Brief report

Neuropsychological performance predicts clinical recovery in bipolar patients

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Abstract

Background: Although a number of investigations have reported cognitive deficits in patients with bipolar disorder, relatively few have focused on the relationship between these impairments and clinical outcome.

Methods: In order to help clarify the pattern of and extent to which cognitive deficits are present at the onset of illness and their relationship to outcome, we examined 26 bipolar patients during their first hospitalization and 20 psychiatrically healthy control subjects. All subjects completed tests of frontal/executive control, psychomotor speed and memory function at baseline and self-reports of clinical recovery (time to recover in days) at 12 months post study enrollment.

Results: At baseline, first episode bipolar patients demonstrated greater deficits relative to control subjects on neurocognitive measures, and a significant association was detected between time to recover and performance on a measure of frontal/executive function (interference condition of the Stroop; $p = .05$; derived interference: $p = .04$). A trend towards significance was also demonstrated between time to clinical recovery and verbal fluency ($p = .06$).

Conclusions: These findings indicate that neuropsychological deficits are seen early in the course of bipolar disorder, prior to the effects of multiple or prolonged episodes, and may be associated with clinical outcome. Future studies are needed to determine whether changes in inhibitory processing or other cognitive function predict clinical outcome or are associated with treatment response.
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1. Introduction

Bipolar disorder has been associated with significant and often persistent impairment in cognitive function (Altshuler, 1993) however, the relationship of these cognitive deficits to clinical outcome has not been well documented. Several investigations have reported cognitive deficits which are suggestive of impairments in executive function, attention, memory and psycho-motor speed (Gourovitch et al., 1999; Dupont et al., 1995), yet relatively little research has focused on how these deficits relate to course of illness. It has been hypothesized that the cognitive deficits present in patients with bipolar disorder are due to residual effects caused by repeated or prolonged affective episodes, however, it is possible that these functional changes represent core features of the illness (Nordenson et al., 2004). Moreover, some studies have reported a progressive decline in cognitive performance over time while others have not, raising the question of whether these deficits are present at the onset of the illness (Altshuler, 1993). Several

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investigations have reported that bipolar patients with a more severe course of illness and higher numbers of affective episodes experience greater cognitive decrements (van Gorp et al., 1998; Kessing, 1998; Denicoff et al., 1999), and that specific variables including age of onset, duration of illness and number of hospitalizations are associated with this neurocognitive profile. Given the importance of understanding the relationship between clinical symptoms and cognition to assess the potentially predictive value of cognitive variables with regard to functional recovery, recent studies have begun to examine neuropsychological performance of bipolar patients at variable points in their illness.

In an investigation by Rubinsztein et al. (2000), investigators compared the performance of 14 bipolar patients in full or partial remission to that of 12 healthy control subjects on a battery of neurocognitive tests, which included a pattern and spatial recognition task, a delayed matching to sample task, and the One Touch Tower of London task, a spatial problem solving task (Elliott et al., 1996). Euthymic bipolar patients performed significantly worse on both the pattern and spatial recognition tasks as compared to controls and made more errors on the delayed matching to sample task. Performance was significantly correlated with total number of months of hospitalization, underscoring the importance of examining the associations between clinico-demographic factors and neurocognitive variables. In a study designed to assess the relationship between course of illness and neurocognitive function, Denicoff et al. (1999) examined 49 bipolar outpatients using a battery of tests, which included measures of inhibitory function (Stroop), verbal fluency (Controlled Oral Word Association Test [COWAT]), verbal learning and memory (California Verbal Learning Test [CVLT]), attention/vigilance (Continuous Performance Test [CPT]), psychomotor speed (Grooved Pegboard), executive function (Wisconsin Card Sorting Test [WCST]) and visual scanning/set maintenance (Letter Cancellation Test [LCT]). The authors reported that duration of symptoms was significantly predictive of the number of perseverative responses on the CVLT, total response time and number correct on the CPT, and performance on the LCT. Similarly, Zubieta et al. (2001) observed a negative correlation between executive function as measured by the WCST, and the number of past affective episodes and hospitalizations due to mania in bipolar I subjects. In a study by Lebowitz et al. (2001) bipolar patients with a history of multiple manic episodes generated significantly fewer words on a phonemic fluency task and made more errors on phonemic and semantic verbal fluency tasks than patients experiencing their first manic episode

and healthy controls. Other investigations have reported inverse correlations between sustained attention and number of affective episodes and hospitalizations (Clark et al., 2001). Psychomotor speed has also been shown to be associated with number of past depressive episodes (MacQueen et al., 2001). In a study of euthymic bipolar patients, El-Badri et al. reported that the while total number of affective episodes was significantly related to cognitive impairment in multiple domains, no significant association was detected between cognitive performance and duration of illness or age of onset (El-Badri et al., 2001). In a recent study by Frangou et al. (2005), remitted bipolar patients showed impairment on a range of tasks requiring executive function relative to control subjects and found that duration of illness predicted loss of inhibitory control (Frangou et al., 2005). Finally, Nehra et al. examined cognitive performance in a group of euthymic bipolar patients following their first episode relative to euthymic multiple episode bipolar patients and control subjects (Nehra et al., 2006). While the study reported that overall, first episode patients performed more poorly than multiple episode patients or controls, multiple episode patients demonstrated significantly worse performance on a subtest of executive functions, specifically perseverative errors on the WCST task, than either of the other two groups. Further, multiple episode patients also achieved lower overall scores on a memory scale than the other groups, raising the question of progressive cognitive impairment with repeated clinical episodes.

These investigations indicate a significant relationship between neurocognitive impairments and clinical variables, including frequency of affective episodes and number of hospitalizations. No study thus far has examined patients during their first hospitalization to document prospectively the relationship between neurocognitive performance and recovery. We examined bipolar patients during their first hospitalization, and hypothesized that compared to normal control subjects, even after becoming clinically stable, these patients would show deficits on neuropsychological tests sensitive to executive function. Further, it was hypothesized that that deficits in cognitive performance would be predictive of clinical recovery, therefore, we examined the extent to which performance on these measures was related to rehospitalization status and time to recover (in days) at 12 months post study enrollment.

2. Methods

Forty six subjects were enrolled in this neuropsychological protocol which included 26 patients admitted