

Letters to the Editor

Differential Effectiveness of Right Unilateral Versus Bilateral Electroconvulsive Therapy in Resistant Bipolar Depression

TO THE EDITOR: The article by Helle K. Schoeyen, M.D., Ph.D., et al. (1), published in the January 2015 issue of the *Journal*, compared electroconvulsive therapy (ECT) with right electrode placement with algorithm-based pharmacotherapy in treatment-resistant bipolar depression. The conclusion was that “the remission rate did not differ between the groups” and “remission rates remained modest regardless of treatment choice.” In order to avoid potential misunderstandings, we feel that the title of the article should have clearly stated that the ECT technique used was exclusively unilateral. Unilateral ECT is known to be less effective—and probably better tolerated—than bilateral ECT (2), and the reported 30% (drug treatment) to 35% (unilateral ECT) remission rates are similar to those found for augmentation strategies in nonbipolar-resistant depression in a real-world setting (3). Furthermore, in the results section, it is clearly apparent that unilateral ECT showed results for higher remission rates that nearly reached statistical significance, compared with algorithm-based drug treatment. Considering that the sample size was not large, suggesting that the study was likely underpowered, caution is needed when making conclusions such as those made in the abstract because they may prompt physicians to disregard ECT as a treatment option, which does not correspond with the available evidence. Before labeling a patient’s symptoms as “treatment-resistant” or “refractory,” months and repeated assays of ineffective drug treatment with drugs of different classes plus augmentation with other treatment methods (antipsychotics, somatic treatments, psychotherapy) is necessary (4, 5). Recent case reports indicate that ECT may abruptly terminate long-persisting psychiatric conditions. ECT is an orphan treatment because there is no marketing supporting it, and it carries some stigma and a bad reputation, which currently is scientifically unjustified. We simply want to emphasize this point in order to pay justice to both treatment options.

REFERENCES

1. Schoeyen HK, Kessler U, Andreassen OA, et al: Treatment-resistant bipolar depression: a randomized controlled trial of electroconvulsive therapy versus algorithm-based pharmacological treatment. *Am J Psychiatry* 2014; 172:41–51
2. McCormick LM, Brumm MC, Benede AK, et al: Relative ineffectiveness of ultrabrief right unilateral versus bilateral electroconvulsive therapy in depression. *J ECT* 2009; 25:238–242
3. Trivedi MH, Fava M, Wisniewski SR, et al: STAR*D Study Team: Medication augmentation after the failure of SSRIs for depression. *N Engl J Med* 2006; 354:1243–1252

4. Pacchiarotti I, Mazzarini L, Colom F, et al: Treatment-resistant bipolar depression: towards a new definition. *Acta Psychiatr Scand* 2009; 120:429–440
5. Vieta E, Colom F: Therapeutic options in treatment-resistant depression. *Ann Med* 2011; 43:512–530

Georgios D. Kotzalidis, M.D., Ph.D.
Isabella Pacchiarotti, M.D., Ph.D.
Chiara Rapinesi, M.D.
Andrea Murru, M.D., Ph.D.
Francesc Colom, Psy.D.
Eduard Vieta, M.D., Ph.D.

From the NESMOS (Neuroscience, Mental Health, and Sensory Organs) Department, Sapienza University, School of Medicine and Psychology, Sant'Andrea Hospital, Rome; and the Bipolar Disorders Unit, Institute of Neuroscience, Hospital Clinic, University of Barcelona, IDIBAPS, CIBERSAM, Barcelona, Catalonia, Spain.

Dr. Pacchiarotti has received CME-related honoraria or consulting fees from ADAMED, Janssen-Cilag, and Lundbeck. Dr. Murru has received CME-related honoraria or consulting fees from ADAMED, AstraZeneca, Bristol-Myers Squibb, Janssen-Cilag, Lundbeck, and Otsuka. Dr. Colom has served as an advisor or speaker for Adamed, AstraZeneca, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Lundbeck, MSD-Merck, Otsuka, Pfizer, Rovi, Sanofi-Aventis, Shire, and Tecnifar, and he has received royalties from Ars Médica, Cambridge University Press, Giovanni Fioriti Ed., Igaku-Shoin Ltd., La Esfera de Los Libros, Mayo Ed. & Columna, Medipage, Morales i Torres Ed, Panamericana, and Solal Ed. Prof. Vieta has received research grants and served as a consultant, advisor, or speaker for Alexza, Almirall, AstraZeneca, Bial, Bristol-Myers Squibb, Eli Lilly, Ferrer, Forest Research Institute, Gedeon Richter, GlaxoSmithKline, Janssen-Cilag, Jazz, Lundbeck, Merck, Novartis, Otsuka, Pfizer, Roche, Sanofi-Aventis, Servier, Solvay, Shire, Takeda, and United Biosource Corp., and he has received research funding from the Spanish Ministry of Science and Innovation, the Stanley Medical Research Institute, and the 7th Framework Program of the European Union. Drs. Kotzalidis and Rapinesi report no financial relationships with commercial interests.

This letter was accepted for publication in December 2014.

Am J Psychiatry 2015; 172:294; doi: 10.1176/appi.ajp.2014.14101366

Response to Kotzalidis et al.

TO THE EDITOR: We appreciate the comments from Kotzalidis et al. regarding our recent article. In our study, linear mixed-effects modeling analysis revealed that ECT was significantly more effective than algorithm-based pharmacological treatment, and the response rate was significantly higher in the ECT group. Furthermore, shorter times to response and remission in the ECT group of better effect on remission rate was a result that fell short of statistical significance. Taken together, we strongly agree with Kotzalidis et al. that these results should not prompt physicians to disregard ECT as a treatment option—on the contrary. We also agree that there is evidence supporting that the use of bilateral electrode placement in ECT may have better effect on depression than unilateral electrode placement. However, whether this is also the case in treatment-resistant bipolar depression remains to be seen, and we cannot base treatment recommendation on anecdotal evidence.

Bilateral electrode placement also seems to carry a higher risk for cognitive side effects (1, 2). In our study, follow-up analysis revealed that the unilateral ECT did not show significantly more cognitive side effects than the algorithm-based pharmacological treatment (3). These results further support the use of ECT for treatment-resistant depression. We assume that the relative low remission rate in our study reflects the chronicity and treatment resistance or the patient group included, but electrode placement may be of importance. This shows that more evidence-based knowledge is needed to optimize ECT treatment strategy in bipolar disorder.

REFERENCES

1. Lisanby SH, Madox JH, Prudic J, et al: The effects of electroconvulsive therapy on memory of autobiographical and public events. *Arch Gen Psychiatry* 2000; 57:581–590
2. Sackeim HA, Prudic J, Fuller R, et al: The cognitive effects of electroconvulsive therapy in community settings. *Neuropsychopharmacology* 2007; 32:244–254
3. Kessler U, Schoeyen HK, Andreassen OA, et al: The effect of electroconvulsive therapy on neurocognitive function in treatment-resistant bipolar disorder depression. *J Clin Psychiatry* 2014; 75:e1306–e1313

Helle K. Schoeyen, M.D., Ph.D.
 Ute Kessler, M.D., Ph.D.
 Ole A. Andreassen, M.D., Ph.D.
 Bjoern H. Auestad, Ph.D.
 Per Bergsholm, M.D., Ph.D.
 Ulrik F. Malt, M.D., Ph.D.
 Gunnar Morken, M.D., Ph.D.
 Ketil J Oedegaard, M.D., Ph.D.
 Arne Vaaler, M.D., Ph.D.

From the MoodNet Research Group and Division of Psychiatry, Stavanger University Hospital, Stavanger, Norway; the MoodNet Research Group and Division of Psychiatry, Haukeland University Hospital, Bergen, Norway; Faculty of Medicine and Dentistry, Clinical Institute, University of Bergen, Norway; NORMENT, KB Jebsen Centre for Psychosis Research, Division of Mental Health and Addiction, Oslo University Hospital, and Institute of Clinical Medicine, University of Oslo, Norway; Research Department, Stavanger University Hospital and Faculty of Science and Technology, University of Stavanger, Norway; the Østmarka Department of Psychiatry, St. Olav University Hospital of Trondheim and Department of Neuroscience, Faculty of Medicine, Norwegian University of Science and Technology, Trondheim, Norway.

The authors' disclosures accompany the original article.

This reply was accepted for publication in December 2014.

Am J Psychiatry 2015; 172:294–295; doi: 10.1176/appi.ajp.2014.14101366r

Electroconvulsive Therapy Versus Pharmacotherapy for Bipolar Depression

TO THE EDITOR: The excellent study by Helle K. Schoeyen, M.D., Ph.D., et al. (1), published in the January 2015 issue of the *Journal*, compares the relative efficacy of a polymedication algorithm with electroconvulsive therapy (ECT) in the treatment of patients with bipolar depression. Despite the fact that their results show the superiority of ECT compared with their pharmacological algorithm on all three assessment outcome scales, the conclusion in their abstract merely states, “Remission rates remained modest regardless of treatment choice for this challenging condition.” An emphasis on a strict, dichotomous remission criterion downplays the clinically significant 74%

response rate in the ECT group compared with a 35% response rate in the medication group in this “challenging condition.”

As with the many options in their choice of medications, they chose the ECT treatment technique of right unilateral electrode placement and brief pulse stimuli, a less than maximally efficient treatment form that may have handicapped the ECT arm in terms of both speed of response and remission rate. Their mean of 10.6 ECT treatments to remission is substantially higher than the approximate mean of 6.0 in the electrode placement study published by the Consortium for Research in Electroconvulsive Therapy group (2). In that study, bilateral electrode placement was associated with a significantly faster speed of response than with either right unilateral or bifrontal electrode placements. For the seriously ill cohort of patients enrolled in the Norwegian study conducted by Schoeyen et al., strengthening the efficacy of the type of ECT used would likely have improved the results, further separating the ECT and pharmacotherapy groups.

Schoeyen et al. indicate that the most severely ill (and most suicidal) patients, for whom ECT is most clearly indicated and perhaps most effective, were excluded from their study because of liability and consent issues. But the patients who were included did volunteer. They were entitled to be informed about the most efficient forms of treatments and not to be disadvantaged for their decision. In real-world clinical settings, the option to use the most potent ECT techniques is an important aspect of optimized, ethical care (3).

REFERENCES

1. Schoeyen HK, Kessler U, Andreassen OA, et al: Treatment-resistant bipolar depression: a randomized controlled trial of electroconvulsive therapy versus algorithm-based pharmacological treatment. *Am J Psychiatry* 2014; 172:41–51
2. Kellner CH, Knapp R, Husain MM, et al: Bifrontal, bitemporal and right unilateral electrode placement in ECT: randomised trial. *Br J Psychiatry* 2010; 196:226–234
3. Ottosson J-O, Fink M: *Ethics in Electroconvulsive Therapy*. New York, Brunner- Routledge, 2004

Charles H. Kellner, M.D.
 Max Fink, M.D.

From the Department of Psychiatry, Icahn School of Medicine at Mount Sinai, New York; and the Departments of Psychiatry and Neurology, Stony Brook University, Stony Brook, New York.

Dr. Kellner has received grant support from NIMH, royalties from Cambridge University Press, and honoraria from UpToDate, Psychiatric Times, and North Shore-LIJ Health System. Dr. Fink reports no financial relationships with commercial interests.

This letter was accepted for publication in December 2014.

Am J Psychiatry 2015; 172:295; doi: 10.1176/appi.ajp.2014.14101284

Response to Kellner and Fink

TO THE EDITOR: We find the point made by Drs. Kellner and Fink regarding efficacy related to ECT treatment technique with reference to our study important and clinically relevant.

When planning our study, the status regarding efficacy and side effects of ECT treatment technique was suggestive but not conclusive of bilateral electrode placement compared with