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CLINICAL PREDICTION OF RATE OF RESPONSE OF ENDOGENOUS DEPRESSION TO ELECTROCONVULSIVE THERAPY

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SUMMARY

In depression, the identification of predictors of fast response is necessary to improve patient selection for ECT. In a double-blind, prospective study of 32 endogenously depressed patients treated with ECT, we attempted to identify the clinical characteristics of ECT responders which predicted fast (requiring $\leq$ 5 treatments to produce maximum recovery) and slow (requiring $\geq$ 6 treatments to produce maximum recovery) response to ECT. Of the 22 ECT responders in the study, 13 were fast and 9 were slow responders. We found that male sex, and greater age associated with lesser initial severity of depression were significantly associated with fast recovery. Surprisingly, factors suggested or expected to predict good outcome with ECT failed to predict fast outcome. Finally, the treatment variables of mean seizure duration and stimulus waveform were found to be unrelated to recovery rate. The findings are briefly discussed.

Introduction

While electroconvulsive therapy (ECT) remains a major therapeutic tool in the psychiatrist's armamentarium in third world countries, legal issues are restricting its popularity in the West. In addition, there is growing apprehension that ECT produces unacceptable neuropsychological deficits. Therefore, important clinical concerns have been the identification of ECT techniques that hasten recovery (Andrade et al 1988a), the identification of ECT techniques that increase likelihood of response (Andrade et al, 1988b), the development of treatment strategies that reduce the number of ECTs required (Andrade et al 1988c), the selection of patients likely to show good response to ECT (Andrade et al 1988d, e, f, g, h), and the selection of patients likely to show fast response to ECT. (Andrade et al 1988g, h). The present study falls into the last-mentioned category.

Hitherto, favourable response to ECT has usually been defined solely in terms of the degree of recovery produced. Also important, however, is the rate at which the patient responds – this is because the reduction of suicide risk and the improvement of quality of life earlier in treatment have obvious clinical advantages; further, the fewer the treatments received, the lesser the ECT-induced cognitive deficits. We hence studied the clinical characteristics of a cohort of ECT-treated endogenously depressed patients in an attempt to identify clinical predictors of rate of response.

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Material and Methods

The sample comprised all endogenously depressed patients (RDC) identified over a 3 month period in 2 adult psychiatry units at the National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore. Informed consent for participation in the study was obtained in writing. Subjects were randomized into sinusoidal wave (SW) or brief-pulse (BP) ECT groups; no concurrent medication was administered.

SW ECT was administered using an ECT machine designed and assembled in collaboration with the Department of Biomedical Engineering at NIMHANS (Gangadhar et al 1988). This constant-voltage SW generator delivers SW stimuli ranging in voltage from 90-190V (in 10v steps). and in duration from 0-2.0secs. (in 0.1sec. steps). Visual display permit the recording of the voltage and amperage of the stimulus delivered during the ECT. The following were the SW stimulus settings employed during the study: 50 Hz, 140V, unmodified alternating current sinusoidal waves, administered for 0.6secs. BP ECT was administered using the MECTA constant-current BP generator. The following were the BP stimulus settings employed during the study: 70Hz, 800mA, 0.75msec. width, biphasic, rectangular pulses, administered for 0.75 secs.

Modified, bilateral (frontotemporal) treatments were administered on alternate mornings, thrice weekly. During each ECT, voltage and current parameters were noted. If the patient failed to convulse, the stimulus was readministered at the next higher setting of stimulus duration. Seizure duration was measured by the cuff method (Addersley and Hamilton, 1953) by 2 trained observers using stopwatches; the mean observed score was recorded.

Severity of depression was rated on the 17-item Hamilton Rating Scale for Depression (HRSD), administered by a blind rater before commencing the ECT course and, again, roughly 30 hours after each ECT. The time was selected to ensure that ECT-related side effects did not falsely inflate scores on the somatically loaded HRSD, and that diurnal variations in depression did not influence ratings of severity.

Treatment was stopped when further amelioration of depression was unlikely. This operationalized as follows: no further reduction in HRSD scores after 3 consecutive ECTs with a minimum of 6 ECTs or occurrence of total/near-total absence of depressive features on the HRSD (HRSD score ≤ 4), whichever obtained earlier.

Satisfactory response to ECT was prospectively defined as $\geq 75\%$ reduction in initial HRSD scores by the end of the ECT course. While many definitions of response have been used in literature, we considered this definition to most appropriately distinguish patients who show satisfactory clinical improvement from those who do not, in an Indian population.

Results

Of the 32 patients entered into the study, 4 developed a transient mania, posited to constitute a side effect of ECT (Andrade et al 1987b, 1988i). Two of these patients were dropped from the study as their manic reaction developed in mid-depression; data from the remaining 2 patients were retained as the manic reaction coincided with the lifting of depression. A further patient was excluded due to withdrawal of consent (due to pressure from relatives) despite satisfactory initial response. These 3 patients did not differ from the rest of the sample on sociodemographic, clinical or treatment variables.

Of the 29 patients completing the study, 22 were deemed to have satisfactorily responded to ECT. These 22 patients received 2-11 (5.7 ± 2.5) treatments to attain maximum recovery; the distribution of number of ECTs required followed a roughly bimodal curve, and the median (5 ECTs) was observed to represent a dividing point between slow and fast responder. Hence, using this median as a yardstick, the responder group was divided into fast (requiring ≤ 5 ECTs to attain maximum recovery) and slow (requiring ≥ 6 ECTs to attain maximum recovery) responders. That this yardstick is a viable one is apparent from traditional clinical wisdom which indicates that depressed patients conventionally require 6-8 treatments for optimum recovery (Taylor 1982), hence, patients requiring 5 or fewer treatments could be considered as fast responders.

There were 9 slow and 13 fast responders. These 2 groups were compared on the variables of age, sex, polarity, affective episode number and duration, initial severity of depression, and status on the Hobson (1953) and Mendels (1967) ECT prognostic indices, as well as (qualitatively and quantitatively) on the Newcastle diagnostic and prognostic indices (Carney et al 1965). The groups were also compared on the treatment variables of mean seizure duration experienced and stimulus waveform. The results are presented in Table 1.

Two variables – greater age and male sex significantly characterized the fast responders, while there was a trend for lesser initial severity of depression to do so. To eliminate/identify interactions between these 3 variables (which, for eg., would answer questions such as 'did males respond faster because they were over-represented in the lesser depressed group?'), further statistical analysis was performed.

Table 1
Clinical and treatment variables in fast and slow ECT responder groups

	Fast (N=13)	Slow (N=9)	Signif.
Number of treatments	2–5 (4.0±1.0)	6–11 (8.1±2.0)	p<0.001 (1)
Sex: Male	10	2	p=0.017
Female	3	7	(2)
Age (years)	25–55 (41.5±10.0)	23–50 (35.0±6.1)	p=0.01 (1)
Unipolar	1	2	NS (2)
Bipolar	5	3	
Unclassifiable	7	4	
Episode number	1–6 (2.5±1.7)	1–7 (3.2±2.4)	NS (3)
Episode duration (months)	0.75–6 (3.6±2.4)	1–6 (3.2±2.4)	NS (3)
Hobson (1953) good prognosis	13	9	NS (2)
Mendels (1967) good prognosis	12	8	NS (2)
Newcastle			
a) good prognosis	9	4	NS (4)
b) prognostic score	6–9	5–9	NS(3)
	0–6 (2.2±1.8)	−3–6 (1.2±3.3)	NS (1)
Newcastle			
a) endogenous	13	8	NS (2)
b) endogenous score	6–9 (7.1±1.0)	5–9 (7.0±1.1)	NS(3)
Initial HRSD score	16–29 (20.5±4.5)	18–40 (24.8±6.6)	p<0.1 (3)
Mean seizure duration (secs.)	18.7–38.5 (27.8±6.2)	21.3–30.6 (24.8±3.0)	NS (1)
Sinusoidal wave	7	6	NS (2)
Brief-pulse	6	3	

(1) Fisher's exact probability (median) test
(2) Fisher's exact probability test
(3) Student's t test
(4) Chi square test

First, males and females were independantly compared (Table 2), it is clear that while males received significantly fewer ECTs (the mean falling in the fast responder range), they did not differ from

Table 2
Specific clinical and treatment variables in male and female ECT responders

	Males (N=12)	Females (N=10)	Signif.
Number of treatments	2–10 (4.6±2.1)	4–11 (7±2.4)	t=2.51* p<0.05
Age (years)	26–55 (41.1±8.8)	23–51 (36.1±10.3)	NS*
Initial HRSD score	17–40 (22.0±8.7)	16–40 (22.5±7.1)	NS*

*Student's t test

females (whose mean was in the slow responder range) in age or initial severity of depression. This indicated that male sex predicted fast response independently of the other 2 variables.

Next, age and initial HRSD scores were correlated (Pearson's product-moment correlation coefficient), a significant, negative relationship between these 2 variables was obtained ($r = 0.46$, $p < 0.05$). This indicated that while no independant effect was demonstrated, lesser initial severity of depression associated with greater age predicted fast response to ECT.

Discussion

While it is generally agreed that the average number of treatment required for optimal therapeutic response of endogenous depression to ECT is 6-8 (Taylor 1982), certain patients may require just 2 to 3 while others may need as many as 10-12 treatments (Kendell 1981). There seems to be a tacit agreement that this variability is largely a function of patient characteristics – an assumption supported by reports that some depressed patients are unusually sensitive to ECT (Keisling 1984, Rich 1984, Andrade et al 1987a). Considering that the clinical prediction of responsiveness to ECT has been accorded to fair degree of attention, it is surprising that the issue of rate of response has been less well studied, that such is necessary has already been pointed out.

While 'rate of response' could strictly be interpreted as the proportion of reduction of depression per treatment, for want of a better term we have used it to qualify the total number of treatments required to produce maximum recovery in those patients who responded to ECT (for obvious reasons, there would be little purpose in including ECT non-responders in the study population). The justification for the demarcation of ECT responders into slow and fast categories has been discussed in the previous section.

Barring a few exceptions in ECT literature, male and female depressed patients have been found to be equally represented amongst ECT responders (see Coryell and Zimmerman 1984). Therefore, the finding that males respond faster than females was somewhat surprising. In contrast, increased age has been suggested to (weakly) predict favourable outcome with ECT (see Fink 1979), and, in consonance with this was the finding that fast responders were significantly older than slow responders. It is worth noting, though, that at least 2 other studies (Price et al 1978, Rich et al 1984) have observed that increased age is associated with slower response, however, the widely differing methodologies and definitions of rate of response do not permit a direct comparision of study results.

Also interesting was the finding that there was a trend for lesser initial severity of depression to predict faster response. This finding could be logically explained in terms of lesser depression requiring lesser treatment. Paradoxically, these 'lesser depressed' patients are the ones to whom

clinicians tend to prescribe antidepressant drugs in preference to ECT despite the disadvantages that these drugs carry-slower recovery rate, more subjective side effects (Gangadhar et al 1982, 1985) and greater suicide abuse potential.

We note that while age was observed to independantly predict rate of response, the significant negative relationship between age and initial severity of depression indicated that increased age predicted rapid response only when associated with lesser initial depression.

We had earlier reported that the Newcastle Prognostic Index identifies ECT responder with high specificity but low sensitivity (Andrade et al 1988d, e). In this study, we examined whether responder/non-responder status on this index predicts fast/slow response to ECT, and whether higher/lower scores on the index have predictive power in this regard. Thus, both qualitative and quantitative analyses were performed, neither differentiated fast from slow responders.

The Newcastle Diagnostic Index scores were similarly examined; again; neither qualitative nor quantitative analyses predicted rate of response to ECT. The former result was obvious as virtually as subjects were diagnosed as endogenous on this index. The latter result was interesting (in view of the the fact that endogenous symptomatology is accepted to predict good response to ECT) as it indicated that more endogenous symptomatology does not indicate likelihood of faster response to ECT.

The (high energy) sinusoidal waveform has been suggested to be therapeutically more effective than the (low energy) brief-pulse stimulus (Andrade et al 1988b), and has also been shown to be asociated with speedier recovery from depression (Robin 1981, Robin and de Tissera 1982).

However, in line with our earlier report (Andrade et al 1988a), in this study stimulus waveform (and hence energy delivery) was unrelated to recovery rate. Likewise, mean seizure duration experienced by the patients did not differ between fast and slow responders. Thus, it would seem that increased seizure duration over and above the hypothetical point of adequacy does not lend itself to hastening the response rate, much as it does not enhance the likelihood of response.

Finally: variables such as polarity (which has been suggested as a predictor of response of endogenous depression to ECT – see Andrade et al 1988e) and affective episode number and duration did not predict the response rate of depression to ECT.

In conclusion: male sex, and lesser initial depression in older patients have been identified as 2 predictors of rapid response of endogenous depression to ECT. Indices suggested to predict favourable outcome with ECT do not predict rate of response. The degree of endogenous symptomatology does not differentiate slow and fast responders, nor does polarity, or affective episode number and duration. Treatment variables such as mean seizure duration experienced and stimulus waveform are likewise unrelated to recovery rate.

Faster response to ECT is associated with reduction of suicide risk and improvement of quality of life earlier in treatment; furtheremore, ECT-induced cognitive deficits are minimized. It is to be hoped that the study of factors influencing the rate of recovery yields predictors that would sensitize clinicians against the traditional practice of prescribing a 'course' of ECT; in fast fast responders, such would unnecessarily

expose the patient to the potentially adverse effects of ECT after maximal recovery has been attained. Lastly, it is to be hoped that identification of predictors of fast response improves patient selection for ECT, much as the identification of ECT responders may have done.

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