

SEIZURE DURATION AND RELATED ISSUES IN ECT FOR ENDOGENOUS DEPRESSION

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SUMMARY

In a study comparing sinusoidal wave and brief-pulse ECT in endogenous depression, seizure duration was monitored by the cuff method in 29 patients over 180 treatment sessions. Mean seizure duration across all treatments was 26.5 secs, and the mean for individual patients across their ECT course ranged from a minimum of 15.7 secs to maximum of 38.5 secs. Regression analysis found no variable which significantly predicted mean seizure duration. Of the 22 good responders in the study, response to ECT was associated with a mean seizure duration of secs in 1 patient, and 0 cs in 11 patients; as just 2 of 7 poor responders to ECT had a mean seizure duration of <20 secs in 1 patients, <25 secs in 11 patients, of the 22 good responders in the study; as just 2 of 7 poor responders to ECT had a mean seizure duration of < 25 secs, it appears that a cuff seizure duration of over 20 secs may suffice for the seizure to be therapeutic in depression. With (constant current) brief pulse ECT, seizure threshold significantly increased with successive ECTs; thresholds did not however differ between the good and poor responders. There was a trend for seizure duration to decrease over time; again, good and poor responders did not differ. These findings provide little support for the anticonvulsant hypothesis for the antidepressant effect of ECT, but support the literature that ECT exerts an anticonvulsant effect.

INTRODUCTION

The ECT seizure duration has received attention on many counts. A minimum seizure duration of 20-25 secs is recommended to ensure therapeutic benefit while seizures lasting for 3 mins or longer are considered to increase risk for adverse effects (Royal College of Psychiatrists, 1989; American Psychiatric Association, 1990). Within this window of 25-180 seconds, while no evidence exists to suggest that longer seizures are more therapeutic (Andrade, 1990), it appears that increased seizure duration increases ECT-induced amnesia (Abrams, 1988).

A cumulative seizure duration therapeutic window has been suggested to exist (Maletzky, 1978; Kramer, 1983), but the evidence for this contention is open to question (Andrade, 1990). Seizure duration decreases across the ECT course and varies inversely as a function of age, seizure threshold, ECT number and barbiturate anaesthesia dose, and directly as a function of the stimulus intensity [although the relationship may be complex outside a narrow range of dosing] (Sackeim et al, 1991). Recently, Agarwal et al (1992) found that seizure duration monitoring during ECT is virtually unheard of in India: lack of such monitoring in research and clinical practice has been criticized (Andrade, 1990; Andrade & Gangadhar, 1990; Channabasavanna, 1992).

In view of the above-mentioned importance attached to seizure duration monitoring during ECT, the data on seizure duration and information related thereto were examined from a double-blind study that sought to compare sinusoidal wave and brief-pulse ECT in endogenous depression. Specific issues that were considered were mean seizure duration, particularly as characteristics of good and poor response to ECT, changes in seizure threshold and seizure duration across time- again, particularly as characteristic of good and poor response and potential determinants of the ECT seizure duration.

MATERIAL AND METHODS

The sample comprised all untreated endogenously depressed patients (definite cases; R.D.C: Spitzer et al, 1978) 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 Biomedical Engineering Department at NIMHANS (Gangadhar et al, 1988). Visual displays permit a read-off of the voltage and amperage of the stimulus delivered during the ECT. For the study, the SW stimulus specifications were 50 Hz, 140 V, unmodified alternating current sinusoidal waves delivered for 0.6 secs. BP ECT was delivered using the (constant current) MECTA ECT device. The BP stimulus settings were 70Hz, 800mA, 0.75 msec width, biphasic rectangular pulse delivered for 0.75 secs. The current delivered between the electrodes was recorded in millicoulombs of charge.

Modified treatments with thiopentone sodium (200mg), succinylcholine (20-30mg) and atropine sulphate (0.65mg) were administered with bilateral frontotemporal electrode placement on alternate mornings, thrice weekly. The duration of the seizure was measured by the cuff method (Addersley & Hamilton, 1953) by 2 observers using stopwatches; the mean value was taken for analysis.

If the subject failed to convulse, the stimulus was repeated at the next higher setting of stimulus duration; if a convulsion occurred, irrespective of its duration, ECT was deemed to have been given.

The ECT course was discontinued when further benefit to the subject was unlikely - i.e., when no clinically meaningful reduction in 17 item Hamilton Rating Scale

for Depression (Hamilton, 1960) scores was seen after 3 consecutive ECTs with a minimum of 6 treatments, or when depression scores fell to 4 or less, whichever occurred earlier. These criteria are in accordance with the observations and findings of McAllister et al (1985), that if depressives improve with ECT, improvement will be discernable within the fifth treatment in the course, and of Barton et al (1973) that no benefit is conferred upon the

TABLE 1
Clinical characteristics of SW and BP ECT good and poor responders.

	SW good responders (n=13)	SW poor responders (n=1)	BP good responders (n=9)	BP poor responders (n=6)
Age (yrs) M ± SD	36.0 ± 8.0	17	42.9 ± 10.7	42.5 ± 13.4
Sex (M:F)	7:6	0:1	5:4	3:3
Polarity				
unipolar	2		1	2
bipolar	4	Uncertain	4	1
uncertain	7	4	3	
Episode duration (M ± SD (mins))	3.0 ± 2.3	2.5	3.9 ± 1.5	3.5 ± 2.2
Episode number (M ± SD)	3.0 ± 2.3	1	2.6 ± 1.4	2.7 ± 1.5
Initial Hamilton Dep. score (M ± SD)	24.2 ± 6.3	28	21.4 ± 2.6	26.8 ± 5.5
Final Hamilton Dep. score (M ± SD)	1.8 ± 2.4	18	0.8 ± 1.8	15.7 ± 6.5

* as the subject had experienced fewer than 3 affective episodes

With the exception of final depression scores ($p < 0.01$ responder groups vs BP poor responders), when the single SW non-responder was excluded, the remaining 3 groups did not differ on any of the above variables (Kruskal-Wallis one way ANOVA / Fisher's exact probability test).

patient by continuing ECT after maximum response is obtained.

A favorable response to ECT was prospectively defined as greater than 75% reduction from the initial depression scores (Andrade & Gangadhar, 1989). This cut-off separated the 'good' from the 'poor' responders. The term poor responders embraces both partial response and non response categories; since, on the average, some 80% of endogenous depressives respond to ECT, it was felt that to separate partial and nonresponders would yield

TABLE 2
M ± SD treatment details of SW and BP ECT good and poor responders.

	SW good responders (n=13)	SW poor responders (n=1)	BP good responders (n=9)	BP poor responders (n=6)
Number of ECTs	6.5 ± 2.5	8	5.7 ± 2.5	6.2 ± 1.2
Cumulative seizure duration (secs)	170.6 ± 56.5	211.1	144.3 ± 58.9	170.1 ± 55.7
Individual mean seizure duration (secs)	27.1 ± 6.0	26.4	25.7 ± 4.6	27.6 ± 7.6

When the single SW poor responder was excluded, the remaining 3 groups did not differ on any of the above variables (Kruskal-Wallis one way ANOVA).

subsample sizes that would be too small for analysis. The study was double-blind: neither patients nor rater were aware of the treatment allotted.

RESULTS

Sociodemographic and treatment details of the 29 patients in the sample are presented in Tables 1 and 2. A total of 180 ECTs were administered. The mean seizure duration for all patients across all treatments was 26.6 secs. Mean seizure duration was < 20 secs in 2 patients - 1 good responder and 1 poor responder, and was between 20 and 25 secs in 11 patients - 10 good responders and 1 poor responder. Mean seizure duration exceeded 25 secs in the remaining 11 good and 5 poor responders.

A stepwise multiple regression analysis was conducted to assess the influence of age, sex, stimulus waveform, number of treatments received and responder status on mean seizure duration; no independent variable predicted a significant proportion of the variance in the dependent variable - in fact, these 5 variables explained barely 8% of the total variance (in mean seizure duration) in the regression analysis.

An attempt was made to match the 6 BP poor responders in the study with 6 BP good responders and 6 SW good responders (as there was only 1 SW poor responder, this category could not be included) on the parameters of age, sex, polarity, episode number and duration, and number of treatments received; fortunately, despite the limited sample from which these 18 patients were drawn, the 3 groups so obtained were reasonably comparable. The Mean ± SD electrical dose delivered in each group for the first 4 as well as the last ECT in the course are presented in Table 3. These data were analyzed separately for SW and BP patients because SW ECT was administered using a constant voltage current device

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TABLE 3: M ± SD electrical dose (coulombs) delivered at different time points during the ECT course.

	ECT 1	ECT 2	ECT 3	ECT 4	
SW good responders (N=6)	304.6 ± 60.6	348.9 ± 41.6	320.8 ± 84.9	356.0 ± 42.3	306.2 ± 76.7
BP good responders (N=6)	66.5 ± 8.6	66.5 ± 8.6	70.0 ± 10.6	73.5 ± 11.5	80.5 ± 20.6
BP poor responders (N=6)	73.5 ± 11.5	80.5 ± 20.6	84.0 ± 18.8	87.5 ± 15.8	91.0 ± 17.1

Statistical inferences are presented in the text

TABLE 4: M ± SD seizure duration (seconds) at different time points during the ECT course.

	ECT 1	ECT 2	ECT 3	ECT 4	Last ECT
SW good responders (N=6)	28.1 ± 10.1	27.9 ± 9.3	24.0 ± 8.6	26.6 ± 5.4	25.1 ± 6.7
BP good responders (N=6)	27.3 ± 7.8	28.1 ± 7.0	27.5 ± 9.5	22.7 ± 9.7	21.1 ± 5.0
BP poor responders (N=6)	34.9 ± 14.0	27.9 ± 12.4	24.2 ± 13.4	27.8 ± 9.1	22.3 ± 10.0

Statistical inferences are presented in the text

(hence, impedance variations would confound SW but not BP stimulus dosages).

A 6x5 one way repeat measures analysis of variance of the SW dosage data revealed no significant changes in the repeating measure. A 2x5 two way repeat measures analysis of variance of the BP dosage data revealed a significant main effect for ECT number ($F_{4,40} = 7.72$; $p < 0.001$) but no significant main effect for response status nor a significant response x ECT number interaction. The Tukey's honestly significant difference (post hoc) test found significant differences across alternate ECT time points - i.e., between ECTs 1&3, 2&4, and 3 and the last in the course. The Mean ± SD seizure duration at these ECT points in these 18 patients are presented in Table 4. A 3x5 two way repeat measures analysis of variance revealed a near significant main effect for ECT number ($F_{4,60} = 2.30$; $p = 0.075$) but no significant main effect for waveform/response status nor a significant waveform/response X ECT number interaction.

DISCUSSION

As a number of patients who showed good response to ECT had a mean seizure duration <25 secs (in one patient it was just 18.7secs!), it appears that there are no grounds to consider motor seizure durations (as measured by the cuff method) between 20 and 25 secs to be invariably sub therapeutic. This may be restated as follows: Motor seizure durations of ≥ 20 secs are likely to suffice for therapy. Further work is required to evaluate the significance of motor seizures between 15 and 20 secs in duration.

The cuff method underestimates the EEG seizure duration by about 10% (Fink & Johnson, 1982) or by a mean of 13 secs. (Warmflash et al, 1987). Therefore, a motor seizure duration in the region of 20 secs is almost certain

to be represented by an EEG seizure close to or in excess of 25 secs. Official available guidelines (e.g. Royal College of Psychiatrists, 1989; American Psychiatric Association, 1990) do not specify the lower limit of acceptability of seizure duration with specific reference to the method of monitoring; the findings of this study may perhaps be helpful in this regard, particularly, as the cuff method is convenient, practical and inexpensive relative to the EEG method and eminently suitable for routine use in developing countries such as India. (Andrade, 1990; Agarwal et al, 1992; Channabasavanna, 1992).

None of the independent variables entered into the regression analysis significantly predicted mean seizure duration. The non significance of sex (Sackeim et al, 1991), stimulus waveform (Andrade et al, 1988) and responder status (Andrade, 1990) have some support in literature. Age, nonsignificant in this study, has been shown to be associated with shorter seizure durations in another study (Sackeim et al, 1991); it is possible that the considerably older sample in that study may have been responsible for this finding. In other words, the effect of age on seizure duration may become identifiable only beyond a certain range.

Curiously, the number of treatments received also did not influence seizure duration. Since the seizure duration decreases with successive ECT (Sackeim et al, 1986), a larger number of treatments could have been expected to be associated with a shorter mean seizure duration (Nettelbladt, 1988). A possible explanation for differences across studies is the parameter chosen for analysis - mean seizure duration (this study), cumulative seizure duration (Andrade et al, 1988), seizure duration at a particular treatment number (Sackeim et al, 1986) etc. The impor-

tance of this dependent variable issue is clearly seen from the results of the analysis of data in Table 4.

It may be noted that 2 sources of variance in seizure duration - seizure threshold and dose of barbiturate anaesthesia - were not addressed in the analysis because the former was not formally titrated for (Sackeim et al, 1986) while the latter was kept constant for all patients.

Maletzky (1978) considered that recovery with ECT occurred within a therapeutic window of cumulative seizure duration between 210 and 1000 secs. From Table 2 it is clear that a considerable proportion of patients showed good response to ECT at cumulative seizure durations well below the minimum specified by Maletzky. This substantiates the opinion that the number of treatments received is more important than the cumulative seizure duration construct.

Although the seizure threshold was not formally titrated for, with constant current BP ECT the electrical dose required to elicit a convulsion was found to increase with successive ECT. This is in accordance with the findings of Sackeim et al (1987) in a study in which careful titration of the seizure threshold was undertaken across the ECT course. The lack of change in dosing in the SW group can be attributed to two factors: [a] the delivered stimulus was of the constant voltage type and hence subject to the vagaries of interelectrode impedance (across patients, and in the same patient across time); and [b] on just 1 occasion in just 1 SW ECT patient was it necessary to increase the stimulus duration to obtain a convulsion (suggesting that the stimulus settings were clearly suprathreshold for the group as a whole).

The absence of difference in dose requirements between BP ECT good and poor responders and the absence of difference in the rate of change of dose requirements across the ECT course between BP ECT good and poor responders suggest that changes in seizure threshold are not germane to treatment response. These findings directly contradict the observations of Sackeim et al (1987) that proportionately greater increases in seizure threshold characterize good response to ECT.

The decrease in seizure duration with successive ECT is in accordance with literature (Sackeim et al, 1986; Michele et al, 1991). The present study further suggests that seizure duration changes are unrelated to treatment response. Overall, therefore, Tables 3 & 4 confirm that ECT has an anticonvulsant action (progressive decrease in seizure duration) but do not support the hypothesis that this anticonvulsant action is related to the antidepressant response (Sackeim et al, 1986; Andrade, 1992) - vide the lack of relationship between seizure threshold and seizure duration changes on the one hand and responder status on the other hand. It is acknowledged, however, that the small subgroup sizes could have decreased the power of the statistical tests to identify a significant association between anticonvulsant construct and antidepressant response; the absence of a perfect one to one subgroup matching is however unlikely to be of importance as none of the variables (selected for conventional reasons) on

which comparison was undertaken have been shown to meaningfully affect response to ECT (Andrade, 1990). The preliminary observations herein reported may however bear substantiation with a larger sample and better matched subgroups.

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