File; ECT; memory

ECT and Memory: Brief Pulse Versus Sine Wave

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The authors evaluated the effects on memory of ECT given with either unilateral or bilateral electrode placement and with brief-pulse or sine-wave stimulus waveform. Clinical criteria determined the mode of ECT and the treatment parameters. As expected, right unilateral ECT produced less memory impairment than bilateral ECT. Brief-pulse ECT resulted in less memory impairment than sine-wave ECT during the first hour after treatment but had similar effects on memory after the first hour. Brief-pulse ECT might produce less memory impairment than conventional sine-wave ECT; however, this can probably be achieved in clinical practice only if treatment parameters that keep stimulation close to the seizure threshold are developed individually for each patient.
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Electroconvulsive therapy (ECT) is an effective treatment for severe depressive illness. Because of the memory dysfunction associated with ECT (1–4), there has been interest in developing alternative modes of convulsive treatment that would result in less memory impairment without compromising therapeutic efficacy. For example, memory is known to be less affected by unilateral nondominant electrode placement than by conventional bilateral electrode placement (5). Therapeutic efficacy has been found to be roughly equivalent, at least when unilateral ECT is administered with a relatively large interelectrode distance (6).

Variations in the stimulus waveform used to administer ECT have also been explored. Stimulation with brief pulses can elicit a generalized seizure with about one-third the electrical energy required for conven-tional sine-wave stimulation and with an apparently equivalent therapeutic result (6). The effect of brief-pulse stimulation on memory has not yet been thoroughly evaluated. Several early studies claimed less confusion and amnesia for low-energy, brief-pulse stimuli, but these studies had methodological problems that made their interpretation difficult (6, 7). The first study to demonstrate an unequivocal advantage of brief-pulse ECT over sine-wave ECT (8) showed that 1 day after the fifth treatment patients receiving brief-pulse stimulation were better able to remember events that had occurred 30 minutes before the treatment. Subsequently, it was shown that brief-pulse stimulation was associated with less anterograde and retrograde amnesia measured 2 to 3 days after the completion of treatment (9). Finally, brief-pulse stimulation has been associated with a more rapid recovery of orientation after ECT than sine-wave stimulation (10–12).

All of the recent information on brief-pulse versus sine-wave ECT comes from a single research setting, where stimulus intensity and electrode placement were determined by uniform criteria. For example, the stimulus intensity associated with each waveform is titrated to be equivalent with respect to seizure threshold and to produce seizures of 25–60 seconds. There have been no comparisons of sine-wave and brief-pulse ECT in purely clinical settings, where treatment parameters are determined exclusively by clinical criteria. The present study assessed memory functions in two different experiments during a period of time ranging from 45 minutes to about 9 hours following a seizure.

EXPERIMENT 1

Method

Subjects. The 43 subjects in the first experiment were 37 psychiatric inpatients who had been prescribed a course of ECT for depression at one of six local hospitals and six depressed inpatients at three of these same hospitals who had not been prescribed ECT (table 1). Patients with neurological disorders, patients with depression secondary to alcoholism or drug abuse, patients who had received ECT during the previous 3 months, and patients over 70 years of age were excluded from the study. Most of the patients (N=26) had not received ECT before this study; 17

TABLE 1. Characteristics of Depressed Patients in Two Comparisons of ECT Modes

Mode of ECT	N	Age (years) Mean	Age Range	Sex M	Sex F	Education (years) Mean	Education Range	Number of Patients Previously Given ECT	ECT Number on Day of Test Mean	ECT Number Range	Electrical Energy (J)[a] Mean	Electrical Energy Range
Experiment 1												
Bilateral sine wave	12	43.2	22–67	4	8	13.4	11–16	5	4.2	3–7	93.3	53.5–131.4
Bilateral brief pulse	13	43.3	21–68	4	9	14.5	12–18	6	4.4	2–7	50.7	6.8–59.1
Right unilateral sine wave	6	51.7	29–68	4	2	14.2	11–16	1	4.5	4–5	53.6	26.7–89.1
Right unilateral brief pulse	6	41.5	29–61	4	2	13.3	12–16	4	4.2	4–5	59.1	—
No ECT control group	6	46.0	27–66	3	3	14.3	12–17	1				
Experiment 2												
Bilateral sine wave	18	44.8	27–66	6	12	12.7	9–17	2	5.0	—	78.5	46.1–116.4
Bilateral brief pulse[b]	7	49.1	30–63	3	4	14.1	12–18	4	5.0	—	53.1	16.9–59.1

[a] Based on an assumed impedance of 220 Ω 9, 13. Data available for only 13 of the 18 patients in experiment 2 given bilateral sine-wave ECT.

[b] Six of these patients had participated in experiment 1.

had received ECT 3 months to 22 years previously (mean=5.7 years). Three of the patients receiving bilateral sine-wave ECT had been given right unilateral ECT immediately before the bilateral ECT (mean number of unilateral treatments=3.7, range=3–4). Similarly, six of the patients receiving bilateral brief-pulse ECT had received right unilateral treatments immediately before receiving bilateral ECT (mean number of unilateral treatments=3.0, range=1–5).

The choice of bilateral or unilateral ECT depended on the preference of the treating psychiatrists and, therefore, was not random. The choice of sine-wave or brief-pulse ECT was determined by the kind of ECT device that was in place at each participating hospital. Two hospitals were using a brief-pulse ECT device at the beginning of the study period in 1982. Two other hospitals began to use a brief-pulse device for administration of ECT in 1984, during the study period, and data collection continued in these same hospitals after the brief-pulse devices were introduced. Ten patients receiving right unilateral ECT reported being strongly right-handed; two were left-handed.

ECT. ECT was administered three times a week on alternate days following medication with methohexital sodium, succinylcholine, and usually an anticholinergic agent, atropine or glycopyrrolate. Patients receiving bilateral sine-wave or brief-pulse ECT had the same bitemporal electrode placement. For patients receiving unilateral brief-pulse ECT, one electrode was placed behind the right ear and the other electrode was placed either in the middle of the forehead (N=3) or on the forehead above the right eye (N=3). For patients receiving unilateral sine-wave ECT, the electrodes were placed on the right side of the head, as described by d'Elia (14) (N=4) or McAndrew et al. (15) (N=2). Electrodes were 1¼ inches in diameter for the patients who received unilateral sine-wave ECT and 2 inches in diameter for patients in the other groups.

Sine-wave treatment (both bilateral and unilateral)

was given with a Medcraft B-24 device (130–170 volts for 0.3–1.0 second). Brief-pulse stimulation (both bilateral and unilateral) was given with a MECTA ECT device (pulse width=0.5–1.5 msec; stimulus duration=1.25–2.0 seconds; frequency=40–70 Hz). For 16 of the 19 patients treated with the MECTA device, treatment was delivered with the maximum value shown here for each of the three stimulus parameters.

In previous studies by Weiner et al. (9, 13, 16), the impedance across the electrodes was measured directly during the electrical stimulus and found to average 220 Ω over a large series of patients. Assuming an impedance of 220 Ω for the patients in our study, we estimated the amount of electrical energy delivered for each group (table 1). For brief-pulse ECT, joules (J)=.64 × impedance (Ω) × duration (seconds) × 2 × frequency (Hz) × pulse width (seconds). For sine-wave ECT, J=(voltage^2/impedance) × duration. (Because estimates were based on a fixed impedance, using coulombs instead of joules as an estimate of ECT dosage does not affect the conclusions of this study.) The assumed impedance of 220 Ω is derived from studies in which ECT was given with electrodes 2 inches in diameter. For the unilateral sine-wave group, which received ECT with 1¼-inch-diameter electrodes, the impedance should have been somewhat higher than 220 Ω, and the electrical energy delivered would therefore have been somewhat lower than the value in table 1.

Materials. We selected 100 target words four or nine letters long from Webster's Pocket Dictionary (average frequency of occurrence per million=40 [17]) and printed them individually on index cards. The 100 target words were randomly assigned to 10 different learning lists of 10 words each. Another 220 words were selected with the same characteristics as the target words. Of these 220 words, 200 were used as distractor words on recognition memory tests and the other 20 formed a pool of fillers (three at the beginning

and two at the end of learning lists) to prevent primacy and recency effects. To construct the recognition memory test, two distractor words were randomly assigned to each of the 100 target words. Groups of three words were then printed on index cards. The position of the target word on the card was random.

Procedure. Testing was scheduled on a single day during the course of ECT, after the fourth or fifth treatment on average (table 1). Three memory tests were scheduled beginning 45 minutes, 65 minutes, and 85 minutes after ECT. At each test time one learning list of 10 words was presented, and retention was always assessed 15 minutes later. To begin testing, patients were first instructed in a study task that they would use during presentation of the learning lists. The use of study tasks in investigations of human memory is intended to reduce variability by bringing under experimental control the cognitive operations that subjects use during learning. Once the study task was understood, words were presented one at a time on index cards and subjects were asked to say the word aloud and to rate (from 1 to 5) how much they liked or disliked the word (1=dislike extremely; 5=like extremely).

The first study list was presented once at 45 minutes after ECT. Fifteen minutes later, recognition was tested by showing patients groups of three words on index cards and asking them to choose the word that had been presented previously. After the first recognition test was completed, a second learning list was presented at the scheduled time 65 minutes after ECT, and it was followed 15 minutes later by another test of recognition memory. Finally, a third learning list was presented, at 85 minutes after ECT, and retention was tested after 15 minutes. Twenty-five of the 37 patients given ECT were also tested on a fourth occasion 6.5 to 11 hours after ECT (mean=8.9 hours). A learning list was presented at that time, and retention was tested 15 minutes later. The 10-word lists were used equally often at each of the four test times. Ten word lists were used instead of four, because some of the patients participated in other experimental conditions on different days (18).

Results

Figure 1 shows memory performance at three times after treatment for the four groups of patients given ECT and for the control group not given ECT. The data for the four ECT groups were first submitted to an analysis of variance involving three factors: electrode placement (bilateral versus unilateral), stimulus waveform (sine wave versus brief pulse), and test session (45 minutes, 65 minutes, and 85 minutes after ECT). All statistical tests were two-tailed. There was a significant effect of electrode placement ($F=25.0$, $df=1,33$, $p<.01$), indicating that patients receiving unilateral ECT performed better overall than patients receiving bilateral ECT. This effect of electrode placement was not affected by excluding the nine bilateral

FIGURE 1. Recognition Memory Three Times After ECT of Depressed Patients Given ECT and a Control Group of Depressed Patients Not Given ECT[a]
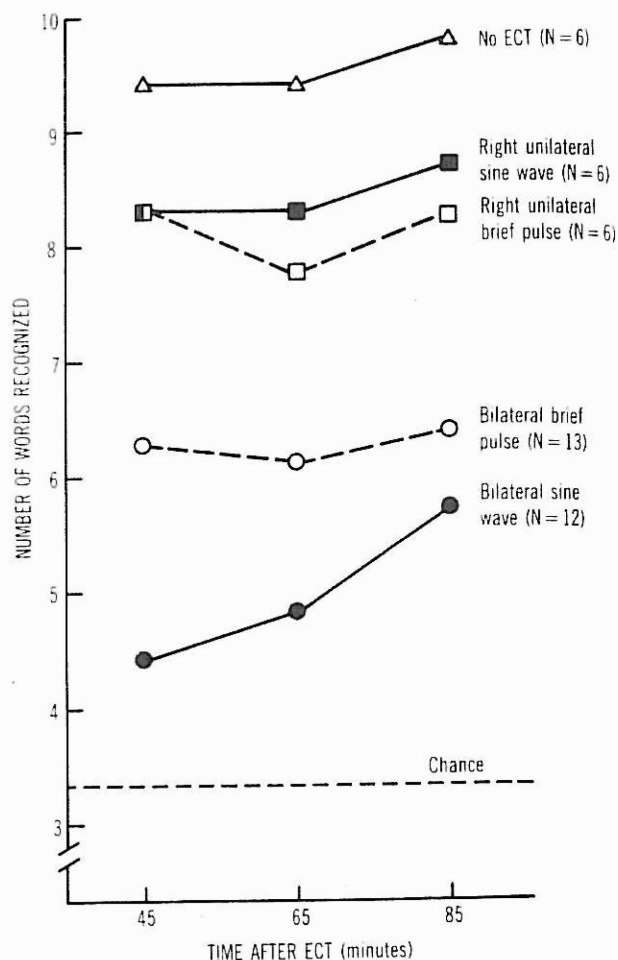
[a]Testing occurred, on average, after 4.3 ECTs; the six patients who did not receive ECT were tested at the same intervals as those who did. For each test, 10 words were presented and a three-choice recognition memory test was given 15 minutes later.

ECT patients who had received unilateral treatments before they received bilateral ECT.

The effect of stimulus waveform did not reach significance ($F=2.34$, $df=1,33$, $p=14$), and none of the interaction terms approached significance. Because stimulus waveform appeared to make a difference in the case of patients given bilateral ECT, the data for bilateral and unilateral ECT were next analyzed separately in analyses of variance involving two factors: stimulus waveform and test session. Patients given unilateral ECT performed similarly regardless of stimulus waveform or time of testing after ECT (all F values < 1). For patients given bilateral ECT there was a marginally significant effect of stimulus waveform ($F=3.99$, $df=1,23$, $p<.06$) and there were no significant interactions.

These results suggest that patients given bilateral

brief-pulse ECT performed differently than patients given bilateral sine-wave ECT. Specifically, when learning occurred only 45 minutes after ECT, patients given bilateral sine-wave ECT performed close to chance (4.4 correct out of 10; 3.3=chance), and the ability to learn and remember new material gradually improved as learning was scheduled at progressively longer intervals after ECT. By contrast, patients given bilateral brief-pulse ECT performed better overall. The difference between the two groups was significant at the earliest test session (45 minutes) (t=2.51, df=23, p<.02) and approached significance at the second test session (65 minutes) (t=1.60, df=23, p<.12). No difference was detectable at the third test session (85 minutes) (t=.80, df=23, p>.10).

Twenty-five of the 37 patients given ECT were tested a fourth time beginning 6.5–11 hours (mean=8.9 hours) after ECT. The recognition memory scores for these four groups were 7.6 (bilateral sine wave, N=5), 7.7 (bilateral brief pulse, N=11), 9.0 (unilateral sine wave, N=3), and 8.7 (unilateral brief pulse, N=6). These data show that during the hours after treatment, improvement in memory functions continued to occur, especially for the two bilateral ECT groups. However, patients given bilateral sine-wave and brief-pulse ECT performed identically. Finally, although patients given bilateral ECT continued to perform more poorly than patients given right unilateral ECT, this difference was not significant by 9 hours after treatment (t=1.6, df=23, p>.10).

The depressed control group not given ECT performed nearly perfectly at each testing session. Comparisons between this group and each of the ECT groups showed that the group not given ECT performed better than the bilateral groups (all t values >3.0, p<.05), but the difference between the group not given ECT and the unilateral groups did not reach significance (all t values <1.2, p>.10).

EXPERIMENT 2

The first experiment showed that bilateral brief-pulse ECT produced less memory dysfunction than bilateral sine-wave ECT, but an advantage for brief-pulse ECT could be observed only during the first hour after treatment, not at later times. It seemed possible that the relatively simple 10-word, multiple-choice memory test used in experiment 1 might not be sensitive enough to detect differences in memory impairment, especially many hours after ECT, when memory functions have improved. Accordingly, for experiment 2 we compared bilateral brief-pulse and sine-wave ECT using three memory tests known to be particularly sensitive to ECT.

Method

Subjects. The subjects were 25 psychiatric inpatients who had been prescribed bilateral sine-wave or brief-pulse ECT for depression at one of five local hospitals (table 1). Data for 11 of the 18 patients in the bilateral sine-wave group have been presented previously (19). The criteria for excluding patients were the same as in experiment 1. Six of the seven patients receiving brief-pulse ECT had participated in experiment 1.

ECT. Treatment was administered as described for experiment 1. For the patients prescribed bilateral sine-wave ECT, treatment was given with a Medcraft B-24 device (130–160 volts for 0.5–1.0 second). For the seven patients prescribed bilateral brief-pulse ECT, treatment was given with a MECTA ECT device (pulse width=0.5–1.5 msec, stimulus duration=2.0 seconds, frequency=60–70 Hz). Electrode placement was bitemporal for all patients.

Materials. Three memory tests were given: prose recall, memory for a geometric figure (diagram recall), and paired-associate learning. For prose recall, one of two equivalent short passages was read to the patient (20). Immediately after learning it, and again the following day, patients were asked to recall as much of it as they could remember. The score was the number of segments recalled out of 20. Patients also copied the Rey-Osterrieth figure (21) or an equivalent figure (22) and were asked to reconstruct it from memory the following day, without forewarning. The score was based on the number of properly located segments (maximum score=36). For paired-associate learning, 10 word pairs (e.g., army-table) were presented on cards three times in succession at the rate of 6 seconds/pair. After each presentation, patients attempted to recall the second word of the pair when cued with the first word (23). The score was the number of words recalled out of 10 on each of the three learning trials. Two forms of this test were available.

Procedure. Patients given bilateral sine-wave ECT (N=11 for prose and diagram recall, N=7 for paired-associate learning) were tested with one form of each test before the first treatment of the series and then again with a different form 6 to 10 hours after the fifth treatment. The order of administration of the test forms was counterbalanced across patients. The seven patients given bilateral brief-pulse ECT were tested 6 to 10 hours after the fifth treatment of the series by using one form of the prose passage and the diagram and alternating between the two forms of the paired-associate test.

Results

Figure 2 shows the results for the three memory tests. Performance was markedly poorer after sine-wave ECT than before sine-wave ECT on all three tests: delayed (24-hour) prose recall (t=4.9, df=10, p<.01), delayed (24-hour) diagram recall (t=3.8, df=10, p<.01), and paired-associate learning (F=111, df=1,6, p<.01). The patients tested after bilateral brief-pulse ECT also performed worse than the patients tested before sine-wave ECT: for delayed prose

FIGURE 2. Performance on Three Memory Tests of Depressed Patients Before and After Bilateral ECT[a]
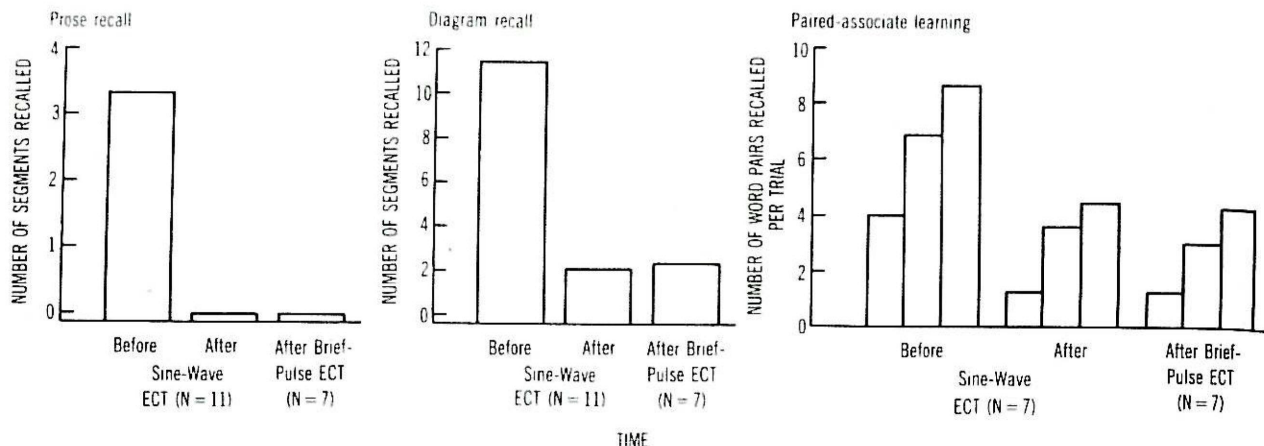
[a]For prose and diagram recall, learning occurred before the first treatment and 6–10 hours after the fifth treatment. Recall was always measured the day after learning. For paired-associate learning, learning was assessed during three trials before the first treatment and during three trials 6–10 hours after the fifth treatment.

recall, t=3.8, df=16, p<.01; for delayed diagram recall, t=2.4, df=16, p<.01; for paired-associate learning, F=6.5, df=1,12, p<.03. Memory functions were just as impaired in patients receiving brief-pulse ECT as in patients receiving sine-wave ECT (all p values>.10). Thus, there was no advantage of brief-pulse ECT over sine-wave ECT.

There was no effect of ECT on immediate recall of the prose passage: before sine-wave ECT, mean=6.1; after sine-wave ECT, mean=5.6; after brief-pulse ECT, mean=6.3. There was also no effect of ECT on the ability to copy the diagram: before sine-wave ECT, mean=28.6; after sine-wave ECT, mean=27.5; after brief-pulse ECT, mean=26.1.

DISCUSSION

Brief-pulse ECT produced less severe anterograde amnesia than sine-wave ECT during the first hour after treatment, but no advantage for brief-pulse ECT was found beyond the first hour. Even when memory was assessed with more sensitive tests requiring overnight retention of material learned several hours after treatment, brief-pulse ECT and sine-wave ECT produced equivalent memory impairment. Right unilateral ECT was associated with less memory impairment than bilateral ECT.

These findings differ from reports of a significant and persisting advantage of brief-pulse ECT over sine-wave ECT with respect to memory functions (8, 9). The latter data come from a research setting, where treatment parameters were applied systematically and matched with respect to seizure threshold. Differences in treatment parameters might account for the persistent advantage of brief-pulse ECT over sine-wave ECT in these reports but not in the present study. At least when the electrical energy delivered is close to what is

required to elicit a seizure, brief-pulse ECT is associated with less postictal depression of the EEG following each treatment and less EEG slowing during the first week after the completion of treatment (16). For these and other reasons it has been proposed that when stimulation is near seizure threshold, sine-wave ECT produces more intense, more generalized seizures than brief-pulse ECT and correspondingly more severe memory impairment (7, 9). When stimulation is delivered at higher energy levels, well above seizure threshold, qualitative differences in seizures might not occur because brief-pulse and sine-wave ECT both produce well-generalized seizures. In this case memory impairment should be familiar. Our previous study in experimental animals (24) is consistent with this idea. We delivered a variety of brief-pulse and sine-wave convulsive stimuli to mice and tested memory in a standard laboratory task. Most stimuli produced equivalent memory impairment, and we were unable to find a brief-pulse waveform that produced less memory impairment than sine-wave stimuli, even when current was delivered at seizure threshold. Perhaps in the relatively small mouse brain, seizures tend to be similar and well generalized. Accordingly, when stimuli were equated with respect to seizure threshold, memory loss was equivalent across waveforms.

In the present study the estimated electrical energy delivered (bilateral sine-wave ECT: 86 J [data were available for 25 of 30 patients in the two experiments]; bilateral brief-pulse ECT: 52 J [N=20]) was higher than in the studies by Weiner et al. (9, 16) (bilateral sine-wave ECT: about 60 J; bilateral brief-pulse ECT: about 25 J). Weiner's group used starting parameters fixed by research criteria: for the Medcraft device, 140 volts and 0.6 seconds' duration; for the MECTA device, 0.75 msec pulse width, 1.25 seconds' duration, and 60 Hz frequency. Parameters were then raised or lowered as needed for subsequent treatments to ensure

a seizure of 25–60 seconds' duration. The psychiatrists participating in our study used higher values for these parameters. Seizure threshold does vary widely among patients (13), and there may have been a preference for stimulus parameters that could elicit a seizure reliably in all patients.

One other possible explanation for why brief-pulse ECT in our study produced no less memory impairment than sine-wave ECT is that our impedance estimate of 220 Ω was too low. Our estimate was based on previous studies where impedance was measured directly during the electrical stimulus (9, 13, 16). However, in those studies special attention was paid to establishing a good scalp-electrode contact, including the clipping of hair under the centroparietal electrode. If in our study the average impedance had been higher than 220 Ω, then our calculations would have overestimated the number of joules delivered by the constant-voltage Medcraft device and underestimated the number of joules delivered by the constant-current MECTA device. However, it seems unlikely that the impedance during ECT in our studies was much more than 220 Ω, because of the findings for the patients given right unilateral ECT (table 1). These patients received an estimated 54 J, which would have to be revised downward if the impedance had been higher than 220 Ω. Yet, the number of joules delivered was probably not much less than 54, because Weiner (13) reported that 47 J were delivered to his unilateral sine-wave group in a study that titrated stimulus intensity so as to stay close to seizure threshold.

In any case, there seem to be two possibilities as to why brief-pulse ECT did not exhibit a persisting advantage over sine-wave ECT. Either brief-pulse stimulation intensity was too high relative to sine-wave stimulation intensity or the impedance was too high. Whichever of these explanations applies, it appears that brief-pulse ECT does not always yield less memory impairment than conventional sine-wave ECT. Brief-pulse ECT was originally introduced as a mode of treatment that might reduce the side effects of ECT on memory. It may be difficult for this promise of brief-pulse ECT to be realized in clinical practice, unless stimulus intensity is titrated individually for each patient across the course of treatment so as to stimulate relatively close to seizure threshold. At the same time, stimulation cannot be so close to the seizure threshold that efficacy is compromised (25).

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