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Impulsivity in bipolar disorder: relationships with neurocognitive dysfunction and substance use history

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Abstract

Objectives—Impulsivity is a core feature in bipolar disorder. Although mood symptoms exacerbate impulsivity, self-reports of impulsivity are elevated even during euthymia. Neurocognitive processes linked to impulsivity (e.g., attention, inhibition) are also impaired in patients with bipolar disorder and a high frequency of comorbidities associated with impulsivity, such as substance use disorders, further highlight the clinical relevance of this dimension of the illness. Our objective was to assess the relationship between impulsivity and cognition in bipolar disorder.

Methods—We evaluated impulsivity in 98 patients with bipolar disorder and its relationship with symptoms, cognition, and substance use history. We assessed self reports of trait-impulsivity [Barrett Impulsiveness Scale (BIS)] and impulsive behaviors on the Iowa Gambling Task (IGT). A comprehensive clinical and neurocognitive battery was also completed. Patients were compared with 95 healthy controls.

Results—Patients with bipolar disorder had higher scores versus healthy controls on all BIS scales. Performance on the IGT was significantly impaired and patients showed a tendency toward more erratic choices. Depressive symptoms were positively correlated with trait-impulsivity and with an increased tendency to attend more readily to losses versus gains on the IGT. We found no significant associations between impulsivity and neurocognition in the full bipolar sample; however, when sub-grouped based on substance abuse history, significant relationships were revealed only in subjects *without* a substance abuse history.

Discussion—Our data support prior reports of increased trait-impulsivity and impairment on behavioral tasks of impulsiveness in bipolar disorder and suggest a differential relationship between these illness features that is dependent upon history of substance abuse.

Keywords

decision making; depression; impulsivity; Iowa Gambling Task; substance use

Impulsivity, clinically defined as “an individual’s predisposition toward rapid, unplanned actions without regard to the negative consequences of these actions to [oneself] or others” (1) is also considered a stable trait characteristic (2). The construct of impulsivity is multidimensional and the nomenclature and understanding of impulsive dimensions have been long debated. Three factors have been generally accepted as separable aspects of impulsivity including attentional impulsivity, motoric impulsivity, and non planning impulsiveness (3).

Several neuropsychiatric disorders are characterized by impulsive behaviors, including attention-deficit hyperactivity disorder (ADHD), substance use disorders, and bipolar disorder. Specifically, during periods of acute mania, patients with bipolar disorder frequently demonstrate an increase in impulsive behaviors (4) such as uncontrolled spending, promiscuity, and suicide attempts (5, 6). Some evidence suggests that there are differential relationships between certain aspects of impulsivity and the polarity of affective symptoms, with motoric impulsivity correlating with mania and non-planning impulsiveness associating more closely with depression (7). Although mood symptoms appear to exacerbate impulsivity in bipolar disorder, data suggest that patients with bipolar disorder rate themselves as more impulsive than healthy controls even during periods of euthymia (8, 9), which implies a trait-like characteristic. Further, neurocognitive processes linked to impulsivity (e.g., attention, inhibition) as measured by behavioral tasks are also impaired in patients with bipolar disorder across all phases of the illness, including affective remission (10). The high frequency of comorbidities associated with impulsivity, including impulse control disorders (11) and substance abuse/dependence (12) in bipolar disorder further highlight the clinical relevance of this dimension of the illness; however, few studies have focused on the potential association between trait impulsivity and neurocognitive performance in patients with bipolar disorder. Thus, the current study evaluated the nature of impulsivity in a large cohort of patients with bipolar disorder and its relationship with current symptom severity, cognitive dysfunction, and comorbid substance use disorders.

Methods

Participants

Participants included 95 healthy control participants and 98 adult inpatients and outpatients age 18–60 years at Zucker Hillside Hospital, a division of the North Shore Long Island Jewish Health System (NSLIJHS). Healthy controls were recruited from the general population from advertisements posted in newspapers and on internet sites. In order to meet inclusion criteria, healthy participants had no history of Axis I or Axis II psychiatric disorder, as evaluated by a structured clinical interview [the Structured Clinical Interview for DSM-IV, Non-Patient edition (SCID-NP) (13)] specifically designed to assess healthy subjects. Healthy subjects had no history of central nervous system trauma, known neurological disorder, ADHD, or learning disability. In addition, healthy participants were excluded if they tested positive for any drug of abuse or had an active, unstable medical problem or were taking any medications that may interfere with cognition (e.g., diphenhydramine).

Participants with bipolar disorder met DSM-IV criteria for bipolar I or II disorder, as per the SCID-Patient version [(SCID-P) (14)]. Diagnoses were confirmed through a rigorous consensus conference process involving psychologists and psychiatrists. All participants with bipolar disorder were treated with psychotropic medications including: mood stabilizers, antidepressants, antipsychotics, anticholinergics, anxiolytics, hypnotics, and/or benzodiazepines. Exclusion criteria for patients were DSM-IV substance abuse/dependence within one month prior to participation in the study, unstable or severe medical illness, history of significant neurological injury, mental retardation, or dementia. Patients treated

with electroconvulsive therapy in the previous 12 months were also excluded. The NSLIJHS Institutional Review Board reviewed and approved all study procedures. All participants provided written informed consent prior to their participation. Data for this investigation were collected from two parallel studies: one set of data (R03MH079995 to KEB) was completed between 07/2007 and 07/2009 and one set of data has been ongoing since 7/2005 (K23MH077807 to KEB).

Assessments

Clinical—The following symptom and mood ratings were administered to participants: Hamilton Rating Scale for Depression-24 items (HAM-D) (15) and Clinician-Administered Rating Scale for Mania (CARS-M) (16). Both of these scales are clinician-administered rating scales that assess for depressive symptomatology (HAM-D) and symptoms of mania (CARS-M) occurring within the previous week. Structured interviews with the SCID assessed for history of psychosis and/or substance use/abuse comorbidities.

Impulsivity—Self-report measurement of trait-impulsivity was conducted with the Barratt Impulsiveness Scale (BIS-11) (17), which served as the primary trait-impulsivity outcome measure in this study. The BIS-11 is a 30-item questionnaire with three subscales that tap self-control of thoughts and behaviors (e.g., acts without thinking, decides on the spur of the moment, does not plan ahead). A total score is derived reflecting overall level of impulsiveness and three subscales are also scored: Attention, Motor, and Non-planning. The *Attention Scale* is thought to reflect a person's tendency to rapidly shift attention and an impatience for complexity; the *Motor Scale* is meant to measure the tendency for hasty or reckless action; and the *Non-planning Scale* taps into a lack of consideration of future consequences.

We also employed a laboratory-based measure believed to assay behavioral impulsivity with regard to risk-taking and reward-based decision-making, the Iowa Gambling Task (IGT), in a *subset* of our healthy controls ($n = 21$) and patients with bipolar disorder ($n = 57$). The IGT is used to assess emotional decision making abilities. The subject is asked to choose cards from four decks (100 choices in total) which result in monetary gains or losses. Decks A and B are disadvantageous (*risky*) in that the subjects obtain large immediate wins, but they also attain intermittent large losses, resulting in a net overall loss. In contrast, decks C and D are advantageous (*conservative*) in that they result in smaller immediate gains but lower long-term penalties and net an overall win. Healthy volunteers are able to discern over five blocks (20 cards each) that choosing from decks C and D is most beneficial and a normal learning curve is typical over the five blocks (18). In addition to learning curve analyses, an expectancy-valence (EV) model can be deployed for this task to determine card-by-card strategy (19). This model results in three indices: *Recency*, which reflects a person's memory for recent consequences of deck choice and discounts past consequences; *Attention to Gains/Losses*, which determines to what degree a person allocates his/her attention to gains made during the task versus losses taken; and *Reliability*, a marker of choice consistency or erratic, impulsive choice behavior. The current study utilized the learning curve and the three EV indices as primary outcome measures for the IGT.

Neurocognitive assessment—All participants, both patients and healthy controls, who met eligibility and provided written informed consent, underwent a comprehensive neurocognitive assessment (20). The Wide Range Achievement Test—Third Edition, Reading (WRAT-3) was employed to assess IQ; Digit Span subtest from the Wechsler Adult Intelligence Test—Third Edition (WAIS-III) assessed auditory attention and working memory; Digit Symbol subtest (WAIS-III) measured visual scanning and graphomotor speed; Trail Making Test Parts A and B measured visual scanning and ability to sequentially

alternate between numbers and letters respectively; Letter and Category Fluency assessed verbal fluency, The Stroop Color Word Test (Stroop) assessed competing response tendencies and ability to suppress interfering stimuli, and the Wisconsin Card Sorting Test (WCST) was used as a measure of cognitive flexibility, novel problem solving, and use of external feedback on a less structured task.

Statistical analyses

First, we examined demographic group differences (bipolar disorder versus healthy controls) using a series of independent *t*-tests or chi-square as appropriate. Demographic variables included age, sex, race (white, nonwhite), and premorbid IQ (estimated with the WRAT-3 Reading test). As our sample included patients with bipolar I and bipolar II disorders, we explored differences between the two subtypes in term of demographic characteristics, clinical presentation, and medications. We then incorporated any demographic measure showing significant group differences as a covariate into subsequent analyses.

To test our primary hypotheses, we utilized multivariate analysis of covariance (MANCOVA) to evaluate group differences on trait-impulsivity ratings (BIS Total and three BIS subscales). IGT data were analyzed in two different ways. First, the number of cards chosen from advantageous decks relative to disadvantageous decks was calculated $[(C + D) - (A + B)]$ over the course of five blocks (trials 1–20, 21–40, 41–60, 61–80, 81–100). Then, a repeated measures ANOVA was conducted to analyze group differences in learning performance, across the five blocks. Next, the card-by-card strategy implemented was assessed using MANOVA with Recency, Attention to Gains/Losses, and Reliability (consistency of response) serving as the dependent variables with group as the fixed factor.

To assess the relationship between current symptom severity and impulsivity, we divided the bipolar disorder group by symptomatic (HAM-D and/or CARS-M scores > 8) or euthymic (HAM-D ≤ 8 and CARS-M ≤ 8) status and re-ran the MANCOVAs. In addition, we conducted Pearson's correlations with CARS-M, HAM-D, BIS scores, and IGT indices. We then tested for associations between trait impulsivity (attention, motor, non-planning, overall impulsivity) and cognitive performance using Pearson's correlations. Finally, in an effort to understand the impact of comorbid substance use disorders, we split the bipolar disorder group based on the presence of a substance abuse history (yes, no) and re-ran correlational analyses between impulsivity and neurocognitive measures. Using the Fisher *r*-to-*z* transformation, we examined whether the correlations between impulsivity and neurocognition were significantly stronger in one group than in the other (with versus without a history of substance use disorders). Given the number of comparisons involved in this correlational analysis, we used the false discovery rate (FDR) with $\alpha < 0.05$ to reduce the risk of type II error.

Results

Participants

The mean age of the final sample ($N = 193$) was 39.36 ± 11.82 years and 49% ($n = 94$) were female. Forty-six percent ($n = 88$) were white and 54% ($n = 105$) were non-white (Asian or Pacific Islander, Black, Hispanic, Other). The bipolar disorder sample included 98 participants with a mean standard deviation (SD) age of 40.40 (12.09) years; 53% ($n = 52$) were female. The patients with bipolar disorder had an estimated premorbid IQ of 98.92 ± 10.59 . Within the bipolar disorder group, 87% ($n = 85$) were diagnosed with bipolar I disorder, 13% ($n = 13$) were diagnosed with bipolar II disorder, and 70 (71.4%) of the patients with bipolar disorder had a history of psychosis during acute episodes. There were no differences between bipolar I and II disorder in terms of age ($p = 0.450$), sex ($p = 0.951$),

race ($p = 0.162$), premorbid IQ ($p = 0.452$), or current symptomatology as measured by the CARS-M or the HAM-D ($p = 0.360$ and $p = 0.317$, respectively). No significant differences were detected when bipolar subtypes were compared in terms of the number of current medications ($p = 0.812$) or class of medications used (all p values > 0.148). Of the 57 patients for whom medication information was available, 10 patients were only taking a mood stabilizer, 22 patients were only taking an antipsychotic, 19 patients were taking both an antipsychotic and a mood stabilizer, and five patients were not taking either a mood stabilizer or an antipsychotic.

The healthy control sample included 95 participants, of which 44% ($n = 42$) were female. Healthy participants had a mean age of 38.29 ± 11.49 years and an estimated IQ = 98.73 ± 12.90 . They did not differ from the bipolar disorder participants on age ($t = 1.24$; $df = 1,192$; $p = 0.22$) or estimated premorbid IQ ($t = 0.11$; $df = 1,192$; $p = 0.91$). However, the healthy control sample did differ from patients with bipolar disorder with regard to race ($\chi^2 = 14.82$; $df = 1,192$; $p < 0.01$). Subsequent analyses included race (white/non-white) as a fixed factor.

Results from the ANCOVA revealed highly significant group differences on trait-impulsivity self-report ratings (Overall MANCOVA: $F = 24.2$; $df = 3,189$; $p = 2.7 \times 10^{-13}$). Patients with bipolar disorder had significantly higher BIS Total scores (mean = 67.2 ± 12.4) as compared with healthy controls [mean = 54.0 ± 9.6 ($F = 69.1$; $df = 1,192$; $p = 1.7 \times 10^{-17}$)] as well as higher scores on each of the three BIS subscales (Fig. 1): Attention ($F = 61.9$; $df = 1,192$; $p = 2.6 \times 10^{-13}$); Motor ($F = 39.7$; $df = 1,192$; $p = 2.0 \times 10^{-9}$); Non-planning ($F = 40.5$; $df = 1,192$; $p = 1.4 \times 10^{-9}$). When including race as a fixed factor in multivariate ANCOVA, the results remained significant ($F = 22.03$, $df = 3,187$; $p = 2.9 \times 10^{-12}$); there was no main effect of race ($F = 0.48$, $p = 0.70$) and the race $\times$ subject type interaction was not significant ($F = 0.58$, $p = 0.63$). Impulsivity was also investigated among the patients with bipolar disorder. A significant statistical difference emerged only for the Attention subscale of the BIS with patients with bipolar II disorder showing a higher score than those with bipolar I disorder (mean = 19.77 ± 4.7 versus mean = 16.29 ± 4.3 ; $F = 7.303$; $df = 1,97$; $p = 0.008$). Compared to subjects taking mood stabilizers alone, patients taking antipsychotics in addition to mood stabilizers demonstrated lower levels of impulsivity on the BIS Motor subscale ($F = 4.19$; $df = 3,55$; $p < 0.05$), the BIS Non-planning subscale ($F = 2.81$; $df = 3,55$; $p < 0.05$), and the BIS Total scale ($F = 4.79$; $df = 3,55$; $p < 0.05$).

In addition, repeated measures MANOVA revealed that performance on the IGT was significantly impaired in patients with bipolar disorder compared with the healthy controls with a main effect of Group ($F = 4.56$; $df = 1,76$; $p = 0.036$); Block ($F = 6.12$; $df = 1,76$; $p < 0.001$); and a Group $\times$ Block interaction effect ($F = 3.98$; $df = 1,76$; $p = 0.004$). Figure 2 depicts the performance by group (bipolar disorder versus healthy controls). When evaluating card-by-card strategy, again significant group differences were noted. Specifically, patients with bipolar disorder showed a tendency toward less consistent, more erratic choices as per the Reliability index from the EV model ($F = 8.68$; $df = 1,75$; $p = 0.004$). Performance on the Recency and Attention to Gains/Losses indices did not differ by group (p -values > 0.24 ; data not shown). No differences in IGT performance were revealed between bipolar subtypes or between medication classes.

Effects of mood symptoms on impulsivity

Groups were divided based on severity of affective symptoms for comparison. Subjects with bipolar disorder were defined as euthymic ($n = 48$) based on cut-off scores ≤ 8 for both CARS-M and HAM-D (mean HAM-D = 4.1 ± 2.3 ; mean CARS-M = 2.7 ± 2.1). The symptomatic group ($n = 50$) included patients with bipolar disorder with CARS-M score > 8

and/or a HAM-D score > 8 (mean HAM-D = 14.6 ± 7.4 ; CARS-M = 8.2 ± 7.3). Of the 50 symptomatic patients, the majority ($n = 30$) were experiencing depressive symptoms while the rest reported symptoms of mania ($n = 9$) or symptoms of both depression and mania ($n = 11$). The euthymic and symptomatic groups did not differ from one another on any demographic or clinical feature (age: $F = 0.15$, $p = 0.70$; premorbid IQ: $F = 0.68$, $p = 0.41$; sex: $\chi^2 = 0.05$, $p = 0.83$; race: $\chi^2 = 0.03$, $p = 0.87$; bipolar subtype: $\chi^2 = 0.05$, $p = 0.83$; history of psychosis: $\chi^2 = 2.76$, $p = 0.10$). The symptomatic bipolar disorder group had significantly higher impulsivity ratings on all BIS measures when compared with the healthy controls (all p -values $< 6.3 \times 10^{-10}$). Moreover, the symptomatic bipolar disorder group had higher impulsivity ratings than the euthymic group on the BIS Total ($p = 0.02$), Attention ($p = 0.02$), and Motor ($p = 0.03$) subscales, but did not differ significantly on the Non-planning scale ($p = 0.19$). Despite the fact that the euthymic sample had significantly lower scores than the symptomatic bipolar disorder subjects, it is important to note that the euthymic patients with bipolar disorder had significantly *increased* BIS scores in comparison to healthy controls on all BIS measures (all p -values < 0.0001) (Fig. 3). There was no interaction between bipolar subtype and mood symptoms on the BIS ($F = 1.14$, $p = 0.323$).

On IGT measures, symptomatic patients with bipolar disorder ($n = 31$) did not differ from euthymic patients with bipolar disorder ($n = 26$) when a repeated measure ANOVA was conducted to determine overall learning curve (Group main effect: $F = 0.17$; $df = 1,55$; $p = 0.69$) nor was there a main effect of Block ($F = 1.26$; $df = 1,55$; $p = 0.29$). Moreover, the Group $\times$ Block interaction effect was not significant ($F = 0.31$; $df = 1,55$; $p = 0.87$). When assessing card- by-card strategy, however, the symptomatic patients with bipolar disorder allocated significantly more attention to losses versus gains than did the euthymic patients with bipolar disorder (Attention Losses/Gains index: $F = 7.35$; $df = 1,54$; $p = 0.009$).

Correlational analyses revealed that the increased trait-impulsivity was positively correlated with more severe depression ratings (HAM-D scores) in the bipolar disorder sample on all BIS scores (BIS Total: $r = 0.29$, $p = 0.004$; Attention: $r = 0.35$, $p = 0.001$; and Motor: $r = 0.21$, $p = 0.04$) except Non-planning. There was no significant relationship between mania ratings (CARS-M) and BIS scores (data not shown). Likewise, higher HAM-D scores were associated with an increased tendency to attend more readily to losses versus gains on the IGT ($r = 0.28$, $p = 0.04$) and there were no significant associations with mania ratings and any index on the IGT. These data suggest that depressive symptoms but not manic symptoms appear to influence patients with bipolar disorder self-reported levels of impulsivity as well as behavioral strategies employed during an emotional decision-making task.

Impulsivity and neurocognitive function in patients with bipolar disorder

Z-scores were calculated based on the healthy control sample to indicate the level of impairment in the bipolar disorder sample across neurocognitive tasks (Fig. 4). Patients were significantly impaired on all measures ($p < 0.01$) with the exception of the Digit Span test ($p = 0.88$) and Animal Fluency ($p = 0.06$) as compared with healthy subjects. In order to assess effects of self-reported impulsivity on cognitive performance, we conducted Pearson's correlations between the BIS Total, the three BIS subscale scores, and neurocognitive performance in the bipolar disorder sample. We found no significant correlations (all p -values > 0.08 ; data not shown).

Effects of substance abuse history on the relationship between cognition and impulsivity

Because of previous data indicating a significant influence of substance abuse history on both impulsivity and neurocognitive function, alongside the very high rates of substance use disorders in patients with bipolar disorder, we carried out exploratory analyses dividing the

bipolar disorder sample based on prior history of substance abuse/dependence and re-ran the correlational analyses. Substance abuse history was characterized by the SCID interviews and, for our purposes, we considered all substances of abuse together (ethanol, marijuana, cocaine, etc.). None of the patients met *current* criteria for substance abuse or dependence but were categorized rather based on their lifetime histories. Fifty-two patients (53%) met criteria for a lifetime diagnosis of either abuse or dependence and 46 subjects (47%) had never met criteria. Abuse groups did not differ from one another on any demographic or clinical feature (age: $F = 0.24$, $p = 0.63$; premorbid IQ: $F = 0.02$, $p = 0.88$; sex: $\chi^2 = 0.06$, $p = 0.81$; race: $\chi^2 = 0.25$, $p = 0.61$; bipolar subtype: $\chi^2 = 3.43$, $p = 0.06$; history of psychosis: $\chi^2 = 0.92$, $p = 0.34$; HAM-D scores: $F = 0.20$, $p = 0.65$; CARS-M scores: $F = 0.07$, $p = 0.79$). Substance abuse groups did not differ from one another in their neurocognitive performance (all p -values > 0.14 ; data not shown); nor did they differ on any of the BIS scales (all p -values > 0.54 ; data not shown). As the correlational analyses in the full sample were not significant, it is interesting to note that we found significant relationships among BIS scores and several cognitive tests in subjects with bipolar disorder *without* substance abuse histories but no significant correlations in subjects with bipolar disorder with substance abuse histories (Table 1).

Using the Fisher r -to- z transformation, several correlations were significantly different between the two groups: BIS Attention and WCST % Perseverative ($z = -1.99$, $p = 0.046$), BIS Non-planning and Digit Symbol ($z = -3.19$, $p = 0.001$), BIS Total and WCST % Perseverative ($z = -2.55$, $p = 0.011$), and BIS Total and Digit Symbol ($z = -2.28$, $p = 0.023$). When corrected for multiple comparisons using the FDR, two of the correlations remained significant (BIS Total and WCST % Perseverative, $p = 0.035$; BIS Non-planning and Digit Symbol, $p = 0.007$) and one achieved a trend-level of significance (BIS Total and Digit Symbol, $p = 0.051$). These results indicate that the relationship between impulsiveness and neurocognitive functioning in patients with bipolar illness is complicated by a history of substance abuse.

Discussion

Bipolar disorder is an episodic illness with alternating periods of depression and elevated or irritable mood (*mania*) (5). Although euthymic phases are present when individuals achieve relative remission of affective symptoms, some aspects of the disorder appear to have a trait-like, persistent course including impulsivity (6, 21) and neurocognitive impairment (10, 22). Results from our study support the persistence of impulsivity in bipolar disorder, as measured by using a self-report inventory, the BIS. Although increased symptom severity, particularly with regard to depressive symptoms was associated with higher BIS scores, euthymic patients with bipolar disorder also reported significantly elevated scores on the BIS in comparison with healthy controls. Likewise, impaired cognitive performance was noted in our cohort of patients with bipolar disorder regardless of mood state at the time of assessment. These data are consistent with our recent work (22) and several meta-analyses (10, 23–25).

The trait-like pattern of impulsivity and at least some aspects of cognitive impairment in patients with bipolar disorder would suggest that these variables may be related to one another. Indeed, individuals with other disorders characterized by impulsivity (e.g., substance use disorders, ADHD, personality disorders) have been shown to have significant cognitive deficits (26–28). At first pass, our data indicate no significant relationship between impulsivity ratings and cognitive performance in our cohort of patients with bipolar disorder. However, an important distinction arises when subdividing the bipolar disorder group based upon a presence/absence of a history of a substance use disorder.

Perhaps surprisingly, we found no significant group differences on any neurocognitive test or impulsivity measure when comparing patients with bipolar disorder with and without substance abuse/dependence histories and groups were well-matched with regard to demographic and clinical features. These data are somewhat inconsistent with several previously published studies (4, 8, 29), with a number of possible explanations for this inconsistency. First, we did not employ lab-based measurements of cognitive tasks that were specifically designed to tap into behavioral impulsivity (e.g., response inhibition or decision-making tests) but rather, we utilized a standard, comprehensive neurocognitive battery. This allowed us to evaluate the effects of trait-impulsivity on cognitive functioning across all of the major neuropsychological domains in a more general manner. Second, although our cohort of patients with bipolar disorder appears to be representative in that just over half of the sample met lifetime criteria for substance abuse or dependence, none of our subjects met criteria for a *current* comorbid substance use disorder, which may account for the lack of group differences noted in this study as compared with prior work (4, 8, 29). Nonetheless, we report a novel finding in this study indicating a significant relationship between high trait impulsivity and impaired cognition on several tasks of processing speed and executive functioning only in patients with bipolar disorder *without* a history of a substance use disorder. In contrast, in the bipolar disorder group with a history of a substance use disorder, we note no such relationship.

There were several limitations to this study that should be addressed. The inclusion of a heterogeneous sample of patients with bipolar disorder who were on a variety of medications may have limited the ability to more directly assess the relationship between impulsivity and neurocognition. Nevertheless, the investigation of such a broad range of patients with bipolar disorder did allow for the examination of a range of potential factors that may be associated with impulsivity, and made possible our finding that depressive symptoms are associated with increased levels of self-reported and behavioral measures of impulsivity. In addition, we did not explore the potential relationship between impulsivity and functional outcomes in this sample. Such an assessment is necessary in order to understand the real-world impact of impulsivity on patients' everyday lives, and is an area worthy of future investigation. Finally, we assessed a large number of variables and the risk of a type I error must be considered. Although we corrected for multiple comparisons when assessing the relationship between impulsivity and neurocognition, future studies replicating our results are necessary in order to confirm the findings.

Our data suggest that trait-impulsivity is elevated and neurocognitive functioning is impaired in patients with bipolar disorder independent of substance abuse/dependence history. Although the patients with a history of a substance use disorder appeared qualitatively and quantitatively similar to the patients without substance histories, the differential relationship between impulsiveness and neurocognitive impairment implies that the common phenotype being expressed across groups may have unique contributing factors within groups. Future studies are needed to more comprehensively assess substance use histories with regard to duration and severity of abuse as well as the specific types of substances misused. In addition, studies that include a non-psychiatric control group with and without histories of substance use disorder might shed light on whether our findings are specific to bipolar disorder.

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References

1. Moeller FG, Barratt ES, Dougherty DM, Schmitz JM, Swann AC. Psychiatric aspects of impulsivity. *Am Psychiatry*. 2001; 158:1783–1793.
2. Swann AC. Mechanisms of impulsivity in bipolar disorder and related illness. *Epidemiologia e Psichiatria Sociale*. 2010; 19:120–130. [PubMed: 20815296]
3. Patton JH, Stanford MS, Barratt ES. Factor structure of the Barratt Impulsiveness Scale. *J Clin Psychology*. 1995; 51:768–774.
4. Swann AC, Dougherty DM, Pazzaglia PJ, Pham M, Moeller FG. Impulsivity: a link between bipolar disorder and substance abuse. *Bipolar Disord*. 2004; 6:204–212. [PubMed: 15117399]
5. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4. Washington, D.C: American Psychiatric Association; 2000.
6. Swann AC, Anderson JC, Dougherty DM, Moeller FG. Measurement of inter-episode impulsivity in bipolar disorder. *Psychiatry Res*. 2001; 101:195–197. [PubMed: 11286822]
7. Swann AC, Steinberg JL, Lijffijt M, Moeller FG. Impulsivity: differential relationship to depression and mania in bipolar disorder. *J Affect Disord*. 2008; 106:241–248. [PubMed: 17822778]
8. Swann AC, Lijffijt M, Lane SD, Steinberg JL, Moeller FG. Interactions between bipolar disorder and antisocial personality disorder in trait impulsivity and severity of illness. *Acta Psychiatr Scand*. 2010; 121:453–461. [PubMed: 20064125]
9. Strakowski SM, Fleck DE, DelBello MP, et al. Impulsivity across the course of bipolar disorder. *Bipolar Disord*. 2010; 12:285–297. [PubMed: 20565435]
10. Bora E, Yucel M, Pantelis C. Cognitive endophenotypes of bipolar disorder: a meta-analysis of neuropsychological deficits in euthymic patients and their first-degree relatives. *J Affect Disord*. 2009; 113:1–20. [PubMed: 18684514]
11. Karakus G, Tamam L. Impulse control disorder comorbidity among patients with bipolar I disorder. *Comprehen Psychiatry*. 2011; 52:378–385.
12. Chengappa KN, Levine J, Gershon S, Kupfer DJ. Lifetime prevalence of substance or alcohol abuse and dependence among subjects with bipolar I and II disorders in a voluntary registry. *Bipolar Disord*. 2000; 2:191–195. [PubMed: 11256686]
13. First, MB.; Spitzer, RL.; Gibbon, M.; Williams, JBW. *Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Non-patient Edition. (SCID-I/NP)*. New York: Biometrics Research, New York State Psychiatric Institute; 2002.
14. First, MB.; Spitzer, RL.; Gibbon, M.; Williams, JBW. *Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Patient Edition. (SCID-I/P)*. New York: Biometrics Research, New York State Psychiatric Institute; 2002.
15. Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry*. 1960; 23:56–62. [PubMed: 14399272]
16. Altman EG, Hedeker DR, Janicak PG, Peterson JL, Davis JM. The Clinician-Administered Rating Scale for Mania (CARS-M): development, reliability, and validity. *Biol Psychiatry*. 1994; 36:124–134. [PubMed: 7948445]
17. Patton JH, Stanford MS, Barratt ES. Factor structure of the Barratt Impulsiveness Scale. *J Clin Psychology*. 1995; 51:768–774.
18. Bechara A, Damasio AR, Damasio H, Anderson SW. Insensitivity to future consequences following damage to human prefrontal cortex. *Cognition*. 1994; 50:7–15. [PubMed: 8039375]
19. Sevy S, Hassoun Y, Bechara A, et al. Emotion-based decision-making in healthy subjects: short-term effects of reducing dopamine levels. *Psychopharmacology*. 2006; 188:228–235. [PubMed: 16915385]
20. Spreen, O.; Strauss, E. *A compendium of neuropsychological tests: administration, norms, and commentary*. 2. New York: Oxford University Press; 1998.

21. Swann AC, Pazzaglia P, Nicholls A, Dougherty DM, Moeller FG. Impulsivity and phase of illness in bipolar disorder. *J Affect Disord.* 2003; 73:105–111. [PubMed: 12507743]
22. Burdick KE, Goldberg TE, Cornblatt BA, et al. The MATRICS Consensus Cognitive Battery in patients with bipolar I disorder. *Neuropsychopharmacology.* 2011; 36:1587–1592. [PubMed: 21451499]
23. Robinson LJ, Thompson JM, Gallagher P, et al. A meta-analysis of cognitive deficits in euthymic patients with bipolar disorder. *J Affect Disord.* 2006; 93:105–115. [PubMed: 16677713]
24. Arts B, Jabben N, Krabbendam L, van Os J. Meta-analyses of cognitive functioning in euthymic bipolar patients and their first-degree relatives. *Psychol Med.* 2008; 38:771–785. [PubMed: 17922938]
25. Torres JJ, Boudreau VG, Yatham LN. Neuropsychological functioning in euthymic bipolar disorder: a meta-analysis. *Acta Psychiatr Scand Suppl.* 2007; (434):17–26. [PubMed: 17688459]
26. Vik PW, Cellucci T, Jarchow A, Hedt J. Cognitive impairment in substance abuse. *Psychiatr Clin North Am.* 2004; 27:97–109. ix. [PubMed: 15062633]
27. Seidman LJ, Biederman J, Faraone SV, Weber W, Ouellette C. Toward defining a neuropsychology of attention deficit-hyperactivity disorder: performance of children and adolescents from a large clinically referred sample. *J Consult Clin Psychol.* 1997; 65:150–160. [PubMed: 9103744]
28. Bazanis E, Rogers RD, Dowson JH, et al. Neurocognitive deficits in decision-making and planning of patients with DSM-III-R borderline personality disorder. *Psychol Med.* 2002; 32:1395–1405. [PubMed: 12455938]
29. Swann AC, Steinberg JL, Lijffijt M, Moeller GF. Continuum of depressive and manic mixed states in patients with bipolar disorder: quantitative measurement and clinical features. *World Psychiatry.* 2009; 8:166–172. [PubMed: 19812754]

Fig. 1. Barrett Impulsiveness Scale (BIS) subscale score: patients with bipolar disorder (n = 98) versus healthy controls (n = 95).

Fig. 2.
Iowa Gambling Task: patients with bipolar disorder (BPD) versus healthy controls (HC).

Fig. 3.
Effects of symptoms on Barrett Impulsiveness Scale (BIS) scores.

Fig. 4. Neurocognitive performance in patients with bipolar disorder (n = 98). CW = Color Word; WCST = Wisconsin Card Sorting Test; Persev = Perseverative.

Table 1

Correlations between Barrett Impulsiveness Scale (BIS) scores and neurocognitive tests based on substance abuse history

Neurocognitive test	BIS Attention	BIS Motor	BIS Non-planning	BIS Total
Without substance history				
Trails A	0.12 (0.44)	−0.14 (0.34)	−0.19 (0.21)	−0.10 (0.51)
Trails B	0.01 (0.94)	0.01 (0.99)	−0.04 (0.78)	−0.01 (0.93)
Digit Span	−0.06 (0.68)	0.10 (0.52)	−0.17 (0.25)	−0.06 (0.72)
Letter Fluency	0.04 (0.80)	0.06 (0.69)	−0.32 (0.03)	−0.10 (0.51)
Stroop Color Word	0.08 (0.58)	0.05 (0.76)	−0.03 (0.86)	0.04 (0.81)
Digit Symbol	−0.21 (0.16)	−0.27 (0.07)	−0.38 (0.01)^b	−0.35 (0.02)^a
WCST % Perseverative	−0.35 (0.02)^a	−0.35 (0.02)	−0.29 (0.06)	−0.39 (0.01)^b
Animal Fluency	0.05 (0.75)	−0.04 (0.78)	−0.32 (0.03)	−0.14 (0.37)
With substance history				
Trails A	−0.05 (0.74)	−0.10 (0.47)	0.17 (0.24)	0.01 (0.95)
Trails B	0.11 (0.45)	−0.04 (0.76)	−0.07 (0.64)	−0.01 (0.97)
Digit Span	−0.09 (0.55)	−0.07 (0.62)	−0.11 (0.45)	−0.11 (0.45)
Letter Fluency	0.09 (0.53)	0.06 (0.66)	0.00 (0.99)	0.06 (0.67)
Stroop Color Word	−0.07 (0.62)	0.17 (0.23)	0.07 (0.64)	0.08 (0.60)
Digit Symbol	0.01 (0.97)	−0.02 (0.92)	0.26 (0.07)	0.11 (0.47)
WCST % Perseverative	0.05 (0.75)	0.02 (0.88)	0.22 (0.13)	0.12 (0.42)
Animal Fluency	−0.17 (0.24)	−0.01 (0.97)	−0.04 (0.80)	−0.08 (0.57)

Values presented as mean (standard deviation). **Bolded** values indicate that the correlation is significant at $p < 0.05$. WCST = Wisconsin Card Sorting Test.

^aCorrelation is significantly different ($p < 0.05$) in subjects without a substance use history compared to subjects with such a history using the Fisher r -to- z transformation.

^bCorrelation remains significant when corrected for multiple comparisons using false discovery rate ($p < 0.05$).