What Do We Know for Sure About Bipolar Disorder?

This year's first issue of *The American Journal of Psychiatry* features four reports dealing with bipolar disorder. Two of the reports study possible etiologic mechanisms. Green et al. present the results of a search for gene loci and a specific candidate gene for the transmission of bipolar disorder. They utilized two pedigrees that showed co-segregation for the transmission of a rare genetically transmitted skin disease: Darier's disorder. They found a locus for a highly penetrant gene for bipolar disorder that agrees with findings from other studies, the 12q23-24 locus. However, the procedures used were unable to locate the gene(s) despite finding overlapping loci in affected individuals in two pedigrees sharing both Darier's disorder and the occurrence of bipolar disorder.

A second study of the P50 wave response to paired auditory stimuli found decreased inhibition in patients with a history of schizophrenia relative to comparison subjects as well as impairment—less in severity but significant—in bipolar disorder patients who had a history of psychosis. These differences were unaffected by current clinical state, severity levels, or medication status. The investigators, Olincy and Martin, found nonpsychotic bipolar disorder patients in general no more impaired than healthy subjects in this putative physiological measure of the capacity to filter incoming stimuli. The authors point out that of the chromosome loci found for the transmission of schizophrenia and bipolar disorder, eight have been found to overlap (including chromosome 15, associated with psychosis), while one has been found only related to schizophrenia. Two chromosomes (including the 12q23-24 locus) have been found to be associated with only the transmission of bipolar disorder. These two studies advance our knowledge of the gene loci possibly associated with phenotypes of bipolar disorder and psychosis, but they leave a vast array of questions and work to be done.

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Two other papers deal with significant issues relating to the clinical management of bipolar disorder. One—a comparative study of insomnia between patients with bipolar disorder, patients meeting the diagnostic criteria for primary insomnia, and good sleepers—found that depending on the self-report measure used, 55%–70% of stable, medicated bipolar disorder patients meet the criteria for insomnia. Yet in this bipolar patient group, Actigraph studies suggested that the same patients slept longer than both comparison groups. These patients also showed decreased activity during the daytime as well. The bipolar disorder patients reported greater anxiety related to sleep and inability to stop thinking when it was time to sleep. Harvey et al. suggest that given data concerning the effectiveness of cognitive therapy approaches to sleep-related anxiety, such techniques may well improve the life quality and rates of relapse of the disorder—which remain quite high despite advances in pharmacologic management—by improving sleep quality and duration in bipolar disorder patients.

A second clinical study focuses on management of the increasingly recognized comorbidity of attention deficit disorder and bipolar disorder. Scheffer et al. point out the hazards of addressing comorbid attention deficit disorder symptoms with stimulants or certain antidepressant medications in terms of inducing mood cycling and worsening of the overall course of illness. They present a study showing that prior stabilization with divalproex followed by the use of methylphenidate for the treatment of attention

deficit disorder symptoms appears to help both conditions with no increased risk of mood cycling during the acute treatment period of 8 weeks or over a 12-week follow-up period. While the follow-up period could be longer to assure the maintenance of a positive result and mood stabilization, the data are valuable given the increasing evidence of significant impairment associated with attention deficit disorder symptoms as well as symptoms of bipolar disorder.

The etiologic studies reporting genetic transmission for the vulnerability to bipolar disorder (as well as overlapping vulnerability to other affective disorders and even schizophrenia) and the relationship of psychophysiological measurements to the presence of psychosis across both bipolar and schizophrenic disorders raise interesting questions about the pathophysiology underlying and distinguishing these conditions. The clinically focused papers raise an entirely new concern that could contribute to more successful management of bipolar disorder as well as provide evidence indicating the possibility of safely addressing significant bipolar comorbidity, which could improve outcomes.

Together these studies also point to the vast areas of ignorance that still exist in our understanding of the causes of bipolar disorder and areas of improvement in the therapeutic management of bipolar disorder that have yet to be discovered. What do we really know about bipolar disorder? We certainly know the course of the illness, the high likelihood of relapse and recurrence over the lifespan, the proportion of time people with this disorder are symptomatic over time (with depression occupying 46.6%–55.8% of weeks of follow-up [1]), the continued liability of recurrence over the lifespan (2), and the continued risk of suicide (3).

While presenting new possibilities for increased understanding and better management, this series of articles most obviously illustrates the need for more research into the causes and treatment of bipolar disorder. We have only scratched the surface with the work that has been done, and what we know for sure about bipolar disorder remains all too limited.

References

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