Emotion perception and executive functioning predict work status in euthymic bipolar disorder

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**A B S T R A C T**

Functional recovery, including return to work, in Bipolar Disorder (BD) lags behind clinical recovery and may be incomplete when acute mood symptoms have subsided. We examined impact of cognition on work status and underemployment in a sample of 156 Euthymic-BD and 143 controls (HC) who were divided into working/not working groups. Clinical, health, social support, and personality data were collected, and eight cognitive factors were derived from a battery of neuropsychological tests. The HC groups outperformed the BD groups on seven of eight cognitive factors. The working-BD group outperformed the not working-BD group on 4 cognitive factors composed of tasks of emotion processing and executive functioning including processing speed and set shifting. Emotion processing and executive tasks were predictive of BD unemployment, after accounting for number of mood episodes. Four cognitive factors accounted for a significant amount of the variance in work status among the BD participants. Results indicate that patients with BD who are unemployed/unable to work exhibit greater difficulties processing emotional information and on executive tasks that comprise a set shifting or interference resolution component as compared to those who are employed, independent of other factors. These cognitive and affective factors are suggested as targets for treatment and/or accommodations.

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1. Introduction

Functional recovery in Bipolar Disorder (BD) has been shown to lag behind recovery from clinical symptoms and may still be incomplete when mood symptoms have subsided (Coryell et al., 1993; Goldberg et al., 1995a; Keck, 2006; Tohen et al., 2000). Only recently have predictors of functional impairment in the specific areas of daily functioning been examined, above using global rating scales that include assessment of mood symptoms. One poorly captured area of functional recovery concerns employment, despite BD being the 6th leading cause of disability world-wide in ages 18–44 year olds (Murray and Lopez, 1997). Several clinical factors, including number of psychiatric hospitalizations and past episodes are weakly related to disability and occupational outcomes in BD, and they have not entirely accounted for disability (Altshuler et al., 2007; Dickerson et al., 2004; Goldberg et al., 1995b; Gutiérrez-Rojas et al., 2011; Staner et al., 1997). Although treatments to limit hospitalizations and reoccurrence of mood episodes likely impact occupational status, it is not clear if or how they could have great clinical utility in specifically improving work related performance and functional independence in BD. Beyond these clinical factors, social supports (Leonardi et al., 2007; Vieta et al., 2007), personality (Bieling et al., 2003; Medard et al., 2010; Pope et al., 2007) and cognitive functioning have been associated with low functioning and disability in BD, although these results also have been modest in nature (for review see Sanchez-Moreno et al., 2009). Despite persistent cognitive deficits in the remitted BD state (Clark et al., 2005; Dixon et al., 2004; El-Badri et al., 2001; Fleck et al., 2005; Mann-Wrobel et al., 2011; Martínez-Arán et al., 2004a, b), the impact of cognitive deficits on occupational outcomes is largely understudied. This is in contrast to other disorders like schizophrenia, where cognition has been shown as a predictor of employment status (McGurk and Mueser, 2004). In a recent study, working memory/attention and speed of processing, were associated with occupational recovery, with cognitive improvements being highly predictive of work recovery three months later (Bearden et al., 2011). Prior studies have demonstrated that better cognitive functioning and less severe clinical symptoms were associated with higher employment status (full time vs. part time or volunteer status) among BD patients, not accounting for mood state (Dickerson et al., 2004; O’Shea et al., 2010). In one small
study, attention and fluency tasks predicted work/school recovery 12 months after initial stabilization from an acute mood episode (Jaeger et al., 2007). Self-report of executive functioning is weakly associated with unemployment status in veterans accounting for 1% of variance in employment (Altschuler et al., 2007). However, these previous studies are limited by small sample sizes, poor comparison groups, failure to account for current mood state, and/or use of broad measures of functioning that do not capture occupational status. Additionally, these studies have demonstrated weak predictive value, and have not indicated treatment targets that might improve recovery and functional independence in BD. The present study examined the impact of clinical factors, health-related quality of life, social support, personality, and cognitive factors on occupational work status in a sample of euthymic BD patients compared to a healthy control group. Identifying significant predictors might be useful in devising targeted clinical treatment plans (and possibly better accommodations within the workplace) for those with greater risk for persistent unemployment.

2. Method

2.1. Participants

Participants were recruited into the Longitudinal Prechter Study of Bipolar Disorder at the University of Michigan. Using the longitudinal cohort consisting of 586 participants, the present study included 156 individuals with a DSM-IV diagnosis of BD in the euthymic state (133 BD-I, 23 BD-II) and 143 healthy controls (HC). Recruitment of all participants, including HC, occurred from 2005 to 2010 through advertisements on the web and in the newspaper, an outpatient specialty psychiatric clinic, and an inpatient psychiatric unit. Participants with BD were excluded from the study if they had a history of schizophrenia or schizoaffective disorder depressive type, any active or current substance use disorder diagnosis, any medical illness specifically associated with depressive symptoms, or any first-degree family member who had been diagnosed or hospitalized for mental illness. All participants gave written informed consent prior to participation. This study was approved by the University of Michigan Institutional Review Board.

All participants underwent an evaluative using the Diagnostic Interview for Genetic Studies (DIGS, Nurnberger et al., 1994), neuropsychological testing, psychiatric symptom and psychosocial questionnaires, Hamilton Depression Rating-17 item (HDRS, Hamilton, 1967) and Young Mania Rating Scale (YMRS, Young et al., 1978). A best estimate process by at least three of the authors was used to confirm diagnoses. We used conservative criteria at the time of the neuropsychological evaluation to validate euthymic state (HDRS < 8) and YMRS (< 8).

Occupational data was obtained as part of the DIGS interview. The DIGS ascertains information on the participant’s current job and classifies it according to occupational categories (e.g., professional specialty, administrative support, unemployed, disabled, student). All participants were divided into two groups based on current working status: working and not working. Participants in the working group consisted of individuals who were currently employed full-time (any occupational category) or enrolled as a full-time student. All participants in the not working group consisted of those who were currently unemployed or were disabled. Unless on disability, information about why a participant was not working was not collected. Participants who were retired (n=12) or a “housewife” (n=8) were excluded to clearly delineate the two working/not working groups. Information on “volunteering” was not collected. In addition, the DIGS collects information about the participant’s most responsible occupational position (whether it was a past position or is their current position and based on the interviewer’s report of “most responsible” position) and those positions were classified using the same occupational category as current occupation. A discrepancy variable was created based on current work classification and most responsible work classification, which provided a measure of who defined in job class. For example, if a participant’s most responsible position was a “professional position” yet their current position is classified as “laborer,” they were considered to have declined in job class.

2.2. Clinical variables

Number of psychiatric hospitalizations, age at onset of first depression/manic/hypomanic mood episode, summation of number of mood episodes, years since first episode and comorbid psychiatric diagnoses (substance abuse/depression, anxiety disorders, eating disorders, and ADHD) taken from the DIGS were chosen based upon prior literature demonstrating that these factors have a potential impact upon functioning (Table 1). There were no significant differences between BD and HC groups for education, F(1, 263) = 12.73, p = 0.0009 and gender, X^2(1, N = 289) = 0.713, p = 0.47, but the BD group was significantly younger than the HC group, F(1, 261) = 13.34, p < 0.001, which is addressed specifically in later analyses, i.e., logistic regression. As expected, the HC had a significantly higher Global Assessment of Functioning (GAF) score than the BD group, F(1, 216) = 98.41, p = 0.001. Among the BD individuals, the only significant difference between the working and not working BD groups for comorbid psychiatric diagnosis was for presence of social phobia, X^2(1, N = 130) = 12.04, p = 0.001 with the not working BD group having a more individuals with a comorbid diagnosis of social phobia (n = 8) vs. the working BD group (n = 3). There were no working/not working BD group differences for total number of past psychiatric hospitalizations, F(1, 262) = 0.001, p = 0.99.

Individuals with BD were taking a number of medications across a range of classes. We examined the influence of medications by adopting a protocol often seen in the literature to assess total medication load. Antidepressant, anxiolytic, mood stabilizer, and antipsychotic medications were coded as absent = 0, low = 1, or high = 2, and converted each other (Hassel et al., 2008; Sackeim, 2001). Antipsychotics were converted into chlorpromazine dose equivalents (Davis and Chen, 2004). We generated a composite measure of total medication load by summing all individual medication codes for each individual medication within categories for each BD participant (Hassel et al., 2008). There were no significant differences between the comparison groups, failure to account for current mood state, and/or difference in ability to interpret each other’s (Hassel et al., 2008; Sackeim, 2001). Antipsychotics were converted into chlorpromazine dose equivalents (Davis and Chen, 2004). We generated a composite measure of total medication load by summing all individual medication codes for each individual medication within categories for each BD participant (Hassel et al., 2008). There were no significant differences between the comparison groups, failure to account for current mood state, and/or difference in ability to interpret each other’s medication regimens.

2.3. Measures

2.3.1. Neuropsychological assessment

Cognitive functioning was assessed via an extended neuropsychological battery focused heavily upon areas known to be adversely affected in BD: Rey-Osterrieth Complex Figure Test (Meyers and Meyers, 1995), California Verbal Learning Test-II (Delis et al., 2000), Purdue Pegboard test (Lezak, 1995), Executive Perception test (Green and Allen, 1997), Facial Emotion Perception test (Rapport et al., 2002), Wisconsin Card Sorting Test (Heaton, 1981), The Stroop Color and Word Test (Golden, 1978), the FAS verbal fluency task of the Controlled Oral Word Association Test and Animal Fluency (Benton and Hamsher, 1978), Digit Symbol from the Wechsler Adult Intelligence Scale-III (Wechsler, 1997), The Trail Making Test-Parts A and B (Armitage, 1946) and the Parametric Go/NoGo task (Langenecker et al., 2007a). Cognitive factor scores were created using standard data reduction techniques to reduce the tests using conceptually and theoretically categorized variables and based on existing knowledge regarding the cognitive constructs (Langenecker et al., 2010, for a full description). A confirmatory factor analysis was computed with the above variables, consistent with our prior work (Langenecker et al., 2010; Ryan et al., 2012). Although factor scores were used in main analyses, Supplemental Table S3 shows group differences for all neuropsychological tests and Supplemental Table S4 shows which cognitive subtests scores were included in each factor, including reliability of the factor scores. Reliabilities for seven cognitive factors with greater than three component variables were all strong. One factor is composed of only two variables; alpha reliability is not an appropriate metric for evaluation of that factor. The respective variables show moderate to strong internal validity using odd-even reliability estimates (Langenecker et al., 2007b). Eight factor scores were used; Auditory Memory, Visual Memory, Emotion Processing, Fine Motor Dexterity, and four executive functioning factors; Verbal Fluency and Processing Speed, Conceptual Reasoning and Set-Shifting, Processing Speed with Interference Resolution, and Inhibitory Control. Vocabulary and Word Fluency from the Wechsler Adult Intelligence Scale (Wechsler, 1999), which was used as a methodological evaluation for premorbid ability, was not significantly different between the diagnostic groups or the work status groups (p > 0.05; Table 1).

2.3.2. Psychosocial and personality measures

The following measures were followed as they have been associated with low functioning and disability in BD (Sanchez-Moreno et al., 2009), The Social Support and Undermining Scale (Abbey et al., 1985), a 17-item scale commonly used to examine relationship dynamics in stressful situations such as unemployment (Vivontur and Van Ry, 1993). The Short Form-36 item Health Survey (SF-36) is a 36-item scale that measures a variety of health concepts. The two summary composite scores (physical and mental health) and one of eight domains were used (Ware, 1996). The Revised NEO Personality Inventory (NEO-PI-R) captures five global dimensions of adult personality traits: neuroticism, extraversion, and openness to experience, agreeableness and conscientiousness (Costa and McCrae, 1992).
3.2. Relationship between clinical, personality and psychosocial variables and work status.

As shown in Table 1, BD participants in the not working group had greater number of mood episodes, lower GAF scores, and reported worse physical health on the SF-36 relative to the working BD group. There were no other significant differences between the working and not working BD participants on other clinical variables, including current mood symptoms on the HDRS and YMRS (p > 0.05), proportion with history of psychosis or between groups for any of the five personality factors or the rating

<table>
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<tr>
<th>Table 1: Demographic characteristics and psychosocial measures for the bipolar and healthy control groups. Data are presented as Mean (SD).</th>
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* Chi-Square. WASI = Wechsler Adult Scale of Intelligence; HDRS-17 = Hamilton Depression Rating Scale 17-item; YMRS = Young Mania Rating Scale; PCS = SF-36 Physical Health Composite Score from SF-36; MCS = SF-36 Mental Health Composite Score from SF-36; NEO = NEO Personality Inventory; VFPS = Verbal Fluency and Processing Speed; CRSS = Conceptual Reasoning and Set-Shifting; PSIR = Processing Speed with Interference Resolution; IC = Inhibitory Control.
of social support, \(F(8, 86) = 1.76, p > 0.09\). There were no significant differences between the working HC and not working HC group on measures of subjective health, social support, or any of the five personality factors, \(F(8, 112) = 1.19, p = 0.314\). Therefore, none of these variables were added as covariates in the comparison between groups for the cognitive factors. In a MANCOVA using work status and both diagnostic groups, both HC groups reported better subjective health, more social support, and lower scores on the NEO neuroticism relative to the BD groups, as well as higher scores on the NEO conscientiousness, \(ps < 0.001\).

A MANOVA with the eight cognitive factor scores as dependent variables and the four groups (working HC, not working HC, working BD, not working BD) as independent variables showed a significant group effect, \(F(24, 615) = 3.06, p < 0.001\). All but Auditory Memory showed significant group differences (\(p < 0.720\)). Post-hoc analyses showed that the working HC group performed similar to the not working HC group, except for lower scores on Visual Memory. The working HC outperformed both BD groups on the Fine Motor, Visual Memory, Verbal Fluency Processing Speed, Conceptual Reasoning Set-Shifting, and Processing Speed Interference Resolution factors and additionally the not working BD groups on the Inhibitory Control and Emotion Processing factors. The not working HC group was not significantly different from the working BD group on seven cognitive factors, performing better on Processing Speed Interference Resolution only. However, the not working BD performed worse than the not working HC on Fine Motor, Verbal Fluency Processing Speed, and Inhibitory Control factors (\(ps = 0.009, 0.004, < 0.001\)). The working BD group outperformed the not working BD group on the Fine Motor, Emotion Processing, Verbal Fluency Processing Speed and Processing Speed Interference Resolution factors (\(ps = 0.010, 0.006, 0.001, \) and 0.002) (Fig. 1). A second analysis was completed in the BD group only. When using age and number of mood episodes as a covariate in comparing the working and not working BD groups, a follow-up MANCOVA showed the same effects. The working BD group outperformed the not working BD group on the Fine Motor, Emotion Processing, Verbal Fluency Processing Speed, and Processing Speed Interference Resolution factors (\(ps = 0.041, 0.050, 0.006, \) and 0.020).

The sample size for the not working BD group was modest, consisting of individuals who were both unemployed and disabled. In a targeted post-hoc analysis, the unemployed group \((n = 13)\) did not perform significantly different from the the disabled group \((n = 20)\), \(F(8, 16) = 2.16, p = 0.09\) for the cognitive factors. There also were no differences between the two not working BD subgroups on any of the clinical or personality variables or the measure of social support \((ps > 0.077)\), suggesting that these groups were appropriate to combine for analyses into one group.

A logistic regression was used to evaluate the relative influences of significant variables (age, number of episodes, Fine Motor, Emotion Processing, Verbal Fluency Processing Speed, and Processing Speed Interference) in predicting work status among the BD patients (working BD vs. not working BD). A test of the full model with the six predictors against the constant-only model was significant, \(\chi^2(9, N = 107) = 36.40, \text{Nagelkerke } R^2 = 0.255\), indicating that the set of predictors reliably distinguished between working HC and working BD. The model correctly classified 69.2% of cases. Again, Processing Speed Interference Resolution made significant contributions above age and the other cognitive variables (Table 2) in predicting work status.

### 3.3. Job class stability/underemployment

Among the BD participants who were in the working group, 25 (25%) declined in job class as compared to their most responsible position (underemployed), compared to 30.1% in the working HC group. The BD patients who declined in job class were not significantly different from BD patients in the not working group in terms of their most responsible job ever held, \(\chi^2(5, N = 55) = 6.44, p = 0.27\), or in terms of premorbid verbal intellect, \(F(1, 108) = 3.845, p = 0.10\). However, those in the declined in job class group performed significantly better than those in the not working group on 3 of the 8 cognitive factors (Emotion Processing factor, \(t(48) = 2.00, p = 0.04\), Verbal Fluency Processing Speed, \(t(48) = 2.95, p = 0.005\), and the Processing Speed Interference Resolution, \(t(45) = 2.94, p = 0.004\)). Those in the declined in job class group had significantly fewer lifetime mood episodes than the not working BD, \(t(39) = -2.10, p = 0.04\), but overall there was no difference between the two groups on other clinical and psychosocial factors.

### 4. Discussion

Now, there is a limited understanding and few clinical tools that might be used to understand, predict, and improve life functioning, such as work status, in BD. The present study represents one of the few studies to show that specific aspects of cognitive dysfunction in euthymic BD are related to employment status using a well-powered sample, despite a more well-established literature base showing specific areas of cognitive dysfunction predicting employability in the schizophrenia population (e.g., attention, processing speed, and set-shifting) (McGurk and Mueser, 2004). Patients with BD who have better cognitive functioning are more likely to be employed. Those who are unemployed or unable to work exhibit greater difficulties in fine motor dexterity, processing emotional information, and on executive tasks comprising a set shifting or interference resolution component compared to BD patients who are gainfully employed. Cognitive factors, particularly those related to emotion processing, executive functioning, and auditory memory, account for a significant amount of variance in work status, independent of other clinical and demographic factors. BD patients have been shown to have greater dysfunction in the areas of executive functions, attention/concentration, and learning/memory compared to healthy controls (Martinez-Aran et al., 2004a,b), with persistent cognitive deficits in the remitted BD state (Clark et al., 2005; Dixon et al., 2004; El-Badri et al., 2001; Fleck et al., 2005; Martinez-Aran et al., 2004a,b); however, little is known about how these persistent deficits impact specific areas of functional outcomes. The current findings add to the few studies indicating that cognitive dysfunction may negatively impact the specific area of employment, but the strength of our findings is linked to having a comparison, nonworking control group, such that effects of unemployment in the BD group can be dissociated from the effects related to greater impact of illness. Further, findings are strengthened by having a large sample of BD patients with an ability to examine the proportion those being unemployed in the BD group compared to a non-affected unemployed group.
Not surprisingly, individuals with BD are less likely to be employed than controls with no psychiatric illness, but our findings indicate that patients with BD who maintained any employment, even if underemployed, exhibit greater cognitive dysfunction than their employed, non-affected healthy counterparts, consistent with recent findings that occupational recovery was associated with better cognitive performance (Bearden et al., 2011). Nearly 26% of the variance in our work status differentiation between diagnoses can be explained by cognitive factors. In particular, speed-related executive functioning measures appear to provide unique information in determining who falls into the employed diagnostic group. Bearden et al. (2011) found that working memory/attention and processing speed were associated with occupational recovery, though recovery was defined to include ratings of quantity and quality of work rather than a comparison of job position stability, which may account for differences in findings.

In addition to cognitive factors predicting who may have BD and who may be employed within the BD group, cognitive factors is related to whether a BD patient is able to maintain employment, regardless if they are underemployed. Employment was affected by emotional processing and executive functioning tasks that have set shifting or interference resolution components. Caution is warranted in over-interpreting these findings as our cross-sectional study and analytical model cannot determine if cognitive functioning is a cause of occupational disability or underemployment or if those who work experience beneficial effects on their cognition as a result. It is tempting to speculate that our results could indicate that BD patients who exhibit difficulties on the job may require assessment of cognitive skills as these may be areas for targeted treatment, accommodations and/or remediation. It may be possible for those who can improve cognitive skills to retain and maintain employment. Need for accommodations or remediation can be identified early in the course of illness, with the opportunity for significantly increased productivity, quality, and job retention. Although not directly addressed in the literature, maintaining any type of employment may provide cognitive or other therapeutic benefits.

This study has a number of strengths and a few limitations. Utilizing employment status as a functional outcome beyond using global assessment of functioning (GAF) scores provides more useful information to clinicians about a specific life domain in which specific treatments can be targeted. The GAF is heavily based on current symptomatology and combines symptoms with overall level of functioning. While using employment status can be seen as a strength of this study, actual employment status does not capture quality or stability of work performance, a particularly important area in understanding functional recovery and warrants future investigation. There are also numerous situational and environmental factors that affect employment that are not routinely captured in our ongoing longitudinal study, but would important to include in future follow up studies (e.g., unemployment rates, access to transportation, regional employment opportunities). We included a large, well-characterized sample of euthymic BD and a well-matched comparison group. Number of mood episodes did not contribute to the prediction of work status despite the not working BD group having significantly more lifetime mood episodes \(M=81.9\) than the working BD group \(M=30.9\) yet equivalent years with the BD illness. This suggests that the not working group may be a sicker group in general and a closer examination of more specific illness severity factors should be examined further in future studies. Our not working
groups, especially the not working HC group was small and may limit some of the generalizations of these findings. However, we have found that including such a small not working HC group, no matter how small, is relatively rare in the literature. As is common among most naturalistic studies of this kind, it is difficult to control for the effects of medication, treatment adherence, and treatment optimization. We evaluated the impact of medication confounds, using a protocol often seen in the literature and accepted by BD researchers to assess total medication load (Almeida et al., 2009; Hassel et al., 2008; Sackeim, 2001) and did not show effects of most medication classes on employment status or a relationship between medication loading and cognition. Our cross-sectional design prevents examination of intra-individual differences in cognitive functioning over time. Future studies could investigate whether changes in cognitive functioning associated with disease progression might be a marker of employment likelihood. Furthermore, information about why or how long participants have been unemployed or disabled was not available to us and having this information might provide valuable insight into other factors that may impact employment status.

4.1. Implications

Bipolar Disorder (BD) is a debilitating and chronic disorder with episodic symptoms. Despite clinical recovery, a substantial portion of BD patients are not working and this is well above the current levels of unemployment in the United States (Statistics, 2011), and a high number of BD patients are not working at their previous levels. Although the portion of unemployed BD patients is not substantially different from the control group, the cognitive factors related to unemployment status provide meaningful information. Treatment for BD generally focuses on clinical remission, but our results indicate that treatments should target areas of cognitive functioning as contributing factors to improve overall functional recovery, such as employability. These neuropsychological tools, with demonstrated ecological validity, can be used to determine the nature and responsiveness of treatment targets in an objective manner. A multidisciplinary approach to management of BD which integrates medication, psychosocial interventions and cognition would enhance functional recovery.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.psychres.2013.06.031.

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