

DOUBLE-BLIND CONTROLLED TRIAL OF ELECTROCONVULSIVE THERAPY (E.C.T.) AND SIMULATED E.C.T. IN DEPRESSIVE ILLNESS

C. P. L. FREEMAN J. V. BASSON
A. CRIGHTON

Department of Psychiatry, Edinburgh University, and Royal
Edinburgh Hospital

Summary 40 patients prescribed electroconvulsive therapy (E.C.T.) for treatment of a depressive illness were randomly allocated to two groups. One group had the first two E.C.T. treatments replaced by simulated E.C.T. on a double-blind basis. The results show that E.C.T. is significantly superior to simulated E.C.T. in the treatment of depressive illness.

Introduction

THE object of the trial was to compare the effectiveness, in the treatment of depressive illness, of bilateral electroconvulsive therapy (E.C.T.) with a treatment which simulated E.C.T. as closely as possible. E.C.T. is an effective treatment for depressive illness¹⁻³ and has tended to become the standard against which novel treatments for depression are assessed. But which parts of the treatment are therapeutically active is not clear.

Critics of E.C.T. say that it is a crude and unscientific therapy which if it works does so through fear, punishment, or non-specific factors such as increased nursing and medical attention. The evidence at present available does not support this view and points towards the seizure as being the important therapeutic agent.⁴

The ideal design for such a trial would have been to have compared a full course of simulated E.C.T. with a full course of real E.C.T. We wanted to conduct the trial on severely and very severely depressed patients for whom E.C.T. is primarily indicated, and we wanted to avoid the criticism that the trial showed E.C.T. to be ineffective because the patients were not those who would usually receive it. We felt it ethically unjustified to withhold for a complete course a treatment generally regarded to be effective and to submit patients to perhaps unnecessary general anaesthesia. The method presented here was therefore a compromise.

Method

Patients

40 patients took part in the trial. The details are shown in

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TABLE I—CHARACTERISTICS OF THE PATIENTS

	Simulated E.C.T. (n=20)	Real E.C.T. (n=20)	Excluded patients (n=7)
Male	5	6	1
Female	15	14	6
M/F ratio	1.3	1.3	1.6
Mean age (yr)	50.5	51	52.8
Have had E.C.T. before	12 (60%)	10 (50%)	6 (86%)
Previous episodes of depression:			
None	6	6	1
One	5	4	0
Two or more	9	10	6
Previous manic illness	5 (25%)	5 (25%)	5 (71%)
Antidepressant medication:			
None	9	13	3
Just started	2	1	0
Regular	9	6	4

table 1. The criteria for admission to the trial were as follows. Inpatients of either sex, aged 20-70 years. A clinical diagnosis of depressive illness defined by the primary manifestation and major symptom of persistent change of mood exceeding customary sadness, accompanied by one or more of the following symptoms: self-deprecation with a morbid sense of guilt; sleep disturbance; hypochondriasis; retardation of thought and action; agitated behaviour. The depression had to be the primary illness and not secondary to other mental illness such as schizophrenia. A minimum score of 15 on both the Hamilton⁵ and Beck⁶ rating-scales for depression. No E.C.T. in the past three months. Absence of a major or progressive physical illness and no symptoms or signs of organic cerebral disease. The patient had to give informed consent to take part in the trial.

Treatment

All patients from four acute units for whom E.C.T. was prescribed were considered. Patients entering the trial were randomly allocated to one of two groups. The group given real E.C.T. (group R) received bilateral E.C.T. twice weekly from an 'Ectron' Mk IV machine. This delivered a bidirectional 60% sine-wave current at 400 V peak to peak for 1.5 s. The group receiving simulated E.C.T. (group S) were given two treatments during which the electrodes were applied to the head but no current was passed. The third and subsequent treatments for this group were normal bilateral E.C.T. In effect, E.C.T. was delayed for one week in the control group and replaced by fake E.C.T.

The anaesthetic procedure was identical for both groups. Premedication was with atropine 600 mg and induction with sodium thiopentone (150-300 mg). Muscle relaxation was with suxamethonium chloride. E.C.T. was always given by the same doctor. This doctor (C.P.L.F.), the E.C.T. nurse, and the anaesthetist were the only people not blind to the patient's group.

Statistical Analysis

All significant values are based on Student's *t* tests. Independent *t* tests were used for between-group sampling and dependent *t* tests within groups.

Results

Overall Outcome

Table II shows the reasons for terminating E.C.T. in the two groups. The 4 hypomanic patients settled without further treatment and were judged to have made a

TABLE II—REASON FOR TERMINATING COURSE OF TREATMENT

Group	Satisfactory response	Inadequate response	Hypomanic episode	Patient refused further treatment
Real E.C.T. (n=20)	14	2	2	2
Simulated E.C.T. (n=20)	18	0	2	0

satisfactory response to E.C.T. The 2 patients who refused further E.C.T. had not improved. 2 patients who continued E.C.T. did not improve. Thus, 36 out of the 40 patients responded well, but all 4 non-responders were in group R.

Number of E.C.T.s Prescribed

If simulated and real E.C.T. are equally effective, then the number of treatments per patient in the two groups should not differ. Conversely, if simulated E.C.T. has no therapeutic effect, then patients in group S would be likely to receive two extra real E.C.T.s. The number of treatments received varied from three to nine per patient for group R and from four to twelve for group S (fig. 1).

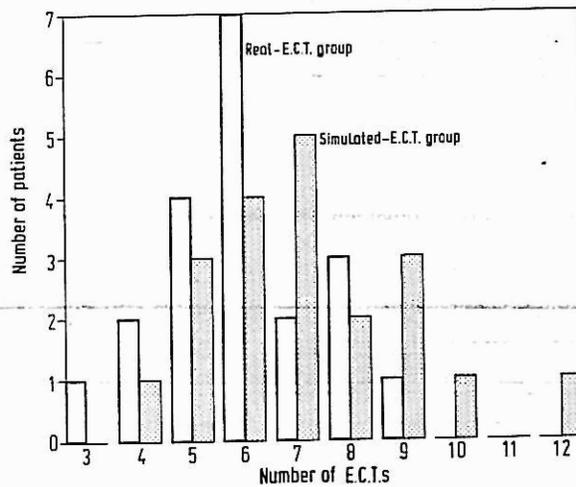


Fig. 1—Number of E.C.T.s prescribed.

For the patients who had simulated E.C.T. the number of treatments indicated includes the simulated treatments.

The wide range indicates that clinicians did not prescribe a fixed course but titrated treatment against outcome. Excluding the 2 patients who refused further E.C.T., the mean number of treatments per patient was 6.0 for group R and 7.15 for group S. The difference is statistically significant ($P < 0.05$).

Depression Rating-scales

Figs. 2 and 3 show the mean scores of the two groups on the Hamilton rating-scale for depression and the visual-analogue scale before treatment, after two, four, and six treatments, and after the final treatment. The

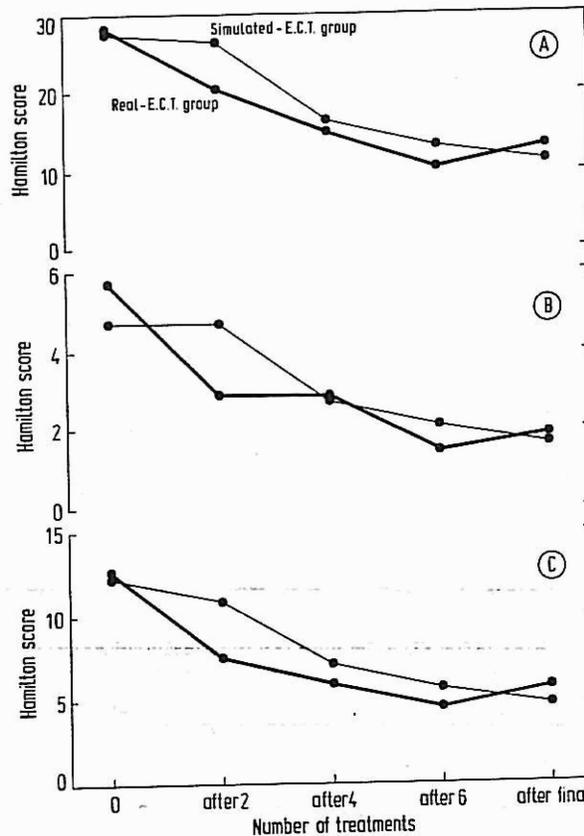


Fig. 2—Mean scores on the Hamilton depression scale.

(A) The full scale. (B) Anxiety items only. (C) Depression items only.

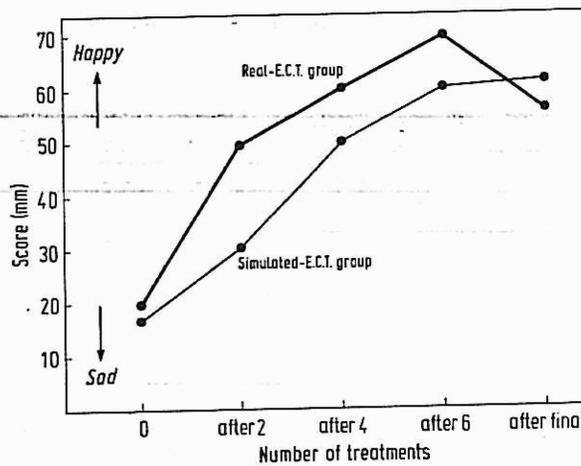


Fig. 3—Mean scores on the visual analogue scale.

Scores were measured in millimetres from the "sad" end of a 10 cm line.

patients were also assessed on the Wakefield and Beck self-rating depression scales.

Before treatment all the measures used showed the two groups to be closely matched for severity of depression. After two treatments all four measures indicate that the patients in group R were significantly less depressed ($P < 0.005$ for Hamilton, Wakefield,⁷ V.A.S.,⁸

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Excluded patients (n=7)

1
6
1-6
52-8

6 (86%)

1
0
6

5 (71%)

3
0
4

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and Beck scales). For group s the scores on the Hamilton and Wakefield scales show virtually no change, but scores on the v.a.s. and Beck scales indicate significant improvement ($P < 0.1$ for v.a.s., $P < 0.05$ for Beck). When groups r and s are compared the former are less depressed at this stage as measured by the Hamilton scale ($P < 0.05$), Wakefield scale ($P < 0.05$), and v.a.s. ($P < 0.05$). The Beck scale did not distinguish between the two groups. Although the simulated-E.C.T. group rated themselves as more depressed than the real-E.C.T. patients until their final treatment, their scores never differed significantly from those of the real-E.C.T. group.

All measures showed that the patients in group s had improved significantly ($P < 0.001$ for Hamilton and Wakefield, $P < 0.05$ for v.a.s. and Beck) after the fourth treatment—i.e., after the second real E.C.T. When the two groups were compared after four treatments group s consistently scored higher (i.e., were more depressed) on all four scales, though the differences were less than they had been after two treatments.

Both groups continued to improve until their final treatments. Comparison after six E.C.T.s was complicated by the fact that more group-r patients had already stopped treatment (2 because they refused further E.C.T. and 7, compared with 4 in group s, because they required fewer than six E.C.T.s to achieve full remission).

When the two groups were compared after their final treatments all measures showed that the patients given simulated E.C.T., having lagged behind throughout treatment, had now caught up. None of the rating-scales showed a significant difference in depression scores at the end of treatment.

Because of a report by Lambourne⁹ that real E.C.T. was no more effective than simulated E.C.T. in relieving depressive symptoms but was more effective in reducing anxiety, we subdivided the Hamilton and Wakefield scales into depression items and anxiety items. Fig. 2B shows the scores of the two groups on items 9, 10, and 11 of the Hamilton scale (agitation, psychic anxiety, and somatic anxiety). The difference in initial scores is not significant. There was a striking relief of anxiety with the first two real E.C.T.s, but simulated E.C.T. produced no decrease in anxiety, and after two treatments patients in group s were significantly more anxious than those in group r ($P < 0.01$). This difference disappeared entirely after four treatments. In both groups nearly all anxiety relief occurred with the first two E.C.T.s, and further E.C.T. produced little additional improvement.

This contrasts with the pattern shown in fig. 2C, which compares the scores of patients in the two groups on the depression items (depressed mood, guilt, suicidal thoughts, loss of interest, retardation, and lack of energy). Improvement on these items was slower, and the gap between group s and group r closed more gradually as treatment progressed. A similar pattern was obtained when the Wakefield scale was artificially split in the same way. On this self-report scale group-s patients rated themselves as more anxious after their two simulated treatments than before.

Rater's and Clinicians' Guesses

Neither the rater nor the clinicians guessed which group the patient belonged to beyond chance expecta-

tion. Both guessed correctly 17 times out of 40, but their guesses were often different.

Discussion

The results show that E.C.T. is clearly superior to simulated E.C.T. A number of factors may have reduced the measured difference in efficacy of the two treatments: the patients had concomitant drug therapy, and there was a slight excess of patients on antidepressants in the simulated-E.C.T. group; by chance all 4 "non-responders" were in the real E.C.T. group; the Hamilton rating-scale is not really designed for measuring day-to-day variations in mood; and the trial was limited to 40 patients. The fact that E.C.T. was significantly superior to placebo under these conditions indicates that it is a very effective and rapidly acting treatment for depressive illness.

All elements of the treatment apart from the seizure and its induction by the passage of electric current across the brain were controlled for in the simulated-E.C.T. group. It has been shown that photic and chemically induced seizures are therapeutically as effective as E.C.T.^{10,11} and therefore that the electric current is not a necessary part of the treatment. The results of our study add to the evidence that the seizure is the essential therapeutic agent⁴ and are incompatible with the suggestion that E.C.T. is a non-specific treatment which works because it is dramatic, frightening, and results in the patient getting more medical and nursing attention. In fact the "placebo" response is slight, especially as measured by the Hamilton and Wakefield scales.

The different rates of response of the anxiety and depression symptoms is interesting but must be treated cautiously. The anxiety measured is occurring in the context of a depressive illness. The splitting of the Hamilton and Wakefield scales as described has no proven validity, though for the former there is a certain face validity. The results do not indicate that E.C.T. has any specific anti-anxiety effect.

The Beck Depression Inventory was the only measure used which did not distinguish between the two groups. This instrument is a lengthy scale containing some American terms. Depressed patients disliked filling it in, and many retarded patients found it impossible to complete. These factors may have contributed to its insensitivity with this particular group of patients.

Finally, it is worth noting that after treatment the majority of both groups were rated as substantially improved on both observer and self ratings. 36 out of 40 patients (90%) showed satisfactory improvement. No patient felt that he had been made worse by the treatment.

Requests for reprints should be addressed to C.P.L.F., University Department of Psychiatry, Morningside Park, Edinburgh EH10 5HF.

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