PROGNOSTIC FACTORS IN THE ELECTROSHOCK TREATMENT OF DEPRESSIVE STATES

I.—CLINICAL FEATURES FROM HISTORY AND EXAMINATION

By

JULIAN M. ROBERTS, M.D., D.P.M.

Lecturer in Psychiatry
University of Leeds and the United Leeds Hospitals

INTRODUCTION

SINCE its introduction in 1938 electroshock therapy (E.C.T.) has become probably the most widely applied form of physical treatment in psychiatry, despite the fact that its method and site of action are still not precisely known. Numerous investigations have been undertaken to delineate more clearly the indications for its use; notwithstanding broad agreement as to its value in depressive states and some schizophrenic syndromes there is still a paucity of evidence on which firm criteria for the prediction of outcome to treatment can be based. Most prognostic studies appeared in the first decade following the introduction of E.C.T. and were based largely on empirical clinical observations during the course of routine psychiatric practice, whereas later investigations have included more intensive and precise researches into possible psychological, physiological, biochemical and pharmacological indices of capacity to respond to electroshock.

The relevant literature is both extensive and yet, on many points, inconclusive. Difficulties of objective assessment of clinical status, both qualitative and quantitative, are partly responsible: Kraepelinian diagnostic terms lack sufficient precision for the purpose of comparing results of treatment, and diagnostic criteria vary considerably among psychiatrists. Estimations of clinical change are also lacking in standard and comparable methods of assessment, and until comparatively recently there has been a lack of awareness of the importance of the initial planning of investigations to allow for the application of simple tests of statistical significance to the results and the avoidance of potential pitfalls, such as neglect of the time factor in assessing the results of treatment (Alexander, 1945).

Predictive value has been claimed, directly or indirectly, for a number of specific factors associated with the treatment of depressive states by E.C.T. These fall broadly into two groups, firstly the possible influence on outcome of clinical features derived from the history and examination, including age, physique and individual symptoms and signs, and secondly the use of more specific tests of various kinds.

In view of conflicting reports in the literature, and the desirability of validating other work in this field, the present investigation was undertaken.

DESIGN OF THE INVESTIGATION

It was decided for various reasons to undertake an intensive and comprehensive study of a relatively small number of patients, without emphasis

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on diagnostic categories, and to determine the relationship of various clinical and specific features to outcome with treatment by means of standard statistical methods. This was designed to detect and assess the influence of individual factors on short-term prognosis, with the possibility of immediate therapeutic guidance; the investigation by Hobson (1953) furnished a convenient starting-point. In this statistically significant associations were found between 20 clinical items and the immediate results of E.C.T. in 127 patients treated at the Maudsley Hospital, almost all with depression.

The most important requirements to avoid serious methodological errors appeared to be (*a*) the presence or absence of specific clinical features as such, within broad diagnostic limits, to avoid the ambiguity often attending diagnostic groupings; (*b*) an attempt to quantify depressive manifestations by means of a rating scale rather than by "global" assessments of clinical status; (*c*) the definition of clinical terms employed as far as possible; (*d*) the setting of a definite time interval for assessment of the results of treatment; and (*e*) the control of such variables as age, technique of treatment, etc. and overall design to allow for the application of standard statistical methods to the interpretation of results.

Selection of Patients

Only women were selected for study, between the ages of 40–60 years. These limits were set to include the involutional period, when many minor or atypical depressions occur, and to exclude older patients where organic factors might increasingly complicate matters. Only those women suffering from a depressive illness sufficiently severe to warrant the application of E.C.T. were included: a "depressive illness" was defined as a sustained primary mood disturbance, leading to subjective or objective inefficiency of mental activities experienced in a mood of sadness, and usually with a diffuse persistent lowering of interests and activity (Mayer-Gross, 1954; Partridge, 1954). E.C.T. was considered justified when symptoms were sufficiently severe to render the patient unfit for her normal occupation, or constituted a serious social handicap, or had led to an apparently genuine attempt at suicide. Patients with depressive symptoms in relation to organic syndromes, other psychoses, etc., were not included, nor were those who had had E.C.T. in the preceding 12 months. No attempt was made initially to place patients in closely-defined diagnostic categories, any otherwise suitable subject showing a sufficient degree of sustained primary mood disturbance being included.

Fifty-four patients were initially investigated, and 50 included in the present study.

Clinical Examination and Assessment

Routine physical examination was carried out on all patients to exclude gross physical disease, and in view of the later administration of methacholine, those with asthma or heart disease were excluded; essential hypertension without evidence of cerebral, cardiac, or renal involvement was not considered a contra-indication. The physical measurements necessary for the calculation of the Rees-Eysenck body index (female) were also made (Rees, 1950); stature, height to symphysis pubis, circumference of chest at xiphisternum midway between inspiration and expiration, and hip circumference at the level of the iliac crests.

Routine history-taking and mental examination were supplemented by particular attention to the various clinical items described by Hobson as being of prognostic significance, and by the quantification of the symptoms and signs of depression and anxiety by the use of an appropriate rating scale. This was derived from a gloss of various depressive symptoms, arranged in appropriate groupings to cover the following headings:

Depressive mood, guilt feelings, suicidal features.
Insomnia—early, middle and late.
Diurnal variation of mood.
Interference with work and activities.
Degree of psycho-motor retardation.
Agitation.
Anxiety—psychic and somatic manifestations.
Depersonalization, derealization, nihilistic ideas.
Paranoid symptoms.
Obsessive–compulsive symptoms.
Hypochondriasis.
Depressive somatic symptoms (e.g. backache, abdominal discomfort).
Loss of weight.
Degree of insight into illness.

The scale has been shown to have a high degree of reliability between observers (Hamilton, 1959); the one used in this study was a slightly modified version.

Features which could be assessed simply as "present" or "absent" were scored 2 or 0 appropriately, occasionally 1 when slight or doubtful: those of varying distribution such as depressive mood, anxiety, etc. were scored on a 5-point scale, from "0—absent" to "4—very severe".

Despite its imperfections the use of this scale allows a higher degree of accuracy than overall clinical judgment, as well as furnishing a quantitative expression of severity of symptoms capable of handling by simple statistical methods.

After clinical assessment and before treatment was begun, various other investigations were completed which included a psychological test, the response to injected methacholine and methedrine, and the sedation threshold to sodium amylobarbitone: these tests form the basis of a separate report.

Treatment and Follow-up

Patients were in all cases treated by E.C.T. modified with thiopentone and suxamethonium chloride following atropine: twice-weekly treatments were usually given until it was felt that maximum benefit had been obtained or that nothing further was to be gained by continuing electroshock. No fixed course was used, and the average number of treatments in the series was between 7 and 8. Most patients were able to be discharged from hospital within 2–3 weeks at most following the cessation of E.C.T. All were in-patients.

Reassessment of clinical status, using the rating scale, was carried out personally on every patient at approximately 30 days after the last treatment, and again 2 months later, i.e. at 1 and 3 months after completion of treatment.

RESULTS

Age

Ages of the 50 patients ranged from 41–60 years (mean 51·1 years). The relationship between age and outcome with E.C.T. at one and three months

respectively was examined by calculation of the coefficient of correlation (r), using age in years and the total symptom-scores derived from the rating scale.

At 1 month after treatment $r=-0\cdot298$ ($P=0\cdot05$)
3 months $r=-0\cdot118$ (not significant).

This negative correlation indicates a tendency for the older patient in the series to have a lower total symptom-score after treatment, i.e. to have a better short-term prognosis, and the reverse for the younger ones. This trend is not a very marked one, however, nor is it sustained at the 3-month interval. In a fairly small series of 50 cases it may be partly due to bias introduced in the initial selection of patients. There is a statistically non-significant correlation ($r=0\cdot265$) between age and initial symptom-scores before treatment, however, which does not suggest a marked selection bias.

Physique

The body-index regression equation for females (Rees), expressed in standard measure, was first converted into an equation in which raw measurements from the patients could be used directly; this was calculated from the means and standard deviations given by Rees (1950) in the original work. The resulting equation did not give a sufficiently wide discrimination between patients of different physique, so that the original regression equation was multiplied 15 times to increase its standard deviation accordingly. From this a further equation was obtained which proved satisfactory: an arbitrary figure of 100 was added to each index-figure in order to obviate negative numbers.

The final equation was:

B.I. (F)$=3\cdot59$ stature$+3\cdot77$ symphysis ht.$-1\cdot91$ chest circumf.$-3\cdot73$ hip circumf.$-159\cdot39$ (measurement in inches).

The index ranged between 19 and 151; the distribution is shown in Table I.

TABLE IA

Distribution of Body-Index (Female)

Body Index	0–20	21–40	41–60	61–80	81–100	101–120	121–140	141–160
Number ..	1	1	4	9	18	12	3	2

This is a normal distribution and provides no evidence to suggest that an undue proportion of patients of a particular physique have been included in the series.

The indices were then correlated with the symptom-scores at 1 and 3 months respectively, the results being:

TABLE IB

	Symptom-score 1 month	Symptom-score 3 months	
Body-Index (F): r=	+0·617	+0·767	(both significant at the 0·001% level)

Previous Hysterectomy

Of the 50 patients, 11 (22 per cent.) had had this operation, all except two in the three years preceding their depressive illness.

No significant differences in mean symptom-scores at 1 and 3 months after treatment, or in diagnostic category, were found between the women who had had a hysterectomy and those who had not.

Clinical Item Score

In addition to the three clinical assessments on the rating-scale for depression, a scoring method devised by Hobson (1953), based on the presence or absence of various clinical items, was also used. These items had been found to be significantly associated with the immediate outcome with electro-shock. The definitions of the various items were those used by Hobson in his original paper, except that "sudden onset" was taken as deterioration to condition on admission within four weeks.

For each of the following allegedly *favourable* clinical features, a score of 1 was given if it was *absent*:

Sudden onset.
Good insight.
Obsessional traits in the previous personality.
Self-reproach (here taken as a score of 2 or more on the "guilt" rating).
Duration of illness of less than a year.
Pronounced retardation (taken as a score of more than 2 on the rating-scale).

For each of the following allegedly *unfavourable* features, a score of 1 was given if it was *present*:

Mild or moderate hypochondriasis (taken as a rating of less than 3).
Depersonalization.
Emotional lability.
Neurotic traits in childhood.
Neurotic traits in adult life.
Hysterical attitude towards symptoms.
Intelligence above average.
Fluctuating course since onset.
Ill-adjusted or hysterical previous personality.

Thus for each patient a clinical item score was made, furnishing a simple numerical assessment which could be compared with outcome: a high rating denoted a presumably poorer prognosis than a low one.

Ratings by this method ranged from 0–12; their distribution and the mean symptom-scores at 1 and 3 months after treatment for each rating are shown in Table II.

TABLE II

Scoring on Clinical Items (Hobson) and Mean Symptom-Score After Treatment

Clinical Item Score ..	0	1	2	3	4	5	6	7	8	9	10	11	12
No. with each rating ..	1	4	7	4	3	10	3	3	7	4	2	1	1
Mean Symptom Score at 1 month	1·0	2·75	3·3	1·2	4·6	5·3	7·3	6·0	8·0	8·0	9·2	13·0	10·0
Mean Symptom Score at 3 months	1·0	4·75	2·8	1·3	5·2	5·9	4·6	11·3	9·1	13·0	11·5	12·0	18·0

n=50.

The distribution is an uneven one, but this is not necessarily of much significance in a comparatively small series of 50 patients.

The mean symptom-score at one month after E.C.T. shows a remarkably consistent rise (apart from 3 minor exceptions) pari passu with the clinical item score, and this is reflected in a correlation of +0·727 between them (significant at the 0·001 per cent. level for 48 degrees of freedom).

A symptom-score at one month of less than 5 points may be regarded as an indication of a "good" result of treatment, and a score of over 6 as "moderately good" to "poor".

Table III shows the distribution of cases with these symptom-scores in relation to the item-scores.

TABLE III

Scoring of Clinical Items (Hobson) and Degree of Recovery

n = 50.

Clinical Item Score (Hobson) ..	0	1	2	3	4	5	6	7	8	9	10	11	12
Number of patients with:													
Symptom-score (1 month) 0–5	1	5	5	4	2	6	1	2	2	0	0	0	0
Symptom-score (1 month) 6+	0	0	1	0	1	4	2	1	5	4	2	1	1

From this table, an item-score of 5·5 points may be taken as an index of a good degree of recovery with treatment. Using this criterion 11 cases are seen to be misclassified, or 22 per cent. of the total. This is in close accord with Hobson's own figure of 21 per cent. of his total of 127 patients who were similarly misclassified.

The close association between the clinical item scoring of Hobson and the symptom score is less marked at three months after treatment (Table IV), the correlation being +0·666 (significant at the 0·001 per cent. level).

The relationship between the various clinical assessments which were made, i.e. the rating-scale assessments before treatment, at one and three months after E.C.T., and the scores on clinical items (Hobson) are demonstrated in Table IV.

TABLE IV

Correlation Between Clinical Assessments

	Clinical Item Score	Initial Symptom Score	1 Month Symptom Score	3 Months Symptom Score
Clinical Item Score (Hobson)	1·0	−0·498	0·727	0·666
Initial Symptom Score ..	−0·498	1·0	−0·353	−0·318
1 month Symptom Score ..	0·727	−0·353	1·0	0·582
3 months Symptom Score ..	0·666	−0·318	0·582	1·0

Initial Assessment and Improvement

The initial symptom-scores before treatment show a closely similar negative correlation between the re-assessments at one and three months after electroshock: r = −0·353 and −0·318 respectively (significant at the 2 per cent. and 5 per cent. levels respectively).

The 50 case histories and clinical records were carefully scrutinized, and the diagnosis of "psychotic" or "neurotic" depression made on the criteria laid down by Mayer-Gross (1954). Some difficulties were experienced in a number of cases, most of which could be satisfactorily resolved after discussion with experienced colleagues, and by taking into account the *predominating* clinical features. Three cases remained where no clear-cut diagnostic differentiation could be made. The "psychotic" group contained 20 patients and the "neurotic" group 27. The number in each diagnostic category was then compared with the clinical-item scores of Hobson (Table V).

TABLE V

Diagnostic Groups and Clinical Item Scores

Clinical Item Score (Hobson)	0	1	2	3	4	5	6	7	8	9	10	11	12
"Psychotic"	1	4	7	2	2	4	0	0	0	0	0	0	0
"Neurotic"	0	0	0	1	1	5	2	3	7	4	2	1	1
Unclassified	0	0	0	1	0	1	1	0	0	0	0	0	0
Totals	1	4	7	4	3	10	3	3	7	4	2	1	1

n=50.

This shows clearly a differentiation into two groups, with a fairly small degree of overlap.

DISCUSSION

It is readily apparent that an investigation such as the present one has necessary limitations, and individual variations and the general complexities of the problem make it futile to expect that prognosis can be reduced to a matter of a few simple figures. To attempt to isolate specific items from the clinical picture presented by each individual patient is clearly to make artificial divisions and to ignore other possible factors in the total situation—the effects of individual and group inter-personal relationships, chance environmental influences and so on. Although many of these factors are operating at random and for the purposes of this study have been ignored, in a comparatively small series of 50 patients their influence cannot be completely dismissed, and it is emphasized that conclusions drawn from the results above are to be interpreted with due caution.

A full review of the relevant literature on the prognostic significance of various clinical features of depressive illnesses, both before and after the introduction of E.C.T., is of considerable interest but cannot be included here. The possible significance of the various findings calls for further mention, however.

Before the advent of electroshock treatment a number of studies on depressed patients stressed the adverse influence of increasing age on the outcome; Strecker *et al.* (1931), Anderson (1936) and Rennie (1942) all remarked on the generally poorer prognosis when the illness occurred after the age of 40. Since the introduction of E.C.T. there has been some evidence that this trend has been at least diminished, and this is confirmed in the present investigation. This tendency for older patients to have a better outcome a month after treatment is not sustained at the three-month interval, however, and the patients concerned were initially selected to exclude those suffering from the organic cerebral complications commoner in the older age group.

The value of morphological indices for prognosis has chiefly been investigated in schizophrenics, the initial impetus to these researches having been given by Kretschmer's observations. Most studies of differences in body-build, and their association with outcome have stressed the better prognosis for individuals of more pyknic than asthenic habitus, but a number of investigators have not found any significant relationship between physique and prognosis. Many reports have been based upon general impressions of the physique rather than actual measurements, and the technique of somatotyping (Sheldon, 1940) has made researches in this field more scientific. A simpler index of somatic morphology is that suggested by Rees (1950) and called the "body-index (female)" obtained by factor analysis of inter-correlations between 15 anthropometric variables from 200 female patients to produce a regression equation

based on 4 simple measurements. Rees found that leptomorphy classified on the basis of this index was associated with dysthymic traits of anxiety and depression in 400 female neurotics, but emphasized that the correlation between physique and psychological studies is probably too small for clinical use in diagnosis or prognosis. The correlations between the body-indices and symptom scores after treatment in the present study are surprisingly high, and on a small series of patients must be treated with reserve. The inference is clear, however, that in the depressed patients observed, those with a lower body-index (i.e. tending towards endomorphy or a pyknic physique) have a distinctly better outcome with E.C.T. than those of a more leptosomatic habitus, and the trend is enhanced three months after treatment. Gildea *et al.* (1936) observed in normal people that high serum lipoids (fatty acids and serum cholesterol) were found in conjunction with pyknic body-build and high energy output; low lipoid levels were found in individuals of asthenic or leptosomatic build and low energy-output. Further studies (Gildea *et al.*, 1940; Gildea and Man, 1943) suggested that the triad of pyknic physique, uncomplicated symptoms of manic-depressive psychosis and high serum lipoids were evidence of a high capacity for recovery in their patients.

In view of conflicting statements as to the importance of such stress factors as physical illness or operations, particularly those involving the genito-urinary system (Malamud *et al.*, 1941), the incidence of women in this series who had had a hysterectomy (22 per cent.) is of interest. The precise nature and extent of the operation, removal of one or both ovaries, etc. was not known in the majority of cases, and it must be remembered that all the patients were between 41–60 years, the age range in which hysterectomy is most frequently performed; nor is it known what proportion of non-depressed women of this age have had the operation. Nevertheless the proportion found seems a large one, although it appears unlikely to carry any prognostic implications for treatment.

The scoring method using clinical items for predicting short-term response to E.C.T. appears to be of definite value. The statistically highly significant correlations found in the present series between clinical item-scores and symptom-scores after treatment ($r=0\cdot727$ and $0\cdot666$ at 1 and 3 months respectively) confirm Hobson's claim that the results of his original investigation "can be of practical assistance in the formulation, treatment, and prognosis by indicating the significance of certain features". The proportion of mis-classifications using this scoring method is also confirmed at about one-fifth of the total. The initial symptom-scores (Table IV) show a similar trend, with correlations with symptom-scores at 1 and 3 months after electroshock of $-0\cdot353$ and $-0\cdot318$ (significant at the 2 per cent. and 5 per cent. levels respectively).

There is thus a clear tendency for those patients with high symptom-scores to begin with to respond rather better to treatment, and vice versa: this is the more so at one month afterwards than at three months. Two explanations for these findings are possible. Either the difference is a quantitative one, as Garmany (1958) and others believe, and the more severe depressives respond better to E.C.T. than milder ones, or there is a qualitative difference with a variety or group of varieties of depression which are characterized by a higher initial symptom-score and a good response to electroshock, and a variety showing the reverse features.

Examination of the relationship between initial assessments and the clinical item score of Hobson gives a correlation of $-0\cdot498$ (significant at

the 0·001 per cent. level). Thus there is an even clearer tendency for the higher initial symptom-scores to be accompanied by low clinical-item ratings and vice versa. To obtain a high score on the clinical-item assessment a fairly large number of neurotic features must be present: Hobson has commented on the high proportion of neurotic traits in his series. If the differences noted above were due merely to different degrees of intensity of depression, it seems unlikely that marked neurotic traits should be so much commoner in the less severely depressed. When the numbers with particular clinical-item scores are classified according to diagnostic category, the higher scores (5 and above) tend to cluster markedly in relation to the group of "neurotic" depression, and it is particularly noticeable that in the present series no patient with a clinical diagnosis of "psychotic" depression, 20 in all, had a clinical item score of more than 5 points, and only 7 out of 27 in the "neurotic" depressive category had a score of 5 or less, and of these only 2 with a score of 4 and 3 points respectively. The evidence here strongly suggests, although it by no means proves, that there may well be a qualitative difference, and that there is a variety of depression, characterized by lower initial symptom-scores for depression on the rating-scale, a higher incidence of neurotic features and thus a higher clinical-item score (Hobson), and a tendency to do less well with E.C.T. Similarly there is a variety, or group, in which the opposite features are found. These clearly correspond to "neurotic" or "reactive" and "psychotic" or "endogenous" depressions. (The terms "reactive" and "endogenous" to imply mutual exclusion and specificity are misleading, as a psychotic depression may well be "reactive" in some senses, and endogenous constitutional predisposition is present in many depressions regarded as "reactive".)

Argument over the question of differentiation of depressive states has waxed and waned for many years, and much of the debate has been admirably and succinctly reviewed by Partridge (1949). Following the now classical historical, clinical and prognostic surveys of "melancholia" by Lewis (1934, 1936), controversy diminished for a number of years, but has again become more topical, and in addition further doubts have been cast upon the concept of "involutional depression" as a clear-cut separate clinical entity (e.g. Mayer-Gross 1954b; Tait *et al.*, 1957). Further evidence favouring the "separatist school" has been reported in recent years, including observations on depressed patients subjected to prefrontal leucotomy (Elithorn, 1958), sedation-threshold studies (Shagass, 1956) and the reaction of depressives to intravenous methyl-amphetamine (Roberts, 1959). The results of the present investigation also point in the direction of there being at least two varieties of depressive illness.

Summary

1. The importance and historical development of the search for reliable prognostic guides for the electroshock treatment of depressive states is briefly indicated.

2. The design of an investigation into alleged prognostic indices is described, using a rating scale of depressive symptoms and signs for the assessment of clinical status. Fifty female patients, aged 41–60, with primary depressive illnesses were investigated, their physique measured, and later treated by E.C.T. Re-assessments of clinical condition were made at 1 and 3 months after the completion of treatment, and the association between specific clinical factors and quantitative symptom-ratings examined statistically.

3. A significant relationship with response to electroshock was found between patient's age, physique and a clinical-item scale (Hobson) derived from the history and examination.

4. Certain of the results support the view that there are at least two clinically separate varieties of depressive illness.

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