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Correlates of Real World Executive Dysfunction in Bipolar I Disorder

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Abstract

Background—Bipolar disorder is characterized by impairments in cognitive functioning, both during acute mood episodes and periods of euthymia, which interfere with functioning. Cognitive functioning is typically assessed using laboratory-based tests, which may not capture how cognitive dysfunction is experienced in real-life settings. Little is known about the specific illness characteristics of bipolar disorder that contribute to cognitive dysfunction in everyday life.

Methods—Participants met DSM-IV criteria for bipolar I disorder ($n = 68$) in a depressed or euthymic state. Everyday executive functioning was evaluated using the Behavior Rating Inventory of Executive Functioning (BRIEF) and the Frontal Systems Behavior Rating Scale (FrSBe). Participants completed clinician rated measures of mood state (Hamilton Depression Rating Scale, Young Mania Rating Scale), prior illness course and co-morbidities (Mini International Neuropsychiatric Interview), as well as self-report measures of psychotropic medication use and medical co-morbidity.

Results—Individuals in this study reported significant impairment in every domain of executive functioning. These deficits were associated with a multitude of illness factors, some directly impacted by mood symptoms and others shaped by illness chronicity, psychiatric comorbidity, medical co-morbidity, and medication use.

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Discussion—Executive functioning problems observed in everyday functioning in bipolar disorder are not entirely mood-state dependent. Cognitive rehabilitation for executive dysfunction should be considered an important adjunctive treatment for many individuals with bipolar disorder.

Keywords

executive function; bipolar; cognition

Introduction

Bipolar I disorder is characterized by episodes of mania and depression that interfere with psychosocial functioning. Rates of attainment of functional milestones are considerably lower in people with bipolar I disorder than the general population (Dean et al., 2004; Hirschfeld et al., 2003). Approximately 50% of patients are unemployed and those who are employed tend to experience diminished work performance (Bowden, 2005). Additionally, many individuals with bipolar disorder do not live independently (Wyatt and Henter, 1995), have unstable relationships (Depp et al., 2010; Kokcu and Kesebir, 2010; Sheets and Miller, 2010), and experience diminished levels of overall life satisfaction (Altamura et al., 2011; Latalova et al., 2011). Thus, understanding features of this illness that cause functional impairment is vital to its treatment as well as improvement in overall level of satisfaction.

Cognitive dysfunction is one illness feature particularly important for understanding impairments in functioning (Dickerson et al., 2004a; Jaeger et al., 2007; Martinez-Aran et al., 2004; Martinez-Aran et al., 2007; Martino et al., 2009; Martino et al., 2008; Zubieta et al., 2001). Acutely ill patients demonstrate dysfunction in several cognitive domains, including attention, psychomotor speed, visuospatial abilities, executive functioning (e.g. planning and organization, cognitive flexibility, reaction inhibition), decision making, memory and learning, and emotion processing (Burdick et al., 2007; Goldberg and Chengappa, 2009; Zarate et al., 2000). Cognitive dysfunctions are present when patients are depressed or manic, but persist during remission to a lesser degree (Malhi et al., 2007; Mann-Wrobel et al., 2011; Rosa et al., 2010; Thompson et al., 2005). The main cognitive domains affected in remitted patients with bipolar disorder are verbal memory, attention, and executive function (Robinson et al., 2006; Torres et al., 2007). Impairment in these neuropsychological domains is associated with impaired global functioning and occupational status (Altshuler et al., 2007; Altshuler et al., 2008; Dickerson et al., 2004b), whereas preserved executive function leads to better vocational performance (Bearden et al., 2011).

Although previous studies have documented links between impairment in objective measures of neuropsychological performance and functioning, it is less clear how mood symptoms relate to the subjective experience of cognitive dysfunction in daily life. Cognitive functioning is predominantly assessed by means of standardized cognitive tests and there is a lack of studies in bipolar disorder investigating how cognitive impairments translate from laboratory settings into the real world. This is particularly important for the area of executive functioning where laboratory based testing has its limitations. That is,

executive functioning (the ability to plan and organize behaviors) can be preserved in structured settings such as during laboratory based testing, but impairments can reveal themselves when individuals are required to organize their own behavior and daily structure. Thus, to better understand the full range of executive dysfunction in bipolar disorder, investigators are increasingly relying on behavioral measures, such as performance-based assessment of functional capacity, third-party ratings of functional behavior, and self-report measures of everyday difficulties, as a compliment to objective, laboratory-based tests of neuropsychological functioning. These methods have been pioneered in schizophrenia where impairments in everyday functioning are common (Sabbag et al., 2011). Daily living deficits in schizophrenia are predicted by a complex combination of illness features including impaired neuropsychological performance, symptoms, and functional capacity (Harvey and Strassnig, 2012). Positive and negative symptoms directly predict certain domains of everyday functioning (Bowie et al., 2006), whereas others are predicted by neurocognition, an effect, which, is largely mediated through functional competence (Bowie et al., 2008; Bowie et al., 2006; Koren et al., 2006; Nakagami et al., 2008; Ventura et al., 2009).

In contrast to the comprehensive body of research assessing determinants of everyday the experience of daily executive functioning in schizophrenia, substantially less is known about the illness characteristics that contribute to the experience of impaired everyday executive functioning in bipolar disorder (Green, 2006; Wingo et al., 2009). This study seeks to address this gap in the literature by examining how mood symptoms are related to the real world experience of executive dysfunction in bipolar disorder. We hypothesized that both mania and depression severity would positively predict self-reported daily executive functioning difficulties. Likewise, we expected that additional clinical features of bipolar disorder, such as psychiatric medication regime, axis-I co-morbidities, co-occurring medical conditions, and illness chronicity, would also contribute to real-world executive functioning impairments.

Method

Participants

Study participants were individuals with bipolar I disorder ($n = 68$). Participants were recruited through the Bipolar Clinic and Research Program at Massachusetts General Hospital (MGH) for studies of individuals in a depressed or euthymic mood state. All participants provided written informed consent prior to participation in the study, in accordance with MGH-approved institutional review board (IRB) consenting procedures. Bipolar diagnoses were determined using the Mini International Neuropsychiatric Interview (MINI). Participants were not eligible for the study if they reported a) a current episode of mania or hypomania on the MINI, b) schizophrenia, schizoaffective disorder, delusional disorder, psychotic disorders not otherwise specified, major depressive disorder, or mood congruent or incongruent psychotic features, c) substance dependence disorders, including alcohol dependence, currently or within the previous 12 months, d) suicidal ideation or severe depressive symptoms requiring a higher level of care, e) history of head injury, or f) current medical conditions affecting the patient's ability to participate in treatment.

Procedure

After the initial screening visit, participants completed a baseline assessment that included a diagnostic interview, clinician rated measures of depression and mania, and self-report measures of medical problems and cognitive functioning.

Measures

Diagnosis—A DSM-IV diagnosis of bipolar I disorder was confirmed using the Mini-International Neuropsychiatric Interview (MINI)(Sheehan et al., 1998) by a trained interviewer. The measure also contains items to assess demographics and mood episode history.

Depressive Symptoms—Severity of depressive symptoms was evaluated using the Hamilton Rating Scale for Depression (HAM-D), 17-item version (Hamilton, 1960). Items were rated by a trained interviewer. Scores range from 0 to 54, with higher scores denoting greater depressive symptoms.

Manic Symptoms—Severity of manic symptoms was assessed with the Young Mania Rating Scale (YMRS) (Young et al., 1978). Items were rated by a trained interviewer. Scores range from 0 to 56, with higher scores indicating greater symptoms of mania or hypomania.

Subjective Executive Functioning—Real world executive functioning behaviors were rated on two scales, the Behavior Rating Inventory of Executive Function – Adult Version (BRIEF-A) and the Frontal Systems Behavior Rating Scale (FrSBe).

(1) BRIEF: This 75-item self report behavior scale rating yields information for nine non-overlapping clinical subscales that measure different aspects of executive functioning (Roth, 2005). The subscales are: Inhibit (impulsiveness or distractibility), Shift (cognitive flexibility), Emotional Control (ability to temper one's emotions when necessary), Self-Monitor (ability to think before acting), Initiate (beginning new activities), Working Memory (attention and focus while completing activities), Plan/Organize (prioritizing and goal-setting), Organization of Materials (the ability to regulate belongings and keep things clean), and Task Monitoring (cognizance of quality during completion of tasks). Items are rated as never, sometimes, or often and higher scores indicate greater impairment in functioning.

Normative data for the BRIEF is available from 1,196 adults (52% female) throughout the United States via internet-sampling methodology (Roth, 2005). The normative sample included individuals 18 – 90 years of age, without history of diagnosis or treatment for psychiatric illness, learning disorder, neurological disorder, or serious medical illness, and without history of any psychotropic medication usage (Roth, 2005). Raw subscale scores were converted into T-scores prior to analyses, so that data could be standardized across demographic characteristics, enabling comparisons to a normative sample.

(2) FrSBe: The FrSBe is a 46-item self-report inventory that assesses executive functioning in adults through three frontal systems behavior subscales: Apathy (14 items), Disinhibition (15 items), and Executive Dysfunction (17 items) (Grace, 2001; Stout et al., 2003). The Apathy subscale contains items related to indifference or lethargy (e.g., “I have lost interest in things that used to be fun or important to me”). The Disinhibition subscale evaluates the ability to regulate and control one’s behavior (e.g., “I do things impulsively”). The Executive Functioning subscale contains items assessing abilities to plan and mentally organize activities (e.g., “I mix up a sequence, get confused when doing several things in a row”). The instrument quantifies behavioral changes over time by including both past and current assessments of behavior. Items are rated on a Likert scale from 1 (almost never) to 5 (almost always), and higher scores indicate greater impairment in functioning.

Normative data for the FrSBe is available from 487 adult US volunteers (57% female) between 18 – 95 years of age (Grace, 2001). The normative sample excluded individuals with history of neurological illness, major psychiatric disorder or substance use in the past two years, and current psychotropic medication use (Grace, 2001). Raw subscale scores for current behavior were converted into scaled T-scores prior to analyses, so that data could be standardized across demographic characteristics and enabling comparisons to a normative sample. All T-scores have a standard deviation of 10, with a T-score of 50 representing the 50th percentile (the normative mean).

Medication Load—Effects of psychotropic medications on cognitive functioning were assessed using an established approach by Phillips et al (2008) (Almeida et al., 2009; Goldberg, 2008; Hassel et al., 2008). This method involves computing a composite measure of a patient’s total medication load that reflects both the dose and variety of different medications. The steps required to compute an index of medication load have been previously reported (Almeida et al., 2009). Briefly, for each participant, the dose of each class of medication (e.g. antidepressant, mood-stabilizer, antipsychotic, and anxiolytic) is coded as absent (0), low (1), or high (2) using the dosing guidelines (Phillips et al., 2008). Next, a composite measure reflecting total medication load is created by summing all individual medication codes for each medication category for each participant (Phillips et al., 2008).

Data Analytic Approach

To assess impairment in real world executive functioning, raw scores were transformed into T-scores. FrSBe raw scores were transformed into age, sex, and education corrected T-scores (Grace, 2001; Stout et al., 2003), and BRIEF raw scores were transformed into age corrected T-scores (Roth RM, 2005). For each FrSBe or BRIEF subscale, the patient means were compared to the T-scores of the normative healthy control comparison cohort (population norms; T=50).

The contributions of mood symptoms, age, sex, education, psychotropic medication load, age of bipolar onset, number of medical conditions, and number of psychiatric co-morbidities to real world executive functioning were investigated using hierarchical multiple linear regression. Specifically, we sought out to investigate whether current mood state

explains unique variance in the experience of real world cognitive impairment beyond the effect of other demographic and clinical factors. Therefore, we conducted a series of linear regression models predicting subjective executive functioning scales, entering a set of demographic and clinical characteristics as control variables on the first step on the model. Manic (YMRS) or depressed (HAMD) mood were entered together on the second step of the model. Given the exploratory nature of this analysis, we focus on findings with medium to large effect sizes (i.e. $r \geq .30$; $R^2 \geq .09$) (Cohen, 1992).

Additionally, separate regression models were used to examine the effect of illness progression on real-world executive functioning in a subsample of participants ($n = 49$ who provided usable information on the MINI regarding the number of prior lifetime episodes of mania and depression. Episode history was grouped into three categories (0–10, 11–20, 20+ episodes) and each entered as a predictor of each FrsBe or BRIEF subscale in separate models. Episode history was dummy coded, such that two dummy variables were created for the 0–10 and 11–20 groups, with 20+ episodes as the comparison level.

Results

Demographic and clinical characteristics of the total sample, including indices of symptom severity, medication, medical conditions, and Axis I co-morbidities are shown in Table 1.

Impairment in Real World Executive Functioning

Means and standard deviations on all subscales of real world executive functioning are provided in Table 2. One sample t-tests revealed that individuals with bipolar I disorder showed significant impairment on all subscales of both the BRIEF and FrSBe relative to population norms (all $ps < .006$). See Table 2.

Do Mood Symptoms Predict Impairment in Real World Executive Functioning?

Table 3 displays the variance explained by the modeling sequence, including over tests of model significance and effect sizes.

Manic Symptoms—In the multivariate models, manic symptoms accounted for unique variance in many aspects of real world cognitive functioning. Manic symptom severity was associated with impairments on the BRIEF subscales of impulsiveness/distractibility ($b = 1.55$, $SE = .49$, $p = .003$), the ability to temper one's own emotions when necessary ($b = 1.77$, $SE = .54$, $p = .002$), attention and focus while completing activities ($b = 1.75$, $SE = .58$, $p = .004$), cognizance of quality during completion of tasks ($b = 1.12$, $SE = .55$, $p = .046$), the ability to regulate belongings and keep things clean ($b = 1.75$, $SE = .54$, $p = .002$), and the FrSBe subscales of behavioral control ($b = 2.19$, $SE = .63$, $p = .001$) and executive dysfunction ($b = 1.42$, $SE = .69$, $p = .045$).

Depressive Symptoms—In the final multivariate models, depressive symptoms also accounted for unique variance in several aspects of real world cognitive functioning. Specifically, depressive symptom severity was associated with impairments in the BRIEF subscales of cognitive flexibility ($b = .54$, $SE = .22$, $p = .021$), tempering one's own emotions when necessary ($b = .52$, $SE = .21$, $p = .018$), beginning new activities ($b = .96$, SE

= .24, $p < .001$), attention and focus while completing activities ($b = .60$, $SE = .23$, $p = .012$), prioritizing and goal-setting ($b = .63$, $SE = .26$, $p = .020$), and the FrSBe subscales of indifference/lethargy ($b = 1.82$, $SE = .29$, $p < .001$), behavioral control ($b = .86$, $SE = .25$, $p = .001$), and executive dysfunction ($b = .84$, $SE = .28$, $p = .003$).

Role of Medication Load, Psychiatric Co-morbidities, and Medical Co-morbidities in Real World Executive Dysfunction

All analyses were conducted to examine the effect of mood symptoms on real world cognitive functioning, above and beyond what could be accounted for by other characteristics that may also influence cognitive functioning (e.g. psychotropic medication use, age at bipolar onset, number of psychiatry co-morbidities, number of medical conditions, lifetime electroconvulsive therapy (ECT), lifetime traumatic brain injury, and lifetime endocrine condition). In the final multivariate models, several of these characteristics remained significant predictors of real world cognitive dysfunction after adjusting for all other predictors in the model.

Medication Load—Higher medication load was marginally associated with impairments in the BRIEF subscales of cognitive flexibility ($b = 1.69$, $SE = .84$, $p = .051$) and attention and focus while completing activities ($b = 1.75$, $SE = .88$, $p = .052$), but not with any other executive functioning subscales on the FrSBe or BRIEF (all p 's $> .082$).

Psychiatric Co-morbidities—More lifetime co-morbid psychiatric conditions were associated with impairments in the BRIEF subscales of impulsiveness/distractibility ($b = 1.34$, $SE = .67$, $p = .050$), the ability to regulate belongings and keep things clean ($b = 1.74$, $SE = .74$, $p = .022$), and the FrSBe subscale of executive dysfunction, ($b = 1.97$, $SE = .94$, $p = .039$), but not with any other executive functioning subscales on the FrSBe or BRIEF (all p 's $> .082$).

Medical Conditions—Higher number of co-morbid medical conditions predicted impairment in the BRIEF subscales of cognitive flexibility ($b = 2.31$, $SE = 1.05$, $p = .032$), and the ability to regulate belongings and keep things clean ($b = 2.18$, $SE = 1.02$, $p = .038$), but not with any other executive functioning subscales on the FrSBe or BRIEF (all p 's $> .111$).

Do Number of Previous Episodes Predict Impairment in Real World Cognitive Functioning?

Of the 68 participants enrolled in this study, 49 provided information regarding the number of prior episodes of mania or depression.

Number of Lifetime Manic Episodes—Chronicity of manic episodes did not predict impairment in real world executive dysfunction on any subscales of the FrSBe or BRIEF (all p 's $> .094$).

Number of Lifetime Depressive Episodes—Chronicity of depressive episodes predicted the ability to temper one's emotions when necessary on the BRIEF, such that

individuals 10 or fewer prior lifetime episodes of depression were less impaired in this domain than individuals with 20+ prior episodes of depression ($b = -11.49$, $SE = 4.96$, $p = .021$). Similarly, participants with 10 or fewer lifetime episodes of depression were less impaired in the ability to think before acting, ($b = -11.08$, $SE = 4.41$, $p = .012$). On the Chronicity of depressive episodes was unrelated to any other subscale of the FrSBe or BRIEF (all p 's $> .072$).

Discussion

Bipolar disorder is characterized by impairments in cognitive functioning, both during acute mood episodes as well as during euthymic periods. However, much of these data are based on laboratory-based paradigms of cognition, which may not capture how cognitive dysfunction is experienced in real-life settings. While it is clear that cognitive dysfunction negatively impacts functional outcomes in bipolar disorder (Almeida et al., 2009), few other studies to date have evaluated the specific illness characteristics that relate to the experience of cognitive dysfunction in everyday life. The present study investigated the degree to which mood symptoms and other clinical features of bipolar disorder predict self-reported executive functioning deficits in real-world settings.

Individuals in this study reported significant impairment in every domain of executive functioning. As hypothesized, severity of mood symptoms robustly predicted impairment, accounting for medium to large effect sizes in nearly all domains of real-world cognitive dysfunction. Symptoms of both mania and depression each predicted numerous cognitive deficits on the BRIEF, and each predicted overall executive dysfunction on the FrSBe scale. Although mood symptoms were the strongest predictor of subjective cognitive dysfunction, the results of this study show that several clinical features of bipolar disorder impact cognitive functioning as well. For example, psychotropic medication load, psychiatric and medical comorbidity, and chronicity of depressive episodes each predicted real-world experience of executive dysfunction, even when accounting for severity of mood symptoms. Similar to the literature on schizophrenia (Bowden, 2005), executive functioning deficits in the daily lives of individuals with bipolar disorder appeared to be influenced by a multitude of illness factors, some directly impacted by mood symptoms and others shaped by illness chronicity, comorbidity, and other characteristics of the disorder. Thus, real-world cognitive functioning problems in bipolar disorder are not entirely mood-state dependent.

Our results are consistent with previous studies reporting a high degree of cognitive dysfunction in bipolar I disorder (Dickerson et al., 2004a; Jaeger et al., 2007; Martinez-Aran et al., 2004; Martinez-Aran et al., 2007; Martino et al., 2009; Martino et al., 2008; Zubieta et al., 2001). Many of the cognitive domains that have been identified as impaired on the basis of laboratory studies (e.g., working memory, attention, and executive function) were also subjectively rated as impaired by participants in the present study, which supports previous research showing that cognitive impairments negatively affect functional outcomes (e.g., Martinez-Aran et al., 2007). The present study extends these findings by exploring particular illness characteristics and their association with deficits in daily activities, such as, memory, attention, and executive functioning. Psychiatric and medical co-morbidity as well as mood symptom severity each predicted deficits in working memory, and attention and executive

function were predicted by mood symptoms. This suggests that domains of cognitive functioning that have been previously identified as impaired among individuals with bipolar disorder in laboratory paradigms are also experienced by these individuals as impairing in their daily lives. However, mood symptoms and illness characteristics also predicted other aspects of cognitive dysfunction not routinely identified in laboratory paradigms, but which are common in daily functioning, such as task monitoring and organization of materials. Together, these findings indicate that the mood symptoms and illness characteristics impact a broad range of everyday aspects of cognitive functioning.

When considering the specific clinical characteristics that emerged as significant predictors of executive dysfunction, several observed outcomes are particularly noteworthy. First, whereas symptoms of depression and mania predicted the same types of cognitive impairment in a number of domains such as attention, cognitive flexibility, and general executive dysfunction, other effects of depression and mania were not entirely parallel. Not surprisingly, current manic symptoms predicted impulsivity and disorganization, while depression predicted difficulties in initiating activity and setting goals. These results are similar to previous findings reporting generally similar though not completely parallel impairment in episodes of depression and mania (Martinez-Aran et al., 2004).

Another predictor of cognitive functioning was psychotropic medication load, which specifically impacted cognitive flexibility and attention. The effects of medication on cognitive functioning in bipolar disorder are frequently identified as a confound to understanding endogenous cognitive impairment in this population; however, these results indicate that medication use significantly predicts impairment in some, but not all, domains of cognitive functioning. Finally, chronicity of past depressive episodes predicted impairments in cognitive functioning, but chronicity of mania did not. This is surprising, given the range of cognitive impairments that were related to current symptoms of mania. This finding may suggest that a history of depression is more detrimental to cognitive functioning than mania, but future research utilizing a longitudinal design is necessary.

Strengths of this study include careful control of medication burden, a relatively large sample size, and the use of standardized self-report assessment measures. Several limitations should also be noted. First, due to the subjective measures of executive functioning, it is possible that participants may have under or over-reported their degree of cognitive impairment. Although these measures capture the self-reported experience of participants in their daily lives, future studies could strengthen this design by incorporating ratings from friends or family members to build on the validity of these findings. It would also have been of value to include objective neuropsychological tests assess their concurrent validity with the subjective measures used in this study. Second, although we included manic symptoms as a predictor of functioning, patients in this study were recruited in either a depressed or euthymic state. Given the limited range of mania scores, our analyses were likely underpowered to detect effects of mania on the experience of executive functioning difficulties. We therefore, can only draw conclusions with regard to the impact of residual manic symptoms and not acute mania. Third, the cross-sectional nature of this study does not allow us to determine how illness characteristics may impact real-world functioning over

time, nor does it allow us to make claims about causality (while mood symptoms may lead to cognitive impairment, impairment may also generate worsening of mood symptoms).

Nevertheless, these results have several important clinical implications. First, these data may help to develop cognitive rehabilitation strategies in this population to improve outcomes, such as task performance, akin work that has been successful in addressing daily functioning deficits in schizophrenia (Krabbendam and Aleman, 2003). Such data is particularly needed for bipolar disorder, as there is a dearth of literature on devoted to cognitive rehabilitation strategies (Deckersbach et al., 2010; Martinez-Aran et al., 2011). The results of one open trial of adults with bipolar disorder found that psychotherapy combining treatment of depression and cognitive remediation strategies was effective in improving psychosocial functioning (Deckersbach et al., 2010) and improving in cognitive functioning (Stange et al., 2011), suggesting that treatments including cognitive rehabilitation may an important adjunctive treatment option. Second, these data suggest that certain illness characteristics including medical and psychiatric co-morbidity and depressive chronicity impact executive functioning. Thus, treatment of cognitive impairment in bipolar disorder may be particularly important when these characteristics are present.

In sum, these findings indicate that individuals with bipolar disorder experience significant impairment in every day executive functioning. Mood symptoms were commonly related to these deficits. However, a number of other illness factors were also associated with executive functioning problems, indicating that everyday functioning in bipolar disorder is not entirely mood-state dependent. Cognitive rehabilitation for executive dysfunction should be considered an important adjunctive treatment for many individuals with bipolar disorder. In particular, these results underscore the need for clinical interventions to address deficits in functioning individuals with bipolar disorder regardless of current mood state.

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Table 1

Demographic and Clinical Characteristics of 68 Individuals with Bipolar I Disorder

	Mean $\pm$ SD	Range
Age	35.21 $\pm$ 13.43	20 – 64
Age at Bipolar Onset	20.69 $\pm$ 9.56	3 – 53
Sex (female) *	31 (46)	-
Education (> 12 years) *	64 (94)	-
Medication Load	3.25 $\pm$ 2.24	0 – 8
<i>Mood Stabilizers *</i>	27 (40)	-
<i>Antidepressants *</i>	30 (44)	-
<i>Antipsychotics *</i>	30 (44)	-
<i>Benzodiazepines *</i>	22 (32)	-
<i>Anticonvulsant *</i>	38 (56)	-
<i>Stimulant *</i>	7 (10)	-
Number of Chronic Medical Conditions	1.99 $\pm$ 1.77	0 – 6
<i>Respiratory *</i>	15 (24)	-
<i>Cardiovascular *</i>	9 (14)	-
<i>Gastrointestinal *</i>	9 (14)	-
<i>Urinary *</i>	6 (10)	-
<i>Reproductive *</i>	4 (6)	-
<i>Blood/Lymphatic *</i>	3 (5)	-
<i>Endocrine *</i>	3 (5)	-
<i>Musculoskeletal *</i>	14 (22)	-
<i>Allergies *</i>	31 (49)	-
<i>Surgeries *</i>	33 (52)	-
<i>ECT *</i>	2 (3)	-
<i>Other *</i>	11 (18)	-
Lifetime Co-Morbidities	3.13 $\pm$ 2.42	0 – 10
<i>Anxiety Disorder *</i>	47 (69)	-
<i>Eating Disorder *</i>	1 (2)	-
<i>Substance/Alcohol Use *</i>	41 (60)	-
<i>ADHD *</i>	8 (12)	-
HAMD	13.69 $\pm$ 7.80	0 – 29
YMRS	4.49 $\pm$ 3.68	0 – 19

* categorical variables are represented as n(%), calculated based on number of valid cases

Table 2

Impairment in Real World Executive Functioning in 68 Individuals with Bipolar I Disorder Relative to Population Norms

	M	SD	t	df	p	Cohen's d
BRIEF						
<i>Inhibit</i>	56.04	12.82	3.89	67	<.001	.53
<i>Shift</i>	61.99	14.43	6.85	67	<.001	.97
<i>Emotional Control</i>	59.41	14.59	5.32	67	<.001	.75
<i>Self Monitoring</i>	54.88	14.29	2.82	67	.006	.40
<i>Initiate</i>	66.66	14.77	9.30	67	<.001	1.32
<i>Working Memory</i>	65.09	15.58	7.98	67	<.001	1.15
<i>Planning</i>	64.21	15.42	7.60	67	<.001	1.09
<i>Task Monitoring</i>	61.44	13.63	6.92	67	<.001	.96
<i>Organization of Materials</i>	57.96	14.62	4.51	67	<.001	.64
BRIEF Total Score	64.09	15.26	7.62	67	<.001	1.09
FrSBe						
<i>Apathy</i>	74.37	21.22	9.47	67	<.001	1.47
<i>Distraction</i>	60.27	16.56	5.11	67	<.001	.75
<i>Executive Dysfunction</i>	67.66	18.22	7.99	67	<.001	1.20
FrSBe Total Score	70.39	18.16	9.26	67	<.001	1.39

Table 3
Hierarchical Regression for Predictors of Real World Executive Functioning (N=68)

1. Demographic & Clinical Controls			2. Manic Symptoms & Depressive Symptoms		
Dependent Variable	F _{model}	R ²	R ²	F _{change}	R ²
BRIEF					
Inhibit	2.43	.27*	.42**	6.57	.15**
Shift	2.75	.30*	.41**	4.78	.11*
Emotional Control	2.13	.25*	.44**	8.44	.19**
Self Monitor	1.55	.19	.03	.98	.22
Initiate	1.24	.16	.36**	7.99	.20**
Working Memory	2.59	.29*	.46**	7.99	.17**
Plan	1.71	.21	.30*	3.17	.09*
Task Monitor	2.06	.24	.34*	3.86	.10*
Organization	3.13	.33**	.45**	5.76	.12**
BRIEF Total Score	2.87	.31*	.48**	8.55	.17**
FrSBe					
Apathy	1.69	.16	.54**	21.17	.38**
Disinhibition	.99	.10	.38**	12.02	.28**
Executive Dysfunction	2.77	.24*	.39**	6.78	.15**
FrSBe Total Score	2.27	.20	.48**	14.16	.28**

* $p < .05$,

** $p < .01$

* BRIEF: Block of demographic & clinical control variables includes sex, education, psychotropic medication use, age at bipolar onset, number of psychiatry co-morbidities, number of medical conditions, lifetime ECT, lifetime traumatic brain injury, and lifetime endocrine condition. The sex variable was dummy-coded with females as the comparison level.

* FrSBe: Block of demographic & clinical control variables includes psychotropic medication use, age at bipolar onset, number of psychiatry co-morbidities, number of medical conditions, lifetime ECT, lifetime traumatic brain injury, and lifetime endocrine condition.