−−
Phenobarbital	250 mg			++			−					++					++			−−		++
Chlorpromazine	10 mg			+			−				−	+			−	−	+		++			++
Chlorpromazine	25 mg									−−					−−			−	++			++
Ditran	1 mg	++				−	−			−−					−							
Dextro-amphetamine	10 mg	++						−	−−	−−					−−				++			
Atropine	1 mg					−			−	−−					−−							−−

J. B. Age 28 years. Dx: Simple schizophrenic.
+ Increase at .05 or better (t-test); ++ increase at .01 or better; − decrease at .05 or less; −− decrease at .01 or less.

TABLE II

Mean values of the EEG computer period analysis measurements during all-night sleep time

(Single drug nights vs *the mean of four placebo nights)*

Drug/EEG variables		Zero cross									First derivative			Amplitude	Arms
		Average frequency	Frequency Deviation	0–3 cps	3–5 cps	5–8 cps	8–12 cps	12–16 cps	16–26 cps	Above 26 cps	Average frequency	22–40 cps	Above 40 cps		
LSD-25	50 mcg					++	++	+			−	++	−	−−	−
Ditran	1 mg		−			+	+	+			−	++	−	−−	−
Chlorpromazine	60 mg						−							+	
Chlordiazepoxide	20 mg			+							−				−
Phenergan	50 mg		−								−−				
Butaperazine	10 mg										++			+	+
Phenobarbital	250 mg		+								++			−	−
Chlorpromazine	10 mg			−		+	+	+			++			−−	−
Chlorpromazine	25 mg		+			+	+	++			++	−−		−−	
Dextroamphetamine	10 mg		−	−		++	+	++			−	++	−	+	++
Atropine	1 mg				+	+	+	+				+	−	−	+
Dilantin	200 mg				+	++		+			−−	++	−	−−	
Stelazine	10 mg		−−		++		+	++	−		−−	++	−−	−−	

J. B. Age 28 years. Dx: Simple schizophrenic.

+ Increase at .05 or better (t-test); ++ increase at .01 or better; − decrease at .05 or less; −− decrease at .01 or less.

TABLE III

Mean values of the EEG computer period analysis measurements during total paradoxical sleep time (Sincle drug nights vs *the mean of four placebo nights)*

Drug/EEG Variables		Zero cross									First derivative			Amplitude	Amplitude variability
		Average frequency	Frequency deviation	0–3 cps	3–5 cps	5–8 cps	8–12 cps	12–16 cps	16–26 cps	Above 26 cps	Average frequency	22–40 cps	Above 40 cps		
Chlorpromazine	60 mg					+									−
Chlordiazepoxide	20 mg	+			−		++							−−	−−
Phenergan	50 mg			+			−				−−				
Butaperazine	10 mg		+		+		−−				++			++	++
Phenobarbital	250 mg	+	+								++			−	
Chlorpromazine	10 mg		+								+			−−	
Chlorpromazine	25 mg		+								+			−−	
Dextroamphetamine	10 mg	++	−			+	++				−	++	−−	−−	
LSD-25	50 mcg	−	−		++	+		++	−		−	++	−−	−−	
Ditran	1 mg					+	++	+				++	−	−−	
Atropine	1 mg					+	++	++							
Dilantin	200 mg	−			+	+		++	−			++	−	−−	
Stelazine	10 mg	−	−−			+	+	+	++		−−	++	−−	−−	−

J. B. Age 28 years. Dx: Simple schizophrenic.

+ Increase at .05 or better (t-test); ++ increase at .01 or better; − decrease at .05 or less; −− decrease at .01 or less.

(20 EEG variables) of the total sleep time showed that after LSD, Ditran, 10 and 25 mg chlorpromazine, atropine, and dextroamphetamine, there was a significant increase in 5–16 c.p.s. activities (5–8, 8–12, and 16 c.p.s. frequency bands) in comparison to placebo nights (Table II). Average frequency in the first derivative analysis decreased after LSD, Ditran, chlordiazepoxide, Phenergan, dextroamphetamine, and Stelazine and increased after butaperazine, phenobarbital, Dilantin and 10 and 25 mg chlorpromazine. Amplitudes increased after 60 mg chlorpromazine, butaperazine, and dextroamphetamine.

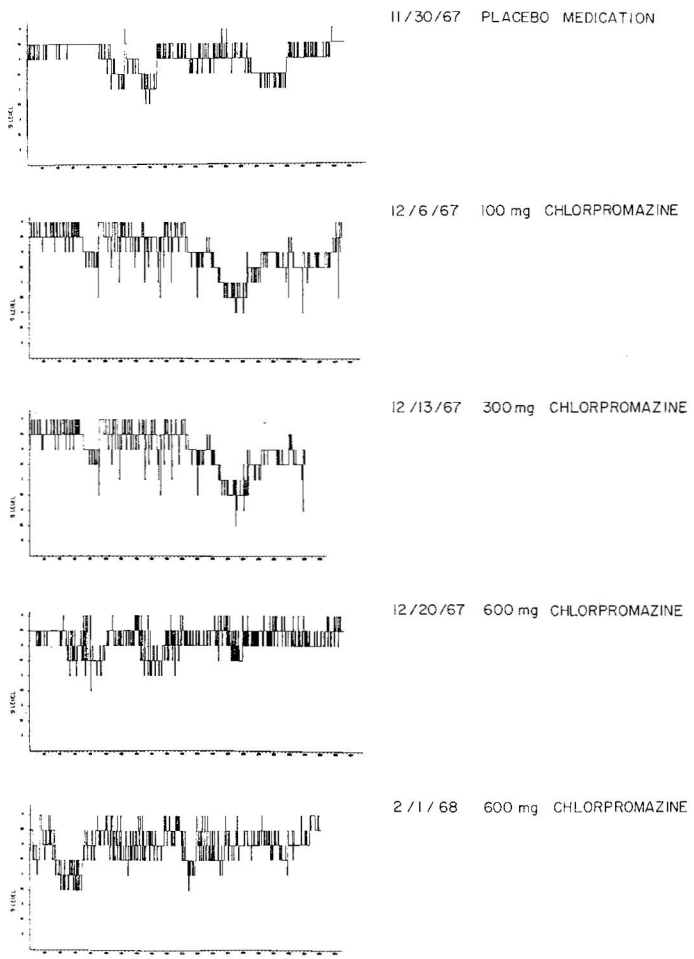

Fig. 12. B. F., 37 years old. Dx: Schizophrenia. Effect of chlorpromazine treatment on sleep print (based on computer period analysis of EEG).

The computer period analysis measurements during paradoxical sleep periods were also altered on drug nights as compared to placebo nights. The average frequency during REM periods was higher after chlordiazepoxide, phenobarbital, and dextroamphetamine, while it was lower after LSD, Dilantin, and Stelazine (Table III). In the zero cross analysis 8–12 c.p.s. activity was significantly greater after chlordiazepoxide, dextroamphetamine. Ditran, atropine, and Stelazine and less after Phenergan and butaperazine than during placebo nights.

II. CHANGES IN SLEEP AFTER CHRONIC ADMINISTRATION OF DRUGS

The chronic oral administration of chlorpromazine induced significant changes in the sleep print. With daily dosages of 100 and 300 mg chlorpromazine, an increase was seen in the depth of sleep during the latter part of the night (Fig. 12). After further treatment with 600 mg chlorpromazine, the cycles of deep sleep decreased. In this dosage range, REM activity increased (Fig. 13). Statistical analysis of the length of sleep stages demonstrated a significant increase of deep sleep stages CD and D (Stage 3) during the course of chlorpromazine treatment without increasing sleep stages DE and E (Stage 4) (Table IV). Stage A (awakening and relaxation) was also increased significantly in all phases of chlorpromazine

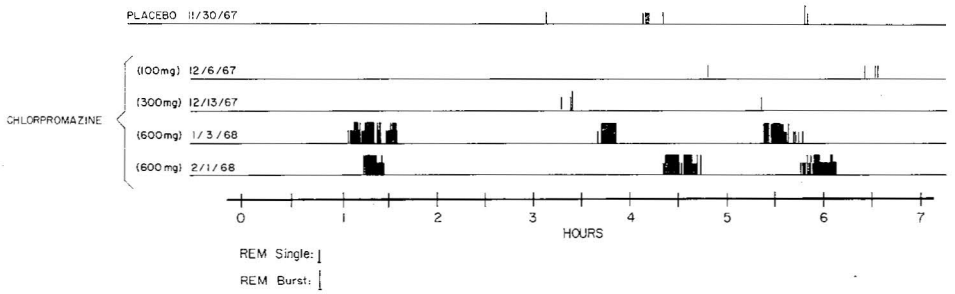

Fig. 13. B.F., 37 years old. Dx: Schizophrenia. Effect of oral chlorpromazine treatment on 'REM' activity.

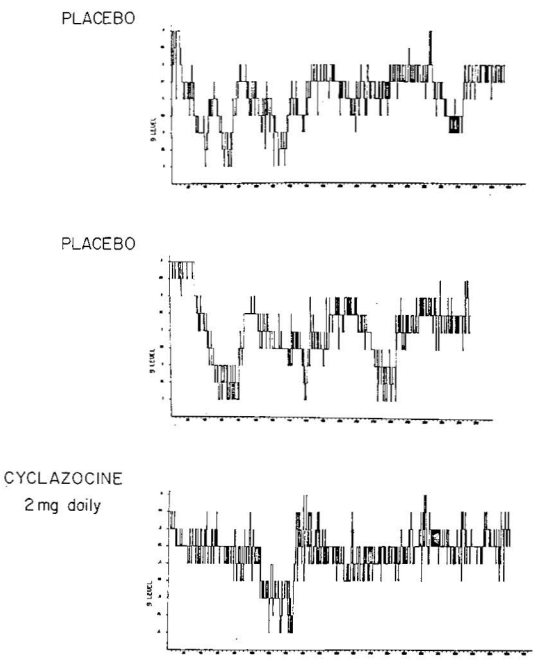

Fig. 14. G. R., 25 years old. Dx: Depression. Effect of cyclazocine treatment on sleep print (based on computer period analysis of EEG).

treatment. There was a marked decrease in the length of paradoxical sleep periods in certain phases of treatment. In contrast, a significant increase in the amount of single and burst REM activity was observed.

During treatment with cyclazocine, a hallucinogenic drug with antidepressive properties, marked alterations in sleep prints were observable in comparison to the sleep activity before treatment. The deep sleep stages and cycles were reduced (Fig. 14). During cyclazocine treatment a marked decrease of REM activity was observed (Fig. 15). Statistical analysis of the length of sleep stages showed a significant increase of light sleep stages A and AB (Table V). At the beginning of treatment there was a marked decrease of deep sleep stages (D, DE, and E) in comparison to placebo nights, while after three weeks of treatment the very deep sleep stage (E or 4) increased significantly. In all treatment periods there was a significant decrease in the length of paradoxical sleep periods, the amount of single and burst REM activity, was well as the number of paradoxical sleep cycles.

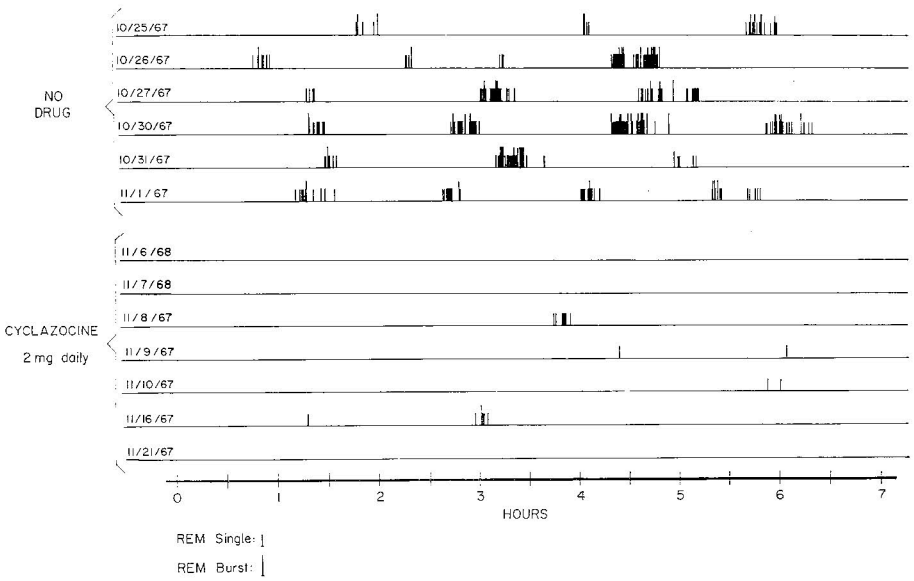

Fig. 15. G. R., 25 years old. Dx: Depression. Effect of cyclazocine treatment on 'REM' activity.

DISCUSSION AND CONCLUSION

Since the discovery of the cyclic variations of the all-night sleep process in association with REM activity and low voltage fast activity in the EEG (Dement and Kleitman, 1957), various investigators have studied the effect of centrally active drugs on the sleep process. In the majority of the drug studies, attention has been focused on the alterations of the paradoxical sleep (REM) periods. It was observed that almost all kinds of drugs—whether they are central stimulatory or inhibitory, effective in schizophrenia or depression, psychotogenic or tranquilizing—reduce the amount of time spent in paradoxical sleep (Oswald *et al.*, 1963; Feinberg, 1964; Rechtschaffen and Maron, 1964; Hartmann, 1967*a*, *b*). Only a few psychoactive drugs such as LSD and reserpine were found to increase paradoxical sleep time (Muzzio *et al.*, 1964; Green, 1965; Hartmann, 1966; Hoffman, 1967). The results of this study do not support the findings of others which show that almost all psychotropic drugs decrease REM periods. We found that 7 different compounds significantly increased the length of the REM periods (paradoxical sleep periods) after administration of single doses. Four different compounds significantly increased paradoxical sleep 'cycles'. An increase in the amount of single

TABLE IV

Effect of chlorpromazine treatment on sleep stages and on REM
(Drug nights (8) vs placebo night)

Chlorpromazine *vs* placebo	Sleep stages: 9 level A	A-B	B	B-C	C	C-D	D	D-E	E	5 level A	B	C	D	E	3 level N	LVF	SWS	REM: Length of periods	Single	Burst
12-6-67 100 mg	++		−−			++	+				−−		++			−−	++	−−		
12-13-67 300 mg	++	−	−−			++					−−		++			−−		−−		
12-20-67 600 mg	++	−	−		−−					++	−	−−			++	−	−−			
12-27-67 600 mg	++	++	−−	−−	−−					++		−−			++	−−	−−			
1-3-68 600 mg	++	−−		++		++	++	++		−−		−−	++	++	−−		++		++	++
1-10-68 600 mg	++	−−				++				−−			++		−−					
1-17-68 600 mg	++	−−	−−	−−	++	++	++			−−	−−	++	++		−−	−−	++			
2-1-68 600 mg	++	−−	−			++				+	−		++		−	−	+	−	++	++

B. F. Age 37 years. Dx: Schizophrenic.
+ Increase at .05 level or better (χ^2-test); ++ increase at .01 level or better; − decrease at .05 level or better; −− decrease at .01 level or better.

TABLE V

Effect of cyclazocine treatment on sleep stages and on REM
(Drug nights (7) vs placebo nights (5))

Drug nights (7) *vs* placebo nights (5)	Sleep stages: 9 level A	A-B	B	B-C	C	C-D	D	D-E	E	5 level A	B	C	D	E	3 level N	LVF	SWS	REM: Lengt of periods	Single	Burst	Number of periods
11-6-67 2 mg		++	++			−−	−−	−−		++	++		−−	−−	++	++	−−	−−	−−	−	−−
11-7-67 2 mg		++		+	+	−	−−	−−		++		++	−−	−				−−	−−	−	−−
11-8-67 2 mg					++		−−	−−	−			++	−−	−−				−−	−−	−	−−
11-9-67 2 mg		++	−	−−	++	++		−−		+	−	+	++	−−	++	−		−−	−−	−	−−
11-10-67 2 mg	++	++	−	−−	++	++	+	−		++	−		++		++	−		−−	−−	−	−−
11-16-56 2 mg		++		−	++	++	−−	−−	++	+		+	+					−	−−	−	−−
11-21-67 2 mg	++	++		−−			−−	−−	++	++		−		+	++		−	−−	−−	−	−−

G. R. Age 25 years. Dx: Depression.
+ Increase at .05 level or better (t-test); ++ increase at .01 level or better; − decrease at .05 level or better; −− decrease at .01 level or better.

REMs or REM bursts was observed, however, after a single dose of only one compound (Stelazine) and at certain times after chronic administration of chlorpromazine. The importance of independent analysis of the paradoxical sleep periods based primarily on the LVF EEG (excluding the drowsiness state) is clearly demonstrated by this study. We observed that various drugs affect the paradoxical sleep EEG period quite differently than they do the amount of REM activity. After a single dose of imipramine, a significant increase in the length of paradoxical sleep periods but a significant decrease in the amount of REM was observed. During chronic treatment with 600 mg chlorpromazine daily a significant decrease in the length of paradoxical sleep periods but an increase in the amount of REM activity was found. Our investigations indicated that in some psychiatric patients single or burst REM activity may not be present during paradoxical sleep periods (low voltage fast EEG periods) whether drugs are used or not. In contrast, we observed the appearance of the most characteristic REM activity during phases of sleep other than the low voltage fast EEG stage in some cases. Because REM and low voltage fast activity in the EEG do not always occur synonymously (dissociation), we prefer to use the term 'paradoxical sleep' introduced by Jouvet *et al.* (1959) to designate this stage of night sleep rather than REM periods. Measurements of the length of paradoxical sleep periods and/or the amount of single and burst REM activity alone are not sufficient to distinguish drugs of different central and clinical effectiveness. The total shape of the sleep EEG (sleep print) and the length of the various sleep stages reflected, however, the characteristic differences that exist between some tranquilizing drugs and hallucinogenic compounds. Furthermore, the study of the mean values of the computer-analyzed EEG characteristics during the total 8-hour sleep process, particularly during the paradoxical sleep time, is a promising parameter in the evaluation of drugs with different clinical effects.

SUMMARY

The effect of various centrally effective compounds on the sleep process was studied after single and multiple doses in psychiatric patients. Alterations of the digital computer-analyzed EEG sleep profiles (sleep prints), the length of sleep stages in the three-, five-, and nine-stage classifications, and the length of paradoxical sleep periods as well as the amount of single and burst REM activity were analyzed after drugs in comparison to placebo nights. On the basis of the amount of REM activity and the length of the paradoxical sleep alone a useful classification of psychotropic drugs could not be made. However, the sleep prints, the length of sleep stages, and the various EEG measurements during paradoxical sleep periods and during total sleep time did reflect the differences between hallucinogenic drugs and tranquilizers. The study demonstrated that the statement that all psychotropic drugs reduce 'REM time' is not true, at least as far as their effects in psychiatric patients are concerned.

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