



Psychotic Symptoms also Contribute to the Uncertain Positioning of Bipolar Disorder

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INTRODUCTION

Bipolar disorder is classically described as clinically significant episodes of depression and elevated mood mania or hypomania interspersed with periods of normal mood resting states. Depending on the duration and severity of mood improvement, a distinction is made between type I and type II bipolar disorder. Indeed, the profile of bipolar disorder is complex and heterogeneous both longitudinally and cross-sectionally, and includes mixed mood states, persistent mood instability, and cognitive impairment. In the case of mood swings, features consistent with psychotic moods delusions and hallucinations may occur. Although present in only a minority of patients, psychotic symptoms describe an early term for manic-depressive psychosis.

DESCRIPTION

Psychotic symptoms also contribute to the uncertain positioning of bipolar disorder within the psychiatric classification, which is placed between schizophrenia and other mood disorders. Significant morbidity of bipolar disorder results primarily from depressive episodes and is frequently comorbid with anxiety disorders and substance abuse. The prevalence, morbidity, mortality and costs associated with bipolar disorder are important goals for effective treatment and ideally prevention in psychiatry. Pharmacology is the mainstay of treatment for all three stages of bipolar disorder (mania, depression, and prophylaxis). The first-line treatment for mania is antipsychotic drugs. Different treatments showed that olanzapine and risperidone had the best efficacy and tolerability profiles. A subsequent update of the literature included several new anti-manic drugs, but reached broadly similar conclusions. Bipolar depression is often long-term and difficult to treat and requires a different approach than unipolar depression. Evidence for effective interventions is limited, and network meta-analyses have reached conflicting conclusions, depending on how studies

were included. There is widespread consensus that quetiapine, olanzapine, antidepressants, lamotrigine, and lurasidone have some efficacy but variable tolerability. Relative efficacy has not been well demonstrated in these analyses. Several recent clinical studies not included in these meta-analyses open new avenues for the treatment of bipolar depression.

There is evidence that the atypical antipsychotic lurasidone may be particularly effective in mixed features of bipolar depression, and preliminary data support the use of armodafinil as add-on therapy. Intravenous ketamine as an add-on therapy to mood stabilizers has shown the potential to produce rapid but often transient antidepressant effects. Finally, recent studies highlight that electroconvulsive therapy remains a useful option for treatment-resistant bipolar depression. Lithium remains the most effective and well-studied monotherapy for preventing relapses in bipolar disorder. Lithium in combination with olanzapine, risperidone, and valproate was significantly superior to placebo in preventing manic episodes, and lamotrigine was superior to placebo in relapsing depression. When considered separately, valproate was no different from placebo. The efficacy of lithium must be weighed against its many side effects and potential toxicity.

CONCLUSION

A better understanding of the mechanism of action of lithium and other potent drugs should generate targets and support new drug development. For example, inhibition of inositol monophosphatase by lithium led to the evaluation of the putative lithium analogue ebselen, which shares this property. Bipolar disorder is undergoing a transition from descriptive psychopathology and incidentally discovered treatments of limited efficacy and tolerability to more effective etiologies and treatments based on a rational understanding of pathophysiology. It illustrates the challenges and opportunities facing psychiatry as it belatedly makes the transition.

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