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The EEG Effects of LSD-25 in Epileptic Patients Before and After Temporal Lobectomy

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The changes produced in the electroencephalogram (EEG) of man by LSD-25 have been the object of various articles in the past. The majority of these studies concerned normal subjects, or psychiatric patients (Gastaut et al. 1953; Bradley et al. 1953; Anderson and Rawnsley 1954; Monroe et al. 1957; Bente et al. 1958; Fink 1963). Such trends as decrease of amplitude, particularly of slower rhythms (if present), and increase in the amount of faster rhythms were described, but contrary and negative results were also reported. The drug was used by Schwarz et al. (1956a) in an attempt to activate the electrographic focus in epileptic patients but without success.

The present study was undertaken with a view to assessing the EEG effects of the drug in a highly selected group of temporal lobe epileptic patients undergoing surgical treatment for their intractable epilepsy. All these patients had a well localized unilateral anterior temporal lobe focus of epileptic activity, half of them in the dominant and the other half in the non-dominant hemisphere. LSD-25 was given before and after operation and comparison was also made according to side of lesion. The clinical and conditioning findings of these patients are being reported separately (Serafetinides 1965a and b).

Material and Method

Twenty patients, who met the criteria of selection for an anterior temporal lobectomy, are the subjects of this study. The criteria, briefly, consist in resistance to medication, seizures of long duration, an anterior temporal lobe focus demonstrable electroencephalographically and absence of evidence for a space-occupying tumour. (More details of the criteria and treatment in Falconer and Serafetinides 1963). The

patients were matched for side of lesion (11 right or non-dominant side, and 9 left or dominant side), sex (12 men and 8 women) age (most between 20—40 years) personality and I.Q. Regarding the latter it should be also added that low I.Q. patients, psychotics and aggressive psychopaths were excluded. Due to the criteria of selection mentioned earlier the patients were also comparable in terms of past medical history, seizure history and findings on clinical and laboratory examination. More details on these patients as well as on their clinical LSD-25 reactions can be found elsewhere (SERAFETINIDES 1965a). Regarding the latter it should be said that these were recorded through the hourly administration of a specially devised questionnaire and were subsequently subjected to analysis of variance, which showed significant differences in the perceptual items among the two groups of patients and also between the pre- and postoperative scores. In contrast to such items, pertaining mainly to visual symptoms, somatic (i.e. of a general, or non-specific, sensory type) and autonomic items were not found to differ between the two groups or according to operation. No subject of this series showed a frank psychotic episode under LSD-25, in the dosage given.

LSD-25 was taken orally by the patients (1 μg/kg of bodyweight) 2—3 days prior to operation and one month after operation. The drug was taken in 5 ml of sterile water at 9.00 a.m. The EEG recordings were as follows: 9:20 a.m., brief run of scalp resting record (8 channel Offner apparatus); 10:15—10:30 a.m., a 15 minutes scalp recording (resting, photic stimulation and overbreathing in that order and of equal duration) by a 16 channel Ediswan apparatus. 12:15 p.m. to 12:30 and 16:15—16:30 repeats of above procedure. For all cases and instances 20 stick on electrodes were used, placed on the scalp, in 3 antero-posterior and 3 transverse bipolar linkages, at constant interelectrode distances. They extended over the frontal, temporal, parietal and occipital areas, on both sides, as it is routinely practiced for ordinary EEG purposes. The "montages" employed were also the routinely recommended ones.

The patients had no breakfast on the LSD-25 day, but they had lunch at 1:00 p.m. Their anticonvulsant medication (various, usually high, combinations of Phenobarbitone, Phenytoin and/or Primidone before operation and after operation a standard combination of Phenobarbitone 35 mg twice daily and Phenytoin 100 mg thrice daily) was not however interfered with.

Preoperative EEG records, with and without LSD-25, were compared separately for hemispheres with and without epileptogenic foci. The same was repeated post-operatively, this time for the hemispheres with and without temporal lobectomy. Only differences of at least 2 c/sec in

comparison with the habitual standard, of a given frequency, were considered noteworthy, whether in the direction of increase or decrease. The amount and amplitude of any given activity present per record, as classified in the tables, was graded according to an arbitrary three point scale, i.e. little, moderate, great. By increase or decrease in amount is meant the transition towards the one or the other end of this scale of a given form of activity under LSD-25. As epileptic activity we mean the presence of spikes and sharp waves and of spike and wave complexes. Intermittent photic stimulation usually at 6, 12 and 18 F/s was administered by a stroboscope at the end of each session with overbreathing (hyperventilation) following as the last event. Again a three point scale (little, moderate and great) was used to assess the amount of "following" or "driving" induced by photic stimulation and the amount of slow and the amount of epileptic activities induced by overbreathing.

Results

Tables 1 and 2 present the results according to side and operation. No consistent changes were induced by the drug on the "normal" sides before or after operation. On the side of the focus, and subsequently, lobectomy, the changes under LSD-25 were not statistically significant either, but some interesting trends, which might suggest further investigation, could be mentioned. Thus, as can be seen (Table 1) LSD-25 influenced the alpha or the fast rhythms little. Whenever, however, a change occured this was, considering the alpha first, of an increased frequency type in the non-dominant group and the opposite in the dominant group, whereas for fast rhythms the changes were the other way round. Operation tended to minimize even further the chances of LSD-25 influence except for the accentuation of the expected postoperative asymmetries (alpha amount) especially obvious here in the non-dominant group. Slow rhythms were also mostly uninfluenced by LSD-25, and again especially so after operation. Whenever changes were observed, however, the two groups again behaved differently; thus more slow was seen in the non-dominant and less slow in the dominant group. Epileptic activity was, if anything, suppressed, especially in the non-dominant group. LSD-25 either did not affect responses to photic stimulation (the majority) or if it did, it did not do so in a consistent manner. Similarly LSD-25 either did not affect the overbreathing results or if it did (the minority) it minimized their extent. In both the last 2 categories the two groups again did not show a similar pattern of changes but it should be remembered that the latter were the minority. Lastly changes after LSD-25, if present, tended to occur on the whole slightly less on the non operated side (Table 2) in both groups and also to be slightly less present at the last (i.e. 4.15 p.m.) recording.

Table 1. *LSD-25 effects on EEG of operated side of the brain*

	Before Operation		After Operation	
	Non-dominant-Group (N 11)	Dominant Group (N 9)	Non-dominant Group (N 11)	Dominant Group (N 9)
Alpha (F)	No change (8) increase (3)	No change (6) decrease (2)	No change (11) —	No change (8) incr. 1.
Alpha (A)	No change (11) —	No change (9) —	Decrease (6) No change (5)	No change (9)
Fast (A)	No change (9) Increase (2)	No change (4) Increase (4)	No change (7) Decrease (3)	No change (7) Increase (2)
Θ (A)	No change (7) Inc-Decr. (2) each	No change (6) Decrease (2)	No change (9) Decrease (2)	No change (7) Incr.-Decr. (1) each
Irregular (A) Slow.	No change (8) Increase (3)	No change (5) Decrease (4)	No change (8) Decrease (3)	No change (8) Increase (1)
Epileptic activity	No change (5) Decrease (4)	No change (7) Incr.-Decr. (1) each	No change (9) Decrease (2)	No change (8) Increase (1)
Photic driving	No change (8) Increase (2)	No change (5) Incr.-Decr. (2) each	No change (7) Decrease (3)	No change (9) —
O. B. (slow)	No change (8) Increase (2)	Decr.-No change (4) each Increase (1)	No change (6) Decrease (5)	No change (7) Increase (2)
O. B. (Epil.)	No change (7) Incr.-Decr. (2) each	Decrease (4) Increase (3)	No change (8) Decrease (3)	No change (8) Increase (1)

(F) = Frequency; (A) = Amount and Amplitude.

Table 2. *LSD-25 effects on EEG of "normal" (non-operated) side of the brain*

	Before operation		After operation	
	Non-dominant Group (N 11)	Dominant Group (N 9)	Non-dominant Group (N 11)	Dominant Group (N 9)
Alpha (F)	No change (8) Increase (3)	No change (6) Decrease (2)	No change (8) Increase (3)	No change (8) Increase (1)
Alpha (A)	No change (11)	No change (9)	No change (10) Decr. (1)	No change (9)
Fast (A)	No change (9) Increase (2)	Incr.-No change (4) each Decrease (1)	No change (7) Increase (4)	No change (6) Increase (3)
Θ (A)	No change (7) Incr.-Decr. (2) each	No change (6) Decrease (2)	No change (10) Decrease (1)	No change (6) Increase (3)
Irregular Slow. (A)	No change (10) Decrease (1)	No change (7) Increase (2)	No change (11) —	No change (8) Increase (1)
Epileptic activity	No change (8) Decrease (2)	No change (9) —	No change (8) Increase (1)	No change (10) Increase (1)
Photic Driving	No change (8) Increase (2)	No change (5) Incr.-Decr. (2) each	No change (7) Decrease (3)	No change (9) —
O. B. (slow)	No change (11) —	No change (5) Decrease (3)	No change (6) Decrease (5)	No change (8) Increase (1)
O. B. (Epil.)	No change (7) Incr.-Decr. (2) each	Decrease (4) Increase (3)	No change (8) Decrease (2)	No change (8) Increase (1)

(F) = Frequency; (A) = Amount and Amplitude.

Discussion

These results make obvious the fact that with the method of investigation and of assessment employed the great majority of our patients did not show any changes after LSD-25. As to the ones that did show a change, their numbers are too small and the changes they show too variable to be worth any form of painstaking analysis. As possible trends one could mention the decrease of epileptic activity (non-dominant group), the contrariness in direction of the changes in the two groups, either before or after operation, in variables like irregular slow, overbreathing responses and alpha and fast rhythms, as well as the fact that more changes seem to occur on the non-dominant group. Preoperatively also more changes seem to be induced than postoperatively for both groups.

Unfortunately, however, we cannot give much attention to these findings. Were they to be valid and also not an insignificant minority they could pose interesting questions in relation to the clinical findings according to which the non-dominant group showed a greater number of perceptual responses after LSD-25 than the dominant group—and that the reaction was richer preoperatively than postoperatively (Serafetinides 1965a).

As things stand now, however, even their simple mentioning may be potentially misleading. The literature shows marked diversity of opinions on this question, and we shall not repeat the trends already mentioned in the introduction. It should be noted, however, that claims of changes after LSD-25 come especially from investigators administering the LSD-25 intravenously (Bente et al. 1958). Oral administration is prone to give no or contradictory results.

This study made once more obvious that electroencephalography as now practised, is a method of investigation which, although useful for the detection of grossly impaired cerebral function, cannot be reliably used either in cases with subtler impairment or in psycho-physiological studies where no impairement in the ordinary sense is postulated. In the latter case the EEG must evolve to a form capable of appreciating and quantitatively analysing and expressing differences in frequency, distribution and amplitude of the various cerebral rhythms. A taste of what might be found with such a method is given by Grey Walter (1957) who demonstrated by toposcopic analysis of the EEG of a subject under LSD-25 that at the time of his visual hallucinations this subject showed a raising of the average frequency of his alpha rhythm from a mean 11.6 cycles per second to 12.7 cycles per second. He also showed great variability in frequencies from region to region even over adjacent areas. Until such methods or their refined and standardized descendants

are employed the present routine methods of EEG even with intracerebral recordings like those of SCHWARZ et al. (1956 b), who also obtained variable effects with LSD-25, cannot offer much in correlational drug studies.

Summary

Two groups of epileptic patients, one (9 patients) with a left (dominant) and one (11 patients) with a right (non-dominant) anterior temporal lobe focus of epileptic activity, were given 1 μg/kg of LSD-25 orally, 2—3 days before and one month after a unilateral temporal lobectomy, undertaken for the treatment of their intractable epilepsy. The two groups were matched for most clinical variables and mental subnormals, psychotics and aggressive psychopaths were excluded. A comparison, according to side of lesion and according to operation, of the effects of the drug on their scalp EEG—judged against the EEG without LSD-25, taken at the time—showed that as a rule the drug did not produce any changes in the amplitude or frequency of the various rhythms. In the minority of cases where changes were noticed, these were of variable direction and were briefly discussed. The limitations of the present EEG methods in pharmacological research in man were stressed and the desirability for quantitative methods of analysis was reaffirmed.

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