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Effects of Mescaline, LSD-25, and Adrenochrome on Depth Electrograms in Man

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In a recent report concerning the reversibility by chlorpromazine of psychoses induced by means of mescaline and *d*-lysergic acid diethylamide (LSD-25), careful attention was given to the clinical and electroencephalographic changes.[1] Although the clinical changes of this reversal effect were immediate and striking, the conventional electroencephalographic changes were minimal, and it was difficult to assess them. It was noted in another recent study that mescaline and LSD-25 failed to activate temporal-lobe epilepsy either clinically or electroencephalographically.[2]

Because of these factors, it was hoped that depth electrographic studies might be fruitful in elucidating the effects of these drugs. It was hoped also that study by means of depth electrography of the effects of adrenochrome might elucidate its reported actions of inducing a psychosis without insight in volunteers[3] and increasing the paroxysmal discharges in the electroencephalograms of epileptics.[4] Scalp electroencephalography and depth electrography were undertaken as specific aids to diagnosis and as preliminary measures to definitive surgical treatment in each patient in our study.

METHOD

After the administration of mescaline and LSD-25, two patients who had intractable epilepsy and psychosis and three who had chronic schizophrenia were studied by means of the techniques of depth electrography developed and defined in this laboratory.* One of the epileptic and two of the schizophrenic patients also received adrenochrome. Each patient had extensive control studies, lasting as long as two weeks per patient, previous to the time of administration of the drug. Further control observations were repeated every day of the study. Electrocardiograms were recorded simultaneously with depth electrograms in two patients.

The dose of mescaline varied between 400 mg. and 1 gm., whereas that of LSD-25 ranged from 50γ to 150γ. The dose of adrenochrome† varied between 50 and 75 mg. The mescaline and LSD-25 were administered orally; the adrenochrome was given intravenously as a freshly prepared solution in 10 cc. of sterile water. At the presumed height of the reactions to mescaline and LSD-25, each patient received an intravenous injection of 50 mg. of chlorpromazine dissolved in 10 cc. of sterile water. The mescaline, LSD-25, and adrenochrome were administered during the fasting state in all instances.

CLINICAL RESULTS

The clinical results are summarized in the accompanying Table. This report is based on 18 observations, 6 with mescaline, 6 with LSD-25, and 6 with adrenochrome. With the doses of drugs used, the clinical effects were moderate when compared with the responses of a series of volunteers[1] and a group of epileptics[2] without psychosis, who received substantially smaller doses than were used in this study.

Mescaline produced autonomic changes consisting of slight pupillary dilatation and facial flushing. In the psychic sphere, three patients who were negativistic in the control

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* References 5 and 6.

† A. Hoffer, M.D., Ph.D., director of psychiatric research, University Hospital, Saskatoon, Sask., Canada, supplied pure adrenochrome.

Clinical Response and Changes in Depth Electrograms Produced by Mescaline, LSD-25, and Adrenochrome

Patient	Diagnosis	Drug and Dose	Clinical Response	Changes in Depth Electrogram	Reversal Effect of Chlorpromazine, 50 mg.	
					Clinical Effect	Effect on Electrogram
1	Chronic paranoid schizophrenia; scalp EEG essentially normal	Mescaline, 1 gm.	Inappropriately silly, loosening of associations, flushed facies, dilated pupils	Diminution in voltage from temporal depths, with increased occurrence of paroxysmal discharges of 2 to 7 cps	Restored to control status	Paroxysmal discharges persisted but were interspersed with slower frequencies of medium voltage and 2 to 3 cps
		LSD-25, 100γ	Persistent silly smile	Synchronous paroxysmal discharges of 2 to 7 cps	Restored to control status; slight drowsiness	Same as above
		Adrenochrome 50 mg.	Body-image disturbances: "My arm wiggles—ha, ha . . . see it happen." Perceived "red" on photic stimulation	Moderate increase in bitemporal paroxysmal discharge of 2 to 7 cps; increased persistence and amplitude of focal temporal sharp-wave discharge from depths	.....	.....
		60 mg.	Essentially the same as with 50 mg.	Same electrographic changes	.....	.....
		75 mg.	Essentially the same as with 50 mg.	Same electrographic changes	.....	.....
2	Chronic catatonic schizophrenia; scalp EEG showed Grade 1 bitemporal dysrhythmia	Mescaline, 1 gm.	Minimal effect; flushed facies	Increased paroxysmal activity	Relaxation	Restoration of occipital depth alpha-like activity
		LSD-25, 100γ	Grinning, laughing; looked in mirror and said, "It looks different"; bit nails; chewing movements, perspiration, flushed facies	Same electrographic changes	Facies restored to control pattern; restless, moaned without apparent reason	Rhythmic fast build-up initially
		Adrenochrome 50 mg.	Pleasant smile on face; waxy flexibility; colors on photic stimulation	Moderate increase in paroxysmal activity	.....	.....
		60 mg.	Very relaxed; waxy flexibility; colors on photic stimulation	Same electrographic changes	.....	.....

3	Chronic catatonic schizophrenia; scalp EEG essentially normal	Mescaline, 400 mg.	Mescaline facies; relatively communicative; posturizing; appears to have hallucinations	Minimal	.....	.....
		LSD-25, 50γ	Grinning, laughing, talking to self, more communicative	Minimal	.....	.....
4 *	Psychosis with convulsive disorder and epileptic deterioration; scalp EEG showed dysrhythmia Grade 3, right sylvian sharp wave	Mescaline, 400 mg.	Talkative, buoyant; "I see bugs—they say I'm not nice"; mescaline facies, pupillary dilatation	Quieting effect on spike activity and background; occipital bursts with eyes closed during music; synchronous waxing and waning of alpha-like activity with music	Restored to control status, other than slight drowsiness	Record resembled control tracing
		LSD-25, 50γ	Talkative; saw "colors of all different shapes" on photic stimulation	Changes similar to mescaline changes but not so clear	Same effect as with mescaline	Same effect as with mescaline
5 †	Psychosis with convulsive disorder and epileptic deterioration; scalp EEG showed dysrhythmia Grade 3, right sylvian sharp wave	Mescaline, 1 gm.	Voluble word salad; euphoric; continuous hallucinations; suggestion of catatonia; posturizing; smacking of lips; perspiration; dilated pupils; mescaline facies	Diminution of epileptic spike discharges with generalized decrease in voltage; appearance of new spike focus in temporal depths, which fired continuously with double spikes 3 times per second; focus stopped firing a few times for 6 to 8 sec. before chlorpromazine was used; continuous focal high-voltage activity from ventromedial region of frontal lobe during pronounced hallucinations	Restored to control state; sullen, negativistic, uncooperative	Record resembled control state; complete abolition of double spikes elicited by mescaline; record changed three times after injection of chlorpromazine
		LSD-25 100γ	Talkative, laughing, euphoric; word salad; flushed facies	As above	As above	.....
		150γ	Restless, difficult to get in contact with, laughing, euphoric, talkative; word salad	As above	As above	.....
		Adrenochrome 50 mg.	Very relaxed; drowsy yet easily aroused; in better contact	High-voltage waves 2 to 3 cps associated with drowsiness	.....	.....

* Patient had excision of local cerebral scar with pronounced gliosis deep in right temporal lobe, as determined by depth studies.

† Clinical effects and changes in depth electrogram produced by mescaline could not be nullified by convulsions produced by pentylenetetrazol (Metrazol).

states became more communicative and euphoric. Their stream of thought showed the same complexes that were noted in the control period; however, further loosening of the associations was noted. In general, these reactions reached their height two to four hours after the drug was given and then subsided immediately after the intravenous injection of chlorpromazine.

patients were in better contact and mood after these studies.

It was difficult to evaluate the effects of adrenochrome on the psyche. The epileptic (Patient 5 in the Table) appeared to be relaxed and became drowsy. One schizophrenic (Patient 1) appeared to show loosening of associations and increase in disturbances of body image; for instance, he

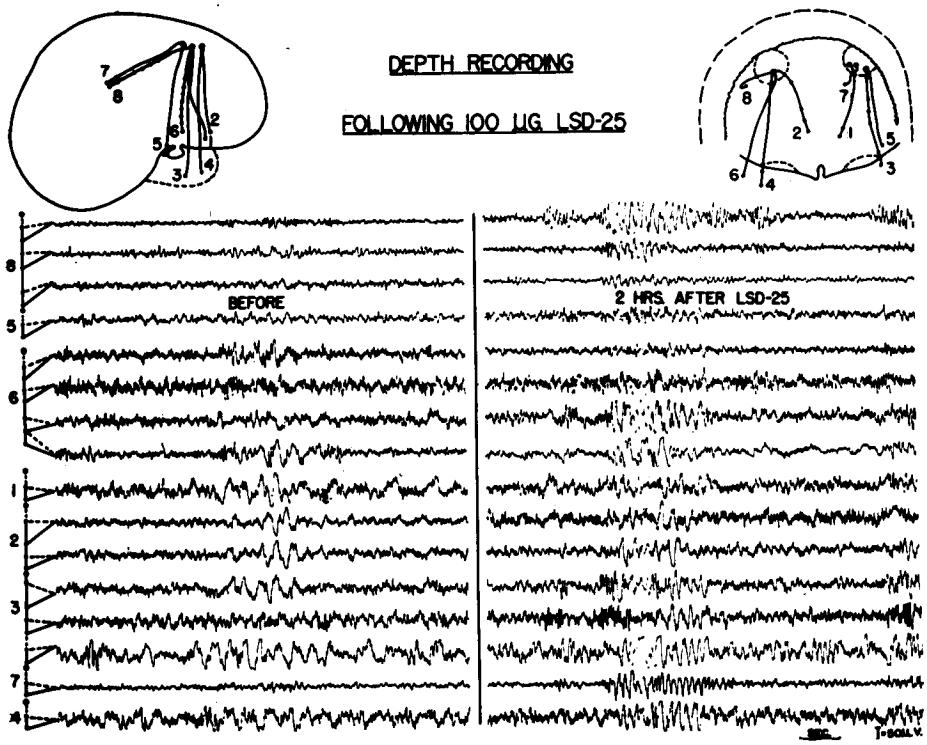

Fig. 1.—Generalized paroxysmal burst in a schizophrenic patient. Before medication, the paroxysms occurred infrequently; after administration of 100γ of LSD-25, they occurred every 10 to 20 seconds.

The clinical effects of LSD-25 closely resembled those of mescaline, although the mescaline reactions in this study appeared to be more intense and were associated with a typical facies. However, inappropriate laughing and giggling were noted more commonly after use of LSD-25 than after administration of mescaline. In several instances when the patients were returned to the ward after receiving mescaline and LSD-25, the nurses volunteered the observation that the

raised his hand, gazed at it, and said, "My arm wiggles and waves—ha, ha!" The other schizophrenic who received adrenochrome (Patient 2) experienced catalepsy on two occasions, which persisted for more than 30 minutes. At these times, his upper extremities were held in unnatural positions that volunteers who served as controls could not maintain for long. This was not his usual reaction, and a similar state did not develop with either mescaline or LSD-25.

EFFECTS ON DEPTH ELECTROGRAM

The effects on the depth electrogram also are summarized in the Table. A generalized diminution in voltage of the depth rhythms from the two epileptic patients was noted approximately 30 minutes to 2 hours after the oral administration of mescaline and LSD-25. The three schizophrenic patients responded to these drugs with an increased paroxysmal activity (Fig. 1). There was no apparent correlation between the dose of these drugs and the effects produced clinically or on the depth electrograms.

In the two epileptic patients, foci of spike waves that existed in the control period on occasions tended to decrease greatly after the administration of mescaline and LSD-25. The tracings from Patient 5, an epileptic, showed a new activity in the form of spike waves recorded from the depths of the temporal lobe. They were double spikes that were present continuously for several hours at the rate of 3 per second (Fig. 2). The pulse rate during the entire test was at no time more than 120 beats per minute. At the time of the persistent double spikes, the patient, as judged by the facial expression, behavioral reactions, and verbal admission, was continuously disturbed, presumably with pronounced hallucinations. Continuous focal high-voltage activity at this stage was recorded from the ventromedial region of the frontal lobe (Fig. 2, bottom tracing). The

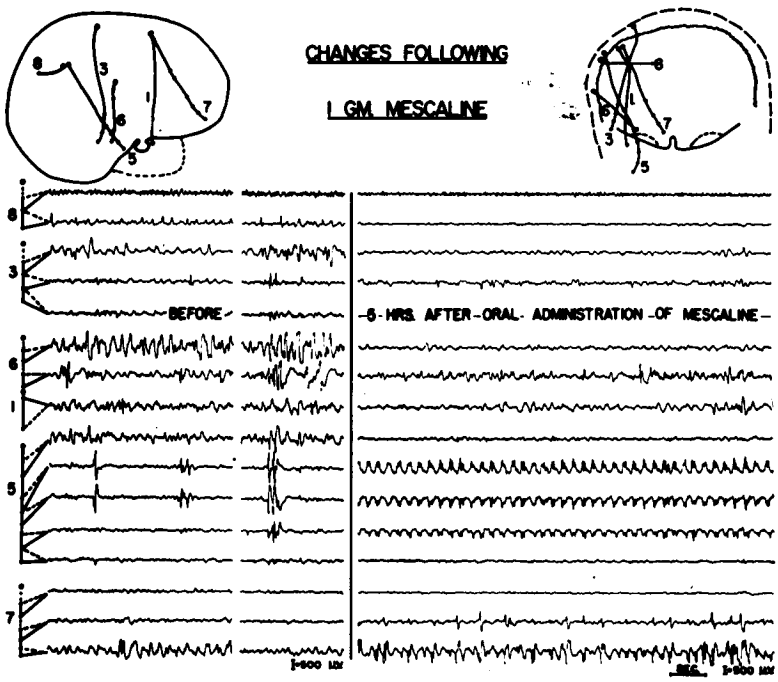

Fig. 2.—Changes in the depth electrogram after administration of 1 gm. of mescaline to an epileptic patient. Note diminution in voltage of the spike discharges and appearance of a persistent new double-spike focus.

temporal double-spike discharge very infrequently ceased during the test for more than six to eight seconds. Patient 4, the other epileptic, at the height of the reaction to mescaline and while having visual hallucinations, showed polyphasic spike discharges from the depths of the occipital region (Fig. 3, upper strip). These were more prominent in the presence of synesthetic visions induced by mescaline. In some respects, these discharges resembled lambda

waves, as seen from electroencephalograms recorded from the scalp. However, in the depth records they consisted of a burst of polyphasic spikes. Lambda waves in depth are monophasic or biphasic,[6] as seen in the top strip of Figure 3.

Patient 4, who was especially cooperative while under the influence of mescaline, also had waxing and waning of the alpha-like spindles from the depths of the occipital region that corresponded with the rhythms of music (Fig. 3, middle and lower strips). For instance, she had one pattern with a relaxing harmonica waltz, another with some swing music, and still a third pattern with a mournful hillbilly tune. This synchronous alpha-like activity occurred at the height of her mescaline-induced state, whereas it never appeared without music or in the control period with music.

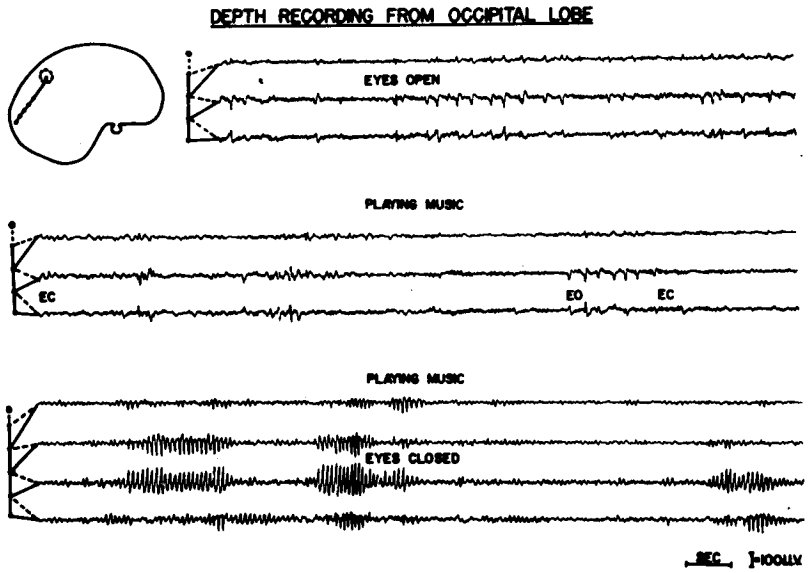

Fig. 3.—Depth electrograms in another epileptic patient. Control lambda waves with the patient looking at a picture are recorded in the top strip. The middle strip illustrates the polyphasic spike discharges associated with synesthetic visions induced by administration of mescaline. The lower strip shows synchronous waxing and waning of alpha-like discharges associated with music during the mescaline effect. All three strips were recorded from the same electrodes.

Within a few minutes after the intravenous administration of 50 mg. of chlorpromazine, the electrographic recordings reverted to the control patterns present before the use of mescaline and LSD-25. However, the reversal process in Patient 5 was characterized by complex changes, as illustrated in Figures 4 and 5. In one instance (Patient 5), the record changed spontaneously before the use of chlorpromazine, with the appearance of fast activity; it then went directly from this state to the premescaline state, with less pronounced complex changes (Figs. 4 and 5). On this occasion, the tracing resembled the premescaline recording for five minutes before it reverted to the mescaline type of recording. As seen in Figures 4 and 5, the double spikes from the depths of the temporal lobe disappeared and the epileptic foci resumed their control appearance. In Patient 4, musically driven occipital bursts associated with visual hallucinations under the influence of mescaline were not present after use of chlorpromazine. Other than occasional slight drowsiness, which was accompanied infrequently by slower frequencies, the pa-

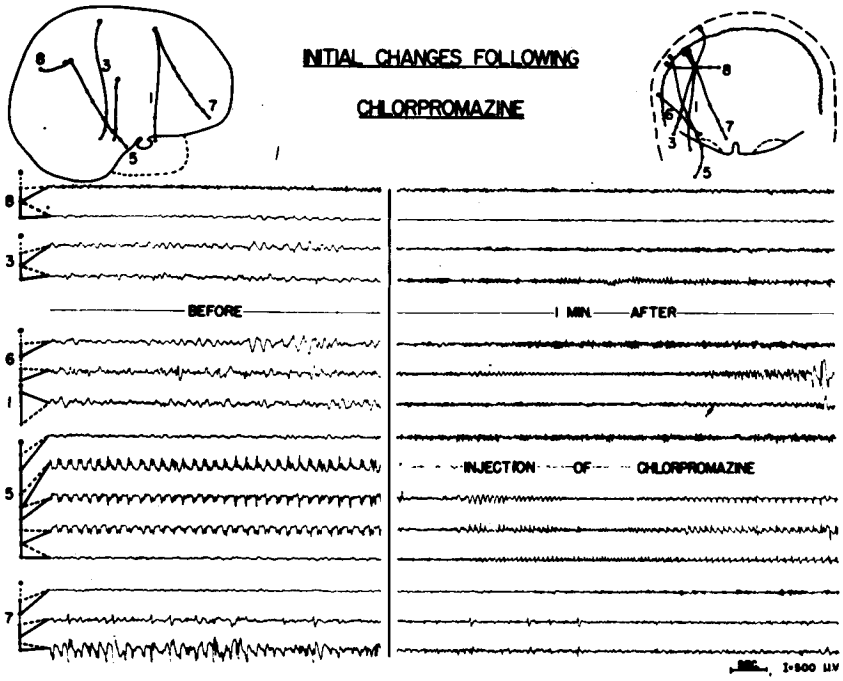

Fig. 4.—Effect of chlorpromazine on the electrogram of an epileptic patient. Note the appearance of fast activity one minute after the intravenous injection of 50 mg. of chlorpromazine.

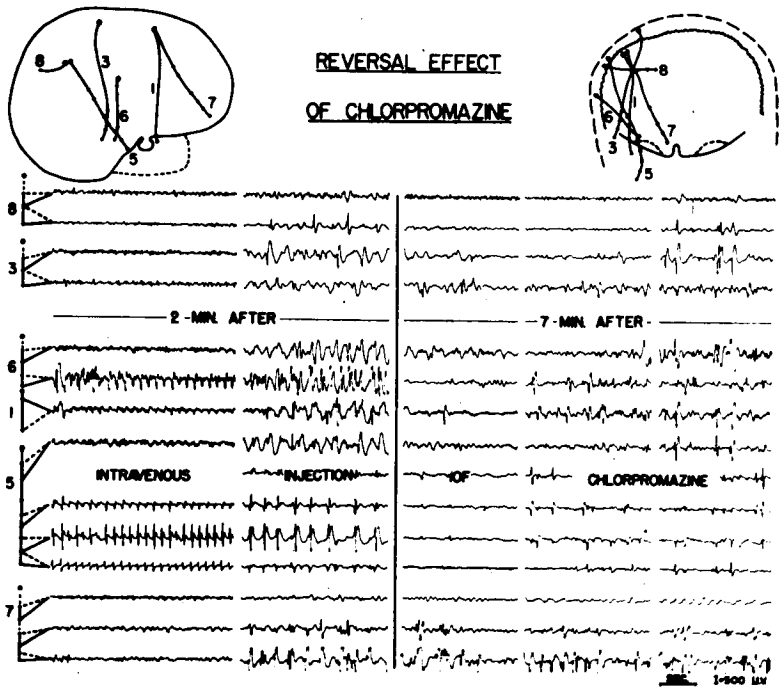

Fig. 5.—Further effects of chlorpromazine in same patient whose electrogram is seen in Figure 4. Note the complex changes before the record reverted to the premescaline stage.

tients clinically resembled their control condition. They were always readily alertable and had clear sensoriums.

An increase in the existing paroxysmal activity was noted in the two schizophrenics (Patients 1 and 2) who received varying doses of adrenochrome at different times. Patient 1 showed a focal sharp wave in activity recorded from the temporal region at rare intervals during the control study. This had some resemblance to similar activity described in an earlier paper.[7] However, in the control period of Patient 1, it was impossible to determine whether he had hallucinations at the time of this focal sharp discharge. After injection of adrenochrome, there was persistent appearance of this focal sharp wave of maximal amplitude from the temporal region (Fig. 6). In the epileptic (Patient 5), the administration of adrenochrome was followed immediately by the appearance of high-voltage waves of 2 or 3 cps, associated with drowsiness. This was not accompanied by any clinical changes other than relaxation.

The electrocardiograms showed no gross changes, as recorded in two schizophrenic patients, between the control states and the states induced by the use of mescaline, LSD-25, and adrenochrome.

COMMENT

It would appear that administration of mescaline, LSD-25, and adrenochrome can cause striking changes in the depth electrogram. Because the observations in this study were confined to two patients who had epilepsy with psychosis and three who had chronic schizophrenia, these definite limitations preclude any general statements with regard to the effects of these drugs. However, it should be noted that the activation of the temporal depths by mescaline and LSD-25 in one patient appeared to coincide with a period of active auditory and visual hallucinations. It should be noted also that

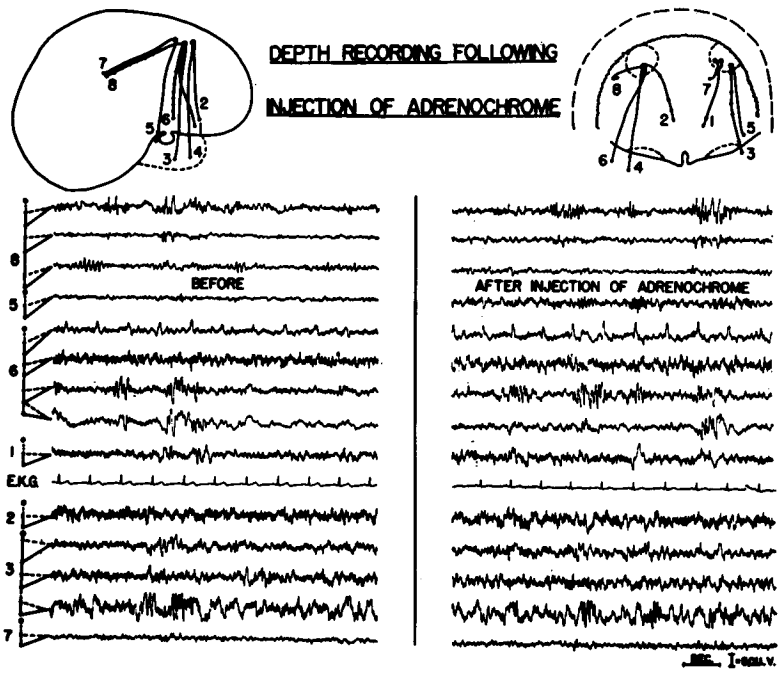

Fig. 6.—Effects of adrenochrome on the electrogram of a schizophrenic. Note the focal sharp wave seen at rare intervals in the control recording and its persistent appearance with higher voltage after administration of 50 mg. of adrenochrome.

the double spikes produced by mescaline and LSD-25 appeared in the proximity of a region from which a similar discharge was found in a patient during spontaneous hallucinations without any previous administration of drugs.[7] A common mechanism might be activated that accounts for the acute psychotic episode. The immediate reversing effects of intravenous administration of chlorpromazine on the clinical and electrographic states induced by means of mescaline and LSD-25 are suggestive of a possible mode of action centered in this region.

The psychic effects and those produced on the depth electrograms in the two schizophrenics by use of adrenochrome are similar to those reported by Szatmari and associates,[4] who described an increase in bilateral paroxysmal abnormalities in electroencephalograms recorded from the scalps of epileptics. The observation that adrenochrome failed to induce clinical and electrographic changes similar to those produced by mescaline and LSD-25 in our epileptic (Patient 5) suggests that adrenochrome or one of its degradation products is not involved in the mediating action of mescaline and LSD-25, as hypothesized previously.

SUMMARY

During depth-electrographic studies, mescaline and *d*-lysergic acid diethylamide (LSD-25) have been administered to five patients; two of them had psychosis with convulsive disorders, and three had chronic schizophrenia. The most striking observation in the epileptics was that mescaline and LSD-25 had a pronounced quieting effect on the spike and sharp-wave foci in depth recordings. An increase in paroxysmal activity characterized by waves of 2 to 5 cps occurred in the patients who had chronic schizophrenia. Mescaline and LSD-25 elicited the appearance of a double-spike focus deep in the temporal lobe in one epileptic patient.

The clinical effects and those on the depth electrogram produced by mescaline and LSD-25 were reversed by the injection of chlorpromazine.

Intravenous administration of adrenochrome to two patients who had chronic schizophrenia produced an increase in paroxysmal activity manifested by waves of 2 to 5 cps. An increase in paroxysmal activity of 2 to 3 cps occurred in a patient who had a psychosis with a convulsive disorder.

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