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The authors report no financial relationships with commercial interests.

This letter (doi: 10.1176/appi.ajp.2010.10020261) was accepted for publication in April 2010.

Response to Kellner et al. Letter

TO THE EDITOR: We appreciate the opportunity to respond to Kellner et al.'s comments underscoring the clinical urgency associated with the treatment of acute catatonia and important aspects of ECT stimulus dosing in this syndrome.

Our stimulus setting for the initial treatment took into account the recommendations of the half-age formula but also accounted for other factors that may have affected seizure threshold. Our patient's age and gender may have reduced her seizure threshold, while recent benzodiazepine treatment, possible dehydration, and use of bilateral electrode placement may have raised it. These complexities preclude a precise dosage determination. Furthermore, Kellner et al.'s suggestion that a more aggressive (suprathreshold) stimulus would have produced a more therapeutic seizure reflects research relevant to unilateral ECT treatment (1). There is no evidence that suprathreshold bilateral ECT yields a more rapid or robust clinical response. The suggestion of en bloc ECT in this setting is interesting but not one we would currently endorse. The evidence base for this treatment approach is anecdotal and includes cases of neuroleptic malignant syndrome. The only prospective, randomized comparison of single- and double-ECT stimulations studied treatment-resistant depressed populations (2). Indeed, catatonic patients are often exquisitely responsive to ECT and may even show response after one treatment (3), making the initial administration of multiple seizures unnecessarily aggressive.

A further variation in treatment not mentioned by Kellner et al., the application of daily rather than thrice weekly treatments for the acutely ill woman, could not be undertaken due to cardiac complications associated with the initial treatment. Interdisciplinary re-evaluation and further consent discussion were necessary before ECT treatment could recommence. The most important factor preventing a more rapid intervention was the legal hurdle of obtaining emergency guardianship. The process took 20 days and might have been further prolonged if an involved, reliable caregiver had not been available. Aggressive legal action and a responsive judicial system are often the most crucial aspects of urgent care.

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The authors' disclosures accompany the original article.

This letter (doi: 10.1176/appi.ajp.2010.10020261r) was accepted for publication in April 2010.

Medication Guesses in Double-Blind Studies

TO THE EDITORS: In their commentary published in the March 2010 issue of the *Journal*, Roy H. Perlis, M.D., M.Sc., et al. (1) should be commended for reminding us of the possible role that correct medication guesses may have in interpreting study results obtained with antidepressants in double-blind trials. Often in these days, when reading "new" kernels of wisdom, I experience a *déjà vu* phenomenon: Have I not seen similar data a long time ago? In fact, in the early 1960s, we published our first paper on doctor medication guesses (2). The results were based on data from several double-blind anti-anxiety studies. After 4 weeks of treatment, in these early days of psychopharmacology, we conducted primarily 4-week anxiety and depression trials; a total of 156/231 (68%) patients who were receiving active drugs were guessed to have been receiving an active drug, and 75/148 (51%) patients receiving placebo were guessed to have been receiving an active drug (χ^2=11.93). Improvement played a big role in these ratings. At the same time period, 73% of improved but only 32.0% of unimproved patients were guessed to have been receiving active medication.

In our second study (3), we had data available from a 6-week anxiety trial. Adverse events became important modifiers, but only at 6 weeks, not earlier. Irrespective of the treatment received, physicians guessed significantly more often that patients with adverse events were receiving an active drug (N=20/22) relative to patients not reporting adverse events (N=68/116; χ^2=7.01). After 6 weeks of treatment, medication guesses correlated with global improvement (r=0.65) and with adverse events (r=0.65). The multiple r between medication guesses and both global improvement and adverse events was 0.87. These data made us conclude that early improvement and, to a lesser extent, adverse events exert influence on physicians' medication guesses during a double-blind controlled study.

And while I agree with Perlis et al. that to include medication guesses into future study designs should be seriously considered, I do not believe that either the use of two raters or the use of active placebos are recommendations that would lead to improved trial methodology.

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