Published in final edited form as:

Bipolar Disord. 2010 May ; 12(3): 319–326. doi:10.1111/j.1399-5618.2010.00808.x.

Factors Associated with Functional Recovery in Bipolar Disorder Patients

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Abstract

Objectives—Among bipolar disorder (BPD) patients, functional recovery, defined as regaining individual premorbid residential and vocational status, is far less common than symptomatic recovery. As several factors have tentatively been implicated in outcomes in BPD, we investigated predictors of functional recovery among BPD patients, including demographic, clinical, and neurocognitive factors.

Methods—We assessed functional recovery status with standardized residential and occupational indices, neurocognitive functioning with performance-based neuropsychological tests, and collected demographic and clinical information for 65 euthymic or residually depressed, SCID-based DSM-IV type I or II BPD patients. We examined predictors of functional recovery with multiple logistic regression modeling.

Results—More education ($p=0.006$), fewer years of illness ($p=0.037$), and being married ($p=0.045$) were associated independently with functional recovery, even after controlling for residual depressive symptoms, diagnostic type (I vs. II), and psychiatric co-morbidity. Functionally unrecovered BPD patients performed less well than recovered patients on verbal fluency ($ES=0.54$, $p=0.03$), a measure of executive functioning, but this difference was not significant when adjusted for residual mood symptoms and education.

Conclusions—Among euthymic or mildly depressed BPD patients, functional recovery was associated with more education, being married, and fewer years of illness.

Keywords

bipolar disorder; functional recovery; neurocognition; education; marital status; illness duration

Psychosocial and occupational impairments in patients diagnosed with bipolar disorder (BPD) are highly prevalent despite modern therapeutic advances (1). A life-long and often debilitating illness, BPD affects at least 2% of the general population (2). As few as 20%–

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Disclosures: Dr Wingo has no relevant potential conflicts of interest. Dr. Baldessarini has recently been a consultant or investigator-initiated research collaborator with Auritec, Biotrofix, IFL, Janssen, JDS, Lilly, Luitpold, Merck, NeuroHealing, Novartis, Pfizer, and SK-BioPharmaceuticals Corporations, but is not a member of pharmaceutical speakers' bureaus, nor does he or any family member hold equity positions in biomedical or pharmaceutical corporations. Dr. Holtzheimer has been a consultant to Advanced Neuromodulation Systems, AstraZeneca, and Tetragenex Corporations. Dr. Harvey has been a recent consultant to Eli Lilly, Johnson & Johnson, Merck, Shire, and Daiippon-Sumitomo/America Corporations, and has current research support from Astra-Zeneca.

40% of BPD patients achieve social and occupational recovery to their own premorbid levels (1). In addition, only 19%–23% of adult BPD-I patients are married, compared to 60% of the general population (1). Of 2839 BPD patients in the Stanley Institute BPD Registry, 64% were unemployed even though 60% had some post-high school education or training, and 30% had completed college (3). Likewise, among the first 1000 BPD patients in the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD), 82% had some college education compared to 52% in the general US population, but 37% were unemployed or disabled compared to 3.7% of the contemporaneous general population (4).

Recovery among BPD patients has been conceptualized as involving several dimensions (5). Typically, *syndromal* recovery is defined as no longer meeting DSM criteria for an acute mood episode, *symptomatic* recovery as having low scores on standard ratings of mania and depression that indicate near-absence of symptoms, and *functional* recovery as regaining individual premorbid levels of psychosocial, residential, and occupational status (5). Using these criteria, the McLean-Harvard First Episode project followed first-episode, type I BPD patients from initial hospitalization for a DSM-IV manic or mixed episode: by two years, 98% achieved syndromal recovery, 72% symptomatic recovery, but only 43% reached functional recovery (6). With similar definitions, another study followed *mid-course* BP-I patients for a year after hospitalization for a manic or mixed episode: only 48% achieved syndromal recovery, 26% symptomatic, and 24% functional recovery (7). These studies suggest that nearly 60% of sometimes hospitalized, type I BPD patients treated by current methods failed to regain their own premorbid functional status within 1–2 years, even from illness-onset, and that prospects for functional recovery may be even poorer after prolonged illness. Moreover, symptomatic recovery does not necessarily lead directly to functional recovery.

An important question is what factors might facilitate or impede functional recovery of BPD patients, particularly considering those in or near symptomatic recovery. Some studies found that higher socioeconomic status (based on years of education and highest level of employment in the previous year), older age at first manic episode, and shorter hospitalization for the first manic or mixed episode predicted functional recovery, as defined above, within 1–2 years (6,7). However, when functional outcome was assessed across 15 studies and for groups rather than on a within-patient basis for occupational, residential, or social functioning, few demographic or clinical characteristics consistently predicted functional outcome (8). Not yet specifically assessed is a relationship between functional recovery and neurocognitive functioning, which can be significantly impaired even among euthymic BPD type I or II patients (9,10), and may influence functional outcomes (11,12).

Regarding neurocognitive functioning, euthymic BPD patients showed medium-to-large effect sizes (ES) for impairments of attention and processing speed (ES = 0.60–0.79), episodic memory (ES = 0.43–0.81), and executive functioning (ES = 0.47–0.71) in a meta-analytic review of 39 studies comparing 948 euthymic BPD patients and 1128 normal controls matched for age, sex, education, and estimated premorbid IQ (13). Cognitive impairment has been associated with impaired psychosocial functioning, even after adjusting for residual mood symptoms and relevant demographic and clinical variables (11). However, these studies used various, often broad, ratings of functional status, such as the Global Assessment of Functioning (GAF) Scale (12,14), Social Adjustment Scale (15), Multidimensional Scale for Independent Functioning (16), and none considered functional recovery based on individual return to baseline status.

Given this background, we evaluated associations of demographic, clinical, and neurocognitive factors with functional recovery, defined as regaining individual premorbid or previous highest level of residential and occupational status, among euthymic or only

mildly depressed BPD patients. We included residually depressed patients since longitudinal studies suggest that BPD patients experience subsyndromal depression or dysthymia during the majority of follow-up time in morbid states, despite access to modern treatments (17–19). We hypothesized that functional recovery would be associated with superior neurocognitive functioning, younger age, or more educational, professional and social accomplishment, including being married.

Methods

We recruited clinically stable BPD patients from the community, a residential and day treatment center, and the Emory University mental health clinics, in 2008 and 2009, with approval by the Emory University Institutional Review Board. Inclusion criteria were: [a] male or female outpatients; [b] age 18–65 years; [c] English as primary language; [d] SCID-supported DSM-IV diagnosis of type I or II BPD; [e] not hospitalized within 3 months; [f] currently stable as reflected by Montgomery-Åsberg Depression Rating Scale (MADRS) scores ≤ 14 (no more than mildly depressed) and Mania Rating Scale (MRS) scores ≤ 11 (no more than mildly hypomanic) at intake (20,21). Exclusion was based on: [a] meeting DSM-IV criteria for a substance-use disorder within the past 30 days or a schizoaffective disorder within a year; [b] pregnancy; [c] unstable medical condition; [d] neuropsychiatric illnesses associated with cognitive impairment; [e] previous brain injury or severe cerebral trauma; [f] any ECT treatment; [g] IQ < 70 . A total of 183 people responded to our advertisements. Of these, 76 were excluded by the preceding criteria, 42 could not be reached, were unable to participate, or changed their minds, and 65 participated after providing written, informed consent.

Clinical assessment

A structured clinical interview (SCID) based on DSM-IV-TR criteria (22) confirmed diagnoses of type I or II BPD of all included subjects. Current mood symptoms were assessed at intake with the MADRS depression (20) and MRS mania (21) rating scales. The presence of co-morbid Axis-I disorders was evaluated by a semi-structured, DSM-IV-based, clinical interview. Clinical and demographic characteristics were recorded. All clinical assessments were performed by an experienced psychiatrist-research fellow (APW).

Cognitive assessment

Cognitive assessment preceded evaluation of functional recovery, and was conducted by the same research fellow (APW) trained and supervised by a cognition expert (PDH). However, scoring of test results was deferred until completion of other assessments, so as to provide substantial “blinding.” Premorbid IQ was estimated with the vocabulary subtest of the Wechsler Adult Intelligence Scale III (WAIS-III; 23). Verbal learning and memory were rated with the Rey Auditory Verbal Learning test (RAVLT; 24). Attention, concentration, and mental tracking were assessed with the WAIS digit-span subtests and Trail-Making Test (TMT), Part A (23,24). Executive functions were evaluated with the Controlled Oral Word Association Test (FAS), Letter-Number-Sequencing Test (LNS) of the WAIS (23), and TMT, Part B (24).

Functional recovery status

Functional recovery was defined as regaining previous highest levels of residential and occupational functioning, using information from patients and corroborative informants (relatives, spouses, or friends who knew the patients well). We used the modified Residential Status Index (RSI) and Vocational Status Index (VSI), adapted from the McLean-Harvard First-Episode project with minor modifications, to rate residential and occupational functioning (6). The modified RSI provides highest-to-lowest ratings, as: [1]

independent (no supervision needed, such as a head of household, functional household member, living alone or with peer); [2] *semi-independent* (some supervision needed, such as in a supervised residence, boarding house, or living with family members under minimal supervision); [3] *dependent* (living under close supervision, such as with family members or in a personal-care home). The modified VSI provides highest-to-lowest ratings, as: [1] *full-time* gainfully *employed*, student, or functional homemaker; [2] *part-time employed* or student; [3] full or part-time *volunteer*; [4] on a medical or psychiatric *leave of absence*; [5] *unemployed*; or [6] *disabled*. Both previous highest and current residential and vocational status were estimated by APW, based on patient-reports and separately by telephone interviews of corroborative informants, by trained research assistants. Rare disparities in ratings were resolved by investigator-consensus. Functional recovery was operationalized as having ratings for current residential and vocational status that equaled or exceeded ratings for previous highest residential and vocational status on the RSI and VSI.

Statistical analyses

Analyses were performed using SAS Software (version 9.2[®] of 2008; SAS Institute, Cary, NC). Demographic and clinical variables were characterized with descriptive statistics. Data are shown as means $\pm$ SD for normally distributed continuous variables and median with interquartile range (IQR) for non-normally distributed continuous variables. Chi-square (χ^2) or Fisher's Exact test was used to compare proportions. Two-sample *t*-test or Wilcoxon rank-sum test was used to compare group means of continuous variables. Raw cognitive scores were standardized against scores from published normative samples (23,25–27) by creating *z*-scores (26). Cognitive scores of functionally recovered and unrecovered patients were compared using multiple linear regression with cognitive *z*-scores as the dependent variable, recovery status as the independent variable, and residual mood symptoms and education as covariates. To explore factors associated with functional recovery, variables with at least suggestive differences ($p < 0.15$) between recovered and unrecovered patients, based on bivariate descriptive statistics, were entered into a multiple logistic regression model using backward, forward, and stepwise selection methods. To that end, 10 covariates considered for the logistic regression model were education, marital status, race, MADRS score, time since the last major mood episode, sex, being treated with or without an antidepressant, number of current psychotropic medications, illness duration, and executive function (FAS *z*-score). Statistical significance required a two-sided *p*-value of 0.05.

Results

Demographic and clinical characteristics of all participants

Of the 65 DSM-IV BPD (64.6% type I, 35.4% type II) study-participants, 49% were women; age averaged (mean $\pm$ SD) 40.1 $\pm$ 13.2 years; 85% were Caucasian; education averaged 15.8 $\pm$ 2.6 years; 63% were employed (full- or part-time); 31% were married, and 43% were rated as having achieved functional recovery (Table 1). Median (IQR) onset-age was 15 (7.0) years; median illness duration was 25.0 (23.0) years; 69% had at least one comorbid psychiatric illness and 52% had at least one medical diagnosis. Current psychotropic drug treatments involved a median of 3.0 (2.0) agents/patient; 60.0% were taking an antidepressant with or without a mood-stabilizer or antipsychotic; 35.4% received only mood-stabilizers with or without antipsychotics, and 4.6% were not taking any medications (Table 1). At intake, 49 (75.4%) were considered euthymic, with MADRS 8 (median [IQR] = 3 [4]); 16 (24.5%) were residually depressed with MADRS scores of 8–14 (median = 11 [2.5]). Median time since last major mood episode was 6.5 (14.1) months.

Demographic and clinical factors associated with recovery

Unrecovered patients had fewer years of education ($p=0.001$), were less likely to be married ($p=0.02$), and more were African-American than Caucasian ($p=0.03$; Table 1). The unrecovered patients also tended to have had less time since a last major mood-episode recurrence ($p=0.07$), higher intake MADRS scores ($p=0.07$), and longer illness duration ($p=0.14$; Table 1). Among unrecovered patients, 67.6% were euthymic (MADRS ≤ 8) and 32.4% were residually depressed (MADRS: 9–14), compared to 86% euthymic and 14% residually depressed among recovered patients, at assessment ($p=0.09$). Among those taking an antidepressant, 35% achieved functional recovery whereas among those not taking an antidepressant, 56% had achieved functional recovery ($p=0.11$; Table 1). Of the 23 type II BPD patients, 35% achieved functional recovery, compared to 48% of the 42 type I patients (Table 1). Functionally recovered and unrecovered patients were similar in age, sex-distribution, onset age, major-depressive, manic or hypomanic, or any BPD episodes/year, proportion with co-morbid psychiatric or medical disorders, percentage with rapid cycling, history of psychosis, number of suicide attempts, number of psychiatric hospitalizations, and the number of current psychotropic medications/patient (Table 1).

Neurocognitive performance and recovery

Based on standardized z-scores, study-subjects, overall, performed 0.2 standard deviations (SD) worse on FAS, and up to 0.5 SD worse on verbal learning and memory, but more than a SD above normative standards on the WAIS vocabulary subtest (Table 2). Differences in cognitive performance between functionally recovered and unrecovered patients based on their standardized effect sizes (ES) indicate that unrecovered patients performed significantly less well than recovered patients on FAS (ES = 0.54; $p=0.03$), vocabulary (ES=0.47; $p=0.05$), and numerically less well on TMT-A (ES=0.32; $p=0.20$), immediate verbal learning and memory (ES = 0.28; $p=0.27$), and digit span (ES=0.27; $p=0.28$) tests (Table 2). However, after adjusting for residual mood symptoms and education using multiple linear regression, differences in cognitive performance between the functionally recovered and unrecovered patients were no longer statistically significant (Table 2).

Multiple regression modeling

Selection by forward, backward or stepwise procedures yielded the same three factors significantly and independently associated with functional recovery—more education, being married, and shorter illness duration (Table 3). The same three factors remained significantly associated with functional recovery after controlling for current depressive symptoms (MADRS score), BPD diagnostic type (I vs. II), and presence of co-morbid psychiatric disorders (Table 3). When time from the last mood episode and MADRS score were adjusted for in the regression model, more education ($p = 0.01$) and shorter illness duration ($p = 0.03$) remained significantly associated with functional recovery while marital status remained suggestive ($p=0.06$). One more year of education was associated with 1.45 (CI: 1.11–1.90) times higher chance for functional recovery. Being ill one year longer was associated with slightly less chance for functional recovery (OR=0.95 [0.91–0.997]). Being married was associated with 4.27 (CI: 1.03–17.7) times higher chance for functional recovery compared to being single or divorced.

Discussion

We investigated demographic, clinical, and neurocognitive factors for association with functional recovery in 65 euthymic or mildly depressed type I (65%) and II (35%) BPD patients. In multiple logistic regression modeling, we found that more years of education, being married, and fewer years from illness-onset were significantly and independently associated with functional recovery, even after adjusting for current depressive symptoms,

BPD subtype (I vs. II), and presence of psychiatric co-morbidity. These findings add to a growing body of knowledge on outcomes among clinically treated BPD patients and may support more informed prognosis.

Our findings are consistent with previous reports pertaining to the three factors found to be associated with functional recovery. First, higher socioeconomic status, based on education and employment, was associated with functional recovery in one study (7). Second, in a report from the Stanley Institute BPD Registry, a striking low proportion of nearly 3000 adult BPD patients (26%) were married (3). Being married may favor functional recovery owing to emotional, psychosocial, or financial support, and perhaps superior social skills (28,29). Among schizophrenia patients, too, the capacity to form intimate attachments with others had been associated with a more favorable prognosis (30). Third, the association of recovery with fewer years of illness is consistent with findings from two longitudinal studies, in which *first-episode patients* were more likely to regain functional recovery (39.5% at 6 months and 43.0% at 24 months [6]) than *mid-course* BPD patients (24% at 12 months of follow-up [7]).

Patients who had not achieved functional recovery despite being 4.5 months from their last illness-recurrence performed less well on verbal fluency, a measure of executive function, as well as on tests of vocabulary, attention, concentration, and mental tracking, and immediate verbal learning and memory. However, these differences were no longer significant after adjusting for residual mood symptoms and education, suggesting that cognitive performance is sensitive to clinical status and associated with educational achievement in the past, and calling for matching on both factors when testing cognition. A previous study found that executive performance, tested with the Stroop Color-Word and FAS tests during a first-lifetime psychiatric hospitalization in BPD patients, was correlated with latency to functional recovery, defined as returning to self-reported baseline functioning within a year (31). However, this Pearson correlation between executive performance and number of days to functional recovery was not adjusted for education or mood symptoms at the time of neurocognitive assessment (31).

Finally, *fewer* type II than type I BPD patients attained functional recovery (35% vs. 48%), although, with the relatively small samples involved, this difference was not statistically significant (Table 1). Nevertheless, this comparison adds to growing evidence that type II patients do not have a lesser illness, but one marked by more time in depressive states, with similar risks of both suicide and disability as in type I BPD (32,33). Moreover, type II BPD patients are reported to have greater disruptions of their health, diet, work, recreation, income, family and social relations, and self-improvement than type I patients (34). The observed tendencies for more functionally unrecovered BPD patients to take antidepressants (68% vs. 27%) and to have mild residual depressive symptoms (MADRS scores: 9–14) than recovered patients (32% vs. 14%) further suggest that even mild residual depressive symptoms may have a deleterious impact on functional recovery in BPD, as noted in other studies (35,36). More studies in BPD type II patients are needed to provide clinicians with more evidence-based guidelines in treating this challenging disorder.

Study limitations

Limitations of this study include its only partially blinded and cross-sectional design, a wide range of time from last major illness-recurrence, small sample-size, mix of types of BPD patients, convenience sampling from potentially heterogeneous sources, and possible recall bias in estimating previous functioning. In addition, the patients evaluated tended to have relatively high levels of IQ and education, and were mainly Caucasian, limiting the generalizability of findings to other groups. We recommend that this first study to investigate associations between objective, performance-based cognitive status and

functional recovery be followed-up with larger prospective studies using a wider range of cognitive measures in patient-subjects with a wider range of cognitive functional status, and with matching on demographic, educational, and clinical variables considered above. To that end, even without such matching, we estimate that approximately 130/group of functionally recovered and unrecovered BPD patients would be sufficient to detect a z -score difference of 0.5 with 80% power at $p = 0.05$, based on the present findings.

Conclusions

This study supports an association between functional recovery and more education, being married, and being ill for fewer years from onset among euthymic or very mildly depressed BPD patients. Depression-prone type II patients, those with even mild residual depressive symptoms, and those taking antidepressants also were less likely to achieve functional recovery. These associations may well reflect deleterious effects of residual depressive morbidity, which remains a major therapeutic challenge in BPD (37). This preliminary investigation provides several leads that require further testing with larger samples and a broad range of cognitive abilities.

Acknowledgments

Supported by an APIRE research fellowship from the American Psychiatric Institute of Research & Education (to APW), a grant from the Bruce J. Anderson Foundation and the McLean Private Donors Research Fund (to RJB), and NIH grant UL1 RR025008 (to APW). We thank Mitchel Klein, Ph.D. and Azhar Nizam, M.S. for valuable statistical advice, and Chloe Ekelem, Carla Heyler and Summer Niazi for excellent assistance with data collection.

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Table 1
Demographic and clinical characteristics versus functional recovery in bipolar disorder patients participated in the study

Factors	All Cases (n=65)	Recovered (n=28)	Unrecovered (n=37)	Test ^a	Statistic	p-value
<i>Sociodemographic characteristics</i>						
Women (n, %)	32 (49.2%)	17 (60.7%)	15 (40.5%)	χ^2	2.6	0.11
Age (years)	40.1 $\pm$ 13.2	39.1 $\pm$ 14.3	40.8 $\pm$ 12.5	<i>t</i>	0.5	0.61
Estimated IQ	120 (25)	120 (12.5)	115 (30.0)	WRS ^b	1028.0	0.17
Education (years)	15.8 $\pm$ 2.6	16.9 $\pm$ 2.2	14.9 $\pm$ 2.6	<i>t</i>	-3.4	0.001
Parent education (years)						
Father	16.0 (6.0)	16.0 (6.0)	16.0 (4.0)	WRS ^b	1007.5	0.26
Mother	14.0 (4.0)	14.0 (4.0)	14.0 (4.0)		977.0	0.36
Employment status (n, %)				χ^2	23.5	<0.0001
Employed (full or part-time)	41 (63.1%)	27 (96.4%)	14 (37.8%)			
Unemployed or disabled	24 (36.9%)	1 (3.6%)	23 (62.2%)			
Marital status				χ^2	5.7	0.02
Married	20 (30.8%)	13 (46.3%)	7 (18.9%)			
Single or divorced	45 (69.2%)	15 (53.6%)	30 (81.1%)			
Race/Ethnicity				Fisher ^b	9.0	0.03
Caucasian	55 (84.6%)	27 (96.4%)	28 (75.7%)			
African America	10 (15.4%)	1 (3.6%)	9 (24.3%)			
<i>Clinical characteristics</i>						
Median onset age (years [IQR])	15.0 (7.0)	15.0 (10.0)	15.0 (6.0)	WRS ^b	997.	0.34
Diagnostic type (n, %)				χ^2	1.0	0.32
Bipolar	42 (64.6%)	20 (71.4%)	22 (59.5%)			
IBipolar II	23 (35.4%)	8 (28.6%)	15 (40.5%)			
Illness duration (years)	25.0 (23.0)	15.0 (25.0)	28.0 (19.0)	WRS ^b	812	0.14
Co-morbid illnesses (n, %) ^c				χ^2		
Psychiatric	45 (69.2%)	18 (64.3%)	27 (73.0%)		0.6	0.45

Factors	All Cases (n=65)	Recovered (n=28)	Unrecovered (n=37)	Test ^a	Statistic	p-value
Medical	34 (52.3%)	13 (46.4%)	21 (56.8%)		0.7	0.41
History of psychosis (n, %)	29 (44.6%)	11 (39.3%)	18 (48.7%)	χ^2	0.6	0.45
Rapid cycling (n, %) ^d	23 (35.4%)	10 (35.7%)	13 (35.1%)	χ^2	0.0	0.96
Lifetime recurrences/year				WRS ^b		
Mania or hypomania	0.8 (1.8)	0.9 (2.4)	0.8 (1.7)		932	0.92
Depression	0.6 (1.6)	0.5 (1.0)	0.7 (1.7)		900	0.75
Any	1.7 (2.9)	1.6 (3.8)	1.7 (2.8)		914	0.90
Suicide attempts/patient	0.0 (1.0)	0.0 (1.0)	0.0 (1.0)	WRS ^b	897	0.68
Hospitalizations/patient	1.0 (3.0)	1.0 (3.0)	1.0 (3.0)	WRS ^b	895	0.70
Current morbidity scores				WRS ^b		
Depressive (MADRS)	4.0 (7.0)	3.0 (5.0)	5.0 (8.0)		783	0.07
Hypomanic (MRS)	1.0 (2.0)	1.0 (2.0)	1.0 (3.0)		909	0.84
Median months from last episode	6.5 (14.1)	10.5 (26.5)	4.5 (9.5)	WRS ^b	1046	0.07
Psychotropics/patient	3.0 (2.0)	2.0 (2.0)	3.0 (2.0)	WRS ^b	810	0.13
Treatments (patients, %) ^e				χ^2	2.5	0.11
With antidepressant	39 (60.0%)	14 (50.0%)	25 (67.6%)			
No antidepressant	23 (35.4%)	13 (46.4%)	10 (27.0%)			

Data are shown as means $\pm$ SD or medians (IQR).

^aStatistics compare functionally recovered vs. unrecovered patients.

^bFisher = Fisher exact test; WRS = Wilcoxon rank sum test

^cLifetime co-morbid psychiatric illnesses: substance use, generalized anxiety, social phobia; obsessive compulsive, post-traumatic stress, or eating disorders; medical illnesses are severe enough to have effects or require treatment.

^dRapid-cycling: 4 recurrent episodes in the past year.

^eAt time of assessment, 3 patients (4.6%) were not taking medications.

Table 2
Cognitive test scores for functionally recovered versus unrecovered bipolar disorder patients

Cognitive domain	z-Scores ^d			z-score Difference ^b	p ^c	Std. ES ^d	Adjusted Difference ^e [95% CI]	p ^f
	All Cases (n=65)	Recovered (n=28)	Unrecovered (n=37)					
Executive function								
Letter-number sequence	0.06 ± 0.92	0.02 ± 0.82	0.08 ± 0.99	-0.06 ± 0.92	0.81	-0.06	-0.19 [-0.70; 0.31]	0.45
FAS ^g	-0.19 ± 1.14	0.15 ± 1.13	-0.44 ± 1.10	0.60 ± 1.11	0.03	0.54	0.42 [-0.17; 1.01]	0.16
Trail Making-B	-0.10 ± 1.31	0.07 ± 1.10	-0.22 ± 1.44	0.30 ± 1.31	0.38	0.23	0.10[-0.95; 1.15]	0.85
Attention, concentration, mental tracking								
Digit span	0.2 ± 0.86	0.33 ± 0.73	0.10 ± 0.94	0.23 ± 0.86	0.28	0.27	0.02 [-0.45; 0.48]	0.94
Trail Making-A	-0.04 ± 0.91	0.13 ± 0.73	-0.17 ± 1.02	0.29 ± 0.90	0.20	0.32	0.14 [-0.36; 0.64]	0.59
Verbal learning and memory								
RAVLT ^h trials I-V	-0.53 ± 1.24	-0.33 ± 1.05	-0.68 ± 1.36	0.35 ± 1.24	0.27	0.28	0.19 [-0.50; 0.88]	0.58
RAVLT ^h immediate recall	-0.29 ± 1.22	-0.14 ± 1.06	-0.40 ± 1.33	0.26 ± 1.22	0.40	0.21	0.12 [-0.55; 0.80]	0.72
RAVLT ^h delayed recall	-0.40 ± 1.18	-0.31 ± 1.04	-0.47 ± 1.28	0.15 ± 1.18	0.60	0.13	0.05 [-0.61; 0.72]	0.87
Estimated premorbid IQ								
WAIS ⁱ vocabulary	1.18 ± 1.07	1.46 ± 0.77	0.97 ± 1.23	0.49 ± 1.05	0.05	0.47	0.17 [-0.39; 0.73]	0.55

^a z score <0 indicates performance below the mean of normative standards

^b Difference in z-scores for functionally recovered vs. unrecovered patients.

^c Probability from t-tests comparing z-scores (age-adjusted) of recovered vs. unrecovered patients

^d Standardized effect sizes (ES) are for z-score differences between unrecovered vs. recovered patients.

^e Difference in z-scores for recovered – unrecovered, adjusted for residual mood symptoms and education by multiple linear regression.

^f Probability for adjusted difference

^g FAS = Controlled Oral Word Association test with 3 word-naming components (trials F, A, and S).

^h RAVLT = Rey Auditory Verbal Learning test.

ⁱ WAIS = Weschler Adult Intelligence Scale III.

Table 3

Factors associated with functional recovery in the multiple logistic regression model

Factors	Multivariate OR [95% CI]	p-value
<i>Significant factors</i>		
More education	1.45 [1.11–1.90]	0.006
Married vs. unmarried	4.27 [1.03–17.68]	0.045
Shorter illness duration	0.95 [0.91–0.997]	0.037
<i>Nonsignificant factors</i>		
MADRS score	—	0.349
BD type (I vs. II)	—	0.411
Co-morbid psychiatric disorder (yes vs. no)	—	0.543

Likelihood ratio for the model: χ^2 [df=6] = 21.1; $p=0.002$.