Brief Pulse and Ultrabrief Pulse Right Unilateral Electroconvulsive Therapy (ECT) for Major Depression: Efficacy, Effectiveness, and Cognitive Effects

To the Editor: We appreciate the contribution to the electroconvulsive therapy (ECT) literature of Spaans and colleagues' careful study[1] comparing brief pulse and ultrabrief pulse stimuli. However, given the study limitations, we suggest that it is premature to conclude that right unilateral (RUL) ultrabrief pulse ECT confers inferior efficacy and no cognitive advantage.

ECT was given twice per week and at 8× seizure threshold, major technique differences from previously published studies,[2] which may have reduced efficacy of ultrabrief pulse ECT as well as cognitive effects of ultrabrief pulse ECT. Regarding the neurocognitive outcome, the study utilized a limited neurocognitive battery, which precluded assessment of important neurocognitive functions, including attention, processing speed, and verbal learning and memory. Also, the statistical analyses were not adjusted for demographic characteristics (eg, age, education, premorbid IQ), which are known to affect neurocognitive outcome. While not statistically significant, there were 6 dropouts (10%) for "confusion/delirium" in the brief pulse group, and 0 in the ultrabrief pulse group. Thus, the most cognitively vulnerable patients were unable to have follow-up neurocognitive assessment, as they exited from the brief pulse condition. Such dropout could have biased the neurocognitive outcomes. Also, the post-ECT neurocognitive testing occurred up to 1 week later, possibly missing immediate posttreatment differences between the 2 groups. Finally, failure to find a difference does not ensure that such a difference does not exist.

Regarding efficacy of the 2 types of ECT, despite the statistically significant differences in remitter rates and number of treatments needed, the decrease in Montgomery-Asberg Depression Rating Scale (MADRS) scores was identical in the intent-to-treat (ITT) sample. Furthermore, the MADRS score at week 5 was actually lower in the ultrabrief pulse group than in the brief pulse group, despite starting at a higher baseline. The authors noted the real-world generalizability of their methods, since they allowed concomitant psychotropics. In the real world, treatment effectiveness is just as important as efficacy. While the authors noted superior ITT efficacy of brief pulse ECT, they failed to discuss the reduced effectiveness of brief pulse ECT, as brief pulse had only a 65.5% completion rate compared with an 84.5% completion rate for ultrabrief pulse ECT. The meaning of the difference in completion rates could have been clarified if Figure 1 had included number of dropouts due to "lack of efficacy."

Our group is currently conducting a clinical trial using RUL ultrabrief pulse ECT (0.25 millisecond pulse width) in geriatric depressed patients (over 200 enrolled to date).[3] While there is no brief pulse comparator group in the study, our efficacy rates (~60% remission) are good. Our preliminary cognitive data suggest that global cognitive function (as based on the Mini-Mental State Examination) remains stable during the acute course. We are conducting a comprehensive neurocognitive battery to assess the effects of ultrabrief pulse ECT on multiple cognitive domains, including processing speed, attention, verbal learning and memory, verbal fluency, and executive function.

We believe that comprehensive evaluation of efficacy and neurocognitive profiles of various ECT techniques is an important research arena because ECT remains a vital treatment option for the most severely ill patients.[4] Optimizing ECT technique through well-conducted clinical trials should continue to be a high priority research goal of our field.

REFERENCES

1. Spaans HP, Verwijk E, Comijs HC, et al. Efficacy and cognitive side effects after brief pulse and ultrabrief pulse right unilateral electroconvulsive therapy for major depression: a randomized, double-blind, controlled study. *J Clin Psychiatry*. 2013;74(11):e1029–e1036.
2. Loo CK, Sainsbury K, Sheehan P, et al. A comparison of RUL ultrabrief pulse (0.3 ms) ECT and standard RUL ECT. *Int J Neuropsychopharmacol*. 2008;11(7):883–890.
3. National Institute of Mental Health. Prolonging Remission in Depressed Elderly (PRIDE). ClinicalTrials.gov Web site. Bethesda, MD: National Library of Medicine. http://clinicaltrials.gov/ct2/show/NCT01028508?term=PRIDE&rank=1. Updated January 27, 2014. Accessed January 10, 2014.
4. Lisanby SH. Electroconvulsive therapy for depression. *N Engl J Med*. 2007;357(19):1939–1945.

Charles H. Kellner, MD
charles.kellner@mssm.edu
Shawn M. McClintock, PhD
W. Vaughn McCall, MD
George Petrides, MD
Rebecca G. Knapp, PhD
Richard D. Weiner, MD, PhD
Robert C. Young, MD
Robert M. Greenberg, MD
Matthew V. Rudorfer, MD
Gabriella M. Ahle, BA
Lauren S. Liebman, BA
Sarah H. Lisanby, MD
for the CORE/PRIDE Group

Author affiliations: Department of Psychiatry, Icahn School of Medicine at Mount Sinai, New York, New York (Dr Kellner and Mss Ahle and Liebman); Department of Psychiatry and Behavioral Sciences, Duke University School of Medicine, Durham, North Carolina (Drs McClintock, Weiner, and Lisanby); Department of Psychiatry and Human Health, Georgia Regents University, Augusta (Dr McCall); Department of Psychiatry, Northshore LIJ Health System, Zucker Hillside Hospital, Glen Oaks, New York (Dr Petrides); Department of Public Health Sciences, Medical University of South Carolina, Charleston (Dr Knapp); Department of Psychiatry, Weill Cornell Medical College, White Plains, New York (Dr Young); Department of Psychiatry, Lutheran Medical Center, Brooklyn, New York (Dr Greenberg); and Somatic Treatments Program, National Institute of Mental Health, Bethesda, Maryland (Dr Rudorfer).

Potential conflicts of interest: **Dr Kellner** has received grant/research support from the National Institute of Mental Health (NIMH) and has received honoraria from LIJ Hospital System and *Psychiatric Times*. **Dr McClintock** has received grant/research support from NIMH. **Dr McCall** has received grant/research support from NIMH and Merck and honoraria from Wolters Kluwer Publishing. **Dr Petrides** has received grant/research support from NIMH, Corcept Therapeutics, St Jude Medical, Amgen, and Proteus. **Dr Young** has been a consultant for and has received grant/research support from the National Institutes of Health (NIH). **Dr Lisanby** has received grant/research support from NIH, Brainsway, NeoSync, ANS/St Jude, and Brain & Behavior Research Foundation. **Drs Knapp**, **Weiner**, **Greenberg**, and **Rudorfer** and **Mss Ahle** and **Liebman** report no potential conflicts of interest relevant to this letter.
Funding/support: PRIDE (Prolonging Remission in Depressed Elderly) is a clinical trial supported by the National Institute of Mental Health in Bethesda, Maryland (ClinicalTrials.gov Identifier: NCT01028508).
J Clin Psychiatry 2014;75(7):777 (doi:10.4088/JCP.14lr08997).

Dr Spaans and Colleagues Reply

To the Editor: We greatly appreciate the comments made by the colleagues from the CORE/PRIDE group with respect to our randomized controlled study[1] in brief and ultrabrief pulse electroconvulsive therapy (ECT), and we welcome the opportunity to clarify a number of issues raised.

Differences in techniques between countries demonstrate that any concept of "the ultimate" ECT technique is still illusory. It is doubtful whether the European twice-weekly schedule reduces efficacy significantly compared to thrice-weekly sessions.[2]

In order to reduce the chance of a less efficacious outcome for ultrabrief pulse ECT, we chose a higher dose, ie, 8× times seizure threshold. Notably, our mean treatment dose of 206 mC in the ultrabrief pulse ECT group was well above the mean charge of 103 mC (6× seizure threshold) in the Sackeim et al study.[3] Therefore, we had expected the efficacy of ultrabrief pulse ECT to be comparable.

It is true that a higher dose usually impacts negatively on cognition.[4] However, although the mean treatment dose in the ultrabrief pulse ECT group was below the charge in the study by Loo and colleagues[5] and the mean treatment dose in our brief pulse group of 495 mC was above the final treatment dose of 469 mC of their brief pulse group, we did not find cognitive differences.

While the practice of ultrabrief pulse ECT has increased,[6,7] the question whether or not this should be the standard of care remains debatable. We sought to further clarify whether ultrabrief pulse right unilateral (RUL) ECT differs in efficacy in severe depression from standard pulse RUL ECT.[3,5,8] In this respect, the clinical issues of clinical response and speed of remission are considered of more importance than the change in Montgomery-Asberg Depression Rating Scale score from baseline, in particular as there was no minimum score for inclusion in our study.

Our focus on retrograde amnesia was based on the knowledge that anterograde amnesia and deficits in other cognitive domains are transient,[9,10] while retrograde amnesia for past memories might show more enduring deficits. Our results did not confirm the hypothesis that ultrabrief pulse ECT produces less severe side effects in retrograde memory.

We agree that the article did not contain a clear description of the covariates. We can confirm that we included age and education as covariates in the cognitive analyses.

The observation that in our brief pulse group more patients (n = 6) dropped out of the study because of confusion, and thus biased the cognitive results, is true. However, the suggestion that we might have missed immediate posttreatment differences between the 2 groups by performing neurocognitive testing up to 1 week after finishing the treatment course is, in our opinion, of little clinical significance.

Finally, we can agree that, at this point in time, with the current state of knowledge, it is premature to draw firm conclusions. It remains unclear whether "ultrabrief ECT should be the new standard of care,'" as Charles Kellner stated 5 years ago.[11] We are looking forward to reading the results of the CORE studies and welcome the wealth of high-quality studies and the attention this discussion brings to the field of ECT.

References

1. Spaans HP, Verwijk E, Comijs HC, et al. Efficacy and cognitive side effects after brief pulse and ultrabrief pulse right unilateral electroconvulsive therapy for major depression: a randomized, double-blind, controlled study. *J Clin Psychiatry*. 2013;74(11):e1029–e1036.
2. Charlson F, Siskind D, Doi SA, et al. ECT efficacy and treatment course: a systematic review and meta-analysis of twice vs thrice weekly schedules. *J Affect Disord*. 2012;138(1–2):1–8.
3. Sackeim HA, Prudic J, Nobler MS, et al. Effects of pulse width and electrode placement on the efficacy and cognitive effects of electroconvulsive therapy. *Brain Stimulat*. 2008;1(2):71–83.
4. McCall WV, Dunn A, Rosenquist PB, et al. Markedly suprathreshold right unilateral ECT versus minimally suprathreshold bilateral ECT: antidepressant and memory effects. *J ECT*. 2002;18(3):126–129.
5. Loo CK, Sainsbury K, Sheehan P, et al. A comparison of RUL ultrabrief pulse (0.3 ms) ECT and standard RUL ECT. *Int J Neuropsychopharmacol*. 2008;11(7):883–890.
6. Galletly C, Paterson T, Burton C. A report on the introduction of ultrabrief pulse width ECT in a private psychiatric hospital. *J ECT*. 2012;28(1):59.
7. van Waarde JA, Verwey B, van den Broek WW, et al. Electroconvulsive therapy in the Netherlands: a questionnaire survey on contemporary practice. *J ECT*. 2009;25(3):190–194.
8. Spaans HP, H Kho K, Verwijk E, et al. Efficacy of ultrabrief pulse electroconvulsive therapy for depression: a systematic review. *J Affect Disord*. 2013;150(3):720–726.
9. Fraser LM, O'Carroll RE, Ebmeier KP. The effect of electroconvulsive therapy on autobiographical memory: a systematic review. *J ECT*. 2008;24(1):10–17.
10. Verwijk E, Comijs HC, Kok RM, et al. Neurocognitive effects after brief pulse and ultrabrief pulse unilateral electroconvulsive therapy for major depression: a review. *J Affect Disord*. 2012;140(3):233–243.
11. Kellner CH. Ultrabrief pulse right unilateral ECT: a new standard of care? http://www.psychiatrictimes.com/articles/ultrabrief-pulse-right-unilateral-ect-new-standard-care. Accessed February 26, 2014.

Harm-Pieter Spaans, MD
hp.spaans@parnassia.nl
Esmée Verwijk, MSc
Pascal Sienaert, MD, PhD
Max L. Stek, MD, PhD
Filip Bouckaert, MD
Hannie C. Comijs, PhD
Rob M. Kok, MD, PhD
Erik J. A. Scherder, PhD
King H. Kho, MD, PhD

Author affiliations: Department of Psychiatry (Drs Spaans and Kho), Clinical Neuropsychology (Ms Verwijk), Old Age Psychiatry (Dr Kok), and ECT (Dr Spaans and Kho and Ms Verwijk), The Clinical Center for the Elderly, Parnassia Psychiatric Institute, The Hague, The Netherlands; Department of Old Age Psychiatry at VU University Medical Center and Academic Department of Old Age of GGZinGeest Amsterdam, Amsterdam, The Netherlands (Dr Stek); Department of Old Age Psychiatry (Dr Bouckaert), University Psychiatric Center–Catholic University of Leuven (Dr Sienaert), campus Kortenberg, Kortenberg, Belgium; EMGO Institute for Health and Care Research, VU University Medical Center, Amsterdam, Amsterdam, The Netherlands (Dr Comijs); and Department of Clinical Neuropsychology of the VU University in Amsterdam, Amsterdam, The Netherlands (Dr Scherder).

Potential conflicts of interest: None reported.
Funding/support: None reported.
Additional information: All authors are members of ResPECT–Research in Psychiatry & ECT.
J Clin Psychiatry 2014;75(7):777–778 (doi:10.4088/JCP.14lr08997a).