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We measured initial seizure threshold by means of a structured stimulus dosage titration procedure in a clinical sample of 111 depressed patients undergoing brief-pulse, constant-current electroconvulsive therapy (ECT). Initial seizure threshold was approximately 60 milli-coumbs (mc) (10 Joules) on average, but varied widely (6-fold) across patients. Initial seizure threshold was predicted by four variables: electrode placement (higher with bilateral), gender (higher in men), age (higher with increasing age), and dynamic impedance (inverse relationship). Use of neuroleptic medication was associated with a lower seizure threshold. EEG seizure duration was inversely related to initial seizure threshold, but no other relations with seizure duration were found. These findings may have important clinical implications for stimulus dosing strategies in ECT.

Key Words: Electroconvulsive therapy (ECT), seizure threshold, stimulus dosage titration

Introduction

Several lines of evidence indicate that both the efficacy and the cognitive side effects of electroconvulsive therapy (ECT) may depend on the extent to which the stimulus dosage exceeds the patient's seizure threshold (Cronholm et al 1963a,b; D'Elia et al 1983; Fraser 1982; Malitz et al 1986; Ottosson 1960; Robin et al 1982; Sackeim 1984; Sackeim et al 1987a, 1993). These findings suggest that optimizing stimulus dosage during ECT requires an ability to estimate seizure threshold.

Previous work on estimating the seizure threshold of depressed patients suggests a wide range in initial ECT seizure threshold (12-fold), with higher values for bilateral electrode placement, male gender, and increasing age (Beale et al 1994; Sackeim et al 1991; McCall et al 1993; however, these data are derived primarily from highly selected research samples that included at least some patients receiving anticonvulsant medications (eg, benzodiazepines, beta blockers), and are based upon versions of an investigational stimulus dosage titration procedure that typically involved multiple restimulations. The present study was designed to address these issues, and to replicate and extend earlier research observations in a large clinical sample of carefully defined depressed patients consecutively referred for ECT.

Methods

Subjects

The subject sample included 111 inpatients with DSM-III (American Psychiatric Association 1980) major depression

Table 1. Subject Characteristics

	Total (n = 111)	Right Unilateral ECT (n = 86)		Bilateral ECT (n= 25)	
		Women (n = 54)	Men (n = 32)	Women (n = 17)	Men (n = 8)
Age, yr (mean ± SD)	57.5 ±17.7	57.6 ±15.5	58.3 ±17.8	57.0 ±22.7	53.6 ±21.8
Pre-ECT MADRS Score (mean ± SD)	35.1 ±10.2	36.7 ± 8.0	35.4 ± 9.2	27.2 ±13.5[a]	39.8 ±12.3
Previous ECT: No. of patients (%)	42 (37.5%)	25 (45.4%)[b]	7 (21.8%)	5 (29.4%)	5 (62.5%)[b]

ECT = electroconvulsive therapy; MADRS = Montgomery-Asberg Depression Rating Scale.
[a]Significantly less than the other three groups (minimum $t = - 2.20$; df = 23, $p < .04$).
[b]Significantly greater than the other two groups ($G^2 = 5.87$; df = 1; $p = .02$).

(n = 85) or bipolar disorder, depressed (n = 14) or mixed (n = 12), selected from among 239 consecutive patients who received ECT at Duke University Medical Center. Patients were excluded who had received ECT within the past 6 months, who were receiving proconvulsant (theophylline, methylphenidate, amphetamine) or anticonvulsant medication (antiepileptics, benzodiazepines [see below], or long-acting beta blockers), or whose ECT administration varied from that described below. Additional subject characteristics are presented in Table 1. There were no differences between the groups with regard to age or frequency of diagnoses. For the purposes of this study, "severity of depressive illness" was defined by the pre-ECT score on the Montgomery-Asberg Depression Rating Scale (MADRS) (Montgomery and Asberg 1979).

ECT Treatment Technique

All patients were free of psychotropic medications at the time of the first ECT treatment, with the exception of as-needed doses of neuroleptics (thioridazine hydrochloride, n = 5; haloperidol, n = 3; thiothixene hydrochloride, n = 2; loxapine hydrochloride, n = 1; and chloral hydrate n = 7). The ECT treatments were administered three times a week. Typical modifications included anticholinergic premedication (glycopyrrolate, n = 68; or atropine sulfate, n = 3), anesthesia (methohexital sodium, 1 mg/kg intravenously), and muscle relaxation (succinylcholine chloride, 1 mg/kg IV) (Coffey and Weiner 1990). Patients received 100% oxygen via mask throughout the procedure. The standard bifrontotemporal and d'Elia (1970) electrode placements were employed for bilateral ECT (n = 25) and right unilateral ECT (n = 86), respectively. The ECT stimulus was administered by a brief-pulse ECT device (MECTA SRI, MECTA Corp; Lake Oswego, OR).

For the purposes of this study, seizure duration was determined retrospectively from two-channel (bilateral fronto-mastoid) EEG by a single rater (ADK) with established reliabilities (Krystal et al 1993) who was blind to ECT treatment number and stimulus dosage. Eight patients had seizures that laster longer than 200 seconds and that were thus terminated by IV methohexital. For these subjects EEG seizure durations were arbitrarily set at 200 seconds.

Determination of Initial Seizure Threshold.

ECT seizure threshold was estimated with use of a modification of the stimulus dosing titration procedure described by Sackeim et al (1987b). These modifications were based upon empirical trials directed towards the development of a clinically optimum dosing schedule (Table 2) that combined the following desirable features: low starting titration dosage (as low as 32 millicoulombs [mc]), adjustment of starting titration dosage for electrode placement and gender (to minimize both the number of restimulations and the number of subconvulsive stimuli across groups), small (50%) increments between dosing steps, and initial adjustment of pulse train duration (to maximize stimulus efficiency). Although it is understood that the adjustment of starting stimulus dose on the basis of electrode placement and gender lends an intrinsic bias to investigation of these factors, it also avoids the potential confounding effects of subconvulsive stimuli on determinations of seizure threshold (Swartz 1990), as well as the potentially harmful cardiovascular effects associated with such stimuli (Decina et al 1984; Welch and Drop 1989; Wells et al 1988; Zielenski et al 1993).

Seizure threshold was arbitrarily defined as the stimulus dosage that elicited an EEG seizure of at least 25 sec (APA 1990). If the initial stimulus dose at the first treatment failed to elicit such a seizure, stimulus charge was increased by approximately 50% (one level in Table 2), and the patient was restimulated. The seizure threshold so determined is an estimate, since the "true" seizure threshold could be somewhere below the defining dosage level in the titration procedure. In all patients, such a seizure was observed by the fourth stimulation (median number of stimulations = 1.0).

Statistical Analyses

The statistical analyses consisted of log-normal regression and log-normal analysis of variance (ANOVA) for continu-

Table 2. ECT Stimulus Dosage Titration Protocol

	MECTA SRI Settings[a]				
Stimulus dosage level	Pulse width (sec)	Frequency (sec^{-1})	Duration (sec)	Current (amp)	Charge (mc)[b]
1 (Right unilateral ECT, women)	1.0	40	0.5	0.8	32
2 (Right unilateral ECT, men; or bilateral ECT, women)	1.0	40	0.75	0.8	48
3 (Bilateral ECT, men)	1.0	40	1.25	0.8	80
4	1.0	40	2.0	0.8	128
5	1.0	60	2.0	0.8	192
6	1.0	90	2.0	0.8	288
7	1.4	90	2.0	0.8	403
8	2.0	90	2.0	0.8	576

ECT = electroconvulsive therapy; sec = seconds; amp = amperage; mc = millicoulombs.
[a]MECTA SRI is a brief-pulse ECT device (MECTA Corp., Lake Oswego, OR).
[b]Charge was calculated as the product of pulse width × 2 × frequency × train duration × current. The increment between stimulus dosage levels is approximately 50%.

ous variables, and log-linear analysis for categorical variables. The choice of log-normal analyses over normal theory analyses is justified on empirical grounds, since the distributions of seizure threshold and seizure duration were skewed to the right (for charge, skewness = 1.4; for J, skewness = 1.32; for seizure duration skewness = 0.66). Log transformation of these data reduced the skewness (for charge, skewness = 0.35; for J, skewness = 0.47; for seizure duration, skewness = −0.35).

Results

Initial ECT Seizure Threshold

Seizure threshold at the first ECT treatment (in units of charge and in units of energy [joules]) and the associated dynamic impedance, were estimated for the entire sample and as a function of gender and electrode placement (Table 3). The range in initial seizure threshold was approximately 6-fold (32–192 mc and 5–28 J). On average, initial seizure threshold was approximately 45% (± 62%) higher than the starting titration dosage.

A two-way ANOVA (electrode placement × gender) on initial seizure threshold (in units of charge) revealed a significant overall effect (overall F = 21.8; df = 3,107; p < .0001) (Table 3). In this analysis there were significant main effects of both electrode placement and gender. On average, initial seizure threshold was approximately 59% higher with bilateral ECT (86.4 ± 34.9 mc, mean ± SD) than unilateral ECT (53.8 ± 24.0 mc, mean ± SD) (F = 35.89; df = 1,107; p < .0001), and approximately 31% higher in men (72.0 ± 24.3 mc, mean ± SD) than women (55.0 ± 31.3 mc, mean ± SD) (F = 22.59; df = 1, 107; p < .0001). There was also a gender × electrode placement interaction (F = 6.94; df = 1,107; p < .01). Women who received unilateral ECT had lower initial seizure thresholds than women who received bilateral ECT (t = −5.84; dp = 69; p < .0001), men who

received unilateral ECT (t = −5.51; df = 84, p < .0001), and men who received bilateral ECT (t = −5.33; df = 60; p < .0001) (Table 3).

With regard to the number of stimulations required to determine seizure threshold (Table 3), 61 (55%) of the 111 patients seized at the starting titration dosage, indicating that their "true seizure threshold" was actually below that dosage level. A two-way ANOVA (gender × electrode placement) on the number of stimulations at the first ECT treatment revealed a significant overall effect (overall F = 115.35; df = 4,107; p < .0001). The number of stimulations was similar for those receiving unilateral (1.63 ± 0.82, mean ± SD) or bilateral (1.72 ± 0.89, mean ± SD) ECT treatments, as well as for men (1.53 ± 0.72, mean ± SD) and women (1.72 ± 0.88, mean ± SD). There was a significant gender × electrode placement interaction however (F = 4.84; df = 1,107; p < .03). For patients receiving bilateral ECT, men required fewer stimulations than women to elicit a seizure (1.13 ± 0.35 (mean ± SD) vs. 2.0±0.94 (mean ± SD), respectively) (t = 2.54; df = 23; p < .018) (Table 3). These data suggest that the starting titration dosage was likely too high for men receiving bilateral ECT (i.e., floor effects with too few restimulations).

Dynamic impedance at the first ECT treatment varied from 138–343 ohms, a 2.5-fold range (Table 3). A two-way ANOVA (electrode placement × gender) on dynamic impedance revealed a significant overall effect (overall F = 21.75; df = 3,107; p < .0001). In this analysis, there were significant main effects of both electrode placement (F = 14.08; df = 1,107; p < .0003) and gender (F = 48.36; df = 1,107; p < .0001). On average, dynamic impedance at the first ECT was approximately 13% greater with right unilateral ECT (222.9±39.5 ohms; mean ± SD) than with bilateral ECT (197.0±31.3 ohms, mean ± SD), and approximately 22% greater in women (232.3±38.3 ohms, mean ± SD) than in men (190.2±23.2 ohms, mean ± SD). There

Table 3. Seizure Threshold, Dynamic Impedance, and Number of Stimulations at the First ECT Treatment

	Total (n = 111)	Right Unilateral ECT (n = 86)		Bilateral ECT (n= 25)	
		Women (n = 54)	Men (n = 32)	Women (n = 17)	Men (n = 8)
Seizure threshold, charge (mc)[a]					
Estimated	61.11 ± 29.99	45.04 ± 18.92	68.50 ± 24.80	86.59 ± 41.21	86.00 ± 16.97
Starting titration dose	42.52 ± 13.03	32	48	48	80
% Difference	45.00 ± 62.00	40.74 ± 59.14	42.71 ± 51.66	80.39 ± 85.84	7.50 ± 21.21
Seizure threshold, dynamic energy (Joules)[b]	10.30 ± 4.56	8.69 ± 3.82	10.84 ± 4.05	13.47 ± 6.11	12.25 ± 2.96
Dynamic impedence (ohms)[c]	217.10 ± 39.18	240.00 ± 37.28	194.16 ± 23.04	207.65 ± 30.97	174.50 ± 17.53
Stimulations, No.[d]	1.65 ± 0.83	1.62 ± 0.84	1.63 ± 0.75	2.00 ± 0.93	1.13 ± 0.35
Restimulations, No.[e] of Patients (%)	50 (44.6%)	22 (40.0%)	16 (50.0%)	11 (64.7%)	1 (12.5%)

ECT = electroconvulsive therapy; mc = millicoulombs; ± indicates mean ± standard deviation.

[a] Seizure threshold in units of charge differed significantly among the four groups ($F = 21.8$; df = 1,107; $p < .0001$). Seizure threshold was higher with bilateral than unilateral ECT ($F = 35.89$; df = 1,107; $p < .0001$) and higher in men than women ($F = 22.59$; df = 1,107; $p < .0001$). Seizure threshold was lowest among females who received unilateral ECT (minimum $t = -5.84$; df = 69; $p < .0001$).

$$\% \text{ Difference} = \frac{\text{estimated seizure threshold} - \text{starting titration dose} \times 100}{\text{starting titration dose}}$$

[b] Dynamic energy was taken from the readings provided on the chart recorder. Seizure threshold in units of energy also differed significantly among the four groups ($F = 7.92$; df = 1,107; $p < .0001$) and was higher with bilateral than unilateral ECT ($F = 15.42$; df = 1,107; $p < .0002$), and in men than women ($F = 5.28$; df = 1,107; $p < .0002$).

[c] Dynamic impedence was taken from the readings provided on the chart recorder. Dynamic impedance differed significantly among the four groups ($F = 21.75$; df = 1,107; $p < .0001$), and was higher with unilateral than bilateral ECT ($F = 14.08$; df = 1,107; $p < .0003$), and in women than men ($F = 48.36$; df = 1,107; $p < .0001$).

[d] The number of stimulations differed significantly among the four groups ($F = 115.35$; df = 1,107; $p < .0001$). Among patients receiving bilateral ECT, men required fewer stimulations than women ($F = 4.84$; df = 1,107; $p < .03$).

[e] The frequency of restimulation differed significantly among the four groups ($G^2 = 5.46$; df = 1; $p < .02$). Men receiving bilateral ECT were less likely to require restimulation than the other three groups.

was no gender × electrode placement interaction, although, as noted above, only a small number of men received bilateral ECT. For the entire sample, a significant negative correlation was observed between seizure threshold in units of charge and dynamic impedance ($r = -.45$; $p < .0001$). Patients with higher seizure thresholds had relatively lower dynamic impedance.

Effects of Age

A regression analysis of initial seizure threshold on age, electrode placement, and gender, and their respective interactions, revealed that age was correlated with initial seizure threshold in units of charge ($r = .35$; $p < .0001$). Older patients required higher stimulus intensity. The regression analysis also revealed no interactions among age, electrode placement, and gender. There was no relationship between age and dynamic impedance at the first ECT treatment.

Predictors of Initial ECT Seizure Threshold

A stepwise multiple regression was computed to examine the amount of variance in seizure threshold that could be accounted for by the variables with which it was associated (viz, electrode placement, gender, age, and dynamic impedance). Overall models were significant in both the analysis of charge ($F = 35.13$; df = 4,106; $p < .0001$) and the analysis of energy ($F = 20.16$; df = 3,107; $p < .0001$), and in both analyses each predictor was significant. (Dynamic impedance was not included in the analysis of energy, since the

unit of energy (J) is in part a function of impedance). In the analysis of charge, these variables (excluding dynamic impedance) accounted for 50% of the variance in seizure threshold, whereas in the analysis of energy they accounted for only 36% of the variance. This difference in predictive value between the two units of seizure threshold pertained primarily to the effects of gender (14% of the variance for charge vs. 5% for energy) and electrode placement (21% of the variance for charge vs. 13% for energy). In the analysis of charge, the addition of dynamic impedance as a predictor increased the cumulative variance by only 2%.

We found no correlation between initial ECT seizure threshold (either in units of charge or energy) and severity of depressive illness (i.e., the pre-ECT score on Montgomery-Asberg Depression Rating Scale), unipolar vs. bipolar diagnosis (seizure threshold has been reported to be lower in mania (Small et al 1986; Mukherjee 1989)), a remote history of treatment with ECT (prior treatment with ECT has been reported to be associated with missed or brief ECT seizures in men (Tomasson et al 1992)), dosage of methohexital anesthesia, benzodiazepine use within 5 days of the first ECT treatment, or the pre-ECT drug-free interval for benzodiazepines. An absence of effects also held when the analyses controlled for the contributions of age, gender, and electrode placement to seizure threshold values. Although no relation was observed in zero-order correlational analyses between initial seizure threshold and neuroleptic use at the time of the first ECT treatment, this relation became significant after adjustment for the effects of age, gender,

and electrode placement ($r = -.30$). Patients receiving neuroleptics at the time of the first ECT treatment (n = 11) had lower initial seizure thresholds (48.0 ± 21.4 mc, mean ± SD) than those not receiving the medications (62.6 ± 30.5 mc, mean ± SD) ($t = -2.28$; df = 106; $p < .02$). Usage of neuroleptics accounted for only a small proportion (9%) of the variance in initial seizure threshold, however.

Relations with Seizure Duration

EEG seizure duration was negatively associated with both initial ECT seizure threshold (in units of charge) ($r = -.25$; $p = 0.007$) and age ($r = -.34$; $p = .0003$). Higher initial seizure threshold and greater age were both associated with shorter EEG seizures at the first ECT treatment. There were no zero-order associations between EEG seizure duration and gender, electrode placement, or dynamic impedance, and no relations were observed with severity of depressive illness, unipolar vs. bipolar diagnosis, a remote history of treatment with ECT, neuroleptic use at the time of the first ECT treatment, benzodiazepine use within 5 days of the first ECT, the pre-ECT drug-free interval for benzodiazepines, or the dosage of methohexital anesthesia. When the effects of age were partialed out however, methohexital dosage was found to correlate inversely with EEG seizure duration ($r = .22$; $p = .02$). Partialing out the effects of age also reduced the correlation between initial seizure threshold and EEG seizure duration ($r = .18$; $p = .07$).

A stepwise regression analysis was computed to examine the amount of variance in EEG seizure duration that could be accounted for by the variables with which it was correlated (viz, age, initial seizure threshold [in units of charge], and dosage of methohexital anesthesia). Significance was achieved in the overall model ($F = 9.10$; df = 2,108; $p < .0002$; $R^2 = .14$), and the significant predictors were age ($t = -4.24$; df = 2,108; $p = .0001$) and dosage of methohexital anesthesia ($t = -1.99$; df = 2,108; $p = .05$); however, these variables accounted for only a small proportion (14%) of the variance in EEG seizure duration. Initial seizure threshold was not a significant predictor of EEG seizure duration.

Discussion

Initial ECT Seizure Threshold

In this investigation of a clinical sample of 111 depressed patients who received brief-pulse, constant-current ECT, we found that the stimulus intensity required to produce a generalized seizure at the first ECT treatment ("initial seizure threshold") was approximately 60 mc (10 J) on average; however, approximately 55% of our sample seized at the starting titration dosage, indicating that their true seizure threshold values were actually somewhere below that dose level. Such floor effects may have led to an overestimation

of initial seizure threshold, particularly for men who received bilateral ECT (88% seized at the starting titration dosage, although there were only eight subjects in this group). This relatively high percentage of subjects seizing at the starting titration dose was unexpected; it was likely due to the heightened efficiency of the stimulus parameter set utilized, as well as the adjustment of initial stimulus dose for electrode placement and gender. While it is clear that these floor effects confounded both the estimate of initial seizure threshold and the investigation of electrode placement and gender effects, our dosing paradigm had other distinct methodologic advantages. These advantages included the clinically desirable minimization of restimulation and an equalization of subconvulsive stimuli across electrode placement and gender conditions. This design variation thus permitted a comparison of such "equalized" data with those produced by studies using the same initial dose for all patients (e.g., Beale et al 1994; McCall et al 1993; Sackeim et al 1991). The fact that our findings were strikingly similar to the observations of these other investigators suggests that determination of initial seizure threshold is not impacted significantly by number of restimulations or exposure to subconvulsive stimuli—an observation that is, in itself, of considerable conceptual and clinical importance.

Prediction of Initial ECT Seizure Threshold

We found that initial seizure threshold could be predicted by certain treatment and patient variables. Taken together, the three variables electrode placement, gender, and age accounted for 50% of the variance in initial seizure threshold in units of charge, but only 36% of the variance in seizure threshold in units of energy (joules). Remarkably similar figures were reported by Sackeim et al (1987c), who observed that these same three variables accounted for 48% of the variance in average seizure threshold across a treatment course in units of charge, and 27% of the variance in units of energy. Our close replication of Sackeim et al's (1987c) original observations, in a clinical sample of depressed patients and with the use of different titration schema, provides strong support for the relations between ECT seizure threshold and stimulus electrode placement, gender, and age.

Among the predictors of initial seizure threshold, stimulus electrode placement accounted for the greatest proportion of the variance (21% in units of charge), followed by gender (14%), age (15%), and dynamic impedance (2%). Similar relations were observed by Sackeim et al (1987b) for average seizure threshold across a treatment course (i.e., 23% of the variance in units of charge for stimulus electrode placement, 16% for gender, and 8% for age).

With regard to stimulus electrode placement, initial seizure threshold in our study was 59% higher on average with bilateral ECT (approximately 86 mc) than right unilateral

ECT (approximately 54 mc). Of course, this modality effect could represent a systematic bias, since our patients were not randomized to bilateral vs. unilateral electrode placement and because our titration schedule utilized a higher starting titration dose for bilateral than right unilateral ECT. Still, our findings agree closely with previous within-patient (bilateral approximately 57% higher) (McCall et al 1993) and between patient (bilateral approximately 70–90% higher) (Sackeim et al 1991) random assignment investigations that used the same starting titration dosages for all patients. Earlier, and less rigorously quantitative, studies also observed higher seizure thresholds with bilateral ECT (Friedman and Wilcox 1942; Goldman 1949; Liberson and Wilcox 1945; Weiner 1980). It should be noted that this modality difference in initial seizure threshold pertains strictly to constant-current, brief-pulse ECT, since other studies using different stimulus configurations (e.g., constant voltage, sine waveforms) have observed either no difference between electrode placements (Cannicott 1963; D'Elia 1970; Impastato and Karliner 1966; McAndrew et al 1967; Weiner 1980) or lower seizure threshold with bilateral electrode placement (Abrams et al 1972; Gottlieb and Wilson 1965; Zamora and Kaelbling 1965).

Gender accounted for 14% of the variance in initial seizure threshold in units of charge; this was in close agreement with the observations of Sackeim et al (1987b) (16% of the variance), despite our adjustment of starting titration dosage for gender. Initial seizure threshold (in units of charge) was approximately 31% higher in men than women, and women who received unilateral ECT had the lowest seizure threshold of any group. Similar relations have been described by others, but the reported differences have been somewhat greater (approximately 40–70% higher in men than women) (McCall et al 1993; Sackeim et al 1993). Again, floor effects associated with starting titration dosages that were above threshold may have led to an overestimation of initial seizure threshold in the women who received unilateral ECT in our study, thereby lessening the extent of gender differences.

Age was a third variable that predicted initial seizure threshold (accounting for 15% of the variance), with older patients evidencing higher thresholds than younger patients ($r = .35$). Several studies have reported a correlation between age and ECT seizure threshold (Bailey 1943; Beale et al 1994; Liberson 1948; Sackeim et al 1991; Shankel et al 1960; Swartz 1993; Watterson 1945; Weiner 1980). Sackeim et al (1987b) also observed that age was a significant predictor (accounting for 8% of the variance) of average seizure threshold over a treatment course. In our study, age was not a strong predictor of initial seizure threshold (accounting for only 15% of the variance in charge), with less impact than gender or electrode placement. These comparisons suggest that the clinician should not base decisions

about ECT stimulus dosage solely on age (Abrams and Swartz 1989).

Other Potential Clinical Correlates of Initial ECT Seizure Threshold

Several other clinical variables were found to be unrelated to initial ECT seizure threshold in our study. There was no association between initial seizure threshold and either severity of depressive illness or a diagnosis of unipolar versus bipolar depression (in agreement with Sackeim et al [1991]), a remote history of treatment with ECT (in agreement with Krueger et al [1993]), dosage of methohexital anesthesia (in agreement with Sackeim et al [1991]), and either recent use of benzodiazepines or the length of the pre-ECT benzodiazepine-free interval (similar negative findings were reported by Krueger et al 1993). These negative findings must be interpreted cautiously, however, given potential error in our seizure threshold measurements associated with floor effects.

Use of neuroleptic medications at the first ECT was associated with a lower initial seizure threshold, after adjusting for the effects of age, gender, and electrode placement. Animal studies also suggest that neuroleptic medications may affect electroconvulsive seizure threshold (Diamond et al 1987; Hashem and Frey, 1988).

Initial Seizure Threshold and Seizure Duration

We found an inverse relationship between initial seizure threshold and EEG seizure duration: higher seizure threshold (i.e., higher stimulus intensity) was associated with a shorter ECT seizure. Others have observed a similar inverse relation between EEG seizure duration and seizure threshold (Krueger et al 1993; Sackeim et al 1987c). Taken together, these data are consistent with the view that EEG seizure duration in ECT is not proportional to *absolute* stimulus intensity. Furthermore, the negative relation between seizure threshold and seizure duration suggests that seizure threshold may provide a window into functional neural activity, specifically, those neural processes that mediate seizure length.

We also observed a negative relation between methohexital anesthesia dosage and initial EEG seizure duration, even though there was no relationship of the former with initial seizure threshold. This dissociation between the effects of methohexital on seizure duration and seizure threshold was also reported by Sackeim et al (1991). While we found no relationship between initial seizure duration and either recent use of benzodiazepines or the length of the pre-ECT benzodiazepine-free interval, benzodiazepine use during ECT has been associated with short seizures and possibly reduced efficacy (American Psychiatric Association 1990; Krueger et al 1993; Nettlebladt 1988; Pettinati et al 1990;

Standish-Barry et al 1985; Stromgren et al 1985). Since our patients were not receiving benzodiazepines during ECT, we could not determine the effects of such usage upon EEG seizure duration.

It has been suggested that seizure duration may serve as one marker for ECT seizure adequacy—the cutoff value usually given is 25–30 seconds (American Psychiatric Association 1990). In our study, the EEG seizure durations at the threshold stimulus dosage (102.8 ± 45.8 sec mean ± SD) clearly met that standard; however, given that Sackeim et al (1987a, 1993) have found that ECT given at barely suprathreshold stimulus intensities is a remarkably weak antidepressant therapy, such data indicate that the clinician cannot rely solely upon seizure duration as a measure of ECT treatment adequacy.

In *summary*, we found that initial ECT seizure threshold in a clinical sample of adult patients with depression could be reliably predicted by four variables—electrode placement, gender, age, and dynamic impedance (although the letter contributed only marginally to the overall variance). These data may provide the basis for an efficient stimulus dosage titration strategy whereby initial ECT seizure threshold may be estimated clinically with relatively few subconvulsive stimulations by adjusting the starting titration dosage for electrode placement, gender, and age. More research is needed to identify variables that account for the still unexplained variance in initial ECT seizure threshold, as well as the neurobiologic mechanisms that mediate seizure threshold in ECT.

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