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Invited commentary

Separating psychotic depression from nonpsychotic depression is essential to effective treatment

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The report of a 92% efficacy rate for patients with psychotic depression compared to a 55% response rate for patients with nonpsychotic depression treated with ECT is a hallmark of modern psychiatric therapy (Birkenhäger et al., 2003). The findings are all the more impressive because they replicate the 95.5% remission rate for the same patient population reported from the four-hospital collaborative study group known as CORE (Petrides et al., 2001). In a sample of 253 severely depressed patients, 77 met SCID criteria (First et al., 1996) for psychotic depression and 176 for nonpsychotic depression. Bitemporal ECT was standardized across the centers and remission was defined as a persisting reduction in $HAMD_{24}$ scores from greater than 60% to below 10. The remission rate for nonpsychotic depression was 83% for an overall remission rate of 87%.

These remission rates with ECT contrast favorably with the 30–40% rates for antidepressant drugs alone, and the 60–70% rates for combinations of antidepressant and antipsychotic drugs for this population (Kroessler, 1985; Parker et al., 1992; Vega et al., 2000).

Studies of psychotic depression enlighten our understanding of therapy-resistant depression, urge a more rational consideration of ECT in treatment algorithms, and increase our understanding of the mechanism of action of ECT.

In treating depressed patients with imipramine in which serum levels were well controlled, Kantor and Glassman (1977) were puzzled when 14 of 21 (66%) nondelusional depressed patients responded, but only 3 of 13 (23%) psychotic depressed did so. When the ten psychotic depressed patients were treated with ECT, nine remitted. Their observations encouraged the re-examination of an Italian study in which 437 depressed patients were treated with 200–350 mg/day imipramine for a minimum of 25 days (Avery and Lubrano, 1979). Of these, 247 (57%) remitted. Most of the 190 nonremitters were also psychotic, and when these were given ECT, 156 (72%) remitted. In the next few decades, the two treatments—ECT and the combination of high doses of an antipsychotic and an antidepressant medicine—were established as effective for psychotic depression (Kroessler, 1985; Parker et al., 1992; Vega et al., 2000).

Therapy resistant depression (TRD) is a puzzling disorder. In pharmacotherapy, the efficiency of medi-

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cations differ according to psychopathology, medication dosing, tolerance, and metabolism. But a common basis for TRD is the unidentified presence of psychosis, and the prescription of inappropriate treatment. Such errors are common since the recognition of the psychotic form of depression is difficult. In a research study of depressed patients treated with ECT at three academic hospitals, Mulsant et al. (1997) reported that only 4% of patients referred for ECT had received adequate trials of medication. Recognition of psychotic depression and its effective treatment will materially reduce the TRD population.

Ever since the discovery that psychiatrically ill patients exhibit gross abnormalities of neuroendocrine functions, the most compelling findings have come from patients with psychotic depression. These patients have the highest levels of serum cortisol and greatest resistance to its suppression with exogenous steroids as measured in dexamethasone suppression tests. The tests normalize when patients are adequately treated (Fink, 2000). Such abnormal neuroendocrine functions and the differential response rates to antidepressant drugs encouraged Schatzberg and Rothschild (1992) to argue that psychotic depression is a unique psychopathologic entity. They have recently treated patients with psychotic depression with mifepristone, a glucocorticoid receptor antagonist, reporting a rapid reduction in both psychosis and depression (Belanoff et al., 2001). These findings are the first suggestion of an effective alternative to ECT.

Treatment algorithms for psychiatric illnesses are fashionable and take on an authoritative aura. The usual algorithm for depression begins with a doctor's choice medicine (Crimson et al., 1999). If the response is slow, an alternate antidepressant from a different chemical class is offered. Then, augmentation and combination tactics are recommended. When ECT is mentioned, it is 'after all else has failed'. Since each trial requires 4–6 weeks, the usual choices in a decision-tree offer inadequate treatment for 3–6 months or longer before ECT is considered. For patients with psychotic depression, such algorithms are tragic because they are associated with unrelieved misery and with suicide. Such failure is also unethical because the principles of justice and nonmaleficence require the prescription of the most effective relief, and ECT warrants consideration much earlier in treatment algorithms. In ECT texts, patients with psychotic depression meet criteria for the primary use of ECT (Fink, 1999; APA, 1990, 2001).

Neuroendocrine dysfunctions and their normalization with effective ECT suggest that these elements are central to the ECT process. Many authors consider the central action of ECT to be its impact on neurohumors, similar to that of antidepressant drugs. But such an association is incorrect. ECT is more broadly effective (e.g. relieving depression, psychosis, mania, catatonia, delirium). We lack replicable neurohumoral changes in ECT that relate to the clinical findings. By contrast, neuroendocrine measures are abnormal in psychiatric illnesses, normalize in remission, and become abnormal again during relapse. It is in the study of patients with psychotic depression that we have found the best elucidation of the ECT mechanism (Fink, 1999, 2000).

The reports by Birkenhäger et al. (2003) and Petrides et al. (2001) on the efficacy of ECT in psychotic depression justify careful consideration. Relief is readily available once psychotic depression is recognized. Such reports should encourage psychiatrists to re-assess their attitudes to ECT.

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