PHOTOCONVULSIVE THRESHOLD IN DEPRESSIVE ILLNESS AND THE EFFECT OF E.C.T.

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FEW techniques are available which have as their aim the quantitative determination of a physiological function of the human brain. Of these the photomyoclonic threshold has received most attention and numerous reports have appeared concerning findings in epilepsy, schizophrenia, other psychiatric conditions and normal controls (2, 4, 5, 9, 10, 11, 14). The precise neurophysiological meaning of the "threshold" is unknown but since the first publications of Gastaut (5) it has been widely assumed that the measure is one of diencephalic function and that a change in the latter can be detected by the resulting threshold change.

The present study is concerned with the photo-convulsive threshold in a group of patients with depressive illness before and after electro-convulsive therapy (E.C.T.). Previously published work on the effects of E.C.T. in this respect has been limited to the study of very few cases (10) or has made use of a different index of "threshold" (3).

MATERIAL AND METHODS

Twenty-seven adults (Table I) diagnosed by the consultant psychiatrist in charge as having a severe depressive illness and admitted to the Maudsley Hospital as in-patients were the subject of the investigation. Of the 18 who had had successful determinations of threshold before and after E.C.T., 7 expressed suicidal ideas and 11 had had previous depressive episodes.

Each patient had an EEG before any further investigation or therapy, a brief "resting" record being followed by successive periods of hyperventilation and photic stimulation.

The technique of measurement of photomyoclonic threshold was a modification of that of Ulett *et al.* (16), 0·5 ml. 1 per cent. hexazole (Azozol, Boots) being injected rapidly into an ante-cubital vein every 30 seconds, each injection being followed after 15 seconds by a 15-second period during which photic stimulation (electronic stroboscope 8 cm. from the closed eyes in a darkened room) at 18 flashes per second was given. The cycle of injection, pause, photic stimulation was repeated at 30-second intervals until spike-and-wave or multiple spikes appeared in the EEG, or myoclonus extending beyond the face was seen in the patient. The threshold so obtained was taken to be the total amount of hexazole in milligrams injected up to the appearance of the end-point

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TABLE I

(1) No.	(2) Age	(3) Sex	(4) Weight Kg.	(5) T_1 mg.	(6) T_2 mg.	(7) No. of E.C.T.	(8) Interval Days	(9) Post-E.C.T. EEG	(10) Clinical Result
1 ..	38	M	77	25	30	5	33	0	U
2 ..	50	M	58	25	25	4	40	0	I
3 ..	44	M	70	25	25	5	27	0	I
4 ..	40	M	73	20	20	6	3	2	I
5 ..	28	M	64	10	15	12	14	1	U
6 ..	60	F	54	20	25	11	8	0	I
7 ..	35	F	56	20	15	5	0	3	I
8 ..	37	M	80	20	—	—	—	—	—
9 ..	37	M	78	35	—	—	—	—	—
10 ..	43	M	64	35	35	6	2	2	I
11 ..	36	M	62	15	—	—	—	—	—
12 ..	56	F	62	15	—	—	—	—	—
13 ..	50	F	42	5	10	10	2	1	I
14 ..	55	M	68	25	—	—	—	—	—
15 ..	38	M	62	30	35	7	2	2	I
16 ..	43	M	97	30	—	—	—	—	—
17 ..	45	M	59	15	15	10	4	1	I
18 ..	47	M	82	35	30	6	9	0	I
19 ..	51	M	70	35	30	5	11	1	I
20 ..	51	M	73	30	25	3	5	1	I
21 ..	34	F	44	25	25	9	5	1	I
22 ..	35	M	70	25	—	—	—	—	—
23 ..	38	M	70	20	—	—	—	—	—
24 ..	59	M	53	20	15	6	4	0	I
25 ..	38	M	75	30	40	7	4	0	I
26 ..	45	M	66	20	—	—	—	—	—
27 ..	58	F	60	25	20	6	9	0	I

(one of more of the above changes). The interval between the last of the series of E.C.T. and the second determination of threshold was largely determined by events outside experimental control but in all cases it was as short as possible.

The E.C.T. procedure was identical in all cases. Atropine (1/100 gr.) was given subcutaneously 30 minutes beforehand, and thiopentone (200 mg.) and Scoline (30 mg.) were injected intravenously before the passage of current. This was delivered by a McPhail-Strauss Plexacon apparatus (30 joules, phase 2 for 30 seconds) and was followed by controlled breathing into a bag of pure oxygen, until spontaneous respiration was re-established. Most treatments were given twice a week, 7 being the average total (range 3–12). The patients were classified as "symptomatically improved or recovered" or as "failed to improve" at the time the post-E.C.T. EEG was recorded, 15 (11 men and 4 women) coming into the first category and 3 (2 men and 1 woman) into the second.

Eighteen patients had post-E.C.T. threshold determinations, the remaining 9 including 3 whose mental state was such that the psychiatrist in charge thought a repetition unwise and 6 who refused.

RESULTS

Column 5 (Table I) gives the threshold value before E.C.T., the mean for the whole group (27 patients) being 23 mg. hexazole. The mean threshold of the 6 females, 18 mg., is considerably lower than that of the 21 males, 25 mg.

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The difference disappears if the threshold is expressed in terms of body weight (column 4), neither males, 0·36 mg./Kg., nor females, 0·34 mg./Kg., showing a significant difference from the group as a whole, 0·36 mg./Kg. The relationship between body weight and convulsive threshold suggested by this finding is shown in Figure 1, the correlation between them being positive and significant

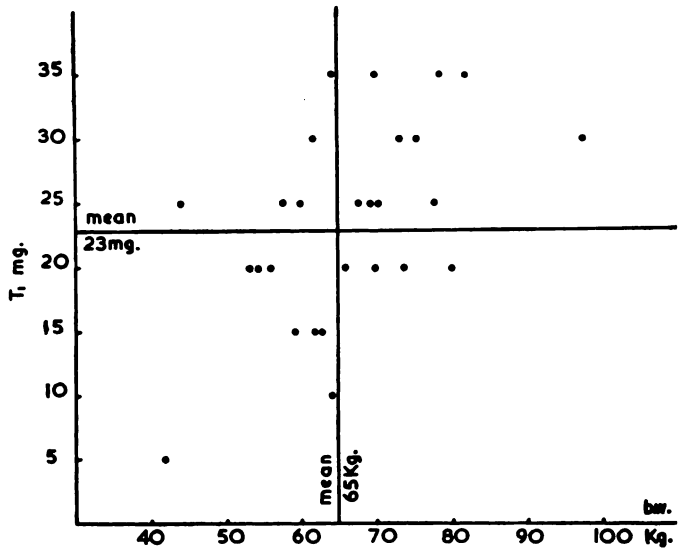


FIG. 1.—Crude threshold in mg. hexazole plotted against patient's body weight in Kg.

at the 1 per cent. level. The mean threshold for this group of depressive patients, 23 mg., is identical with that found (for the same end-point) by Ulett *et al.* (16) in a group of 27 subjects, 22 of whom were schizophrenic. A subsequent paper (14) from the same laboratory showed that the mean threshold for a group of 30 schizophrenic subjects was not significantly different from that of a mixed group of 20 non-schizophrenic and mental hospital patients. In this latter investigation the end-point taken was that of generalized myoclonus and the mean value (33 mg.) therefore appears higher than the figures found in the earlier paper and in the present study. However, if it is multiplied by the factor 23/31 suggested by Ulett's mean dose figures for various end-points the results are virtually identical. Comparison with the findings of other workers is difficult since leptazol (Cardiazol, Metrazol) has been used by most. Ulett's work suggests that for investigations of the present type hexazole is about 15 times as potent as leptazol weight for weight, and use of this factor gives a mean leptazol-equivalent threshold in the present series of 350 mg. or 5·5 mg./Kg., a figure which is comparable with that found in most published work, though low compared with Gastaut's original findings.

Column 6 (Table I) gives the threshold (T_2) values in those cases where satisfactory post-E.C.T. determination was possible. There is no significant difference between the T_2 means (13 males, T_2=26 mg.; 5 females, 19 mg.; total 18 patients, 24 mg.) and the T_1 means of the same 18 patients (26, 19, 24 mg. respectively) or that of the total 27 patients (given above). It appears probable that the difference found in any given patient between the T_1 and T_2

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measures is within the limits of experimental error but as Figure 2 shows there is a tendency for those patients who had most therapeutic convulsions (column 7)

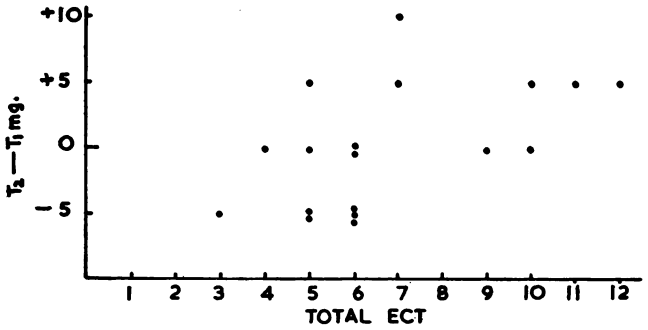


FIG. 2.—Difference between post-E.C.T. (T_2) and pre-E.C.T. (T_1) estimates of crude threshold plotted against total E.C.T. given.

to have a rise in threshold and for those with fewer E.C.T. to have a fall. On the other hand, there appears to be no relationship between the direction of change in threshold and the interval between the last induced convulsion and the second threshold measurement (column 8) even when the interval is small (Fig. 3).

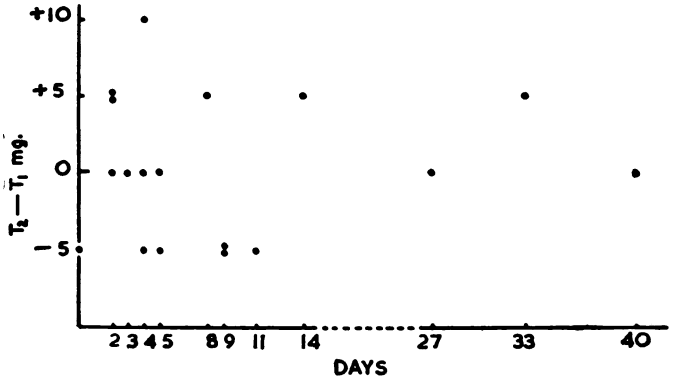


FIG. 3.—Difference between post-E.C.T. (T_2) and pre-E.C.T. (T_1) estimates of crude threshold plotted against the period in days between the last therapeutic convulsion and the post-E.C.T. determination of threshold.

The pre-E.C.T. EEG of each of the 19 patients having satisfactory T_2 determinations was normal and no abnormality arose following a 3-minute period of overbreathing or a series of rhythmic photic stimulations over a wide range of flash rates (1 to 30 f/sec.). The post-E.C.T. EEG in each case was placed in one of four categories according to the abnormalities found. These are given in column 9, Table I, the categories being: 0, no change, i.e. a normal record; 1, showing low voltage 6–8 c/s; 2, moderate voltage 4–6 c/s and 3, high voltage 3–6 c/s. ("Moderate" voltage representing roughly the amplitude of the alpha rhythm, "low" and "high" being about half and at least twice this.) As seen in Figure 4, there is a definite relationship between the "abnormality" of the post-E.C.T. record and the period since the previous convulsion, early post-E.C.T. records being the most abnormal. There is, however, no relationship between abnormality in the EEG and a change in convulsive threshold.

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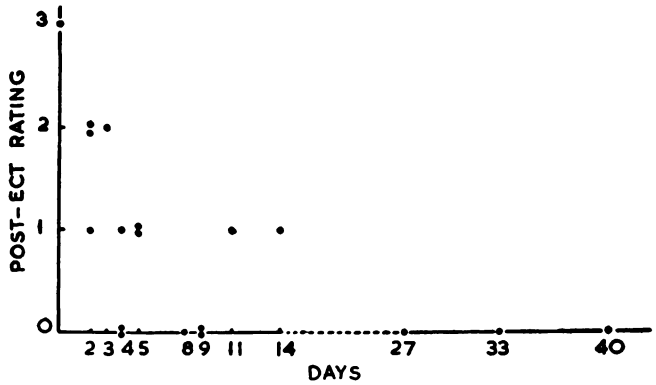


FIG. 4.—Post-E.C.T. rating (see text) plotted against the period in days between the last therapeutic convulsion and the post-E.C.T. determination of threshold.

Column 10, Table I, gives the short-term assessment of the patient's clinical state following E.C.T., the only 3 unimproved (U) cases showing no consistent difference in any variable from the remainder (improved, I).

DISCUSSION

The close similarity between the mean "threshold" in this group of 27 patients with depressive illness and that found by other workers in a wide variety of subjects—normal and abnormal—suggests that if psychiatric patients differ from each other and from the "normal" population neurophysiologically they do so in a way not susceptible to discovery by a single measurement of photoconvulsive threshold made under standardized laboratory conditions. It would appear, then, that the threshold has negligible clinical significance in its present form.

That there was no rise in threshold after a course of E.C.T. contrasts with the results of other workers. Leffman and Perlo (10) reported a rise in 4 schizophrenic patients, 2 of whom showed an initial elevation of threshold shortly after E.C.T., but a return to the original level a month later. Brockman *et al.* (3), in a larger series of chronic paranoid schizophrenic patients, found that a significant increase in threshold followed a course of 12 convulsions whether the latter were induced by "photo-shock" or conventional "electro-shock" methods. The greater change (increase from 31·2 to 75·6 mg. hexazole) was following "photo-shock" therapy, the lesser (increase from 30·5 to 49·7 mg. hexazole) following E.C.T. Several points deserve attention in comparing these findings with those reported in the present work. The increase in threshold found by both groups may be related to a failure in schizophrenia of a homeostatic mechanism which remains intact in depressive patients. However, as the larger series showed no difference between improved and unimproved patients with respect to threshold changes it is unlikely that this is an adequate reason.

A further point of importance is the possible influence of the number of convulsive seizures upon threshold change. Each of the Brockman *et al.* series had 13 seizures (one for threshold measurement and 12 therapeutic) before the final estimate of threshold, i.e. a much greater number than those of the present work (range 3 to 12, mean 7). It may be that the function measured is affected by convulsant therapy but only as a result of cerebral changes secondary to the convulsions. As seen in Figure 3 there is a tendency in the present work for those patients with the greatest number of E.C.T. to have

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higher second (T_2) than first (T_1) thresholds but the rise is very small compared with that found by Brockman *et al.*

Lastly in this connection is the difference in techniques used to measure "threshold" and the difficulty in strict comparison of results that arises. Brockman *et al.* estimated the amount of drug (hexazole) needed to produce an EEG or clinical end-point (myoclonus) in each case but the "convulsive threshold" as given in their results was determined by a different technique, a single large injected dose being followed by a continuously flashing stimulus until a generalized convulsive seizure occurred (additional injections being given if necessary). Although Ulett *et al.* showed that there was a high correlation between the amount of convulsant drug needed to lead to a valid "end-point" and the amount needed to produce a generalized epileptic seizure no evidence was presented that the latter arises simply by an increase in the intensity of the former. The fact that consciousness is lost in the major seizure suggests that a qualitative change in cerebral activity has taken place and it appears possible that the ease or otherwise of inducing this change may be affected by a number of shock therapies whereas the usual "end-point" phenomena are less affected.

That it is diencephalic function which is assessed quantitatively by the photoconvulsive technique was suggested by Gastaut following estimations of threshold in psychiatric patients (5) and experiments on laboratory animals (6). The work of Starzl *et al.* (15) and Hunter and Ingvar (8) indicated that in the cat under metrazol the visual cortex was responsible for the rapid spread of irradiated responses to the rest of the cortex. The diencephalon was involved only as part of a slower pathway. Similar experimental evidence is unlikely to be available in human subjects and the validity or otherwise of Gastaut's hypothesis can be determined only indirectly.

The neurophysiological effects of E.C.T. are not known with certainty, but subcortical rather than cortical structures are predominantly involved (1, 7). The effects of E.C.T. on the EEG—especially in relation to subsequent intravenous injection of thiopentone—suggest that the site of action of E.C.T. is the diencephalon (12, 13). If this is so the present finding, that no change in "threshold" follows E.C.T., offers some evidence that the pathway concerned in the measurement of threshold, though not necessarily that demonstrated in cats, is not affected by a change in diencephalic function.

Summary

Estimation of photoconvulsive threshold was made in 27 patients with a severe depressive illness. The findings did not differ from those reported elsewhere in other psychiatric categories and normal subjects.

It was concluded that the threshold had no clinical differentiating value.

The estimation was repeated in 18 patients after a course of electroconvulsive therapy. No change in threshold was observed.

It was concluded that although no positive evidence of primary cortical involvement in the photoconvulsive mechanism was available it was unwise to assume that any aspect of diencephalic function was assessed by an estimate of the photoconvulsive threshold.

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