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Improving the understanding of the link between cognition and functional capacity in schizophrenia and bipolar disorder

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ABSTRACT

Objective: Deficits in cognitive functioning are related to functional disability in people with serious mental illness. Measures of functional capacity are commonly used as a proxy for functional disabilities for cognitive remediation programs, and robust linear relationships between functional capacity and cognitive deficits are frequently observed. This study aimed to determine whether a curvilinear relationship better approximates the association between cognitive functioning and functional capacity.

Method: Two independent samples were studied. Study 1: participants with schizophrenia (n = 435) and bipolar disorder (n = 390) aged 18–83 completed a neuropsychological battery and a performance-based measure of functional capacity. Study 2: 205 participants with schizophrenia (age range = 39–72) completed a brief neuropsychological screening battery and a performance-based measure of functional capacity. For both studies, linear and quadratic curve estimations were conducted with cognitive performance predicting functional capacity scores.

Results: Significant linear and quadratic trends were observed for both studies. Study 1: in both the schizophrenia and bipolar participants, when cognitive composite z-scores were >0 (indicating normal to above normal performance), cognition was not related to functional capacity. Study 2: when neuropsychological screening battery z-scores were >−1 (indicating low average to average performance), cognition was not related to functional capacity.

Conclusions: These results illustrate that in cognitively normal adults with serious mental illness, the relationship between cognitive function and functional capacity is relatively weak. These findings may aid clinicians and researchers determine who may optimally benefit from cognitive remediation programs, with greater benefits possibly being achieved for individuals with cognitive deficits relative to individuals with normal cognition.

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1. Introduction

Cognitive deficits are a prominent and stable feature of many patients with serious mental illness, and, in addition to mood and psychotic symptoms, account for high rates of disability and service utilization. Patients with schizophrenia average between one to three standard deviations below the mean of normal comparison subjects across a wide range of cognitive domains (Heinrichs and Zakzanis, 1998; Saykin et al., 1991). These cognitive deficits have been found to pre-date illness onset (Allen et al., 2003), thus suggesting impairment in cognition may be a core feature of the pathophysiology of the disorder irrespective of positive and negative symptoms typically attributed to illness severity.

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Although cognitive and functional impairment appear to be key features of severe mental illnesses, they may not be universal. For example, although most patients experience neuropsychological deficits, approximately 20–25% of patients with schizophrenia have been found to have neuropsychological function within normal limits (i.e., not greater than 1 standard deviation from average performance) (Malhi et al., 2007; Palmer et al., 2009). This is even more characteristic of patients with bipolar disorder, with an estimated prevalence of 57% performing within normal limits on neuropsychological assessments (Gualtieri and Morgan, 2008). Similarly, whereas the vast majority of patients with schizophrenia and bipolar disorder show reduced rates of employment and independent living (Depp et al., 2012), other patients exhibit milder functional impairments. Given this variability in both cognitive and functional outcomes, it is imperative to determine how deficits in cognitive functioning relate to functional disability in people with serious mental illness.

Recent studies suggest that cognitive functioning may be differentially related to functional outcomes depending on the severity of the cognitive impairment. For example, one recent study of community dwelling adults with schizophrenia found that a supported employment + cognitive remediation intervention had significantly better employment outcomes than supported employment alone, but only among lower functioning participants (Bell et al., 2014). These results suggest that improvements in cognitive functioning are not associated with universal gains in functional outcomes, but rather that cognition may be more strongly related to functional outcomes among individuals with more severe cognitive impairment. In other words, a differential relationship on treatment outcome appears to exist as a result of the association between cognition and functioning.

The aim of the current study was to test whether cognitive function is more strongly related to functional capacity in persons with more severe cognitive impairment, a relationship which, to our knowledge, has not been previously tested. We tested linear and quadratic trends using two independent samples of patients with schizophrenia and a sample of patients with bipolar disorder. To assess functional capacity, we used the UCSD Performance-Based Skills Assessment-Brief (USPA-B) (Mausbach et al., 2007) as our primary outcome measure. We hypothesized that a linear relationship would provide valuable estimations of this relationship; however, we further postulated that a curvilinear relationship would be more accurate in improving model fit. A curvilinear relationship suggests that as cognitive functioning improves, it's relationship to functioning becomes weaker. If a curvilinear relationship between cognitive functioning and functional capacity is confirmed, this may indicate there are ceiling effects for the UPSA-B and a more sensitive instrument of assessing functional capacity is needed for patients with higher levels of cognition. Additionally, a curvilinear relationship may indicate that cognitively normal patients have the capacity to be functionally normal as well.

2. Method: Study 1

The aim of this study was to examine the nature of the relationships between neurocognition and everyday functioning in a sample of adults with schizophrenia and a sample of adults with bipolar disorder. This study used a Neurocognitive Composite Score to measure neurocognitive ability and the UPSA-B to measure functional capacity.

2.1. Participants

Eight hundred and twenty-five individuals diagnosed with serious mental illnesses were included in this study, including 435 participants having a diagnosis of schizophrenia and 390 having a diagnosis of bipolar I disorder. All participants were enrolled in a parent study in the Epidemiology–Genetics Program in Psychiatry at the Johns Hopkins School of Medicine, as well as a subsequent study of clinical and neuropsychological factors associated with daily functional outcomes. Participants are of full or mixed Ashkenazi Jewish background, which was determined from ancestry of four grandparents. Participants were enrolled in the parent study between 1996 and 2006, at which time diagnosis was determined. Diagnosis was obtained by skilled clinicians (master's or Ph.D. level) using the Diagnostic Interview for Genetic Studies (Nurnberger et al., 1994), as well as collateral review of medical records and informant reports by at least two clinicians (Ph.D. or psychiatrist). The procedures for the consensus diagnosis are described in detail elsewhere (Chen et al., 2009; Fallin et al., 2003, 2004, 2005). The follow-up study of genetic study participants was conducted between 2007 and 2012 and focused on neurocognition and functional capacity. At this time, participants who were diagnosed with schizophrenia, schizoaffective disorder or bipolar disorder in the parent study were contacted regarding participation in the follow-up study. The study protocol was approved by the Johns Hopkins Medicine Institutional Review Board, and all participants provided written informed consent. The assessments were completed in participant's homes or in residential outpatient treatment settings.

2.2. Measures

2.2.1. Neurocognitive ability

Estimated premorbid intelligence was assessed with the Wide Range Achievement Test (WRAT; Jastak, 1993) Reading subtest. A Neurocognitive Composite Score (NCS) was used to assess neurocognitive ability. The NCS battery of tests was administered to measure executive functions, attention, verbal working memory, episodic learning, verbal fluency, and information processing speed. The NCS included the following: total learning from trials 1 to 5 on the Rey Auditory Verbal Learning Test (RAVLT; Schmidt, 1996), total time on Trail Making Test Parts A and B (Reitan and Wolfson, 1993), number of correct responses on WAIS-IV Letter Number Sequencing and Digit Symbol Coding (Wechsler, 2008), total unique correct responses on Animal Fluency (Spreen and Strauss, 1998), perseverative errors standard score from the 64-card computerized Wisconsin Card Sorting Test (Heaton et al., 1993), and Continuous Performance Test Identical Pairs Version, 4-digit condition, d-Prime (Cornblatt et al., 1988). Raw scores were adjusted for age, gender, and education on the basis of published normative data. Variables were transformed to equally weighted standardized scores (z-scores; Mean = 0, SD = 1) and averaged to obtain the NCS.

2.2.2. Functional capacity

The UCSD Performance-Based Skills Assessment, Brief version (UPSA-B; Mausbach et al., 2007) was used to assess functional capacity. The UPSA-B is a measure of functional capacity that measures two domains of functioning: finances and communication (Mausbach et al., 2007, 2010; Patterson et al., 2001). During the *Finance* subtest, participants are required to role-play various financial tasks, such as counting change and paying a utility bill. The *Communication* subtest requires participants to role-play exercises using an unplugged phone (e.g., make an emergency call, dial a number from memory, call and reschedule a doctor's appointment). The UPSA-B takes approximately 10–15 min to complete, and scaled scores range from 0–100, with higher scores indicating better functional capacity. Psychometric properties for the UPSA-B are very good (Mausbach et al., 2007, 2009; Velligan et al., 2013), including high test-retest reliability and correlations with the full-length version of the UPSA (Patterson et al., 2001).

2.2.3. Clinical symptoms

The Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987) was used to assess symptoms of psychopathology. The total Positive and Negative domain scores were used in this study, with higher scores indicating greater severity of symptoms. Depressive symptoms were assessed with the Beck Depression Inventory-II (BDI-II) (Dozois et al., 1998) and manic symptoms were assessed with the PANSS-

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