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Increased trait-like impulsivity and course of illness in bipolar disorder

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Abstract

Background—Impulsivity as a trait characteristic is increased in bipolar disorder and may be a core factor of the illness. We have investigated relationships between trait-like impulsivity, measured by the Barratt Impulsiveness Scale (BIS-11), and demographic and illness-course characteristics of bipolar disorder.

Methods—We studied 114 subjects with bipolar disorder and 71 healthy comparison subjects. Diagnoses were based on the Structured Clinical Interview for DSM-IV. In addition to impulsivity, we examined age, education, gender, psychiatric symptoms, and characteristics related to course of illness. We used general linear mixed model analysis to evaluate the manner in which the variables contributed to BIS-11 scores.

Results—All BIS-11 subscale scores were higher in bipolar disorder than in comparison subjects. There were less consistent independent effects of education and age. Elevated BIS-11 scores were associated with early onset, more frequent episodes of illness, and a history of suicide attempts. These relationships persisted when age, gender, and education were taken into account.

Discussion—These results show that, after accounting for common confounding factors, trait-like impulsivity was substantially higher in subjects with bipolar disorder than in nonbipolar comparison subjects, regardless of symptoms. Within subjects with bipolar disorder, high trait impulsivity was associated with a more severe course of illness.

Keywords

age at onset; attempted suicide; bipolar disorder; impulsive behavior; impulsivity; recurrence; substance abuse

Impulsivity results from dysregulation of the initiation of action (1,2), an integral part of bipolar disorder (3). Operationalized as a predisposition to action without reflection or without regard for consequences (2), impulsivity is increased in bipolar disorder (4–6). Potential consequences of this increased impulsivity include substance abuse (7,8), suicidal behavior (9–11), and other serious behavioral problems (12).

Impulsivity has interacting state- and trait-like characteristics (5,13). Trait impulsivity, as measured by the Barratt Impulsiveness Scale (BIS-11) (1), is increased in bipolar disorder, even when patients are euthymic (4,13,14). Impulsivity may also be related differentially to mania, depression, and anxiety (13,15,16). Increased impulsivity is consistent with many

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characteristics of bipolar disorder (6), but there is relatively little evidence directly linking measurements of impulsivity to specific illness-course characteristics of bipolar disorder.

Patients with bipolar disorder vary substantially in their course of illness. Early onset and more frequent episodes are associated with susceptibility to mixed states (17) and with resistance to lithium treatment (18–20). Trait impulsivity is potentially related to the long-term course of bipolar disorder, whether as a consequence of unstable illness or as an expression of biological factors predisposing to a severe course (17), and may further worsen course of illness by contributing to substance abuse (8) and nonadherence to treatment (21). Patients with early-onset or highly recurrent bipolar disorder have characteristics consistent with impulsivity, including substance use disorders, aggression, and suicide attempts (22–24), but there is little direct evidence about impulsivity in these patients. Education and age can influence impulsivity and may confound the interpretation of variations in impulsivity relative to illness course; for example, either severe bipolar disorder or impulsive behavior could interfere with completion of education, while education could potentially provide cognitive tools for counteracting impulsivity (25,26). We examined trait impulsivity in bipolar disorder in relation to demographic characteristics, symptoms, and course of illness. After characterizing relationships to age, education, and gender, we investigated relationships between trait-like impulsivity and age of onset, frequency of episodes, substance use disorders, and suicidal behavior.

Methods

Subjects

Potential subjects, who were referred by clinicians or who responded to advertisements that had been approved by the Institutional Review Board, were fully informed of the procedures, risks, and benefits of the study, and signed informed consent documents before any study-related procedures took place. The study was approved by the Committee for the Protection of Human Subjects, the Institutional Review Board for the University of Texas Health Science Center at Houston. Healthy comparison subjects did not meet criteria for any Axis I or Axis II disorder according to the Structured Clinical Interview for DSM-IV (SCID) I or II (27). Subjects with bipolar disorder included subjects who met past criteria for substance use or alcohol use disorders (77 of 108) in order to ensure a clinically generalizable group of subjects, and were recruited to cover a wide range of symptomatic and clinical characteristics. All subjects were required to have negative breath alcohol and urine screens for drugs of abuse when they were tested.

Diagnostic and symptom measures

Diagnoses, including substance abuse or dependence, were rendered by the SCID (27). Symptoms were rated using the Change version of the Schedule for Affective Disorders and Schizophrenia (SADS-C) (28), which is designed to measure depressive, manic, anxious, and psychotic symptoms concomitantly. The augmented version of the SADS-C used in this and our previous work (29) had all 10 mania rating scale items used in the full SADS (30,31), rather than the subset of five items in the conventional SADS-C (28). Raters were trained in these instruments using standard rating tapes and materials. Diagnoses were confirmed in consensus meetings that included coauthors ACS, FGM, and JLS.

Impulsivity

Impulsivity was assessed using the BIS-11 (1). This 30-item self-rated scale has three oblique factors: attentional/cognitive, which measures toleration for cognitive complexity and persistence; motor, which measures the tendency to act on the spur of the moment; and nonplanning impulsivity, which measures the lack of sense of the future (32). Items are rated

from 1 (absent) to 4 (most extreme). Therefore, the possible scores range from 30–120; nonpsychiatric controls generally score in the range of 50–60 (33). Internal consistency was good across several different samples of subjects ($\alpha > 0.79$).

Statistical methods

For normally distributed variables, we used general linear model (GLM) analysis of variance or linear multiple regression analysis. GLM analysis of variance was used to evaluate prediction of continuous dependent variables by continuous and categorical predictor (independent) variables. Separate univariate fixed-effects model analyses were carried out with BIS-11 total or subscale scores as dependent variables. Dependent and independent variables for specific analyses are given in the text. Continuous data were normally distributed (Kolmogorov-Smirnov test). Post hoc comparisons, when appropriate analysis of variance interactions were significant, used the Duncan multiple range test. Correlation coefficients were compared using the Fisher *r-z* transformation. Numbers of subjects vary across analyses according to completeness of data.

Results

Demographic

Age, gender, and education—Table 1 compares demographic characteristics of bipolar and healthy comparison subjects. Men with bipolar disorder were older than comparison men, but women with bipolar disorder were not older than comparison women, leading to an interaction between group and gender with respect to age. As previously reported (26), comparison subjects had more years of education than subjects with bipolar disorder, and men had slightly, but significantly, more years of education than women, with no group-gender interaction in this group of subjects.

Characteristics of subjects with bipolar disorder—Subjects with bipolar disorder were recruited to encompass a representative range of symptoms and clinical characteristics. Fifty subjects had made suicide attempts, and 77 subjects had histories of alcohol or substance abuse or dependence. SADS-C depression scores ranged from 0–36 (mean ± SD: 14.2 ± 9.1), mania scores ranged from 0–37 (9.6 ± 8), anxiety scores from 0–22 (7.2 ± 4.7), and psychosis scores from 0–8 (1.9 ± 1.9). By DSM-IV-TR criteria, 29 subjects were euthymic (14 men and 15 women), 19 were hypomanic (10 men and 9 women), 33 were depressed (23 men and 10 women), and 25 combined depression with hypomania (9 men and 16 women). Analysis of variance revealed no significant relationships between clinical state and age [$F(3,98) = 1.3$] or education [$F(3,89) = 1.2$]. Chi-squared analysis of state versus gender showed a borderline-significant effect [χ^2 (df = 6) = 6.9, p = 0.08], largely reflecting the preponderance of women in mixed states versus men in other states.

BIS-11 scores

BIS-11 and psychiatric symptoms—Table 2 summarizes BIS-11 and symptom rating scale scores in euthymic, depressed, hypomanic, and mixed subjects with bipolar disorder. Neither BIS-11 total scores (Table 2) nor subscale scores (not shown) differed significantly across affective state. Symptom scores, on the other hand, showed the expected differences and varied widely. For comparison, among healthy comparison subjects depression scores were 0–10, mania 0–3, anxiety 0–3, and psychosis 0–1.

Within subjects with bipolar disorder, depression scores correlated modestly but significantly ($p < 0.05$; n = 104) with BIS-11 total ($r = 0.2$), nonplanning ($r = 0.2$), and attentional ($r = 0.24$) scores, and mania correlated significantly with BIS-11 attentional ($r = 0.2$) score. There were no other significant correlations between BIS-11 and symptom rating scores among subjects

with bipolar disorder. Among comparison subjects, there were no significant correlations between BIS-11 and symptom scores; there was little variance in symptom scores (see above), although BIS-11 scores varied appreciably among comparison subjects (mean 56.6, range 39–89, 25th–75th percentile range 50–61). Therefore, correlations between BIS-11 and symptom scores were minimal in subjects with bipolar disorder and nonsignificant in comparison subjects.

BIS-11 total, attentional, motor, and nonplanning scores were all substantially higher in subjects with bipolar disorder than in healthy comparison subjects, as shown in Table 3. Despite the limited correlations between symptoms and BIS-11 scores, we evaluated any role of psychiatric symptoms in differences between comparison and bipolar subjects by conducting multiple regression analyses, with each BIS-11 score as dependent variable and depression, mania, anxiety, and psychosis scores as independent variables, for bipolar and comparison subjects. As shown in Table 3, the y-intercepts (extrapolated scores at zero symptoms) of the BIS-11 scores differed substantially between the subject groups. In addition, BIS-11 scores were significantly higher in euthymic bipolar subjects than in comparison subjects (BIS-11 total score 80.2 ± 13.8, $n = 29$ versus 56.6 ± 9.4, $n = 71$; $t = 9.2$, $p < 0.001$). Therefore, psychiatric symptoms did not appear to contribute to differences in BIS-11 scores between subjects with and without bipolar disorder.

BIS-11 and education in bipolar disorder—BIS total and subscale scores had negative correlations with years of education in subjects with bipolar disorder ($n = 113$): BIS total, $r = -0.297$, $p < 0.005$; BIS nonplanning, $r = -0.396$, $p < 0.005$; BIS motor, $r = -0.207$, $p < 0.05$; and BIS attentional, $r = -0.213$, $p < 0.05$. There were no significant correlations between BIS-11 scores and education in comparison subjects ($p > 0.4$, $n = 71$). Correlations between education and BIS-11 scores differed significantly between subjects with bipolar disorder and comparison subjects for total score ($z = 1.65$, $p = 0.05$) and attentional score ($z = 2.03$, $p = 0.02$) and at a trend level ($p = 0.06$–0.07) for motor and non-planning scores. These differences could have resulted in part from greater variance of BIS-11 scores among subjects with bipolar disorder than among comparison subjects (for total BIS-11, F ratio for variances was 2.1, $p < 0.001$; F ratio was smaller but still significant for subscale scores).

We next investigated the role of education, age, symptom ratings, and gender in these differences. We conducted GLM analyses with age and education as continuous predictors and gender as a categorical (fixed) predictor, and BIS-11 total, attentional, motor, or nonplanning score as dependent variables. As shown in Table 4, there were marked differences between comparison subjects and those with bipolar disorder for each BIS-11 score. Education significantly contributed to total and nonplanning BIS-11 scores after statistically controlling for the main effects of experimental group. Age contributed significantly to nonplanning impulsivity but not to BIS-11 total or other scores.

BIS-11 scores and course of illness in bipolar disorder

Elevated BIS-11 scores and unstable course of illness—High trait impulsivity may be associated with a more severe or unstable course of illness in bipolar disorder. Examining the relation between impulsivity and frequency of episodes is complicated by a large number of subjects reporting too many episodes to count, and by problems in recall of individual episodes in subjects who have had many episodes. Therefore, number of episodes was categorized. Based on the distribution of number of episodes, with a substantial number of subjects reporting too many to count reliably, ‘many episodes’ was defined as too many episodes to count of either depression or mania. Among subjects with bipolar disorder, those with many episodes had higher BIS-11 total scores than those without many episodes [BIS-11

total score: many episodes (n = 40) 83.8 ± 13.8, without many episodes (n = 31) 76.9 ± 9.9, *t* (df = 69) = 2.5, p = 0.016].

Education and age could significantly contribute to any relationship between course of illness and impulsivity. Education was significantly lower in subjects with many episodes (13.1 ± 2.9 versus 14.7 ± 1.7, *t* = 2.9, p = 0.004). Duration of illness (years from onset until the age when studied) did not differ between those with versus without many episodes (20.1 ± 8.6 years versus 21.8 ± 12.4, *t* = 0.7), confirming that 'many episodes' reflected increased episode frequency rather than merely having been ill longer.

We investigated effects of current age, age of onset, and years of education as continuous predictor variables, and presence of many previous episodes as a dichotomous categorical variable, on BIS-11 scores. The results, summarized in Table 5, showed that, even after accounting for effects of gender and education, there were consistent relationships between BIS-11 scores and course of illness, with younger age of onset and many episodes predicting higher BIS-11 total, motor, and attentional impulsivity scores. Age contributed significantly to BIS-11 motor scores, and education to BIS-11 nonplanning scores, after statistically controlling for onset age or history of frequent episodes. There were no significant effects of gender.

The results in Table 5 suggest that current age and age at onset were differentially related to BIS-11 scores. One would not expect current age and age at onset to be unrelated, and they correlated significantly ($r = 0.35$, $p < 0.001$). We investigated relationships between age factors and BIS-11 scores in bipolar disorder by conducting GLM analyses identical to Table 5, except that age and age at onset were replaced by one variable, 'years ill', calculated as the difference between age at onset and current age. For total BIS-11 score, characteristics of 'years ill' were the mirror image of age at onset, with similar *F* ratios; 'years ill' contributed more strongly than age at onset to motor impulsivity ($F = 12.9$ versus 6.8 for age of onset in Table 5), but did not contribute significantly to attentional impulsivity ($F = 0.01$ versus $F = 7.4$ for age at onset in Table 5). GLM analyses analogous to Table 5 but omitting current age revealed no significant effect of age at onset on nonplanning or motor impulsivity, but a strong effect on attentional impulsivity ($F = 15.3$). Neither of these analyses altered relationships between a history of many episodes and BIS-11 scores. These findings suggest that increased motor impulsivity is related most strongly to duration of illness, whereas increased attentional impulsivity is related to early onset, and nonplanning impulsivity may have little relationship to age-related factors.

While the course of bipolar disorder is dominated by depression for the average patient, there are predominately mania-prone and depression-prone presentations (34). Depressive and manic episodes may contribute differentially to impulsivity. Separately including many depressive and many manic episodes as dichotomous predictor variables revealed that many manic episodes contributed more strongly than many depressive episodes to BIS-11 total scores, with $F(1,59) = 8.7$ (p = 0.005) for many manic episodes and $F(1,59) = 2.5$ (p = 0.12) for many depressive episodes. A history of many depressive episodes contributed significantly to BIS-11 nonplanning score [$F(1,59) = 4.1$, p = 0.04] and at a trend level to BIS-11 motor score [$F(1,59) = 3.6$, p = 0.06], but not to other scores.

BIS-11 scores and high-risk behavior in bipolar disorder—Total BIS-11 scores were significantly higher in subjects with bipolar disorder who had made suicide attempts than in those who had not [83.8 ± 13.1, n = 50 versus 77.4 ± 12.7, n = 53; *t* (101) = 2.5, p = 0.01]. BIS-11 scores were also elevated in subjects with histories of substance abuse or dependence [82.7 ± 11.2 versus 77.1 ± 15.6, *t* (106) = 2.12, p = 0.037]. Subjects with bipolar disorder who did not have a substance/alcohol use disorder still had higher BIS-11 scores than comparison subjects [total score 77.1 ± 15.6, n = 31 versus 56.6 ± 8.8, n = 71; *t* (100) = 8.4, p < 0.001],

confirming that elevated BIS-11 scores in bipolar disorder are not entirely due to the presence of substance abuse disorders.

Risk of suicide attempt may be increased in subjects with substance abuse, and interpretation may also be confounded by effects of education or age. Among subjects with bipolar disorder, we conducted GLM analysis with BIS-11 scores as dependent variables, history of suicide attempt and history of substance use disorder as dichotomous categorical predictor variables, and age and education as continuous predictor variables. Because of possible relationships between substance use disorders and suicide attempt history, we included both in the analysis. The results are summarized in Table 6. History of suicide attempt was consistently associated with increased BIS-11 scores. Lower education contributed to total and nonplanning scores. There was an interaction between substance use disorder and suicide attempt history in non-planning impulsivity. This interaction reflected increased nonplanning impulsivity in subjects with either a substance use disorder or suicide attempt history alone, but these increases were not additive in subjects who had a substance use disorder and a history of suicide attempt: scores were similar in subjects with either or both histories.

Discussion

Trait-like impulsivity, measured by the BIS-11, was substantially higher in subjects with bipolar disorder compared to healthy nonbipolar comparison subjects. Further increases in BIS-11 scores were associated with histories of early onset of illness, frequent episodes, substance abuse, or suicide attempts. Subjects with bipolar disorder who lacked these characteristics still had higher BIS-11 scores than comparison subjects. Education appeared to be more strongly related to impulsivity in subjects with bipolar disorder than in comparison subjects, but neither education nor age, gender, or psychiatric symptoms accounted for the relationships between BIS-11 scores and diagnosis of bipolar disorder or course of illness.

Definitions and components of impulsivity

Impulsivity represents a pattern of behavior that occurs without the opportunity for reflection on action or consequences (2). The BIS-11 identifies three components of impulsivity. Attentional/cognitive impulsivity is a lack of cognitive persistence, with inability to tolerate cognitive complexity; motor impulsivity is a tendency to act on the spur of the moment; and nonplanning impulsivity refers to a lack of sense of the future (32).

Impulsivity is complex. Underlying mechanisms include inability to delay reward and inability to withhold or modify response to a stimulus (35). Specific measures of these characteristics correlate poorly with each other, but significantly with the BIS-11 (33,36). Subscales of the BIS-11 are related differentially to other measures of impulsivity. In controls, motor impulsivity correlated with performance on a stop-signal task, consistent with impaired motor inhibition; nonplanning impulsiveness correlated with complex reaction time, interpreted as impaired response organization; and cognitive impulsivity correlated somewhat more weakly with errors in time production, considered consistent with impaired temporal regulation (37). We have reported BIS-11 nonplanning and motor impulsivity to correlate with performance on tests of the ability to delay reward, and nonplanning impulsivity to correlate with increased commission of errors on a continuous performance task (33). Among patients with bipolar disorder, Christodoulou et al. (38) reported that BIS nonplanning scores were correlated with poor Iowa Gambling Task performance, while BIS attentional scores were correlated with poor performance on a sentence-completion task designed to measure response inhibition. These results suggest that elevated impulsivity in subjects with bipolar disorder is related to deficiencies at more than one level of cognitive functioning.

Impulsivity and clinical characteristics

Mechanisms underlying impulsivity may vary across clinical entities (39). Attention-deficit hyperactivity disorder, like bipolar disorder, is associated with impulsivity and increased motor activity, but their underlying mechanisms and psychopharmacology appear distinct (39,40). These differences underscore the importance of understanding the neurobiology of impulsivity-like symptoms in different clinical contexts in order to develop rational diagnosis and treatments (2).

Most studies of impulsivity in bipolar disorder reported elevated BIS-11 scores regardless of clinical state (6,13,14). One study reported BIS-11 scores in subjects with bipolar disorder in remission that resembled BIS-11 scores from controls reported in other studies, but that study had no nonbipolar comparison group (38). Depending on populations, motor impulsivity may be elevated further in manic subjects (8,13). Depressed patients with bipolar disorder have elevated BIS-11 scores (14) and are more likely than unipolar depressed patients to have concomitant impulsecontrol disorders (41). The BIS-11 is intended to measure impulsivity as a stable trait, but has been reported to be influenced by clinical state as well (13), declining with improvement in unipolar major depressive episodes (42). Most studies have been cross-sectional, so it is not possible to differentiate whether differences in BIS-11 scores across clinical states are due to true state dependence, differential characteristics of subjects with predominately depressive or manic courses of bipolar disorder, or differences among patients with bipolar disorder who are predisposed to having more severe or recurrent illness and therefore more likely to be symptomatic when they were studied. Impulsivity can ‘undermine mood stability’ and is consistent with many prominent complications of bipolar disorder (6, 8,43,44).

Impulsivity may be affected by education. Education can be compromised by either impulsive behavior or bipolar disorder. Our observation of lower educational attainment in subjects with bipolar disorders than in comparison subjects is consistent with an earlier report by Glahn et al. (26). We found a stronger correlation between education and impulsivity in subjects with bipolar disorder than in comparison subjects, and lower educational attainment in subjects with more severe course of illness. Bipolar disorder, therefore, may reduce educational attainment through severely recurrent symptoms and through impulsivity. These mechanisms of reduced educational attainment are consistent with the report that educational attainment was less in subjects with bipolar disorder than in controls, but IQ did not differ (26).

There is surprisingly little evidence directly relating impulsivity to course of illness in bipolar disorder. The current results confirm our earlier report that BIS-11 scores were higher, regardless of clinical state, in subjects with bipolar disorder who also had a substance use disorder (8). Grunebaum et al. (23) reported that in subjects with bipolar disorder, a history of substance use disorder was associated with earlier onset of illness and history of aggressive behavior. Oquendo et al. reported more previous depressive episodes in subjects with suicide attempts in a retrospective study of hospitalized patients (45), and increased impulsivity among those who attempted suicide in a prospective study of patients with bipolar disorder (46). Early onset of bipolar disorder was associated with increased risk for substance use disorders, suicidal behavior, and other problems that are potentially related to impulsivity (24,44). None of these studies directly measured impulsivity relative to course of illness. The data in Table 5 and related analyses suggested that early onset was associated with increased attentional impulsivity, while duration of illness, to which early onset contributes, was related to motor impulsivity. This suggests that an early age of onset and duration of illness could affect different aspects of impulsivity, with different biological substrates.

In the current study, increased impulsivity was most pronounced in patients with a severely unstable course of illness, reflected by more frequent episodes, early age of onset, and histories

of substance use disorders and suicide attempts. This finding underscores the importance of early clinical assessment and intervention. High impulsivity could be part of the familial association of unstable and complicated course of illness and lithium resistance (20). Alternatively, elevated impulsivity scores could reflect neural effects of previous drug exposure (47) or multiple episodes of illness (48). Prospective or developmental studies may enhance our understanding of these relationships.

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Table 1

Demographic characteristics of subjects with bipolar disorder and healthy comparison subjects

Group	Current age	Education
Comparison subjects		
Women	33.8 ± 11.9 (40)	14.3 ± 2.1 (40)
Men	31.5 ± 10.1 (31)	15.1 ± 2.2 (31)
Bipolar disorder		
Women	34.1 ± 8.5 (52)	13.4 ± 2.5 (52)
Men	37.8 ± 8.7 (60)	14.1 ± 2.3 (60)
F (diagnosis) (p)	5.2 (0.024)	7.1 (0.008)
F (gender) (p)	0.2 (0.64)	3.9 (0.05)
F (diagnosis × gender) (p)	4.2 (0.042)	0.02 (0.9)

Units are years, given with SD and number of subjects (n). *F* ratios are from two-way factorial analysis of variance, with p-values in parentheses.

Table 2

Barratt Impulsiveness Scale (BIS-11) and psychiatric symptom scores in subjects with bipolar disorder

State (n)	BIS-11 Total	Depression	Mania	Anxiety	Psychosis
Euthymic (29)	80.2 ± 13.8	6.4 ± 3.2	5.0 ± 3.3	3.2 ± 2.9	0.7 ± 0.9
Hypomanic (19)	76.9 ± 17.1	6.1 ± 3.6	17.1 ± 7.3	7.0 ± 3.5	1.9 ± 2.3
Depressed (33)	79.3 ± 11.4	21.6 ± 6.4	3.7 ± 2.7	8.9 ± 4.1	2.0 ± 1.4
Mixed (25)	84.3 ± 11.5	20.1 ± 6.9	17.3 ± 6.4	10.1 ± 4.8	3.2 ± 2.4
F (df = 3,102)(p)	1.2 (0.3)	68 (10^{-6})	63 (10^{-6})	17 (10^{-6})	9.9 (10^{-5})

Affective states are according to DSM-IV-TR, except for mixed, which denotes combined depression and hypomania. Symptom ratings are from the Change version of the Schedule for Affective Disorders and Schizophrenia.

Table 3

Barratt Impulsiveness Scale (BIS-11) scores in subjects with bipolar disorder and in healthy comparison subjects

	Comparison (n = 70)	Bipolar disorder (n = 114)	t^a	Extrapolated to zero symptoms		
				Comparison	Bipolar	t^b
Total	56.6 ± 8.8	80.3 ± 12.4	13.9	56.6 ± 1.6	75.1 ± 2.3	4.7
Nonplanning	21.4 ± 4.3	29.6 ± 5.7	10.7	21.2 ± 0.8	27.9 ± 1.3	3.3
Motor	21.5 ± 4.1	28.8 ± 5.3	10.1	21.6 ± 0.7	27.9 ± 1.2	3.2
Attentional	13.8 ± 3.5	21.8 ± 4.4	13.2	14.0 ± 0.6	19.2 ± 0.9	3.4

Means for BIS-11 total or component scores are given with standard deviations. Extrapolated values are y-intercepts calculated from multiple regression analyses, with BIS-11 score as dependent variable and depression, mania, anxiety, and psychosis scores as independent variables, as described in the text, and are given with standard error of the fit.

[a] For all direct comparisons, $p < 10^{-6}$.

[b] For all comparisons of extrapolated values, $p < 10^{-4}$.

Table 4

Barratt Impulsiveness Scale (BIS-11) scores in subjects with bipolar disorder versus comparison subjects: effect of age, gender, and education

	BIS total	BIS nonplanning	BIS motor	BIS attention
Current age	0.04 (0.83)	1.9 (0.16)	0.19 (0.66)	**4.4 (0.04)**
Education	**8.8 (0.004)**	**13.4 (0.0003)**	2.6 (0.11)	2.7 (0.1)
Bipolar versus comparison	**157 (10^{-6})**	**84.7 (10^{-6})**	**84.1 (10^{-6})**	**162.4 (10^{-6})**
Gender	0.45 (0.5)	0.71 (0.4)	0.5 (0.48)	2.2 (0.14)
Group × gender	0.07 (0.8)	0.001 (0.9)	0.38 (0.54)	0.02 (0.9)

Table shows *F* ratios from general linear model analysis; *F* df = 1,135. Age and education were continuous predictor variables; diagnosis and gender were dichotomous categorical predictor variables; BIS-11 scores were dependent variables. Statistical significance is in parentheses (p). Significant *F* ratios are shown in **bold** type.

Table 5

Course of illness, education, and gender effects on Barratt Impulsiveness Scale (BIS-11) in subjects with bipolar disorder

	BIS total	BIS nonplanning	BIS motor	BIS attention
Age at onset	**8.2 (0.006)**	2.4 (0.12)	**6.8 (0.012)**	**7.4 (0.009)**
Current age	1.6 (0.2)	0.6 (0.43)	**11.5 (0.001)**	3.4 (0.07)
Education	3.52 (0.07)	**5.4 (0.024)**	0.3 (0.7)	2.4 (0.13)
Gender	1 (0.3)	1.7 (0.2)	0.6 (0.5)	3.7 (0.06)
Many episodes	**5.8 (0.02)**	**4.5 (0.04)**	**4.2 (0.04)**	2.1 (0.15)
Gender × many	0.2 (0.7)	0.2 (0.67)	2.1 (0.15)	3.4 (0.07)

Table shows *F* ratios from general linear model analysis; *F* df = 1,53. Age at onset, current age, and years of education were continuous predictor variables; gender and presence of many episodes were dichotomous categorical predictor variables; and BIS-11 scores were dependent variables. Statistical significances of *F* ratios are in parentheses (p). Significant *F* ratios are shown in **bold** type.

Table 6

Relationships between Barratt Impulsiveness Scale (BIS-11) scores and history of suicide attempt or substance use disorder in subjects with bipolar disorder

	BIS total	BIS nonplanning	BIS motor	BIS attention
Current age	0 (1)	0.8 (0.4)	0.2 (0.7)	3.7 (0.06)
Education	**5.67 (0.02)**	**9.2 (0.003)**	2.35 (0.13)	1.6 (0.21)
Suicide attempt	**6.92 (0.01)**	**5.8 (0.018)**	**7.54 (0.007)**	1.18 (0.28)
Substance abuse	0.74 (0.4)	1.7 (0.2)	0.2 (0.65)	0.04 (0.85)
Suicide attempt × substance abuse	3.5 (0.065)	**8.1 (0.006)**	2.1 (0.15)	0.02 (0.9)

Table shows *F* ratios from general linear model analysis; *F* df = 1,83. Age and years of education were continuous predictor variables; history of suicide attempt or substance use disorder was a dichotomous categorical predictor variable; and BIS scores were dependent variables. Statistical significance is in parentheses (p). Significant *F* ratios are shown in **bold** type.