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Severity of bipolar disorder is associated with impairment of response inhibition

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Abstract

Background—Pathological impulsivity in bipolar disorder could be related to deficiencies in mechanisms involved in attention or response inhibition. We investigated these mechanisms in subjects with bipolar disorder and examined relationships to severity of course of illness, use of medication, affective state, age, education, and gender. We measured two complementary aspects of response inhibition: attention-based and reward-based.

Methods—Subjects with bipolar disorder ($n=112$) and healthy controls ($n=71$) were recruited from the community. Diagnoses were rendered using the SCID for DSMIV. Impulsivity-related measures included the Immediate Memory Task (IMT), a form of the Continuous Performance Task, and the Single Key Impulsivity Paradigm (SKIP), an operant procedure measuring ability to delay responding for a reward.

Results—Subjects with bipolar disorder had fewer correct detections (Effect Size (ES)=0.5), prolonged reaction times (ES=0.88), and decreased discriminability (ES=0.57) on the IMT compared to controls. History of frequent episodes, substance use disorders, or suicide attempts predicted faster reaction times, especially to a commission error. Subjects with bipolar disorder who also met criteria for an Axis II disorder had fewer correct detections, more commission errors relative to correct detections, and poorer discriminability on the IMT than other subjects with bipolar disorder. Subjects with bipolar disorder made more responses on the SKIP than did controls (ES=0.5), with a shorter maximum delay (ES=0.62), consistent with inability to delay reward. Probit analysis showed that faster reaction time to a commission error on the IMT was associated with history of substance use disorder, suicide attempt, or many previous episodes. Effects of medication or affective state did not account for these differences.

Discussion—Bipolar disorder was associated with impairment in attention and response inhibition, encompassing impaired inhibition of rapid responses and an inability to delay reward, and resulting in impulsivity. Response inhibition mechanisms are impaired further in subjects with more severe complications of illness.

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Keywords

Bipolar disorder; Impulsive behavior; Continuous performance test; Attention; Recurrence; Substance-related disorders; Reward; Suicide; Attempted

1. Introduction

Impulsivity is a core component of bipolar disorder, prominent across all phases of the illness (Swann et al., 2007). Abnormal response inhibition may underlie this increased impulsivity. Two complementary mechanisms for response inhibition include rapid-response impulsivity, with inability to completely assess a stimulus before responding, and reward-delay impulsivity, where the individual cannot delay responding for a larger reward, related to accelerated discounting of delayed reward (Evenden, 2000).

Rapid-response impulsivity can be measured by continuous performance tasks (CPT) (Dougherty et al., 2003a; Swann et al., 2002). Studies using CPT showed that subjects with bipolar disorder have fewer correct detections of target stimuli (Wilder-Willis et al., 2001), and slower reaction times (Fleck et al., 2001; Wilder-Willis et al., 2001), suggesting impaired sustained attention. Subjects made more commission errors, especially if they were manic (Fleck et al., 2005b; Sax et al., 1998; Swann et al., 2003), suggesting inability to inhibit responses before a stimulus is completely evaluated (Swann et al., 2002). Commission errors were increased in subjects with bipolar disorder and a substance use disorder (Swann et al., 2004), or history of a medically severe suicide attempt (Swann et al., 2005), but otherwise there is little data relating it to course or clinical characteristics.

Reward-delay impulsivity can be assessed using the Single-Key Impulsivity Paradigm (SKIP) (Dougherty et al., 2003a, 2005), where the subject can press a button to receive a reward, and is told that a larger reward is obtained by waiting longer. Unlike attention-based models, there is no discrete stimulus. More responses may reflect a deficit in delaying response for a reward (Dougherty et al., 2003a). History of suicidal behavior (Dougherty et al., 2004), high trait impulsivity (Marsh et al., 2002), and history of conduct disorder (Dougherty et al., 2003a) are associated with more SKIP responses. To our knowledge, direct evidence of reward-delay inhibition, including SKIP responding, is lacking in bipolar disorder.

In the current study, we measured performance on the Immediate Memory Task (IMT), a CPT developed to measure rapid-response impulsivity (Dougherty et al., 2000), and the SKIP in healthy controls and in subjects with bipolar disorder. We also investigated potential confounds including education, age, and pharmacological treatments. Hypotheses were: 1) IMT would be impaired in bipolar disorder, with reduced correct detections, increased commission errors, and slower reaction times; 2) IMT impairment would be worse in subjects with early onset, many episodes, or severe complications of illness; and 3) subjects with bipolar disorder would make more frequent SKIP responses than controls. We also explored effects of course of illness on SKIP performance.

2. Methods

2.1. Subjects

Subjects were referred by clinicians or responded to advertisements. After full information on procedures, risks, and benefits, with an opportunity to have any questions answered, subjects signed written informed consent before any study-related procedures took place. Subjects with bipolar disorder who were not in treatment were given referral information and, if needing immediate treatment, referred to an appropriate facility. 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. The authors were not involved in the subjects' treatment.

Diagnoses, including substance abuse or dependence, were rendered by the Structured Clinical Interview for DSM-IV (SCID-I and -II) (First et al., 1996). Healthy controls did not meet criteria for any Axis I or Axis II disorder. Subjects with bipolar disorder met criteria for at least one past depressive and hypomanic/manic episode. Symptom ratings used the Change version of the Schedule for Affective Disorders and Schizophrenia (SADS-C), designed to measure depressive, manic, anxious, and psychotic symptoms concomitantly (Spitzer and Endicott, 1978b). The augmented SADS-C used in this and our previous work (Bowden et al., 1994) had all ten mania rating scale items in the Mania Rating Scale of the full SADS (Spitzer and Endicott, 1978a), rather than the subset of five items in the conventional SADS-C (Spitzer and Endicott, 1978b). Raters were trained using standard rating tapes and materials. Diagnoses based on SCID-IV and clinical interview were confirmed in consensus meetings that included coauthors A.C.S., F.G.M., and J.L.S. Data on course of illness, substance use disorder, suicide attempts, and medication were derived from interviews and from medical records. Only subjects where consensus meeting determined the presence or absence of such histories were used in the relevant analyses. We recruited 71 control subjects, and 112 subjects with bipolar disorder (86 bipolar I and 21 bipolar II). Subjects were required not to have addition, discontinuation, or dose change of 20% or more for any psychotropic treatment for two weeks before testing, and to have negative breath alcohol and urine screens for drugs of abuse on testing days.

2.1.1. Course of illness—A life chart of episodes was based on the SCID and available records. Thirty-seven subjects had too many manic episodes to count, and 35 had too many depressive episodes to count. These groups overlapped: 20 subjects had too many depressive and too many manic episodes to count, while 32 had too many depressive or manic episodes. Fifty subjects had made at least one suicide attempt, 62 had not; 63 had met DSM-IV criteria for alcohol or drug use disorder, 47 had not; 26 had a history of a cluster B personality disorder (SCID-II), while 85 did not.

2.1.2. Psychopharmacological treatment—Seven subjects were prescribed lithium (none as monotherapy), 60 were taking an anticonvulsant (20 monotherapy), 36 were prescribed an antipsychotic (5 monotherapy), and 29 were prescribed an antidepressant (6 monotherapy). Twenty-one subjects were taking no medicines, 35 one class, 36 two classes, 8 3 classes, and 2 were taking four or more classes.

2.1.3. Clinical characteristics—Among subjects with bipolar disorder, SADS-C depression scores ranged from 0–36 (mean $13.8 \pm SD 9.4$), mania from 0–37 (9.4 ± 7.8), anxiety from 0–22 (7.2 ± 4.8) and psychosis from 0–8 (1.8 ± 1.9). Affective state on the day of testing (SCID), was euthymic in 33 subjects (16 men and 17 women), hypomanic/manic in 19 (11 men and 8 women), depressed in 33 (9 men and 24 women), and combined depression with hypomania/mania in 25 (12 men and 13 women). There were no significant relationships between affective state and age ($F(3,107)=1.32$), education ($F(3,98)=1.57$), or gender ($\chi^2(df=6)=6.6, p=0.08$). Controls had depression scores from 0–10, mania 0–3, anxiety 0–3, and psychosis 0–1.

2.2. Impulsivity measures

The Immediate Memory Task (CPT) is a CPT (Dougherty et al., 2000). Subjects are shown 5-digit numbers on a computer screen, for 0.5 s, separated by 0.5-second intervals, and are instructed to respond if a set of digits matches the previous set. Responses are: correct

detections of matching sets, commission errors with response to a set with 4 of the 5 digits correct, and random errors with response to a set of five completely different digits. Commission errors are interpreted as responses to a stimulus that has not been fully evaluated, or impulsive responses (Dougherty et al., 2003a,b; Swann et al., 2002). Signal detection methods can obtain measures of discriminability (A') and response bias (β) (Donaldson, 1992; Green and Swets, 1966).

The Single Key Impulsivity Paradigm (SKIP) (Dougherty et al., 2003a, 2005) assesses the rate and pattern of operant responses for reward. In a 20-min session, the participant can respond whenever desired by clicking a computer mouse button. Each response adds earnings in direct proportion to the interval since the previous response. The more a response is delayed, the greater the reward. The session lasts 20 min regardless of responding. Total responses, the average delay to a response (essentially redundant with total responses), the shortest delay, and the longest delay are recorded.

2.3. Statistical methods

Distributions were tested for normality (Kolmogorov–Smirnov test) and, if necessary, normalized with log transformation. Group differences were analyzed with independent samples t -tests, and additionally expressed as an effect size (ES), the difference between group means divided by the standard deviation weighted and pooled across both groups, corrected for differences in sample size (Lipsey and Wilson, 2001) (p 198). We used univariate analysis of variance to test differences between histories of episodes, drug/alcohol use disorder, suicide attempt, number of medication classes prescribed, and affective states. Post-hoc comparisons used the Newman–Keuls test. Relationships between SKIP or IMT measures, as dependent variables, and multiple predictors were analyzed using General Linear Model (GLM) analysis. Relationships between SKIP and IMT as independent variables and dichotomous dependent variables (for example, history of many previous episodes) were analyzed using probit analysis (Gibbons and Hedeker, 1994). Numbers varied according to completeness of data. Data are reported as means with standard deviations.

3. Results

Subjects with bipolar disorder were older than controls (controls: men 31.5 ± 10.1 ($n=31$) and women 33.8 ± 11.9 ($n=40$) vs bipolar: men 36.2 ± 9.3 ($n=48$), women 36.1 ± 13.9 ($n=64$)), ($F(1,179)=5.5$, $p=0.02$). Control subjects had more years of education than subjects with bipolar disorder (controls: men 15.5 ± 2.2 , women 14.3 ± 2.1 vs bipolar: men 13.6 ± 2.5 , women 13.9 ± 2.3), ($F=7$, $p=0.009$). We therefore included age, education, and gender in our analyses. There was no significant main effect of gender or diagnosis $\times$ gender interaction for either age or education. The 86 subjects with bipolar I and 21 with bipolar II disorder did not differ significantly ($p>0.3$) in any of the demographic, symptomatic, or response-inhibition measures analyzed, so they were combined.

3.1. IMT performance

3.1.1. Diagnosis and demographics—Fig. 1 summarizes group differences for IMT results. Effect sizes were large for reaction times and moderate for correct detections and discriminability. GLM analysis (Table 1) revealed that diagnosis of bipolar disorder was related significantly to fewer correct detections, prolonged reaction times, and signal-detection parameters reflecting poor signal/ noise discrimination (A') and positive response bias (β). Age contributed to slower reaction time for correct detections; education contributed to β and accounted for the difference between controls and bipolar disorder in commission error rates relative to correct detections (Fig. 1).

3.1.2. Course of illness—Reaction times were faster in subjects with bipolar disorder who had histories of many manic or depressive episodes ($E.S.=0.64$), suicide attempts ($E.S.=0.48$), or alcohol/substance use disorder ($E.S.=0.44$) than in those lacking these characteristics (Table 2, GLM). Subjects with a history of alcohol use disorder had more correct detections than subjects without that history. Subjects with Axis II disorders had fewer correct detections and more commission errors/ correct detection, with a trend ($E.S.=0.38$, $p=0.08$) toward faster reaction times. Subjects without these characteristics still had significantly fewer correct detections, more commission errors/correct detections, slower reaction times, and lower discriminability than controls.

GLM analysis showed that many episodes contributed significantly to commission error reaction time ($F(1,43)=7.7$, $p=0.008$), while alcohol/substance use disorder ($F=2.4$), personality disorder ($F=1.4$) and suicide attempt ($F=2.7$) did not. Alcohol/substance use disorder was also no longer related to correct detections. Presence of a cluster B personality disorder was associated with increased commission errors relative to correct detections ($F=5.3$, $p=0.02$).

3.1.3. Pharmacological treatment—Subjects taking medication from any of the four classes (lithium, anticonvulsant, antipsychotic, antidepressant) did not differ on IMT performance from subjects not taking a drug in that class. Subjects taking one medication had fewer commission errors relative to correct detections ($F(3,90)=3.7$, $p=0.015$) and slower reaction times to correct detections ($F(3,90)=3.2$, $p=0.03$) or commission errors ($F(3,90)=2.9$, $p=0.04$) than those taking no medication or taking medication from more than one class (one-way ANOVA and Newman–Keuls test). Subjects taking no medication were identical on the IMT to those taking more than one class. Comparisons between controls and subjects with bipolar disorder excluding those taking one medication, or between controls and subjects with bipolar disorder taking no medicines, revealed the same differences as in Fig. 1. There were no significant differences in prescribed medicines (Fisher Exact Test >0.2) between patients with and without histories of many depressive, manic, or total episodes, substance/alcohol use disorders, or suicide attempts. Subjects taking one medicine class were less likely to have many depressive episodes (Fisher Exact Test $=0.04$), with a similar trend for total episodes (Fisher Exact Test $=0.08$). Subjects taking one medicine did not differ in early onset, history of suicide attempt, or alcohol or substance-use disorder (Fisher Exact Test >0.2).

3.1.4. Affective state—Two-way analysis of covariance GLM analysis among subjects with bipolar disorder with hypomanic/manic or depressive state (absent or present) as dependent variables (mixed states were scored as having both hypomania/mania and depression present), and age and education as covariates, showed no differences on IMT variables across affective states ($F<2.6$, $p>0.1$).

3.2. SKIP performance

3.2.1. Diagnosis, demographics, and course of illness—Fig. 2 shows that subjects with bipolar disorder made more responses on the SKIP, with shorter maximum delayed response times, than control subjects. Age correlated with number of responses and shortest delay in the bipolar group ($r=0.25$ and -0.29 , $p<0.05$), but not controls ($r=-0.16$ and 0.18). Number of responses correlated significantly with education ($r=-0.27$, $p<0.01$) across all subjects combined, with qualitatively similar but nonsignificant correlations within the control ($r=-0.23$) and bipolar groups ($r=-0.19$). Longest delay correlated with education across all subjects ($r=0.29$, $p=0.005$) and within controls ($r=0.39$, $p=0.001$).

Within subjects with bipolar disorder, GLM analysis revealed no significant relationships between measures of course of illness (as predictor variables) and SKIP performance (as

dependent variables), except that presence of a cluster B personality disorder was associated with a shorter minimal response time ($F(1,50)=4.9, p=0.03$).

3.2.2. Pharmacological treatment—SKIP performance was not significantly related to the number of medication classes that subjects simultaneously took ($F(3,74)<1.0; p>0.40$). The only significant pharmacological effect was that subjects taking an antipsychotic agent had longer maximum delays ($4.9\pm 2.1, n=51$ vs $6.9\pm 2.9, n=22; t=3.6, p<0.005$), still substantially shorter than controls (9.06 ± 1.05 , see Fig. 2).

3.2.3. Clinical characteristics—Mania scores correlated significantly with number of responses ($r=0.237, n=80, p=0.04$). Two-way analysis of covariance GLM for SKIP variables, with education and age as covariates, showed no relationships between affective state and SKIP approached significance ($F<2, p>0.2$). The effect of diagnosis remained significant after controlling for age, education, gender, depression, anxiety, mania, and psychosis: subjects with bipolar disorder still had increased total responses (GLM $F(1,94)=5.7, p=0.02$), and shorter maximum delay ($F(1,94)=4, p<0.05$). Years of education was related to decreased total responses ($F(1,89)=6.4, p=0.012$).

3.3. Relationships of IMT and SKIP performance with course of illness

Among controls, total SKIP responses correlated negatively with IMT reaction times to a correct detection ($r=-0.293, n=61, p=0.02$) or to a commission error ($r=-0.274, n=61, p=0.03$). Among subjects with bipolar disorder, maximal response delay correlated negatively with commission errors relative to correct detections ($r=-0.231, n=82, p=0.04$) and positively with discriminability ($r=0.227, n=82, p=0.04$).

In probit analysis (Table 3), IMT reaction times, especially to a commission error, were associated with histories of suicide attempt, drug/alcohol use disorder, or many episodes. SKIP performance as a predictor variable was related to course of illness as a dependent variable in probit analysis. Number of responses was related to alcohol/substance use disorder and history of many episodes, and shorter minimum response delay was related to presence of an Axis II disorder. Education was related to history of alcohol/substance use disorder.

4. Discussion

We investigated attention and response inhibition in bipolar disorder, and explored their potential relationships with course of illness and affective state. The results supported our hypotheses of fewer correct detections and slower reaction times in bipolar subjects than in controls. Subjects with bipolar disorder made more SKIP responses than did controls, suggesting a deficit in response inhibition reflected by inability to delay response for a larger reward. Subjects taking only one medication made fewer commission errors, suggesting that subjects with a more severe history or who were less responsive to monotherapy had deficient inhibition of rapid IMT responses. Alternatively, this may represent subtle adverse behavioral effects of polypharmacy. IMT responses were faster and SKIP response delays were shorter in subjects with bipolar disorder who had experienced many episodes of illness. Thus, bipolar disorder with a more severe course of illness is associated with deficient attention and deficient response inhibition.

4.1. IMT performance

Our results confirm that subjects with bipolar disorder were impaired on the CPT, with poor discriminability, reduced correct detections (Wilder-Willis et al., 2001), slow reaction times (Fleck et al., 2001; Wilder-Willis et al., 2001), and increased commission errors relative to correct detections (Swann et al., 2003). Affective state did not relate to IMT commission errors

when education and age were taken into account (Table 1). Most subjects with bipolar disorder in this report had histories of alcohol or substance use disorders, reported to reduce state-dependence of commission errors (Swann et al., 2004). IMT has been related to impulsivity in other contexts, including parents of children with conduct disorders (Hrdina and Du, 2001), disruptive behavior disorders (Dougherty et al., 2000), alcohol-dependence (Bjork et al., 2004), adolescents with substance-related or conduct disorders (Thompson et al., 2006), and healthy controls in interactions with serotonergic function (Walderhaug et al., 2007).

The higher rate of commission errors in bipolar disorder (Fig. 1) was accounted for by fewer years of education (Table 1). Subjects with bipolar disorder did not differ from controls in IQ, but had significantly lower educational attainment (Glahn et al., 2006). Reduced educational attainment relative to IQ could result from disruption of educational careers by affective symptoms and episodes, while education could protect against consequences of impulsivity or enhance compensatory abilities (Nusslock et al., 2008).

4.2. SKIP performance

We know of no previous reports on reward-delay performance, including SKIP performance, in bipolar disorder. SKIP parameters differed between subjects with bipolar disorder and controls, with more responses and shorter maximum response delay in subjects with bipolar disorder. Bipolar disorder therefore was related to diminished ability to withhold a response for a larger reward.

4.3. Response inhibition and course of illness

Performance impairments on IMT and, to a smaller extent, SKIP, were associated with an unfavorable course of illness, including multiple episodes, suicide attempts, substance use disorders, and cluster B Axis II personality disorder. Subjects with bipolar disorder who had histories of many episodes, alcohol/substance use disorder, or suicide attempts had faster reaction times than other subjects with bipolar disorder (Tables 2 and 3), although subjects with bipolar disorder, as a group, had slower reaction times than controls (Fig. 1). Faster reaction times were related most strongly to history of many manic or depressive episodes (Table 2). Characteristics of suicide attempters were consistent with our earlier report that reaction times were accelerated in all subjects with suicide attempts, while commission errors were only increased with medically severe attempts (Swann et al., 2005).

Bipolar disorder may be associated primarily with a deficit in attention or in response inhibition associated with inefficient stimulus processing (Wilder-Willis et al., 2001). Delayed reaction time may be an adaptation to this deficit in regulation of attention (Fleck et al., 2005a). Subjects with a more severe course of illness may have a superimposed sensitization-like phenomenon where behavioral responses are accelerated, resulting in loss of compensatory slowing, faster reaction times to commission errors and susceptibility to the severe behavioral consequences associated with strongly recurrent bipolar disorder.

Manifestations of bipolar disorder and criteria for Axis II cluster B personality disorders overlap. The two diagnoses share affective instability and impulsivity. About 20% of the subjects with bipolar disorder met criteria for a cluster B personality disorder; presence of personality disorder did not affect differences between bipolar disorder and controls. The groups differed in correct detections (combined disorders lower), commission errors relative to correct detections (combined disorders higher), discriminability (combined disorders lower), and speed of the fastest SKIP response (combined disorders faster) (Tables 2 and 3). The differences were all consistent with disturbances similar to, but more severe than, those in subjects with bipolar disorder without an Axis II diagnosis.

4.4. Response inhibition and psychopharmacological treatments

Medication class had no significant effects on IMT or SKIP, except that subjects with antipsychotic treatment had longer maximum SKIP response delays, still substantially shorter than in controls. Subjects treated with only one drug type differed from other subjects, having fewer commission errors and slower reaction times, independent of the specific monotherapy. Subjects receiving one drug appeared less likely to have many depressive or total episodes (Fisher Exact Test=0.04 and 0.08). Subjects with a milder course of illness, requiring only one medication, may be more efficient in inhibiting rapid responses. Alternatively, this finding may be related to subtle behavioral impairment due to polypharmacy.

4.5. Limitations

Interpretation of these data must take potential problems, generally consequences of naturalistic design and of ethical and safety considerations, into account: 1) State- vs trait-dependence: a) the study was cross-sectional, making it impossible to assess trait- vs state-like characteristics directly; neither IMT nor SKIP appeared strongly related to current symptoms; b) exclusion of subjects with recent pharmacological changes may have reduced the detection of potential state-dependence by biasing the study toward more stable subjects; c) course of illness was determined retrospectively. 2) Pharmacological treatments: a) subjects were receiving a variety of medicines; the major findings were significant even in subjects with no current medicines, but the results suggested that patterns of treatments may interact with course of illness in a manner that could influence behavior and cognitive functioning; b) the study was generally adequately powered to detect differences associated with each medicine class and with the number of medicines taken, but not for the complete range of interactions among the four pharmacological classes.

5. Conclusion

These results suggest that attention and response inhibition are impaired in bipolar disorder, are associated with a more severe course of illness, and could be promising endophenotypes for bipolar disorder. Specificity of these abnormalities for bipolar disorder, relationships to neurobiological measures, and their presence in subjects at high risk for bipolar disorder, remain to be determined.

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Fig. 1.

IMT performance in subjects with bipolar disorder compared to controls. The bars show effect sizes for differences between controls and subjects with bipolar disorder. T-values are given above each bar. Below each bar, means with standard deviations are given: CD = Correct Detections as percent; CE = Commission Errors as percent; CE/CD = commission errors relative to correct detections; CD RT and CE RT are reaction times for correct detections and commission errors, respectively, in ms; A is discriminability, and B is response bias. Probability of *t*-tests: **p*<0.05; ***p*<0.001; ****p*<0.0001.

Fig. 2. SKIP performance in subjects with bipolar disorder vs controls. The bars show effect sizes. *t*-test values and their 2-tailed significances are given above each bar. Below each bar, log-transformed means and standard deviations are given for Total responses, time to the shortest response delay, and time to the longest response delay.

Table 1
Effects of diagnosis, age, gender, and education on IMT performance

GLM <i>F</i> (1,149)	CD	CE	CE/CD	CD RT	CE RT	A'	Beta
Diagnosis	9.2 (0.003)	0.1	2.2	31.5 (0.0001)	31 (0.0001)	8.6 (0.004)	4 (0.04)
Age	0.4	1.2	1.7	7.6 (0.006)	2.2	1.8	0
Education	0.4	10.7 (0.002)	9.5 (0.002)	2.1	1.4	3.4	4.8 (0.03)
Gender	0.1	0.8	0.8	0.4	0	0.3	1
Dx×gender	1.5	0	0	0	0.8	0.9	1.5

F ratios are given with the statistical significance in parentheses. Significant *F* ratios are shown in bold print. CD is correct detections; CE, commission errors; CE/CD, ratio of commission errors to correct detections; CD RT, the reaction time to a correct detection; CE RT, the reaction time to a commission error; A', discriminability; and beta, response bias.

Table 2

IMT performance and course of bipolar disorder

	Many episodes (<i>n</i>)		Suicide attempt (<i>n</i>)		Alcohol/substance abuse (<i>n</i>)		Axis II cluster B (<i>n</i>)	
	No (21)	Yes (31)	No (45)	Yes (35)	No (39)	Yes (45)	No (79)	Yes (25)
CD	80.9±13.1	78.0±14.0	76.7±14.2	76.9±15.5	73.9±16.1	81.9±12.2 ^{**}	79.8±13.6	71.4±14.8 ^{**}
CE	25.8±16.3	32.1±13.5	27.0±14.5	29.4±13.9	27.7±12.7	29.5±16.0	26.7±15	30.8±13.4
CE/CD	0.32±0.19	0.42±0.18	0.36±0.19	0.39±0.16	0.39±0.17	0.36±0.19	0.34±0.17	0.44±0.18 [*]
CD RT	542±98	512±61	547±93	529±71	539±75	530±87	546±83	512±77
CE RT	554±104	496±58 ^{**}	562±105	518±75 [*]	562±87	521±96 [*]	549±95	513±86
A'	0.851±0.076	0.811±0.079	0.825±0.084	0.824±0.076	0.812±0.082	0.843±0.078	0.845±0.073	0.787±0.083 ^{**}
Beta	-0.127±0.481	-0.238±0.482	-0.088±0.482	-0.152±0.551	-0.05±0.512	-0.254±0.477	-0.149±0.504	-0.035±0.518

Significantly different values are shown in bold print. CD is percent correct detections; CE, percent commission errors; CE/CD, ratio of commission errors to correct detections; CD RT, the reaction time (ms) to a correct detection; CE RT, the reaction time (ms) to a commission error; A', discriminability; and beta, response bias. Significance of differences, Student *t* test:

* <0.05,

** <0.01.

Table 3
Contribution of IMT and SKIP performance to course of illness: probit analysis

	Suicide at tempt		Alcohol/substance abuse		Many episodes		Axis II cluster B	
	Wald	p	Wald	p	Wald	p	Wald	p
<i>IMT</i>								
CD	0.2	0.6	5.81	0.02	1.61	0.2	10.4	0.001
CE	1.12	0.3	1.13	0.3	0.2	0.6	1.96	0.16
CD RT	6.76	0.009	8.37	0.004	1.34	0.25	0.28	0.6
CE RT	6.52	0.01	9.27	0.002	6.9	0.009	1.91	0.17
<i>SKIP^a</i>								
Total responses	1.14	0.3	4.07	0.04	5.56	0.02	1.24	0.26
Shortest delay	1.37	0.24	2.46	0.12	1.03	0.3	6.46	0.01
Longest delay	0.5	0.4	1.37	0.24	2.07	0.15	0.22	0.64
<i>Demographics</i>								
Age	0.03	0.8	0.12	3.36	0.1	0.8	0.6	0.4
Education	0.2	0.7	4	0.04	0.6	0.5	0.01	0.9

The table shows Wald statistics and their significances. CD = correct detections, CE = commission errors, CD RT is reaction time to a correct detection, and CE RT is reaction time to a commission error.

^a All SKIP measures were log transformed. Significant relationships are shown in bold face.