Introduction

The Use of Mood Stabilizers in the Treatment of Psychiatric Disorders

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The symposium that led to the interrelated scientific articles published in this issue accomplished 2 goals that should be of interest and utility to readers of *The Journal of Clinical Psychiatry*. Specific topics in the field of bipolar disorders are addressed with up-to-date information. These include treatment strategies for acute mania, bipolar depression, mood disturbances in schizophrenia, and diagnostic perspectives in the complex area of patients who have concurrent psychotic and mood symptoms. Kane's article on tardive dyskinesia reminds us that the recently introduced atypical neuroleptics provide notable advantages in reduced risk of extrapyramidal adverse effects over first generation neuroleptics despite their similar limitations in regard to full efficacy. Calabrese and Rapport's article on maintenance study design issues may seem technical for the reader who views himself strictly as a clinician, but the issues raised are highly relevant to important aspects of clinical care. Furthermore, it addresses the second goal that these articles achieve: raising the case for a more dimensional perspective on diagnosis and treatment selection in the spectrum of bipolar disorders.

The DSM is a powerfully useful system—principally in assuring that the criteria that we apply to arrive at a diagnosis are explicit and uniformly applied regardless of who or where we may be. However, in the case of bipolar disorder the strictly syndromal and cross-sectional approach tends to provide specificity at a cost of lost sensitivity. Here are 2 examples. To call a patient a rapid cycler, DSM-IV requires that consecutive episodes in the same mood direction be separated by at least 2 months of euthymia. However, many patients with a full array of positive symptoms of mania may have more than 1 episode within a week, or even within a day.[1,2] Similarly, DSM-IV designation of mixed mania requires that all of the symptoms needed for diagnosis of a major depressive episode be present for at least 1 week. Recent evidence consistently indicates that milder and shorter pure depressive symptoms in the context of a manic syndrome more accurately define this subgroup phenotypically in relationship to illness course and therapeutic responsiveness.[3,4]

Just as practicing psychiatrists led the initial interest in valproate and carbamazepine as alternatives to lithium treatment of bipolar disorder, they also are, in many ways, responsible for the current interest in dimensional constructs in diagnostic assessment. Rather than exclude from consideration the use of a mood stabilizer in a patient with schizophrenia or dementia, psychiatrists have shown interest in identifying core positive components of bipolar psychopathology and, on that basis, then adding mood stabilizers to the patient's regimen in a trial fashion. Particularly in the area of dementias, this practice has yielded a consistently positive series of reports regarding the efficacy of valproate and carbamazepine, either alone or in combination treatment. To date, most of these reports are limited to small open series, yet their consistency is impressive, and controlled trials are near the point of publication.[5] As a generalization, the common theme one sees in these reports is a focus on impulsive aggressive behavior.[5,6] These usually include episodic, labile onset and offset of verbal or physical aggression, and, frequently, various manifestations of motor hyperactivity. At present, terminology unfortunately varies across studies. However, there is clearly potential to use a refined dimensional definition of impulsive aggression as a guide to treatment decisions and a more clearly defined target set of behaviors expected to be ameliorated. Furthermore, there is some evidence that impulsive aggression may aid in fundamentally differentiating unipolar from bipolar depressions.[7]

A similar clinician-driven interest accounts for much of the broad use of neuroleptics in bipolar disorder and other nonschizophrenic disorders that may incorporate psychotic features. Although some authorities discourage other than very short-term use of neuroleptics in bipolar disorder, systematic descriptions of treatment practices in large series indicate that longer term use of neuroleptics is common.[8,9] Data consistently indicate that psychotic features are associated with poor prognosis in bipolar disorder, certainly with lithium-based treatment.[10] Maas et al.

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provide a cogent argument and data supporting the notion that neuroleptics are generically effective in psychotic states, rather than having specific antischizophrenic effects in a full syndromal sense.[11]

It is likely that the better adverse effect profile—albeit still far from ideal—of newer neuroleptics such as olanzapine and quetiapine are contributing to heightened interest in such applications just as the favorable adverse effect profile of divalproex compared with lithium has affected use in impulsive aggressive states.

Consider also the dilemma posed by recurrent major depression. Both investigators and clinicians understand that some percentage of persons with depressive episodes fundamentally suffer from bipolar disorders but cannot be so diagnosed in the absence of a manic or hypomanic episode. Illness course and family history criteria suggest characteristics that may sharpen early correct diagnosis and therapeutic intervention. The features that are more associated with bipolar disorder than with unipolar depression include early age at onset, high episode frequency, a strong family history of mood disorders, subthreshold hypomanic symptomatology, and greater psychomotor impairment (Swann AC, Bowden CL, Dilsaver SC, et al., unpublished data, 1998), as well as more specific disruption in noradrenergic metabolism.[12] Application of some constellation of these features holds the potential for fundamentally correct early identification and treatment, rather than waiting until full syndromal diagnostic criteria are met.

It is not likely that dimensional constructs such as these will fully displace syndromal and categorical diagnosis, but the evidence is strong that greater application of dimensional diagnostic approaches can enhance the effectiveness of our therapies in psychiatric disorders.[13] Furthermore, such strategies are also likely to advance our knowledge regarding disturbances in biological systems that are fundamental to the pathophysiology of serious mental disorders.

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