Bipolar Depression and Cognitive Impairment

Shared Mechanisms and New Treatment Avenues

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KEYWORDS

• Neuropsychology • Mood disorders • Aging • Brain function • Health behavior

KEY POINTS

- Depressive symptoms and cognitive impairment together account for most disability experienced by people with bipolar disorder.
- Bipolar depression and cognitive impairment seem to share neurobiological determinants, such as inflammation, as well as behavioral risks, such as sedentary lifestyles.
- Novel treatment avenues that may jointly target depression and cognitive impairment include pharmacologic agents and modification of health behavior.

INTRODUCTION

For many years, bipolar disorder (BD) was not believed to be associated with durable cognitive problems. A return to normal cognitive function was believed to be one of the main distinguishing features of BD compared with schizophrenia. However, over the past 15 years, scores of studies have accumulated to indicate that BD is associated with clinically significant cognitive impairments evident both during mood episodes and during clinically euthymic periods. Collectively, depressive symptoms and cognitive impairment account for most of the disability produced by BD. There remains a great need for efficacious treatments targeting either bipolar depression or cognitive dysfunction. Emerging research has shifted away from efforts to parse cognitive deficits from mood symptoms toward examining their shared neurobiological mechanisms, behavioral determinants, and treatment avenues.

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PREVALENCE AND DISTRIBUTION OF COGNITIVE IMPAIRMENTS IN EUTHYMIC PATIENTS

The distribution of cognitive deficits in BD, as with most aspects of this illness, is heterogeneous and complex. Approximately 40% to 60% of patients with BD show clinically significant cognitive impairment.[1] Thus, although cognitive impairment may enact a marked impact on functioning at the population level in BD, global cognitive impairment is not evident in approximately half of patients. Within the BD spectrum, there is some evidence that risk of cognitive impairment varies by diagnostic subtype and clinical features. Some studies[2] have found that cognitive deficits are more prominent in patients with bipolar I versus bipolar II disorders, although this finding is not consistent.[3] A history of psychotic features, more common in bipolar I compared with bipolar II, is also associated with a greater likelihood of cognitive impairment.[4]

Some cognitive abilities seem more affected by BD. In meta-analyses that have examined cognitive performance in euthymic patients compared with performance in healthy control individuals,[5,6] deficits are apparent at medium to large effect sizes in the areas of verbal memory, executive function, processing speed, and sustained attention. In contrast, vocabulary, naming, and verbal fluency abilities are generally observed to be comparable with those of healthy comparators. A recent study by Burdick and colleagues[7] used cluster analysis to indicate that roughly 40% of patients showed normal cognition, 30% showed selective deficits in verbal memory, processing speed, attention, and social cognition yet with normal functioning, and 30% were globally cognitively and functionally impaired.

An increasing number of studies have investigated domains of cognition that extend beyond traditional neuropsychological foci, such as social cognitive abilities. In a recent meta-analysis in euthymic patients across a range of social cognition measures,[8] deficits were present in theory of mind and emotional reasoning tasks, whereas basic emotion recognition tasks were preserved.

COMPARISON OF COGNITIVE DEFICITS IN BIPOLAR DISORDER WITH THOSE IN OTHER PSYCHIATRIC ILLNESSES

Compared with schizophrenia, the neuropsychological deficits of BD seem to be less severe and more selective. The rate of global cognitive impairment in schizophrenia is 90%, and a meta-analysis of cognitive function comparing schizophrenia with BD[9] reported a mean difference between these disorders of about a half of a standard deviation, with individuals with BD performing better. Severity distinctions compared with unipolar depression are less clear and seem to vary by clinical state and medication status. For example, one study[10] indicated greater impairment in unmedicated unipolar depressed patients compared with patients with bipolar II disorder. Another longitudinal study[11] found evidence of increased dysfunction in patients with bipolar I after treatment of acute depression but similar cognitive test performance during acute depression, and, in another study,[12] similarities in brain activation between bipolar and unipolar acutely depressed patients were seen. Thus, the balance of evidence indicates that on a spectrum of cognitive impairment, BD is intermediate between unipolar depression and schizophrenia, particularly when comparing across mood disorders in euthymic states.

STUDIES OF THE SHORTER-TERM EFFECT OF BIPOLAR DEPRESSION ON COGNITIVE FUNCTION

Several studies have evaluated cognition in samples of patients with BD during the presence of active depressive symptoms versus euthymic or hypo/manic states.