

EEG Manifestations during ECT: Effects of Electrode Placement and Stimulus Intensity

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This study examined the ictal electroencephalographic (EEG) characteristics of four forms of electroconvulsive therapy (ECT) known to differ in efficacy. Previously, we demonstrated that titrated, low-dose right unilateral ECT reliably produces generalized seizures of adequate duration, but is remarkably weak in antidepressant effects. Using a new rating scale, we found that specific features of the ictal and immediate postictal EEG varied significantly with ECT stimulus intensity and electrode placement. The low-dose right unilateral condition differed from more effective forms of ECT in having the longest polyspike phase duration, averaging twice that of the other conditions; it was also the condition least likely to manifest bioelectric suppression immediately following seizure termination. In contrast, high-dose bilateral ECT—a treatment with particularly rapid antidepressant effects—resulted in the greatest peak slow-wave amplitude in both hemispheres. Total seizure duration did not differ among the four treatment conditions. These findings indicate that seizure duration is not a useful marker of therapeutic efficacy, and instead provide preliminary evidence that other features of the EEG may be more useful markers of treatment adequacy.

Key Words: Electroconvulsive therapy, electrode placement, electroencephalogram, seizure, stimulus dosing

Introduction

Despite the proven efficacy of electroconvulsive therapy (ECT), we lack a reliable marker of optimally therapeutic treatment (Scott 1989). There had been a long-standing belief that ECT exerts maximal antidepressant effects as long as generalized seizures of adequate duration are produced (Ottosson 1960; d'Elia et al 1983; Rose 1985). How-

ever, recently it has been found that, depending on stimulus intensity and electrode placement, generalized seizures of "adequate" duration may be produced that consistently lack therapeutic effects (Sackeim et al 1987a; Sackeim et al 1993). It had also been postulated that the cumulative duration of seizures provide a guide to the number of ECT treatments needed to achieve therapeutic response (Malletzky 1978). Subsequent research failed to support this hypothesis (for review, see Sackeim et al 1991). Consequently, clinicians remain without a measure that informs treatment administration. Indeed, there is no biological marker that distinguishes effective seizures from less effective seizures or that indicates when sufficient ECT has been administered.

The electroencephalogram (EEG) has been used as a

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Received January 4, 1993; revised April 29, 1993.

research tool since the early days of convulsive therapy. Such work was motivated by interest in demonstrating EEG changes that correlate with either the therapeutic or deleterious effects of the treatment. Most studies have focused on interictal EEG recordings of the resting state during or following the ECT course (for reviews see Small 1974 and Abrams 1992). Some workers have recently suggested that lateralized differences in the interictal EEG correlate with the relative therapeutic efficacy of unilateral and bilateral ECT (Abrams et al 1987; Abrams 1989; Abrams et al 1989). However, findings in this area have been inconsistent (Small et al 1988; Abrams et al 1992).

Some studies of the ictal EEG have also focused on lateralized differences in the seizures produced by right unilateral (RUL), left unilateral, and bilateral (BL) ECT (d'Elia and Perris 1970; Small et al 1970; Kriss et al 1978; Krystal et al 1992). Other work has examined phases of the ictal EEG in an attempt to characterize patterns of seizure initiation and propagation (Staton et al 1981; Brumback and Staton 1982; Gerst et al 1982). In a within-patient study, Robin et al (1985) demonstrated differences in amplitude and duration measures of ictal EEGs among BL ECT conditions that differed in stimulus intensity. They found that higher intensity stimulation was associated with greater integrated amplitude of the ictal EEG and greater postictal bioelectrical suppression. These findings were particularly important since Robin and deTissera (1982) had earlier reported that these ECT conditions also differed in speed of clinical response. However, an important limitation in this work was the confounding of differences in stimulus intensity with differences in electrical waveforms (low-intensity ultrabrief pulse, high-intensity brief pulse, and high-intensity sine wave). At least with respect to interictal effects, it is well established that sine wave stimuli produce greater EEG changes than brief pulse stimuli (Weiner et al 1986). Nonetheless, the Robin et al (1985) work indicated that the ictal EEG may vary as a function of the modality of ECT that a patient receives.

In an earlier study, we found that brief pulse RUL ECT, given at a stimulus intensity that was titrated to be just above seizure threshold, produced seizures of adequate duration by motor and EEG criteria, but were remarkably weak in therapeutic effects (Sackeim et al 1987a). Low dose RUL ECT had a response rate of 28%, whereas with low dose BL ECT, 70% of patients were responders. In a recent second study, we again compared RUL and BL ECT, with stimulation for both electrode placements set at either low dosage (just above seizure threshold) or higher dosage (150% above seizure threshold) (Sackeim et al 1993). This study replicated the finding that low-dose RUL ECT results in generalized seizures of adequate duration that lack therapeutic properties, with a response rate of

17%. The other three treatment conditions were markedly superior in therapeutic effects, when compared to the low-dose RUL condition, with response rates ranging from 43% to 65%.

As we routinely monitored two channels of ictal EEG, this study provided an opportunity to contrast the ictal EEG characteristics associated with treatment conditions that reliably differed in therapeutic properties. We developed a new rating scale for evaluating ictal and immediate postictal EEG characteristics, in part following the descriptions by Weiner and colleagues (Weiner 1982; Weiner et al 1991). Our major aim was to identify a set of EEG features that distinguish effective forms of ECT from low-dose RUL ECT, a treatment condition associated with poor efficacy.

Method

Subjects

Inclusion criteria for the depressed sample have been described elsewhere (Sackeim et al 1993). Inclusion in this EEG substudy also required that the same ECT device with the same EEG instrumentation amplifiers be used for all patients. This resulted in dropping the first 22 patients of the 96 that participated in the parent study. As described below, 11 other patients were excluded.

Table 1 presents descriptive characteristics for the sample of 63 patients. Analyses of variance (ANOVAs) with electrode placement (RUL versus BL) and dosage condition (low versus high dose) as between-subject factors yielded no significant main effects or interactions for the continuous variables. Log-linear analyses indicated that females were overrepresented in the RUL groups and there was a trend toward a greater representation of females in the high-dose conditions as compared with the low-dose conditions. In addition, bipolar depressives were more common in the unilateral and high-dose conditions. However, neither gender nor the bipolar-unipolar distinction showed significant relations with any of the EEG characteristics, and these patient variables were not further considered.

Table 1 also presents scores on the Hamilton Rating Scale for Depression [HRSD, 24-item (Hamilton 1967)] 1 week following the end of the ECT course and rates of clinical response. Response classifications were based on previously described criteria (Sackeim et al 1987a; 1993). In line with the parent study, the low-dose RUL patients included in this substudy had a remarkably poor clinical outcome, with only 13.3% classified as ECT responders. ANOVAs and log-linear analyses indicated that the low-dose RUL group differed significantly from each of the other groups in both postECT HRSD scores and in re-

Table 1. Descriptive Characteristics of the Patient Sample

	Low dose unilateral (n = 15)		High dose unilateral (n = 14)		Low dose bilateral (n = 15)		High dose bilateral (n = 19)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Age in years	60.40	13.56	53.86	14.89	60.87	11.12	55.79	14.76
Sex (% female)	73.3		85.7		40.0		68.4	
PreECT HRSD	34.40	9.40	30.93	7.84	31.60	6.33	34.26	7.75
Polarity (% bipolar)	20.0		57.1		6.7		26.3	
Length of current episode in weeks	40.80	30.64	42.14	38.59	48.53	36.07	46.42	35.93
Number of previous episodes	4.00	3.49	3.29	3.12	2.50	2.68	3.32	3.83
Number of previous psychiatric admissions	1.73	1.71	2.64	2.59	1.80	2.04	2.00	2.31
Age at illness onset in years	41.29	19.89	41.14	19.38	41.80	19.02	42.53	16.84
Previous history of ECT (% yes)	46.7		42.9		46.7		36.8	
One week post-ECT HRSD	24.13	12.10	11.79	9.76	12.20	9.42	12.84	10.78
Percentage of ECT responders	13.3		64.3		66.7		57.9	

sponse rates. High-dose RUL ECT was somewhat more effective in this subsample than in the parent study.

Electroconvulsive Therapy

Methods of ECT administration have been previously described (Sackeim et al 1993). Patients were withdrawn from psychotropic medications, except for lorazepam (up to 3 mg/d) as needed, for a minimum of five days prior to the start of ECT. Mean lorazepam dose during the study for patients in each of the four treatment groups did not differ (Table 2). Lorazepam was withheld at least 8 hr prior to each treatment. Patients did not receive any other medications known to affect seizure threshold or duration. Using an upper limit of 30 days, the average medication washout prior to ECT was 15.68 days (SD = 6.99). Pharmacological modification consisted of atropine [0.4 mg intravenously (IV) 2 min prior to anesthetic], methohexital (0.75 mg/kg IV bolus) and succinylcholine (0.5 mg/kg IV bolus). After the first treatment, methohexital and succinylcholine doses were individually adjusted. Mean anes-

thetic doses are presented in Table 2. ANOVAs with electrode placement and stimulus intensity revealed no significant main effects or interactions.

The d'Elia placement was used for RUL ECT and the standard bifrontotemporal placement was used for BL ECT. A custom-modified MECTA (Lake Oswego, OR) device (SR1) was used to provide a constant current, bidirectional, brief pulse electrical stimulus. The device had extended ranges of pulse frequency (20–140 Hz) and stimulus duration (0.5–4.0 sec). Standardized procedures were used for preparation of the scalp for ECT and EEG electrodes (American Psychiatric Association 1990).

STIMULUS DOSING. To estimate seizure threshold, the empirical titration method was used in all patients at the first and last treatments (Sackeim et al 1987b). At all other treatments, patients in the high dose conditions received a stimulus intensity that was 150% above, or 2.5 times, the minimal charge found necessary to produce an adequate generalized seizure in their first treatment. Through-

Table 2. Treatment Characteristics

	Low dose unilateral (n = 15)		High dose unilateral (n = 14)		Low dose bilateral (n = 15)		High dose bilateral (n = 19)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Lorazepam (mg/d)	1.57	1.09	0.88	0.96	0.95	0.87	1.16	1.16
Methohexital (mg)	54.18	14.73	50.51	12.82	53.78	10.59	55.73	10.05
Succinylcholine (mg)	39.91	12.72	36.54	8.78	42.24	15.51	42.53	16.30
Charge (mQ)	88.88	29.94	160.17	80.67	233.98	208.76	363.16	168.36
Energy (J)	17.20	4.16	29.82	14.18	28.80	23.22	49.17	20.82
Motor duration (sec)	44.97	11.97	47.41	13.02	45.09	9.87	42.47	9.28

out the treatment course, patients in the low-dose conditions received an electrical stimulus intensity that was just above their seizure threshold. Table 2 presents descriptive statistics on electrical stimulus parameters in those ECT sessions in which the ictal EEG was rated. All statistical analyses of stimulus intensity and seizure duration measures were performed on logarithmically transformed values to achieve normal distributions. ANOVAs with electrode placement and stimulus intensity were conducted on the average charge and energy administered at the treatments included in this study. In both analyses, there were significant main effects of electrode placement and of dosage condition (p values < 0.0001), with no significant interaction. The significant effect of electrode placement corresponded to the higher seizure threshold associated with BL ECT (Sackeim et al 1987b).

SEIZURE MONITORING. The "cuff technique" was used to monitor the duration of ictal motor activity (Addersley and Hamilton 1953). Two channels of EEG were recorded using the MECTA amplifiers, with potential differences measured between prefrontal (~2 in above the midpoint of the eyebrow) and ipsilateral earlobe silver/silver chloride electrodes (14 mm diameter). The criterion of an adequate seizure over the first five treatments was a motor seizure of at least 25 sec. In rare instances when there was uncertainty about the motor criterion, 30 sec of EEG seizure manifestations were required. To account for the spontaneous decrease in seizure duration during the ECT course (Sackeim et al 1987c), after five treatments, the motor and EEG cutoffs for adequacy were reduced to 20 sec and 25 sec, respectively. As indicated in Table 2, the four treatment conditions were equivalent in motor seizure duration, as ANOVAs with electrode placement and dosage condition revealed no significant main effects or interactions.

EEG Rating Scale

We developed a rating scale to evaluate both qualitative and quantitative EEG features of generalized, tonic-clonic seizures. As illustrated by Weiner (1982), the onset of the seizure consists of high-frequency rhythmic activity, or "epileptic recruiting rhythm," which is variously present, and is followed by chaotic polyspike activity. Chaotic polyspike activity is almost invariably present, and we refer to this initial phase of the ictal EEG as the "polyspike" phase. This early rapid polyspike activity may last for several seconds before the polyspikes become more regular and slow-wave activity is discernible. This reflects the transition from late polyspike to early slow-wave ictal activity. The slow-wave phase proper is

characterized by high amplitude polyspike and slow-wave activity, and is followed by a termination phase in which the polyspike and slow-wave activity becomes more irregular and diminishes in amplitude. For purposes of brevity, we refer to the period of high-amplitude polyspike and slow-wave activity and its termination collectively as the "slow-wave" phase of the ictal EEG.

Using the right hemisphere channel of the digital recorder output, we assessed the duration of both the polyspike and slow-wave phases of the seizure. The polyspike phase was defined as starting with the offset of stimulation and terminating at the point at which visually discernible slow-wave activity fully replaced early chaotic polyspike activity (see Figure 1). The slow-wave phase was defined as the period from this time point until seizure termination. Maximal amplitudes (μ v) during the polyspike and slow-wave phases were quantitatively assessed, and defined by the largest peak-to-peak deflections in the relevant phases.

A variety of qualitative ratings were scored on 7-point Likert-like scales ranging from 0 to 3, in increments of 0.5. These included global seizure strength, global seizure patterning (stereotypy), two indices of the termination phase (extent of amplitude and frequency reduction), and degree of immediate postictal suppression (suppression of bioelectric activity). Seizures were rated as having greater strength if slow-wave activity of high amplitude predominated during the slow-wave phase. Seizures were rated as more stereotypic if there was a clear progression from low amplitude chaotic polyspike activity to high amplitude slow-wave activity without the reappearance of chaotic polyspike activity or marked variability in amplitude during phases. Ratings for some of these features for prototypic examples of ictal activity are provided in Figure 1. In addition, ratings of total seizure duration and measurement of peak slow-wave amplitude were also made for the left hemisphere channel. Symmetry between left and right channels was rated on a scale from -3.0 to $+3.0$, again with 0.5 increments, with -3.0 representing markedly greater seizure strength in the left hemisphere lead, and $+3.0$ indicating an opposite pattern of asymmetry (see Figure 1).

All ratings were performed by one of us (MSN), at a point in time after all subjects had completed the study. This rater was blind to all patient information, including electrode placement, stimulus dose, treatment session number, and clinical outcome. To be included in this data set, the sensitivity settings (gain) on both of the MECTA EEG amplifiers had to be set at 1.0, thereby avoiding extraneous rating variance due to differences among the sessions in the gain of EEG recordings. Across the sample, 83% of treatment sessions of these patients met this criterion. The first and last sessions of all patients were excluded, as titration procedures were administered resulting

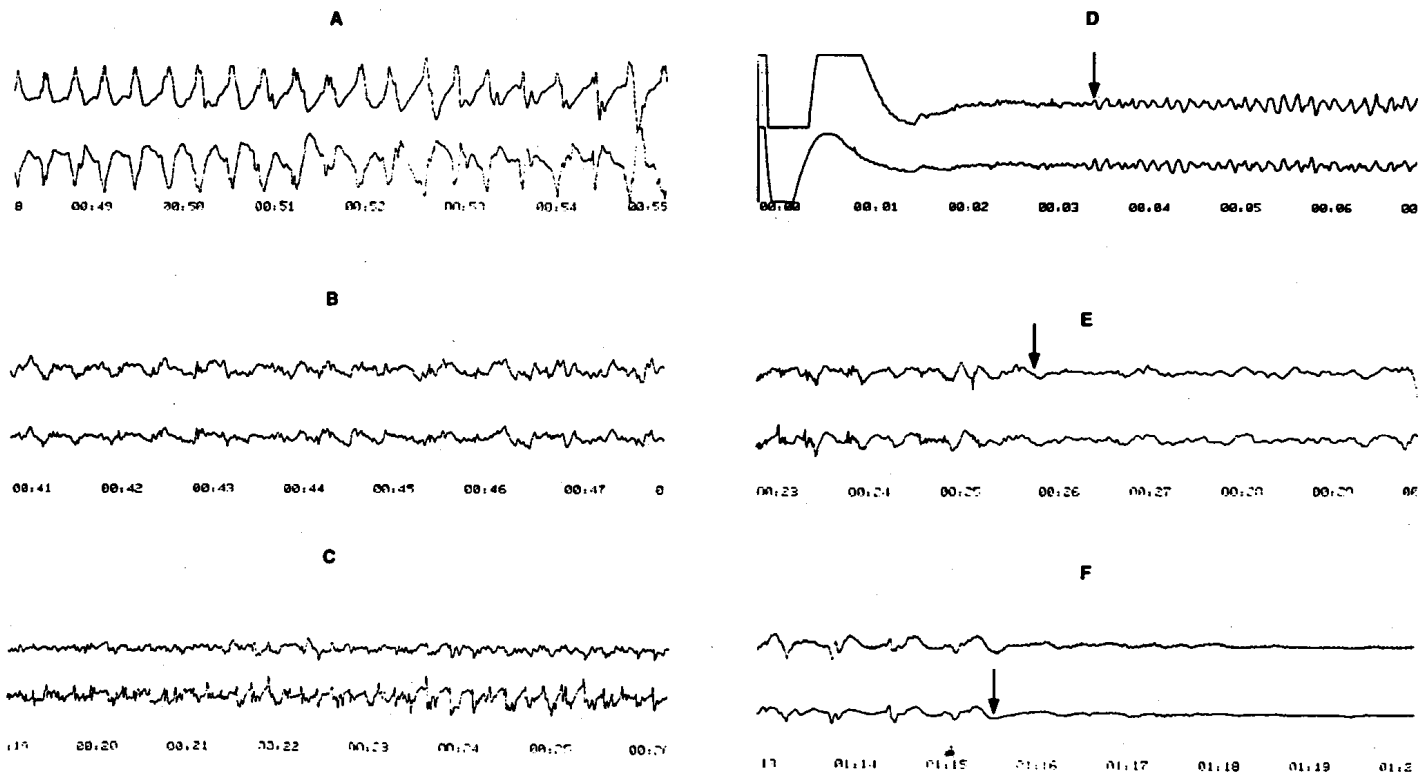


Figure 1. Examples of seizure ratings. (A.) A seizure that was rated as both fairly robust (2.5 out of 3) and stereotypic (score = 2.5). (B.) In contrast, a segment from a seizure that had an overall rating of "definite seizure but not robust" (score = 1) and "seizure patterns there but not distinct" (score = 1). (C.) This seizure had a maximal score of 3 on symmetry, with the right channel (bottom) "markedly more robust" than the left. (D.) Illustrates the transition from polyspike to slow-wave seizure activity. The top channel is marked @ 3.6 sec where slow-wave activity has replaced early chaotic polyspike activity. (E.) An example of little bioelectric suppression immediately following the seizure termination (marked by arrow). This tracing was rated as "terminates in rhythmic activity" (score = 0). (F.) In contrast, a rating of 3 ("definitely suppressed") for postictal suppression (seizure terminus marked by arrow).

in low-dosage stimulation, regardless of treatment group. Sessions beyond the tenth treatment were excluded to minimize the influence of particularly long ECT courses on the ratings. Finally, some sessions were excluded when excessive artifact prevented reliable ratings of duration or peak amplitude, or when the left or right channels were not clearly labeled. Using these criteria, on average each patient was rated at 3.76 treatments (SD = 1.83). ANOVA indicated that the treatment conditions were equivalent in the number of treatments contributing to mean scores, in the average point of the rated sessions during the treatment course, and in the variability of these measures.

A second judge (MS) blindly rated 50 randomly selected EEG records. Intraclass correlation coefficients (ICCs) ranged from 0.75 to 0.94 for measurements of peak slow-wave amplitude in the right and left channels and for judgments of seizure duration (left and right channels), global strength, symmetry, and the extent of immediate postictal bioelectric suppression. Acceptable reliability was also obtained for ratings of time to onset of slow-wave activity and global seizure patterning. Poor reliability was obtained

for the measurement of peak amplitude during the polyspike phase and the judgments of amplitude and frequency reduction at seizure termination. Consequently, these variables were not further considered. The first judge also rerated the duration of the polyspike phase in the right channel and the total seizure duration in both the left and right channels for 25 randomly selected records more than a year after making the original ratings. The ICC for the polyspike phase duration was 0.74 and the ICCs exceeded 0.99 for the measures of total duration.

Results

Scores on the seizure rating scale were averaged across all of the treatment sessions for each of the 63 patients. For the dependent measures listed in Table 3, analyses of covariance (ANCOVAs) were conducted on each measure with electrode placement (RUL versus BL) and dosage condition (low dose versus high dose) as between-subject factors. Age and the average absolute electrical dose (charge) administered served as covariates. To achieve normal dis-

Table 3. Mean Values for Ictal EEG Ratings*

	Low dose unilateral (n = 15)		High dose unilateral (n = 14)		Low dose bilateral (n = 15)		High dose bilateral (n = 19)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
<i>Right Hemisphere</i>								
Duration of polyspike phase (sec)	10.29 ^a	6.17	5.60 ^b	2.01	6.78 ^b	2.42	5.58 ^b	3.54
Duration of slow-wave phase (sec)	40.60 ^a	13.75	52.23 ^b	19.76	44.44 ^b	10.38	45.37 ^b	12.65
Total duration (sec)	50.89	13.89	57.83	19.06	51.22	11.48	50.95	12.32
Peak slow-wave amplitude (μV)	550.83 ^a	166.24	526.07 ^a	158.02	466.77 ^a	127.84	633.73 ^b	171.88
Overall strength	1.28 ^a	0.58	1.50 ^{a,b}	0.69	1.23 ^a	0.41	1.63 ^b	0.60
Overall pattern	1.38 ^a	0.67	1.78 ^b	0.62	1.51 ^{a,b}	0.49	1.78 ^b	0.50
Postictal suppression	1.09 ^a	0.67	1.64 ^b	0.93	1.95 ^b	0.43	1.78 ^b	0.77
<i>Left Hemisphere</i>								
Total duration (sec)	53.67	12.70	58.37	19.27	52.88	13.02	51.09	12.51
Peak slow-wave amplitude (μV)	515.33 ^a	209.92	548.91 ^a	168.96	457.34 ^a	157.11	598.95 ^b	201.99
Overall symmetry	+0.19	0.89	+0.29	0.90	+0.38	0.74	+0.70	1.17

*Groups with differing superscripts (e.g., *a* versus *b*) differed in pair-wise *t*-tests on least-squares adjusted means at trend or significant levels (all *p*'s < 0.1, two-tailed).

tributions, logarithmic transformation was applied to the duration and amplitude measures, prior to submitting them to these analyses. Age was used as a covariate as this factor has been found to be a powerful correlate of ECT seizure characteristics (Shankel et al 1960; Weiner 1980; Sackeim et al 1991). In this sample there was considerable variability in initial seizure threshold, with approximately a 20-fold range. Therefore, patients in the low-dose conditions with high seizure thresholds often received higher absolute electrical doses than patients in the high-dose conditions with low seizure thresholds. By using absolute electrical dose as a covariate, we could test whether absolute electrical dose or dose relative to threshold (low versus high) was a more critical determinant of EEG effects. Table 3 presents descriptive statistics for the four treatment groups on the EEG characteristics.

The ANCOVAs yielded a significant main effect of electrode placement only for postictal suppression (*p* = 0.03). In addition, there were trends toward main effects of electrode placement for duration of the slow-wave phase (*p* = 0.07), and peak amplitude during the slow-wave phase (*p* = 0.08). In line with previous reports (Small et al 1970; Abrams et al 1973; Staton et al 1981; Krystal et al 1992), bilateral ECT was associated with greater postictal suppression than unilateral ECT. However, this effect was conditioned by a marginally significant interaction between electrode placement and dosage condition (*p* = 0.06). Post hoc *t*-tests on least squares adjusted means indicated that the low-dose RUL group resulted in less postictal suppression than each of the remaining three con-

ditions at trend or significant levels (*p*'s ≤ 0.09) (Table 3).

There were several main effects of dosage condition. The seizures produced in the high-dose conditions tended to be rated as globally stronger and more stereotyped in patterning than low-dose seizures (*p*'s = 0.07). High-dose treatments were associated with longer slow-wave phase duration (*p* = 0.03), although despite the absence of a significant interaction, post hoc comparison of the least squares adjusted means suggested that this effect was carried by particularly short slow-wave duration in the low dose RUL group (Table 3). In addition, significant main effects of dosage condition were obtained for the duration of the polyspike phase (*p* = 0.02) and for the peak amplitude during the slow-wave phase in both the left and right channels (*p*'s ≤ 0.03). These effects were also conditioned by interactions between electrode placement and dosage condition. As seen in Table 3, the polyspike phase was considerably longer in the low-dose RUL condition. Each of the remaining three groups had significantly shorter durations and did not differ from each other. In contrast, for both of the measures of peak slow-wave amplitude (left and right channels), the high-dose BL group had significantly higher values than all the remaining conditions, which did not differ from each other. Symmetry of seizure expression did not yield any significant effects.

Age was a significant covariate for measures of total seizure duration (left and right channels) (*p*'s ≤ 0.04), slow-wave phase duration (*p* = 0.04), peak slow-wave amplitude (left and right channels) (*p*'s ≤ 0.01), overall

strength ($p = 0.001$), and overall patterning ($p = 0.0002$). Older patients had significantly shorter total seizure durations, shorter slow-wave phase duration, lower peak slow-wave amplitudes, and globally weaker and less stereotyped seizures. Absolute electrical dose was related to total seizure (p 's ≤ 0.03) and slow-wave phase duration ($p = 0.01$) and to peak slow-wave amplitude (in both left and right channels) (p 's ≤ 0.03). It is important to note that higher absolute dose, due to higher initial seizure threshold, was associated with shorter total seizure duration, shorter slow-wave phase duration, and lower peak slow-wave amplitude. The effects of absolute electrical dose were independent of the age-related effects.

These analyses indicated that several parameters distinguished the ECT treatment conditions. Such parameters may have potential as markers of the therapeutic potency of treatments. To examine this issue more directly, relations between the EEG measures and clinical outcome should be determined. ANCOVAs were conducted using response categorization (responder versus nonresponder) as a between-subject term and age as a covariate. ECT responders ($M = 1.84$, $SD = 0.59$) had significantly higher ratings for postictal suppression than nonresponders ($M = 1.41$, $SD = 0.88$) ($p = 0.03$). No other differences were significant. To determine whether this association was a by-product of the cutoffs used to classify response status, correlations were computed between the percentage change in HRSD scores and the ictal measures. Patients who manifested greater symptomatic improvement also manifested significantly greater postictal suppression ($p < 0.05$).

Discussion

The major findings of this study indicated that specific qualitative and quantitative features of the ictal EEG vary with the stimulus intensity and the electrode placement used in ECT. This study examined four forms of ECT, one of which was low-dose RUL, a type of treatment now known to lack antidepressant effects (Sackeim et al 1987a, 1993). Traditionally, the measure of the adequacy of ECT treatment has been the duration of the seizure (Fink 1979). However, replicating previous findings (Sackeim et al 1987a), we found that motor and EEG measures of seizure duration were equivalent across the four treatment conditions. Rather, the treatments differed in other ictal EEG characteristics. Consequently, these findings contribute to the growing evidence that the traditional measure of treatment adequacy—motor or EEG seizure duration—has little relation to the effectiveness of treatments, at least when minimum seizure durations are required at each treatment (Weiner et al 1986; Sackeim et al 1991). Further, the findings suggest that other features of the ictal and im-

mediate postictal EEG have greater potential in developing a valid marker of effective treatment.

The low-dose RUL condition was characterized by exceptional patterns. The duration of the polyspike phase of the seizure was longest with this treatment, averaging twice that of the other conditions. This finding indicated that the onset of predominately slow-wave phase activity was delayed with low-dose RUL compared to the other conditions. In addition, the low-dose RUL condition was associated with the shortest duration of slow-wave activity and was the condition least likely to manifest suppression of bioelectrical activity following seizure termination. High-dose BL ECT was the treatment condition in the parent protocol associated with a particularly marked and rapid clinical response (Sackeim et al 1993). Peak slow-wave amplitude within the right hemisphere was greatest in the high dose BL condition; there was a similar trend within the left hemisphere.

In general these findings are consistent with previous reports of higher integrated EEG voltage (d'Elia and Perris 1970) and more profound postictal suppression with BL relative to unilateral ECT (Small et al 1970; Abrams et al 1973; Staton et al 1981; Krystal et al 1992). Similarly, Robin et al (1985) observed lower peak amplitudes and a less marked postictal isoelectric period in association with low stimulus intensity. However, it is problematic to generalize results across studies that employ different waveforms (i.e., sine wave versus brief pulse) or different electrode placements (widely versus closely spaced) for unilateral ECT.

No previous study of ictal and immediate postictal EEG characteristics employed titration of stimulus intensity to seizure threshold, and thus none could determine the degree to which the electrical dose administered exceeded patients' individual seizure thresholds. Overall, in our study, the high intensity conditions resulted in stronger and more stereotyped seizures, with slow-wave phases of longer duration and greater peak amplitude. After accounting for treatment condition assignment (low or high dose relative to threshold), the remaining variability in absolute electrical dose was mainly due to individual differences in seizure threshold. Patients with higher thresholds required a more intense stimulus to elicit seizures. These patients had shorter slow-wave and total seizure duration and smaller peak slow-wave amplitude. Therefore, the intensifying effects of higher levels of electrical stimulation on ictal EEG manifestations appear to be due to whether or not the electrical dosage substantially exceeds seizure threshold and not to the absolute dose administered. In essence, increasing the electrical dose above the threshold resulted in stronger and more stereotyped seizures. In contrast, patients who had a high seizure threshold had seizures of shorter duration and lesser amplitude. This study joins a

growing body of evidence suggesting that a number of the therapeutic, adverse cognitive, and neurophysiological effects of ECT are related more to electrical dose relative to threshold than the absolute dose used (Sackeim et al 1993; Nobler and Sackeim 1993). This pattern is in line with basic research indicating that the seizure threshold may be a filter for many of the effects of electrical stimulation on neural tissue (Zornetzer 1974).

We found that patients who responded to ECT were more likely to manifest postictal bioelectric suppression than nonresponders. Furthermore, the weakly therapeutic low-dose RUL condition was characterized by less postictal suppression than each of the other three ECT conditions. This finding is in line with the classic study by Ottosson (1960), contrasting suprathreshold BL ECT with and without pretreatment with intravenous lidocaine. Lidocaine pretreatment resulted in inferior efficacy and also interfered with the expression of the seizures, decreasing seizure duration by nearly two-thirds. Indeed, these findings had provided the grounds for the suggestion that seizure duration may serve as a marker of efficacy. However, given less attention was the observation that lidocaine-modified seizures were also less likely to result in postictal bioelectric suppression. Postictal suppression, then, appears to be a particularly promising measure with respect to clinical outcome with ECT.

In our study, patients received psychoactive compounds known to affect the EEG. Barbiturates such as methohexital can have profound EEG effects, both being proconvulsant at lower doses (e.g., Wyler et al 1987), and aborting seizures at higher doses (Engel 1989). Indeed, we have previously found that even in the relatively low-dose range we employed (0.75 mg/kg) higher absolute methohexital dose was associated with shorter seizure duration, although it had no effect on seizure threshold (Krueger et al 1993). However, as per our ECT protocol, methohexital dose in each patient was adjusted for body weight in a standardized fashion, and, in fact, did not differ among the treatment conditions. Some patients also received lorazepam during the ECT course. We have previously shown that lorazepam dose is not related to seizure threshold, but, like methohexital, higher doses are related to decreased seizure duration (Krueger et al 1993). Patients within each of the four treatment conditions did not differ significantly in daily lorazepam dose. The relatively low dosage of succinylcholine (0.5 mg/kg) may have diminished the magnitude of differences among the treatment conditions. High frequency electromyographic and movement artifacts

would tend to obscure differences in EEG effects. Despite these limitations, reliable differences among the treatment groups emerged.

Generalized seizures are composite phenomena that reflect the opposing contributions of excitatory and inhibitory neural processes. For example, the spike and wave complex characteristically observed during the slow-wave phase is typically thought to reflect a widespread excitatory discharge as manifested in the spike, followed by spreading inhibition, as seen in the slow negative wave (Engel 1989). As a general rule, the amplitude of the slow wave is felt to reflect the spatial extent of the neuronal populations subject to inhibition.

Speculatively, the findings of this study suggest that the low-dose RUL condition resulted in a relatively weak inhibitory process to terminate the seizure. The onset of predominantly slow-wave activity (reflecting bouts of excitation and inhibition) was delayed in this treatment group. The duration of the slow-wave phase was shorter relative to the other treatment conditions and low-dose RUL also manifested the weakest postictal bioelectrical suppression. Of note, previous data from this research program has indicated that the low-dose RUL condition is weak in anticonvulsant properties, resulting, for instance, in the smallest elevations of seizure threshold over the course of ECT (Sackeim et al 1987c; 1993). The findings of this study suggest that specific ictal and immediate postictal EEG features may index the magnitude of inhibitory processes that result in seizure termination and may be related to the anticonvulsant properties of ECT (Post et al 1986). It has been suggested that the anticonvulsant properties of ECT provide the basis for its antidepressant effects (Sackeim et al 1983).

It is also noteworthy that we failed to observe lateralized asymmetry in the ictal EEG patterns, despite contrasting unilateral and bilateral ECT. This may be related to using global visual judgments that were insensitive to small but consistent patterns of asymmetry, to the use of only two channels of EEG recording, or to confounding effects of movement artifact. For this and related reasons it will be valuable to validate the findings obtained here with fully quantitative, multichannel recordings of ictal EEG. This would provide an opportunity to examine the topography of the ictal and immediate postictal effects, using a more automated and objective approach to measurement.

This work was supported in part by grants MH35636 and MH47739 from the National Institute of Mental Health

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