Ultrabrief Pulse Right Unilateral ECT: A New Standard of Care?

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While ECT remains a remarkably safe and effective treatment for severe depression, its broad application has been hampered by concerns—both perceived and real—about its cognitive effects. Worry about memory loss make some patients reluctant to undergo this therapy and some practitioners reluctant to refer patients for it. Within the field of ECT itself, there has been tension for some years between the wish to maximize (the already excellent) antidepressant and antipsychotic efficacy of ECT and the competing wish to minimize any effects on memory.

Several studies conclude that right unilateral (RUL) electroconvulsive therapy (ECT) given with ultrabrief pulse-width stimulus packages causes less cognitive impairment than other techniques. I review this evidence and discuss how these findings can be interpreted to direct optimal clinical practice.

While ECT remains a remarkably safe and effective treatment for severe depression, its broad application has been hampered by concerns—both perceived and real—about its cognitive effects. Worry about memory loss make some patients reluctant to undergo this therapy and some practitioners reluctant to refer patients for it. Within the field of ECT itself, there has been tension for some years between the wish to maximize (the already excellent) antidepressant and antipsychotic efficacy of ECT and the competing wish to minimize any effects on memory. This tension has resulted in several important enhancements in ECT technique which, taken together, make contemporary ECT far better than the ECT of decades past. Major enhancements to ECT technique include RUL electrode placement, brief pulse stimulus currents, improved anesthesia techniques, the “dose titration” technique to individualize treatment stimulus dosing, and the discovery of the dose-response relationship between electrical stimulus dosing and antidepressant outcome (largely with RUL electrode placement.)

Is ultrabrief pulse stimulus ECT to be the next advancement added to this list? It has long been established that the induction of a cerebral seizure is central to the neurobiological changes that result in the antidepressant effects of ECT. For decades, an electrical stimulus has been used to initiate this seizure event, replacing earlier methods that used chemicals. Interestingly, the characteristics of the electrical stimulus affect the effectiveness and cognitive outcomes of the seizure. Sine wave stimuli have been replaced with rectangular pulses on modern ECT devices, leading to a substantial decrease in cognitive effects. The width of these pulses, measured in milliseconds, may be important too. Contemporary ECT devices can be set to deliver pulse-widths between 0.25 and 2.0 milliseconds. Stimuli between 0.5 and 2.0 milliseconds are called “brief,” and those less than 0.5 millisecond are called “ultrabrief.” Sackeim and colleagues state that the “optimal width for neuronal depolarization is estimated to be at most 0.1 to 0.2 millisecond” and cite earlier work in this area. They also believe that wider pulse-widths are less efficient at inducing seizures, thus raising seizure threshold and perhaps contributing to cognitive effects.

Sienaert and associates randomized 81 patients to either bifrontal (BF) (n = 40) or RUL (n = 41) ECT; all given with ultrabrief (0.3 millisecond) stimuli. The BF was given at 1.5 times seizure threshold and the RUL at 6 times seizure threshold. At the end of the ECT course, the response rate (measured by decrease in the Hamilton Rating Scale for Depression [HRSD] score of 50% or greater) in the BF and RUL groups was equal (78%). Using remitter criteria (HRSD score of 10 or below), the rates were 59% in the BF group and 72% in the RUL group. Using even stricter remitter criteria (HRSD score of 7 or lower), the rates fell to 34% in the BF group and to 44% in the RUL group. None of the group differences was significant.

A cognitive battery of tests was administered at baseline and at 1 and 6 weeks after ECT. Global cognitive function, verbal memory, attention, executive function, and autobiographical memory improved from base-line to after ECT, with no significant differences between the electrode placements. While patients in the RUL group needed fewer treatments (mean = 7.76) than did those in the BF group (mean = 10.08) to reach response criteria, there was no difference in number of treatments needed to reach the 2 levels of remission (HRSD, 10 and 7).
Loo and colleagues\textsuperscript{1} carried out a naturalistic study in which patients were given ECT with either standard brief pulse RUL ECT (pulse-width = 1.0 millisecond; \( n = 22 \)) or ultrabrief RUL ECT (pulse-width = 0.3 millisecond; \( n = 74 \)). In this context, “naturalistic” meant that the treating psychiatrist decided the type of ECT (either of the 2 groups), the number of treatments, and when to switch to bilateral placement because of lack of antidepressant response. Remission rates were very low (RUL = 36\%, RUL-ultrabrief [RUL-UB] = 27\%), both absolutely and when compared with those reported by Sackeim and coworkers\textsuperscript{2} and Sienaert and colleagues.\textsuperscript{3,4} There were no significant differences in the Montgomery Asberg Depression Rating Scale (MADRS) scores between the 2 groups across the treatment course. However, MADRS scores declined more slowly in the RUL-UB group, and more treatments were required (10.3 vs 7.6). RUL-UB was superior to RUL on 1 measure of retrograde amnesia, the Autobiographical Memory Inventory–Short Form (30-item). Full results of the other tests in the cognitive battery were not reported.

Sackeim and coworkers\textsuperscript{2} randomized 90 patients with depression to 1 of 4 treatment groups:

1. RUL at 6 times seizure threshold with a standard pulse-width of 1.5 milliseconds
2. RUL at 6 times seizure threshold with a pulse-width of ultrabrief 0.3 millisecond
3. Bilateral (BL) ECT at 2.5 times seizure threshold with a pulse-width of 1.5 milliseconds
4. BL ECT at 2.5 times seizure threshold with a pulse-width of 0.3 millisecond

Patients were assessed for depressive symptoms and cognition at baseline, during and after the acute course of ECT, and at 2 and 6 month time points. Responders were monitored for 1 year. Reported remission rates were 73\% for ultrabrief RUL, 65\% for brief pulse BL, 59\% for brief pulse RUL, and 35\% for ultrabrief BL. Ultrabrief pulse RUL produced less severe cognitive effects than the other 3 treatment groups, both acutely and long-term, on multiple measures in several cognitive domains, including subjective assessment of memory function. Relapse in the year following acute ECT was unrelated to treatment group. These authors concluded, “the use of an ultrabrief stimulus coupled with high-dosage RUL stimulation is a strategy that appears to retain the therapeutic properties of ECT, although substantially reducing its potential for adverse cognitive side effects.”

While the conclusions of these 3 studies are similar, some differences in methodology and results should be noted. The Sienaert study used BF placement at 1.5 times seizure threshold, while the Sackeim study used standard BL placement at 2.5 times seizure threshold. The latter strategy is likely to accentuate cognitive differences between the BL and RUL groups. The low remission rate in the Sackeim study of BL ultrabrief pulse ECT in 23 patients is surprising, at odds with the superior rate of the slightly different BF placement in the Sienaert study, and requires replication. Finally, pulse-widths used for “standard” brief pulse treatment varied between the Sackeim (1.5 milliseconds) and Loo (1.0 millisecond) studies.

Discussion

These studies constitute an exciting and intriguing preliminary body of data. While these are the only readily accessible published data, undoubtedly there are more data out there. Because standard ECT devices used in the United States and around the world have had the capability to deliver ultrabrief pulse-widths for several years, many patients have been treated clinically with this modality—most likely with all 3 commonly used electrode placements (BL, BF, and RUL). Such anecdotal data may be helpful to provide hints about safety and effectiveness but cannot replace systematically collected data from clinical trials, randomized or naturalistic.

With fewer than 200 patients reported in these trials, is it reasonable to adopt ultrabrief pulse ECT in routine clinical practice? Are we sacrificing efficacy? Are ultrabrief pulse stimuli appropriate for use with BL electrode placements?

Further studies are needed to answer these questions. Such important questions beg the even more important question: “How much evidence is needed, in evidence-based medicine, to change clinical practice?” Ideally, the studies discussed would quickly lead to replications that would prove the point, one way or the other. Unfortunately, in ECT, the resources to conduct well-designed studies that would definitely answer the question are often unavailable. We are left with a smattering of data, not all collected with the best methodology, from which clinical decisions must be made. Prudence and caution are always needed in clinical decision making, and we should clearly “first, do no harm.” But what is the greater harm? Depriving a seriously depressed patient of the most effective treatment, or exposing the patient to more cognitive impairment from the treatment? There is no simple answer, but I suggest that we tell our patients that there is a new technique, about which less is known than more standard techniques, but one that has the potential to relieve depression with fewer memory effects. Thus included in the decision-making process, the practitioner and patient together can arrive at a treatment plan that is informed by the available,
albeit limited, data. Fortunately, the nature of ECT is such that if, after several RUL treatments with ultrabrief pulse stimuli, the patient is not responding adequately, the treatment technique can be switched, either to a different waveform or electrode placement, or both.

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