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Correlates of recovery of social functioning in type I and II bipolar disorder patients

Aliza P. Wingo, M.D.^{a,*}, Ross J. Baldessarini, M.D.^b, Michael T. Compton, M.D., M.P.H.^a, and Philip D. Harvey, Ph.D.^a

^aDepartment of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, GA 30322

^bDepartment of Psychiatry and Neuroscience Program, Harvard Medical School, Boston, MA; Psychopharmacology Program and International Consortium for Bipolar Disorder Research, Mailman Research, Center, McLean Division of Massachusetts General Hospital, Belmont, MA 02478-9106

Abstract

Since bipolar disorder (BPD) patients are often functionally impaired, and factors associated with recovery from disability are largely unknown, we investigated demographic, clinical, and neurocognitive correlates of current social functional recovery in 65 stable participants diagnosed with DSM-IV type I (n=42) or II (n=23) BPD. Regaining highest previous levels of social functioning was rated with the Interpersonal Relationships Questionnaire. We also considered neuropsychological test findings as well as demographic and clinical information including mania and depression symptom-ratings. We examined factors associated with social recovery status using univariate analyses and then multiple logistic regression modeling. Of all subjects, 30 (46%) achieved current social functional recovery and 35 (54%) did not. Younger age ($p=0.005$) and lesser current depressive symptoms ($p=0.02$) were associated with social functional recovery, even after controlling for time since the last major mood episode, diagnostic type (II vs. I), co-morbid psychiatric illness, and executive functioning status. The findings are consistent with deleterious effects of even residual depressive symptoms in BPD patients.

Keywords

bipolar disorder; depression; neurocognition; social functional recovery; age

Correspondence to: Dr. Aliza P. Wingo, Emory University, Department of Psychiatry and Behavioral Sciences, 101 Woodruff Circle, NE (Suite 4000), Atlanta, GA 30322; Tel 404-727-9253; Fax: 404-727-3233, aliza.wingo@emory.edu.

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1. Introduction

Impairment in social functioning is strikingly prevalent among patients diagnosed with bipolar disorder (BPD), despite modern therapeutic advances (Carlson et al., 1974; Coryell et al., 1993; Gitlin et al., 1995; Robb et al., 1997; Huxley & Baldessarini, 2007; Druss et al., 2009). In the recent National Comorbidity Survey replication study, respondents diagnosed with BPD reported more interference by illness symptoms with their social and interpersonal relationships, even during periods of relative euthymia, than persons with various chronic medical disorders, including cancer, heart disease, diabetes mellitus, rheumatoid arthritis, and renal failure (Robb et al., 1997). Social impairment in BPD patients can persist for many years, even with sustained resolution of mood symptoms (Coryell et al., 1993). Recovery of past social functional levels was attained by only 45% of type I BPD patients within nine years (Carlson et al., 1974). Factors suggested as potentially related to high rates of sustained social dysfunction despite treatment include residual depressive symptoms, limited illness-insight, and impaired executive functioning (Gitlin et al., 1995; Yen et al., 2007; Yen et al., 2009). However, since studies of factors associated with social functional recovery defined as regaining one's own premorbid or highest previous level of social functioning remain rare, we investigated demographic, clinical, and neurocognitive factors associated with social functional recovery among euthymic or only mildly depressed BPD subjects, in the community.

2. Methods

In this cross-sectional study, in 2008–2009, we recruited clinically stable subjects diagnosed with DSM-IV BPD from the community, a residential and day treatment center, and Emory University affiliated mental health clinics by advertisements. The study was approved 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] having no history of hospitalization within the past 3 months; [f] currently clinically stable, supported 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 the time of assessment (Spitzer & Endicott, 1978; Montgomery & Asberg, 1979). Exclusion was based on: [a] meeting DSM-IV criteria for a substance use disorder within 30 days, or given a schizoaffective diagnosis within the past year; [b] pregnancy; [c] a severe and unstable medical condition; [d] neuropsychiatric illnesses associated with cognitive impairment; [e] previous brain injury or severe cerebral trauma; [f] any history of electroconvulsive treatment (ECT); [g] IQ < 70 as assessed by the Wechsler Adult Intelligence Scale vocabulary subtest (Wechsler D., 1987).

A total of 183 candidates responded to our advertisements; 76 were excluded by the preceding criteria and 42 were unable to participate; 65 participated after providing written, informed consent. This sample was involved in a previous study of factors associated with functional recovery based on regaining individual premorbid occupational and residential status (Wingo et al., 2010).

2.1. Clinical assessment

A structured clinical interview based on DSM-IV-TR criteria (SCID; (First et al., 1997) confirmed diagnoses of type I or II BPD. Current mood symptoms were assessed with the MADRS and MRS rating scales for depression and mania, for the previous week (Spitzer & Endicott, 1978; Montgomery & Asberg, 1979). Co-morbid Axis-I disorders were evaluated by semi-structured, DSM-IV-based, clinical interview. Clinical and demographic

characteristics were recorded. Clinical assessments were carried out by an experienced psychiatrist-research fellow (APW).

2.2 Social functional recovery

Functional recovery was defined as regaining highest previous level of social functioning. Both *current* and *highest previous* social functioning ratings were obtained from study participants using the Interpersonal Relationships questionnaire (IRQ) of the Functioning Assessment Short Test (FAST), a standardized, interviewer-administered instrument that addresses current functioning in the preceding two weeks and highest previous level of functioning at any time (Rosa et al., 2007). Among patients with BPD, the FAST has shown high internal consistency (Cronbach's $\alpha > 0.9$), strong concurrent validity, discriminant validity, and test-retest reliability for current functioning (Rosa et al., 2007). The IRQ includes six questions: Do you have difficulty in [a] maintaining one or more friendships, [b] participating in social activities, [c] maintaining good relationships with people close to you, [d] living with your family, [e] having satisfactory sexual relationships, [f] being able to defend your wishes or interests? Each item was rated for severity of difficulty using a 3-point Likert scale: 0 = no difficulty; 1 = mild; 2 = moderate; or 3 = severe difficulty. *Social functional recovery* as the outcome measure was operationalized as having scores for current social functioning equal to or less than scores for previous highest social functioning on the IRQ.

2.3 Cognitive assessment

Cognitive assessment preceded evaluation of functional recovery, was conducted by the same research fellow (APW) trained and supervised by a cognition expert (PDH), and 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 (1987) Adult Intelligence Scale III (WAIS-III). Verbal learning and memory were rated with the Rey Auditory Verbal Learning test (RAVLT) (Lezak et al., 2004). Attention, concentration, and mental tracking were assessed with the WAIS digit-span subtests and Trail-Making Test (TMT), Part A (Wechsler D., 1987; Lezak et al., 2004). Executive functions were evaluated with the Controlled Oral Word Association Test (FAS) (Lezak et al., 2004), Letter-Number-Sequencing Test (LNS) of the WAIS (Wechsler D., 1987), and TMT, Part B (Lezak et al., 2004).

2.4 Statistical analyses

Analyses was performed using SAS Software (Version 9.2© of 2008; SAS Institute, Cary, NC). Demographic, clinical, and neurocognitive variables were characterized with descriptive statistics. Data are shown as means $\pm$ standard deviations (SD) for normally distributed continuous variables, or medians with interquartile ranges (IQR) for non-normally distributed continuous variables. Two-sample *t*-tests or Wilcoxon rank-sum tests compared group means of continuous variables. Chi-square (χ^2) or Fisher's-Exact (*p*) tests compared proportions. Raw cognitive scores were standardized against scores from published normative samples (Wechsler D., 1987; Tombaugh et al., 1999; Tombaugh, 2004; Strauss et al., 2006) by creating *z*-scores (Strauss et al., 2006). Within each cognitive domain, *z*-scores were averaged to provide a composite, pooled *z*-score. To explore factors associated with social functional recovery, variables with at least suggestive differences ($p < 0.15$) between socially recovered and unrecovered patients based on univariate descriptive statistics (Table 1), were entered into a multiple logistic regression model using stepwise selection method. Statistical significance required a two-sided *p*-value of < 0.05 .

3. Results

Of the 65 DSM-IV BPD (42 type I, 23 type II) study-participants, 49% were women; mean age was 40.1 ± 13.2 years; median illness-duration was 25 (IQR = 23; range = 3–55) years; 85% were Caucasian; education averaged 15.8 ± 2.6 years; 63% were employed at least part-time; 31% were married; and 46% were rated as having achieved social functional recovery to their highest previous individual levels.

Regarding IRQ social *disability* scores (higher score means lower ability), overall (N=65 cases), median score for previous highest levels of functioning was 2 (IQR = 5; range 0-15) and for current functioning was 4 (IQR = 6; range 0-17). The 30 recovered patients (with current social-function scores equal to or better than their best previous scores) had median *current* scores of 1.5 (IQR=4; range 0–7) versus their own estimated best previous score of 3.0 (5; 0–15). The 35 unrecovered patients had *current* median social dysfunction ratings of 7.0 (6; 1–17), which were substantially greater (lower functional levels) than their highest previous scores of 2.0 (5; 0–15). The recovered and unrecovered subgroups had similar *previous* highest levels of social functioning, as reflected by their similar IRQ scores for previous highest social functioning (Wilcoxon rank-sum statistic = 1023, $p=0.66$).

Regarding characteristics of the socially recovered and unrecovered subgroups, both were similar in sex-distribution, ethnicity, estimated IQ, years of education, parental education, employment, and marital status (Table 1). However, recovered subjects were significantly younger ($p=0.004$), and had been ill for fewer years ($p=0.04$) than the unrecovered subjects. Both subgroups also were similar in attention, concentration, and mental tracking, verbal learning and memory, and executive functioning (Table 1).

Of all 65 study-participants, 49 (75%) were clinically euthymic with MADRS total scores ≤ 8 (median [IQR] = 3.0 [4.0]), and 16 (25%) were mildly depressed (MADRS = 9–14 (11.0 [2.5])). Socially unrecovered participants had higher MADRS scores at the time of assessment, had been ill longer, and received more psychotropic medications than the socially recovered participants (Table 1). However, the subgroups were similar in onset-age; proportions of BPD-subtypes; prevalence of co-morbid psychiatric or medical illnesses; past psychosis and rapid cycling; annual rates of lifetime major depressive or manic/hypomanic episodes or total mood episodes; number of suicide attempts; number of hospitalizations, and proportions taking antidepressants (Table 1). Median number of months (IQR) from the last major mood episode was 10 (25) for socially recovered participants and 5.5 (9.5) for unrecovered participants (Table 1).

3.1 Multiple regression modeling

Selection by stepwise inclusion of potential factors suggested by preliminary univariate analyses found two factors to be significantly and independently associated with social functional recovery: younger age ($p=0.005$) and lower current MADRS depression scores ($p=0.020$). These two factors remained significantly associated with social functional recovery even after controlling for time since the last major mood episode, presence of co-morbid psychiatric disorders, executive-function ratings, and BPD subtype (I versus II), based on multiple logistic regression modeling (Table 2).

4. Discussion

In this cross-sectional study of 65 euthymic (75%) or mildly depressed (25%) BPD type I and II study-participants, we investigated sociodemographic, clinical, and cognitive factors associated with social functional recovery. Social recovery was defined as returning to or exceeding one's own highest previous levels of social functioning. Younger age and lower

current depression scores were independently and significantly associated with social functional recovery. It is notable that even mild depressive symptoms (MADRS total scores of 9–14) were associated with non-recovery of social functioning, underscoring previous evidence of deleterious effects of residual depressive symptoms on functional recovery in treated BPD patients (Altshuler et al., 2006; Kauer-Sant'Anna et al., 2009). The association of younger current age with recovery of social functioning is consistent with at least one previous study ((Rosa et al., 2009), suggesting adverse effects of prolonged illness. This association, if replicated, would appear to encourage earlier intervention and systematic treatment.

The relatively small numbers of subjects of specific bipolar diagnostic types, and the cross-sectional design of this study preclude firm conclusions about chances of their social functional recovery, but type I (n=42) and II (n=23) BPD subjects appeared to be similarly likely to experience substantial current social dysfunction. This tentative impression is consistent with a previous longitudinal study (Judd et al., 2005). We also found previously that types I and II BPD were similarly disabling as reflected in non-recovery of individual best previous residential (independent living) and occupational status; factors associated with such dysfunction included less education, being unmarried, and longer illness (Wingo et al., 2010). These several findings add to growing evidence that type II patients do not have a lesser illness, but one marked by more time in depressive states and with similar suicide risks as in type I BPD (Tondo et al., 2007; Mantere et al., 2008).

This appears to be the first systematic study to examine a range of factors associated with current social functional recovery among stable or only mildly depressed BPD subjects. Nevertheless, our findings need to be confirmed with larger, and ideally longitudinal, studies that include assessments for time since last highest previous level of functioning, and with ratings that do not depend on participants' recall. It is unlikely, as suggested by one study, that changes in severity of mania or hypomania are consistently associated with differences in social functioning, especially when co-occurring depressive symptoms were adjusted for (Simon et al., 2007). Particular limitations of this study include relatively small subsamples, incomplete blinding, a cross-sectional design, and risk of recall bias in estimating previous highest social dysfunction. Moreover, the IRQ scale for rating social dysfunction requires further validation as a retrospective measure. Future studies should also examine the pattern of social functional recovery or non-recovery to determine whether social functioning is recovered after each mood episode, or gradually degrades over time, or remains at a chronically low or sub-optimal level in BPD patients.

Intensive psychosocial intervention, including cognitive-behavioral therapy, family-focused therapy, or interpersonal and social rhythm therapy, in combination with mood-stabilizing pharmacologic treatments appears to enhance social and other measures of functioning in BPD patients (Miklowitz et al., 2007a). Such psychosocial interventions have been particularly beneficial in enhancing stabilization from BP depression (Miklowitz et al., 2007b). Finally, both positive and adverse effects of various treatments should be studied further to compare social, residential, and occupational recoveries in type II as well as type I BPD patients.

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Table 1
Demographic, clinical, and cognitive characteristics versus social functional recovery status in 65 bipolar disorder I or II patients

Factors	Recovered (n=30; 46%)	Unrecovered (n=35; 54%)	Statistic	p-value
<i>Demographic Characteristics</i>				
Gender, female (n, %)	14 (46.7%)	18 (51.4%)	$\chi^2 = 0.15$	0.70
Current age (years)	35.1 $\pm$ 12.3	44.4 $\pm$ 12.6	$t = 2.99$	0.004
Estimated IQ	120 (15)	120 (30)	WRS = 1095	0.17
Education (years)	15.7 $\pm$ 2.6	15.9 $\pm$ 2.7	$t = 0.29$	0.77
Parent education (years; median [IQR])				
Father	16.0 (8.0)	16.0 (4.0)	WRS = 1105	0.12
Mother	16.0 (4.0)	13.1 (4.0)	WRS = 1090	0.12
Employment status (n, %)			$\chi^2 = 2.52$	0.11
Employed (full or part-time)	22 (73.3%)	19 (54.3%)		
Unemployed or disabled	8 (26.7%)	16 (45.7%)		
Marital status			Fisher Exact	0.29
Married	7 (23.3%)	13 (37.1%)		
Single or divorced	23 (76.7%)	22 (62.9%)		
Race/Ethnicity			Fisher Exact	0.74
Caucasian	26 (86.7%)	29 (82.9%)		
African American	4 (13.3%)	6 (17.1%)		
<i>Clinical Characteristics</i>				
Onset age (years; median [IQR])	15.0 (6.0)	15.0 (7.0)	WRS = 991	0.99
Diagnostic type (n, %)			$\chi^2 = 0.71$	0.40
Bipolar I (n=42)	21 (70.0%)	21 (60.0%)		
Bipolar II (n=23)	9 (30.0%)	14 (40.0%)		
Illness duration (years; ; median [IQR])	16.0 (21.0)	28.0 (25.0)	WRS = 834	0.04
Co-morbid illnesses (n, %) ^a				
Psychiatric	21 (70.0%)	24 (68.6%)	$\chi^2 = 0.01$	0.90
Medical	15 (50.0%)	19 (54.3%)	$\chi^2 = 0.12$	0.73
History of psychosis (n, %)	12 (40.0%)	17 (48.6%)	$\chi^2 = 0.48$	0.49
Rapid cycling (n, %) ^b	10 (33.3%)	13 (37.1%)	$\chi^2 = 0.10$	0.75
Lifetime recurrences/year (median [IQR])				

Factors	Recovered (n=30; 46%)	Unrecovered (n=35; 54%)	Statistic	p-value
Mania or hypomania	0.8 (2.3)	0.9 (1.5)	WRS = 1000	0.90
Depression	0.7 (1.6)	0.5 (1.4)	WRS = 1039	0.52
Any	2.2 (3.1)	1.6 (2.9)	WRS = 1015	0.74
Number of past suicide attempts	0 (1)	0 (2)	WRS = 951	0.56
Number of past hospitalizations	1 (3)	1 (3)	WRS = 1011	0.78
<i>Current symptom scores (median [IQR])</i>				
Depressive (MADRS)	1.5 (7.0)	6.0 (7.0)	WRS = 747	0.002
Hypomanic (MRS)	1.0 (2.0)	1.0 (3.0)	WRS = 921	0.35
Months since last major episode (median [IQR])	10.0 (25)	5.5 (9.5)	WRS = 1086	0.14
Number of psychotropics (median [IQR])	2 (1)	3 (2)	WRS = 814	0.02
<i>Treatments (n, %)^c</i>			$\chi^2 = 1.39$	0.24
With antidepressant	16 (53.3%)	23 (65.7%)		
No antidepressant	13 (43.3%)	10 (28.6%)		
<i>Cognitive functioning (z scores)</i>				
Executive function (median [IQR])	0.2 (0.7)	-0.4 (1.4)	WRS = 1114	0.11
Attention, concentration, mental tracking	0.1 ± 0.7	0.1 ± 0.7	t = 0.24	0.81
Verbal learning and memory	-0.3 ± 1.2	-0.5 ± 1.1	t = -0.49	0.62

Data are shown as mean ± SD or median (IQR)

Statistics compare functionally recovered vs. unrecovered patients; WRS = Wilcoxon rank-sum test.

^aLifetime co-morbid psychiatric illnesses: substance use, generalized anxiety, social phobia; obsessive compulsive, post-traumatic stress, or eating disorders; medical illnesses producing symptoms or requiring treatment.

^b≥4 recurrent episodes in the past year.

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

Table 2
Multiple logistic regression model for social functional recovery in 65 bipolar disorder subjects

Factors	Adjusted OR [95% CI]	p-value
<i>Significant factors</i>		
Older vs. younger age	0.93 [0.89–0.98]	0.005
Higher vs. lower MADRS depression ratings	0.82 [0.69–0.97]	0.020
<i>Nonsignificant factors</i>		
Months since last major episode	—	0.611
Co-morbid psychiatric illness	—	0.704
Executive function	—	0.571
BPD diagnostic type (I vs. II)	—	0.724

Likelihood ratio for the model: χ^2 [df=6] = 19.2; $p=0.004$.

Adjusted OR = adjusted odds ratio for achieving social functional recovery.