

Over 60 years since its introduction, electroconvulsive therapy (ECT) remains controversial but unsurpassed in efficacy as a treatment for depression. Fortunately, new data keep rolling in about this old treatment, which remains a mainstay in our modern armamentarium. My friend and colleague Max Fink, M.D., is a tireless advocate for the study and proper use of ECT. His commentary provides a useful summary and cogent recommendations from new research.

—A.J.G.

Editorial

Electroconvulsive Therapy Update: Recognizing and Treating Psychotic Depression

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“Therapy resistance” is an increasing burden in patient care. Despite our many medications and psychotherapies, we see an increasingly larger frustrated population of therapists and families as more patients fail to respond to treatment and are labeled “pharmacotherapy-resistant.” The frustration is all the worse because effective treatment is available for some diagnoses when properly made. Psychotic depression is one such treatable condition that is difficult to recognize.

In the 1970s, Glassman and associates at Columbia University treated hospitalized depressed patients with imipramine at serum drug levels considered to be therapeutic.¹ But a cohort of depressed patients failed to improve despite adequate serum drug levels for seemingly adequate durations of treatment. These patients did respond, however, and did so dramatically, to electroconvulsive treatment.² By examining patients’ psychopathology, the researchers discerned the presence of delusional thoughts as a common feature.

The presence of psychosis became a marker of differential treatment response. By 1985, we knew that antidepressant drugs alone (mostly tricyclic antidepressants) resulted in a 34% improvement rate in depressive symptoms. Antipsychotic drugs resulted in a 50% improvement rate, increasing to 70% with both medication classes together.³ Similar differential improvement rates are reported in more recent assessments.^{4,5}

The efficacy of ECT in psychotic depression is best seen in the National Institute of Mental Health (NIMH)-supported 4-hospital CORE study of ECT in patients with major depressive disorder.⁶ The study assesses the merits of continuation ECT and continuation pharmacotherapy after a successful course of ECT. The patients receive bitemporal ECT at 1.5× the calibrated seizure threshold 3 times a week. The remission criterion is a greater than 60% reduction on the 24-item Hamilton Rating Scale for Depression to 10 or less for 1 week (before assignment to either of the 2 continuation treatments).

Of the overall sample of 253 patients, 217 (86%) completed the full trial. Remission of depression was achieved in 87% of the completers (75% of the overall intent-to-treat sample). Seventy-seven (30%) met Structured Clinical Interview for DSM-IV criteria for psychotic depression. The remission rate was 83% for the nonpsychotic depressive patients and 95% for the psychotic depressed patients. And, the time to remission was shorter for the psychotic depressed than the nonpsychotic, with 53% achieving full remission by 7 or fewer ECT treatments, and 75% by the 10th ECT treatment.

Psychosis is a marker of differential treatment response among depressed patients, warranting either ECT or the combination of an antipsychotic and an antidepressant for effective treatment. For effective patient care in depression, identifying the presence of psychosis is essential.

But are such patients identified and “adequately treated” before referral? In an examination of the records for adequacy of prior medication trials in the 3-hospital collaborative ECT study program,⁷ only 2 of 52 patients with psychotic depression had received adequate medication trials (combined antipsychotic and antidepressant

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drug trials at effective dosages for 6 or more weeks). This finding reflects failure to identify those with psychotic depression or the lack of an effective treatment regimen.

How are we to define “therapy resistance” in depression? Is the failure of patients to respond to 2 or more treatment trials, “adequate” in duration and dosing, sufficient for such a designation? Almost all patients referred for ECT fail multiple treatment trials until “the last-resort” option is recommended. Almost all treatment algorithms include ECT as the fourth or later option in successive treatments.⁸ Such designations are also common for bipolar disorder and schizophrenia.

Psychotic depression is a chronic disabling disorder with a high mortality rate. It is not responsive to antidepressant treatments alone, but it does remit with ECT and does so rapidly. Were ECT a pill or a single surgical intervention, it would be considered a primary treatment for psychotic depression. But it is not a pill, and its proper administration requires repeated inductions of anesthesia. Societal and professional stigma associated with its use has relegated ECT to the last-resort option.

Safety is a consideration. Because treatments are given under professional supervision of psychiatrist, anesthesiologist, and nurse, the treatment is remarkably safe. There are no absolute contraindications to its use, and modern practice has lessons on how to manage ECT even in the presence of severe systemic illnesses.⁹

But the stigma of ECT and the reiterated complaints that it brings prolonged memory effects that some patients and some psychologists find intolerable are severe hurdles that need to be overcome. The public perception of ECT, as the treatment pictured in *The Snake Pit* and *One Flew Over the Cuckoo's Nest*, needs to be changed.

Another complication in this assessment is the description of “ECT-resistant depression.”¹⁰ On the basis of such reports, some therapists argue that even if ECT is effective in the short-run, its high relapse rate makes its use inefficient. But these reports come mainly from studies that use inefficient forms of ECT. An NIMH-supported 3-hospital program¹¹ reported a 55% recovery rate, with relapse rates of 84% (placebo), 60% (nortriptyline alone), and 39% (nortriptyline and lithium combination) in continuation treatment. Almost all the treatments were given as low-energy electric currents through unilateral electrode placements, treatments that are now known to be ineffective.¹²

Even at higher energies, unilateral electrode placement is inefficient. At 8× the calibrated seizure threshold, treatment with unilateral electrode placement elicited a 60%

antidepressant response rate, compared with a 73% rate for bilateral ECT (at 1.5× seizure threshold).¹³ The authors claim “no significant difference in response,” a conclusion that is not supportable since the sample size is too small (N = 40 for unilateral and N = 37 for bilateral) to discern the probable difference.

The failure to offer effective ECT is a better explanation of the poor clinical results and high relapse rates in studies that label their failures as “ECT resistant.”

CONCLUSIONS

Diagnostic tools need to be refined to assure better identification of psychotic depression and its effective treatment. In treatment algorithms, ECT is a late consideration, usually after 3 or 4 medication trials have failed. Such prescription leads patients to months of medication trials, suffering, loss of employment, and the possibility of suicide. It is a high-risk option. Perhaps it is timely to reconsider the place for ECT in treatment algorithms for psychotic depression, even to consider it as a primary treatment, especially in those with suicidality, severe weight loss, insomnia, and agitation.

The greater responsiveness to ECT of patients with psychotic depression, a more severe form of nonpsychotic depression, is counterintuitive. How can this observation be explained? Psychotic depressed patients exhibit greater degrees of neuroendocrine abnormality in cortisol and thyroid metabolism. With ECT, these abnormalities are reversed, and their reappearance heralds a recurrence of the illness. Such observations are the basis for a neuroendocrine explanation of the mode of action of ECT.¹⁴ They are also the basis for the ongoing clinical trials with mifepristone (a central nervous system glucocorticosteroid antagonist) in psychotic depression.¹⁵ Were these trials to be successful in treating psychotic depression, they may provide a chemical equivalent to ECT.

The report of a remarkable and rapid responsiveness of patients with psychotic depression to bilateral ECT encourages its greater consideration as the treatment for this disorder and encourages its reassessment in treatment algorithms. The stigma of ECT is a significant hurdle that needs to be overcome to be able to offer patients effective and safe treatment.

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