Published in final edited form as:
Psychiatry Res. 2013 December 30; 210(3): . doi:10.1016/j.psychres.2013.04.006.

Everyday functional ability across different phases of bipolar disorder

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Abstract

Bipolar Disorder (BD) is a chronic illness characterized by significant neurocognitive impairment and functional deficits. Functional status is typically assessed with self-report or observer ratingslimited by poor participant insight and subjective judgment, while application of performance-based measures has been limited. We assessed functional ability in manic, depressed, and euthymic BD individualsusing the UCSD Performance-Based Skills Assessment (UPSA-2), which simulates real-world tasks such as medication management. UPSA-2 was administered to 17 manic or hypomanic BD, 14 depressed BD, 23 euthymic BD, and 28 healthy comparison (HC) participants matched for age, education, and IQ. Psychopathology was quantified with the Young Mania Rating Scale (YMRS), Hamilton Depression Rating Scale (HDRS), and the Positive and Negative Syndrome Scale (PANSS); executive functioning was assessed with the Wisconsin Card Sorting Task (WCST). All BD groups exhibited functional ability deficits on the UPSA-2 and impaired performance on the WCST compared to HC. UPSA-2 scores were lower in manic/hypomanic subjects relative to other BD participants and mania symptoms correlated with functional impairment. Poor WCST performance was also associated with worse UPSA-2 function. In summary, BD functional deficits occur across different phases of the disorder and may be impacted by symptom severity and associated with executive dysfunction.

Keywords

mania; depression; euthymic; everyday function; performance-based; neurocognitive

1. Introduction

Bipolar Disorder (BD) represents one of the leading causes of disability worldwide (The World Health Organization, 2001), creating a substantial economic burden driven by expensive medical care and lost productivity (Laxman et al., 2008). While BD was once primarily viewed as an episodic disorder with substantial recovery during remission, mounting evidence indicates people with this illness exhibit a poor prognosis distinguished by enduring cognitive impairment and functional decline (Martinez-Aran et al., 2007;

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Goodwin et al., 2008). Recent studies have found that over half of BD individuals experience persistent unemployment while 40% self-report impairment in social, cognitive, work, or household functioning (Tohen et al., 2000; Huxley and Baldessarini, 2007; Shippee et al., 2011). Prominent neurocognitive deficits in domains such as executive function persist during manic, hypomanic, and euthymic states (Bearden et al., 2001; Quraishi and Frangou, 2002; Savitz et al., 2005; Bora et al., 2009) and are predictive of disability in social relationships and vocational success (Wingo et al., 2009). Although standard neuropsychological tests remain the primary gauge of BD cognitive deficits, these measures are restricted by limited applicability to real-world functioning(O'Shea et al., 2010). While impaired everyday function has been reported across all phases of BD, most studies have used subjective and imprecise measures such as the Global Assessment of Functioning Scale (GAF) and/or relied on self-report and survey tools that do not control for demographic or socioeconomic factors (Sanchez-Moreno et al., 2009; Martino et al., 2011; Torres et al., 2011). Application of these techniques is particularly challenging for BD, where self-appraisal of functional status may be significantly biased by affective symptoms such as manic grandiosity or low self-esteem in depression. Recent initiatives such as the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) have emphasized the need to utilize objective, performance-based measures of treatment outcome, rather than the traditional reliance on reducing acute symptoms and improving standardized neuropsychological performance (Green et al., 2008). Over the past decade, a series of studies have quantified functional ability in schizophrenia using the UCSD Performance-Based Skills Assessment (UPSA) (Patterson et al., 2001a), a battery of performance tests designed to objectively assess everyday functioning across 5 domains representing real-life activities. A more recent version of the task, the UPSA-2 (Patterson, 2005), quantifies functional ability across 6 domains, including: 1) planning recreational activities, 2) finance, 3) communication skills, 4) transportation, 5) household skills, and 6) medication management. The UPSA is characterized by strong inter-rater and test-retest reliability (Patterson et al., 2001a; Patterson et al., 2001b; Leifker et al., 2010; Light et al., 2012), is highly correlated with neuropsychological deficits, and predicts real-life outcomes such as unemployment status, social and communication skills, and living independence (Twamley et al., 2002; Bowie et al., 2006; Mausbach et al., 2008; Bowie et al., 2010). Although initially designed to determine functional deficits in geriatric psychosis, the UPSA has also been administered successfully to younger cohorts (Heinrichs et al., 2006; Pietrzak et al., 2009), Swedish and Latino samples (Patterson et al., 2005; Harvey et al., 2009), drug-dependent individuals (Henry et al., 2010)and participants with Alzheimer's disease (Goldberg et al., 2010). It has been favorably compared to other measures of functional capacity and selected as the optimal marker of functional assessment by the MATRICS project (Moore et al., 2007; Green et al., 2011; Keefe et al., 2011).

In contrast to the extensive body of literature describing performance-based functional deficits in schizophrenia, relatively few reports have assessed similar measures in BD(McIntosh et al., 2011). Previous work indicates impaired functional performance in older BD patients (mean age 60–73 years), including a correlation between self-care and cognitive deficits in a direct observational study (Gildengers et al., 2007), impaired UPSA performance in a community-dwelling BD sample (Depp et al., 2009), and worse medication management ability (Depp et al., 2008). Other reports have used the brief version of the UPSA (UPSA-B), which tests everyday functioning in only two domains (finance and communication), to demonstrate that this performance-based measure predicts residential independence and work skills in both BD and schizophrenia (Bowie et al., 2010; Mausbach et al., 2010). However, functional ability has not been explicitly examined in different phases of BD using this performance-based measure, as existing studies have been conducted in euthymic individuals or did not specify participant mood state(Depp et al., 2009; Bowie et al., 2010). In addition, while variants of the UPSA task have been

administered to BD subjects, the full version of the battery has not been assessed in younger individuals. Thus, more work is required to determine the extent to which objectively quantified functional impairment represents a state- vs. trait-based phenomenon in this disorder, similar to existing reports of persistent neurocognitive deficits (Bora et al., 2009). Performance-based assessment of functional capacity during various illness states would serve as a useful adjunct to self-report data and improve the ability of the clinician to determine if BD patients are capable of functioning independently in the community.

The purposeof the current study was to assess everyday functional ability in manic, depressed, and euthymic adult BD subjects (mean age 34–39 years) using the UPSA-2 task. Previous work suggests that BD cognitive deficits and disability are most pronounced during affective episodes, but also persist during remission(Rosa et al., 2010). Therefore, we hypothesized that BD participants across all phases would exhibit functional deficits relative to healthy comparison subjects, but individuals in a manic or hypomanic state will exhibit the most pronounced functional impairment. We also administered the Wisconsin Card Sorting Task (WCST) as a neuropsychological measure of executive function. Given that impaired WCST performance in schizophrenia is associated with lower UPSA scores (Kurtz and Wexler, 2006), we hypothesized a similar association among BD subjects independent of the phase of their illness.

2. Methods

2.1 Participants

54 participants between the age of 18 and 60 who met SCID (Structured Clinical Interview for DSM-IV) criteria for BD were recruited from inpatient and outpatient psychiatric clinics located at the University of California San Diego (UCSD) Medical Center. We compared three groups of BD participants, including manic (n = 17), depressed (n = 14), and euthymic (n = 23) patients. Euthymic individuals did not meet criteria for current mania or depression, scored 12 or lower on the Young Mania Rating Scale (YMRS) and under 10on the Hamilton Depression Rating Scale (HDRS)(Tohen et al., 2002). Participants selected for the manic group were characterized by a YMRS score of 13 or higher and included 13 individuals who met criteria for a current manic episode (YMRS above 20) and four patients in the hypomanic range (YMRS 13 to 19). BD subjects in the depressed group exhibited moderate to severe depression at the time of testing defined by an HDRS score of 13 or higher and included 9 individuals who met criteria for a current major depressive episode. Approximately 9% of euthymic participants, 76% of manic participants, and 43% of depressed participants were recruited from an inpatient setting. 28 healthy comparison (HC) participants who had never met SCID criteria for an Axis I psychiatric disorder were recruited from advertisements in the San Diego community. All groups were matched for age, education, ethnicity, and had equivalent premorbid IQ as assessed by the Peabody Picture Vocabulary Test (PPVT) (Dunn and Dunn, 1997) (Table 1).

Participants were excluded for: 1) current alcohol or substance dependence, 2) a history of neurological conditions or head trauma, 3) treatment with electro convulsive therapy, 4) stroke, myocardial infarction, or cardiac disease, and 5) a positive result for cocaine, amphetamine, or PCP on a urine toxicology Rapid Drug screen (Pharmatic Inc., San Diego,CA) administered during the test session. All subjects provided written informed consent to the current protocol approved by the UCSD institutional review board.

2.2 Measures

UCSD Performance-Based Skills Assessment (UPSA-2)—The UPSA-2 (Patterson, 2005) is a performance-based instrument designed to assess the ability of individuals to

perform tasks in 6 areas requisite for successful everyday functioning, including: 1) comprehension and planning, 2) financial ability, 3) communication ability, 4) transportation, 5) household skills, and 6) medication management. Each type of task requires approximately 5 to 8 minutes to complete, for a total administration time of about 40 minutes. Participants receive a raw score for each subscale that is converted to a domain score ranging from 0 to 20 points. The 6 domain scores are summed to create a total UPSA-2 score between 0 and 120, with higher scores indicating improved performance.

The UPSA-2 begins by the examiner asking participants to read a fictional article about the opening of a theme park. Comprehension and planning skills are assessed by having individuals describe the park activities and select items required for a trip to the recreational facility. The finance portion of the test includes counting change (e.g., purchasing an item at a store) and reading a utility bill. Communication skills are assessed by role-play tasks with an unplugged telephone and include rescheduling a medical appointment. The transportation domain involves reading and interpreting a generic bus route and planning the use of a public bus system. Household skills are evaluated by having subjects examine a mock pantry of food items to prepare a shopping list. Finally, participants are asked to plan out a medication routine using 4 different drugs taken over the course of one day (i.e., arranging how the medications should be administered together or separately, with or without meals, etc.).

Wisconsin Card Sorting Task (WCST)—To assess cognitive performance, participants were administered the Wisconsin Card Sorting Test-64 Card Version (WCST-64) (Heaton, 1993), a measure of executive function. The WCST constitutes a set shifting task that quantifies the ability to demonstrate cognitive flexibility in response to altering schedules of reinforcement. It is a rule-generation paradigm designed to assess frontal functions that include strategic planning, goal-directed behavior, and perseverative behavior, a tendency to engage in repetitive and maladaptive responses linked to frontal cortex pathology (Goldberg and Miller, 1986; Perry and Braff, 1998). Participants are required to sort cards based on three distinct dimensions (color, shape, and number) and are provided feedback to enable identification of the correct matching rule. The card sorting category changes after a number of correct responses. Dependent measures include 1) total number of errors, 2) perseverative errors, and 3) number of categories completed. Perseverative responding is represented by a failure to abandon the previous sorting rule when it has been explicitly changed (e.g., from shape to color). Error scores for the task are converted to T scores corrected for age and education, where a higher T score indicates improved performance.

Clinical Assessment—Symptom severity was assessing using three scales, the YMRS, HDRS, and the Structured Clinical Interview – Positive and Negative Syndrome Scale (PANSS)(Bech et al., 1975; Young et al., 1978). The YMRS is a widely used interview-based scale consisting of 11 items rated on 5 defined grades of mania, including elevated mood, pressured speech, decreased need for sleep, irritability, and increased motor activity. The HDRS is a 17 item semi-structured interview rating scale that evaluates depressed mood, cognitive symptoms of depression, and comorbid anxiety. The PANSS consists of a 30 item rating scale that determines the extent of “positive” psychotic symptoms that include paranoia, hallucinations, or unusual thought content, “negative” symptoms that include flat affect, emotional withdrawal, and lack of spontaneity, and miscellaneous symptoms of general psychopathology that include anxiety, poor attention, and somatic concerns.

2.3 Statistical Analyses

Statistical analyses were performed using SPSS and data were examined for normality of distribution and homogeneity of variance. Transformations were conducted as needed to

limit skew and kurtosis values to between −1 and 1 for UPSA-2 variables (reflected $\log_{10}$ for total score, medication and financial domains; reflected square root for transportation and household scores). UPSA-2 performance across the four groups (HC, euthymic BD, manic/hypomanic BD, depressed BD) was assessed using multivariate analysis of variance (MANOVA), followed up by univariate ANOVAs for the total score and each of the 6 domains. Group differences in clinical ratings and WCST scores were also evaluated using univariate ANOVAs. Since the manic group had a higher proportion of male subjects (chi-square = 8.0, p = 0.05), gender was also included as a covariate in the UPSA-2 analyses. Post hoc differences were examined using Bonferroni-adjusted multiple t-test comparisons and effect sizes assessed with Cohen's d.

Spearman's rho was used to compare relationships between the UPSA-2 and scores on the YMRS, HDRS, PANSS, and WCST with the level of significance set to P<0.05. We also examined the correlations between functional capacity and BD illness characteristics such as age of onset, illness duration, and number of hospitalizations. While all BD participants were evaluated with the YMRS, two subjects in the manic group were not administered the HDRS, while four participants (2 BD, 2 comparison subjects) were not administered the PANSS. Seven subjects out of 82 did not complete the WCST task, while neuropsychological data was collected for 26 HC, 22 euthymic BD, 13 manic BD, and 14 depressed BD subjects. Potential medication effects were examined by comparing UPSA-2 data in BD individuals treated solely with antipsychotic drugs, those receiving only mood stabilizers, and patients withboth types of medication. To examine the impact of dopamine antagonists on functional capacity, the doses of antipsychotic medications were converted to chlorpromazine equivalents and the correlation between medication dose and UPSA performance was assessed with Spearman's rho. The most common antipsychotic medications included risperidone, aripiprazole, and quetiapine. Given that the manic and depressed BD cohorts were characterized by a mix of inpatient and outpatient recruitment, we also compared UPSA-2 performance between inpatient and outpatient participants in each group using the nonparametric Mann-Whitney test.

3. Results

The MANOVA performed for the UPSA-2 data indicated a main effect of group [$F(21,222) = 2.5$, $P < 0.01$]. Subsequent univariate ANOVAs revealed significant group differences for the total UPSA-2 score [$F(3,78) = 14.9$, $P < 0.001$] and in communication [$F(3,78) = 8.1$, $P < 0.001$], comprehension [$F(3,78) = 8.9$, $P < 0.001$], and medication management [$F(3,78) = 8.6$, $P < 0.001$] domains, with a trend towards disparity in the finance task [$F(3,78) = 2.2$, $P = 0.09$] (Table 2). No differences were observed for transportation or household skills. Post hoc tests indicated that healthy comparison subjects exhibited higher performance on the total UPSA score and the comprehension task relative to all the BD groups, regardless of mood state($P < 0.05$). We observed a large effect size for comparisons between the HC and all three BD groups for overall UPSA performance (Cohen's d between 1 and 1.6) and between the HC and manic participants for the communication and medication tasks (d = 1.4 to 1.5). Effect sizes were in the medium to small range for differences between the HC and BD groups in the financial, transportation, and household domains (d = 0.2 to 0.7). Manic individuals performed more poorly overall compared to both the euthymic and depressed BD, with significant deficits in medication management versus the other two patient groups, along with a trend towards lower financial performance relative to healthy comparison subjects ($P = 0.10$). Notably, euthymic BD subjects did not differ from the depressed participants on any UPSA measure, although both demonstrated lower functional ability as measured against the comparison subjects. Participant gender was not a significant factor for any UPSA domain and did not affect the outcome when included as a covariate. Outpatient participants in the manic group (n = 4) did not differ from inpatient manic participants (n =

13) on UPSA-2 performanceas assessed with Mann-Whitney, and the mean total UPSA-2 score was similar for both groups (outpatient =82, inpatient = 81). Inpatient BD depressed participants (n = 6) exhibited slightly better comprehension scores compared to outpatient BD depressed participants (n = 8) ($P<0.05$), but did not differ on the total UPSA-2 score or any other domain.

As expected, there was a main effect of group on all the symptom rating scales administered, including the YMRS [$F(3,78) = 98.2$, $P< 0.001$], HDRS [$F(3,74) = 70.8$, $P< 0.001$], PANSS total score [$F(3,75) = 31.5$, $P< 0.001$], PANSS positive symptoms score [$F(3,75) = 35.1$, $P< 0.001$], and PANSS negative symptoms score [$F(3,75) = 11.4$ $P< 0.001$] (Table 1). Post hoc tests indicated significant differences among the four groups on most measures, with predictably higher YMRS scores in the manic group($P< 0.001$) and the highest HDRS score in depressed BD participants relative to all the other groups ($P< 0.001$). Across all BD subjects, total UPSA-2 performance was negatively correlated with the YMRS score (rho = −0.34, P< 0.05), while impaired medication management was associated with higher ratings on the YMRS (rho = −0.34, P< 0.05), PANSS total score (rho = −0.32, P< 0.05) and PANSS positive score (rho = −0.29, P< 0.05). For BD euthymic subjects alone ($n = 22$), we observed a negative correlation between HDRS and both the total UPSA ($r = −0.46$, $P< 0.05$) and medication ($r = −0.43$, $P<0.05$) scores, indicating that higher depression ratings associated with worse function. We did not observe any correlation between functional ability and BD age of onset or number of hospitalizations, although longer duration of illness was weakly associated with lower scores on the household task ($r = −0.30$, $P< 0.05$). Medication did not significantly impact UPSA-2 performance in this cohort and we did not observe any relationship between the dose of antipsychotic treatment and functional capacity. BD groups exhibited impaired WCST performance relative to comparison, including more total errors [$F(3,71) = 5.4$, $P< 0.01$], more perseverative errors [$F(3,71) = 6.6$, $P< 0.01$], and fewer categories completed [$F(3,71) = 6.5$, $P< 0.01$], but did not differ from each other. For all participants, worse WCST performance (lower T scores) was associated with lower total UPSA-2 scores and lower scores in all domains, with the exception of household skills (Table 3). For BD subjects alone, poor WCST scores were also significantly correlated with impaired overall function and lower scores on the medication management domain.

4. Discussion

Despite major therapeutic advances, individuals with BD frequently exhibitchronic functional and cognitive impairment (Bora et al., 2009; Martino et al., 2011). While some patients achieve effective functional recovery, it is estimated that between 30% and 60% of BD individuals demonstrate marked disability in social, work, and family interactions (Sanchez-Moreno et al., 2009). Consequently, clinicians are often faced with the difficult task of determining patient capacity to function independently and subjective evaluation on measures such as the GAF is often inadequate (Roy-Byrne et al., 1996). Everyday functioning has been commonly evaluated by rating scales that review more defined aspects of employment, living independence, and social interaction (Tohen et al., 1990; Gitlin et al., 1995), but these methods may also be limited by variable precision and poor participant insight. Recent work indicates that performance-based measures are an effective means of predicting real-world independent living ability (Moore et al., 2007; Mausbach et al., 2009) and may be particularly useful in evaluating treatment efficacy and clinical outcome for BD patients uniquely affected by diverse state- and trait- based pathology (Mausbach et al., 2010). The findings from the current study indicate that BD participants demonstrate impaired functional ability across all phases of the disorder relative to healthy comparison subjects matched for age, education, and premorbid IQ. Notably, subjects ina manic or hypomanic state also exhibited significantly lower performance on the total UPSA score and the medication management portion of the task compared to the euthymic or depressed

groups, indicating support for state-based effects. While many factors are reported to influence functional outcome in this disorder, including age of onset, illness duration, medication side effects, and number of hospitalizations (Martinez-Aran et al., 2007), previous work is inconsistent (Mann-Wrobel et al., 2011) and these variables were generally not predictive of UPSA-2 performance in the current cohort. Group differences were not observed in the household skills and transportation domains and effect sizes were smaller for these tasks, consistent with other applications of the UPSA paradigm (Depp et al., 2009; Henry et al., 2010). It is possible that the restricted score range in the household task (0–4 points) may limit observation of group differences in this domain (Henry et al., 2010), while greater familiarity with bus schedules(several BD subjects self-reported frequentuse of buses as their primary transportation) may influence the results in this portion of the battery. Overall UPSA performance was congruent with prior work. Depp and colleagues (2009) reported that older euthymic BD individuals received a total score of 78.5 on a 5-domain 100-point UPSA version. When normalized to the same scale, the total score for our current euthymic BD sample was 77.4, while the healthy comparison subjects received a slightly lower mean total score of 86.9 (vs. 92.6 in the Depp study) (Depp et al., 2009).

Several studies have included the UPSA in attempts to construct path analysis models that define the complex relationship among neurocognitive deficits, psychopathology, functional ability, and real-world functional outcomes (Bowie et al., 2006; Bowie et al., 2010). UPSA performance is strongly correlated with both neuropsychological impairment and real-world disability, while less consistently related to symptom severity (Bowie et al., 2010). The association between clinical variables and UPSA scores may also depend significantly upon participant age and background. In older schizophrenia patients, poor UPSA performance correlates specifically with elevated negative symptoms on the PANSS (Patterson et al., 2001a; Kasckow et al., 2008). In contrast, both positive and negative symptoms were related to worse functioning in a heterogeneous sample of middle-aged BD outpatients where illness phase was not specified (Mausbach et al., 2010). Depp and colleagues (2009) also noted that UPSA scores in a euthymic BD sample were not significantly correlated with depression ratings, but that study did not include use of the YMRS (Depp et al., 2009). In the current report, we observed that more severe manic symptoms were linked to worse UPSA performance across all BD subjects, suggesting that mood state, especially during acute and severe affective episodes, does appear to be a factor on this performance-based measure. Contrary to Depp et al., (2009), our data also indicates a negative correlation between HDRS depression and both the total UPSA score and medication domain in our euthymic group, although interpretation of this finding is tempered by the relatively small sample size.

It has been recently proposed that functional deficits, similar to cognitive impairment, represent an endophenotype for severe mental illness, including schizophrenia and BD (Harvey et al., 2011). Although the link between genetic factors, functional ability, and real-world functioning has yet to be elucidated, our findings support the endophenotype concept insofar as demonstrating that functional declineoccurs to some extent in a state-independent manner. Similar to previous reports, we also observed impaired WCST performance in both euthymic and manic/depressed BD groups relative to healthy comparison participants. These data correspond with numerous studies indicating that cognitive deficits persist in euthymic BD and strong associations exist between neurocognitive and functional deterioration in this population(Savitz et al., 2005; Moore et al., 2007; Bora et al., 2009). Our data also show that poor performance on the WCST was correlated with worse function across most UPSA domains in all participants and with impaired medication management in BD participants. These results support earlier work indicating that more errors on the WCST are associated with lower UPSA scores across multiple functional domains in schizophrenia patients and drug-dependent individuals (Henry et al., 2010; Lysaker et al., 2011). It is important to note,

however, that UPSA performance appears to associate with multiple cognitive abilities, including processing speed and attention/working memory, in addition to executive functioning (Twamley et al., 2002; McClure et al., 2007; Bowie et al., 2008). While the WCST is a set-shifting task traditionally considered to be an indicator of cognitive flexibility, it does not constitute a comprehensive measure of neurocognitive impairment or fully address other faculties that may impact UPSA performance. The WCST-medication management relationship in BD participants may suggest that arranging a complex medication routine represents asuperior analog of executive functions (strategic planning, efficient goal-directed behavior), but administration of a more comprehensive neuropsychological battery in future studies would assist in clarifying this finding. BD is characterized by marked anomalies in frontal cortex, including decreased neuronal density and reduced cerebral blood flow (Drevets et al., 1997; Rajkowska et al., 2001), that could potentially mediate defective WCST performance and also play a role in everyday functional impairment(Frangou et al., 2005; Lovstad et al., 2012). As many other factors may influence both phenomena, future studies that combine neuroimaging, neuropsychological assessment, and performance-based functional measures will help to elucidate the underlying neurobiological mechanisms.

There are a number of limitations to consider in the interpretation of the current data. The size of the clinical sample was relatively small and included a mixed sample of inpatients and community-dwelling outpatients, so other factors associated with acute hospitalization besides mood state may have a significant impact on this performance-based measure. We did not observe evidence of worse functioning in inpatients compared to outpatients in either the manic or depressed BD group, although the small sample size precludes drawing a definitive conclusion. Previous studies have been restricted to stable outpatient samples with mild symptoms (Depp et al., 2009; O'Shea et al., 2010), but are conversely limitedby the inability to generalize findings to acutely symptomatic BD individuals. Various reports have also used different criteria to define euthymia in BD, including limits on the upper bound of the YMRS score that can range from 6 to 12 (Suppes et al., 2005; Dickerson et al., 2007). While euthymia was more liberally defined in the current study as YMRS ≤ 12, other work assessing performance-based deficits in BD use more stringent definitions (e.g., YMRS ≤ 8) (O'Shea et al., 2010). There fore, while our current data confirm earlier reports of functional deficits in BD remission, the results could be more significantly impacted by the presence of residual mood symptoms. Future studies with larger sample sizes to assess differential mood states in both outpatient and inpatient samples will be useful to confirm the contribution of these factors to functional ability.

In conclusion, a cross-sectional sample of manic, depressed, and euthymic BD individuals exhibited impaired functional ability on the UPSA-2 compared to a healthy comparison group. Deficits in functional ability were correlated with poor performance on the WCST and more severe manic symptoms. These data support previous self-report and survey findings that indicate functional deficits are pervasive among people with BD and appear across the spectrum of the disorder. Objective performance-based measures such as the UPSA-2 could be utilized to assess BD treatment efficacy and assist in determining patient capacity to function real-world settings.

Acknowledgments

This manuscript was supported by a grant from the National Institute of Mental Health (NIMH) (R01-MH071916).

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Table 1

Description of demographic factors and clinical variables for healthy comparison (HC) (n = 28), euthymic bipolar (BD) (n = 23), manic/hypomanic BD (n = 17), and depressed BD subjects (n = 14). Premorbid IQ was quantified with the Peabody Picture Vocabulary Test (PPVT) and psychiatric symptoms assessed with the Young Manic Rating Scale (YMRS), Hamilton Depression Rating Scale (HDRS), and the Positive and Negative Syndrome Scale (PANSS).

Parameter	HC	Euthymic BD	Manic/hypo BD	Depressed BD	Group Differences
Age (years)	**34.9 ± 11.3**	**39.2 ± 8.7**	**33.8 ± 11.4**	**34.4 ± 8.7**	**ns**
Gender (male/female)	**11 M, 17 F**	**8 M, 15 F**	**13 M, 4 F**	**6 M, 8 F**	**b,** *D*
Education (years)	**14.4 ± 2.0**	**15.0 ± 2.3**	**13.8 ± 2.0**	**13.8 ± 1.8**	**ns**
Ethnicity (n)					**ns**
Caucasian	**17**	**13**	**16**	**10**	
Latino	**4**	**2**	**0**	**1**	
African-American	**5**	**8**	**1**	**3**	
Asian	**2**	**0**	**0**	**0**	
BD Duration of Illness		**10.8 ± 8.1**	**10.7 ± 7.6**	**9.1 ± 8.6**	**ns**
BD Age of Onset		**28.5 ± 9.1**	**22.5 ± 6.9**	**25.4 ± 9.3**	**ns**
Number of BD Hospitalizations		**2.5 ± 3.0**	**3.2 ± 2.7**	**3.6 ± 4.4**	**ns**
Medication					
Antipsychotic alone		**8**	**3**	**2**	
Mood stabilizer alone		**9**	**3**	**5**	
Antipsychotic + Mood stabilizer		**4**	**7**	**5**	
Other medications		**2**	**2**	**0**	
Not medicated		**0**	**2**	**2**	
PPVT	**102.8 ± 11.8**	**98.3 ± 13.0**	**101.0 ± 17.3**	**104.3 ± 14.4**	**ns**
YMRS	**0.7 ± 1.5**	**5.8 ± 4.0**	**25.7 ± 8.7**	**6.7 ± 4.1**	*A,B,C,D,F*
HDRS	**1.9 ± 2.1**	**5.6 ± 2.7**	**9.9 ± 5.2**	**20.1 ± 6.2**	*A,B,C,***d**,*E,F*
PANSS Total Score	**33.0 ± 2.9**	**45.3 ± 9.0** †	**77.0 ± 27.0**	**64.1 ± 18.9**	*B,C,D,E*
PANSS Positive Symptoms	**7.9 ± 1.2**	**11.0 ± 2.4**	**21.8 ± 8.3**	**12.3 ± 3.8**	*B,***c**,*D,F*
PANSS Negative Symptoms	**7.8 ± 1.0**	**8.0 ± 1.0**	**14.3 ± 6.6**	**12.4 ± 6.6**	*B,C,D,***e**

Data are shown as the means ± standard deviation.

Significant differences between individual groups are denoted as follows;

(a,b,c,d,e,f $P < 0.05$; A,B,C,D,E,F, $P < 0.01$).

A HC and euthymic BD

B HC and manic BD

C HC and depressed BD

D euthymic and manic BD

E euthymic and depressed BD

F manic and depressed BD.

† indicates a trend towards a difference between the labeled BD group and HC ($P < 0.1$).

Table 2

Description of functional assessment on the UCSD Performance-Based Skills Assessment (UPSA-2) and cognitive performance on the Wisconsin Card Sorting Task (WCST) for healthy comparison (HC) (n = 28), euthymic bipolar (BD) (n = 23), manic/hypomanic BD (n = 17), and depressed BD (n = 14) subjects. WCST total and perseverative errors are presented as T scores where a higher score indicates improved task performance.

Measure	HC	Euthymic BD	Manic/hypo BD	Depressed BD	Group Differences
UPSA-2 Total Score	**104.3 ± 4.8**	**92.9 ± 11.5**	**81.3 ± 20.9**	**94.9 ± 11.8**	*A,B*,**c, f**
UPSA-2 Comprehension	**16.4 ± 2.4**	**13.4 ± 2.6**	**12.7 ± 3.4**	**13.2 ± 3.0**	*A,B,C*
UPSA-2 Financial	**18.5 ± 1.6**	**17.0 ± 3.0**	**15.6 ± 4.7** †	**17.0 ± 3.7**	**ns**
UPSA-2 Communication	**16.9 ± 2.3**	**14.5 ± 3.0**	**12.3 ± 4.1**	**15.0 ± 3.2**	**a,** *B*
UPSA-2 Transportation	**16.3 ± 2.3**	**14.7 ± 3.0**	**14.1 ± 4.8**	**14.6 ± 3.3**	**ns**
UPSA-2 Household skills	**16.8 ± 2.4**	**16.3 ± 2.7**	**14.4 ± 5.6**	**17.5 ± 3.2**	**ns**
UPSA-2 Medication	**18.8 ± 1.4**	**17.0 ± 3.2**	**12.3 ± 7.3**	**17.6 ± 3.0**	*B*,**d,f**
WCST Total Errors	**51.8 ± 8.7**	**43.1 ± 12.8** †	**37.9 ± 12.4**	**43.1 ± 10.5** †	*B*
WCST Perserverative Errors	**50.1 ± 8.9**	**40.5 ± 9.3**	**36.5 ± 12.7**	**45.2 ± 10.4**	*A,B*
WCST Categories completed	**4.2 ± 1.1**	**3.0 ± 1.6**	**2.2 ± 1.7**	**2.9 ± 1.6**	**a,** *B* **,c**

Data are shown as the untransformed means ± standard deviation.

Significant differences between individual groups are denoted as follows;

(a,b,c,d,f $P < 0.05$; A,B,C,C,D,F, $P < 0.01$).

A HC and euthymic BD

B HC and manic BD

C HC and depressed BD

D euthymic and manic BD

F manic and depressed BD.

† indicates a trend towards a difference between the labeled BD group and HC ($P < 0.1$).

Table 3

Spearman rho correlations between Wisconsin Card Sorting Task (WCST) measures and UPSA-2 domain scores for all participants and BD subjects separately. WCST total and perseverative error data are calculated as T scores normalized for age and gender. Higher T scores indicate improved performance (fewer errors) that was consistently associated with better function on the UPSA-2.

All Participants (n = 75)	WCST Total Errors T score	WCST Perseverative Errors T score	WCST Categories Completed
UPSA-2 Total Score	**0.43** ***	**0.43** **	**0.45** ***
UPSA-2 Comprehension	**0.44** ***	**0.40** ***	**0.48** ***
UPSA-2 Financial	**0.31** **	**0.41** ***	**0.40** **
UPSA-2 Communication	**0.31** **	**0.36** **	**0.30** **
UPSA-2 Transportation	**0.29** *	0.22	**0.30** *
UPSA-2 Household skills	0.05	0.08	0.11
UPSA-2 Medication	**0.51** ***	**0.52** **	0.51***

All BD Participants (n = 49)			
UPSA-2 Total Score	**0.29** *	0.25	0.27
UPSA-2 Comprehension	0.26	0.21	0.29
UPSA-2 Financial	0.17	0.27	0.21
UPSA-2 Communication	0.22	0.23	0.19
UPSA-2 Transportation	0.27	0.20	0.23
UPSA-2 Household skills	−0.04	−0.07	−0.12
UPSA-2 Medication	**0.46** **	**0.47** **	**0.38** **

Asterisks indicate significant correlations;

* $P < 0.05$

** $P < 0.01$

*** $P < 0.001$.