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The duration of inpatient admission predicts cognitive functioning at discharge in patients with bipolar disorder

Boaz Levy^{*}, Matthew R. Stephansky, Kris C. Dobie, Benedetta A. Monzani, Anna Marie Medina², and Roger D. Weiss

¹Department of Psychiatry, Harvard Medical School/McLean Hospital, 115 Mill St. Belmont, Massachusetts, USA

²Gonzaga University Psychology Department, Spokane, Washington, USA

Abstract

Previous studies of cognitive functioning in bipolar disorder generally indicate that a more severe course of illness is associated with greater cognitive impairment. In particular, a history of greater number and longer duration of mood episodes predicts enduring cognitive deficits in euthymic patients. Shifting the focus of this investigation to the cognitive effects of a discrete mood episode, the current study aimed to explore whether patients who require a longer hospitalization to stabilize from an acute episode of mood disturbance present with more compromised cognitive functioning during the phase of early recovery. For this purpose, the study examined the link between the duration of inpatient admission and neuropsychological test scores at the time of discharge in 41 patients with bipolar disorder. Participants were assigned to long (n=20) and short (n=21) stay groups, using a median split (M=12). Results indicated that longer admissions were associated with more severe deficits in executive functioning at discharge, after controlling for residual mood symptoms and previous number of psychiatric admissions. Findings from the current study may inform discharge planning for patients with bipolar disorder following an extended hospital stay.

Keywords

Cognitive Impairment; Neuropsychology; Bipolar Disorder; Inpatients

1. Introduction

Patients with bipolar disorder often exhibit impairment in cognitive functioning (1). The cognitive dysfunction associated with bipolar disorder tends to be most severe and least differentiated during phases of acute mood disturbance (2). Although deficits typically diminish and narrow in scope over the course of remission, the presence of debilitating cognitive impairment sometimes persists into periods of euthymia (3,4).

Studies investigating cognitive impairment in bipolar disorder consistently find an association between persistent cognitive dysfunction and different measures of illness severity such as the frequency and duration of mood episodes, age of onset, and the number of inpatient admissions (1,5,6). These findings have advanced the notion that enduring disturbance in mood leads to neuro-degeneration and cognitive decline in patients with bipolar disorder (3). While efforts to examine this hypothesis have generally focused on the

^{*}Corresponding author. boaz_levy@hms.harvard.edu.

course of illness, the characteristics of a discrete mood episode that may be related to cognitive functioning during early remission from acute disturbance have received little attention. Examining the relationship between different characteristics of a discrete mood episode and cognitive functioning during early remission may be important for treatment planning, especially at the time of discharge from inpatient care.

The current investigation examined the link between the duration of an inpatient admission and cognitive functioning at the time of discharge in patients with bipolar disorder. Specifically, the study aimed to determine whether bipolar disorder patients who require a longer psychiatric hospitalization to stabilize an episode of mood disturbance suffer from greater cognitive deficits during the phase of early recovery. We hypothesized that longer hospital stay would predict poorer performance on neuropsychological tests at discharge, after controlling for residual mood symptoms and previous number of psychiatric admissions.

2. Method

2.1 Subjects

Forty-one inpatients at McLean Hospital who met DSM-IV diagnostic criteria for bipolar I disorder (manic=29, depressed=6, mixed=6) completed the neuropsychological battery. We classified participants into two groups based on a median split of hospital stay (i.e., number of hospital days). Above and below the median hospital stay of 12 days formed the longer (n=20) and shorter (n=21) hospitalization groups, respectively. Participants included 20 men and 21 women, of whom 33 identified themselves as Caucasian and 8 indicated an affiliation with an ethnic minority group. Twenty-one participants were single, 10 were married, and 10 were divorced. These patients participated in a larger study that explored neurocognitive functioning in patients with co-occurring bipolar and substance use disorders. However, to rule out the confounding effects of substance use on cognitive functioning, none of the participants included in the present study met diagnostic criteria for a lifetime substance use disorder. The admission notes documented 9 cases (6 in the short stay group and 3 in the long stay group) where patients discontinued medication without medical supervision prior to admission. With respect to medications with known cognitive side effects, 2 patients were prescribed anticholinergic drugs (both patients were assigned to the short term group) and 1 patient (in long term group) was prescribed topiramate. The use of first generation antipsychotic medication was not present in the current sample. Overall, the treatment of patients over the course of hospitalization was primarily psychopharmacological in nature. This treatment was supplemented by educational, art, support, relapse prevention and discharge plans groups.

2.2 Inclusion/Exclusion Criteria

Participants in this study were inpatients, age 18 to 59, who met DSM-IV diagnostic criteria for bipolar I disorder. To control for the cognitive effects of severe mood symptoms, inclusion criteria also required a Beck Depression Inventory – Second Edition (BDI-II) score < 15 (7), a Beck Hopelessness Scale (BHS) score < 10 (8), and a Young Mania Rating Scale (YMRS) score < 15 (9) at the time of testing. Patients who received electroconvulsive therapy during the 12 months prior to admission or who presented with a history of neurological illness or injury were excluded from the study. A review of medical records and a structured interview with patients yielded this information.

2.3 Diagnosis and Procedure

All participants were recruited for the study only after the hospital treating physician established a diagnosis of bipolar I disorder, based on information from clinical interviews,

family members, and outpatient treatment providers. After obtaining informed consent, a trained clinician administered the Structured Clinical Interview for DSM-IV (10) – Part I to confirm participants' diagnosis. Upon enrollment, participants' clinical status was monitored through a daily review of updates in the medical chart and verbal communication with the treatment team. Following a treatment team determination that the patient was sufficiently stable for discharge, a trained examiner administered the neuropsychological battery and mood measures. This procedure occurred 24–48 hours prior to discharge.

2.4 The Neuropsychological Battery

Standardized measures with well-established reliability and validity were used to assess memory, executive functioning, attention and working memory, and IQ. We assessed perceptual organization and visual memory, using the Rey Complex Figure test (RCF; 11). To evaluate verbal memory, we administered the Logical Memory subtest from Wechsler's Memory Scale-Revised (12), and the California Verbal Learning Test II – Short Form (13). Measures of executive functioning included the Stroop Color-Word Interference Test (14), the Controlled Oral Word Association Test (COWAT) – FAS letters format, and Animal Naming Task (15) – and the Wisconsin Card Sorting Test – 64 Card Version (16). We administered several measures to examine attention and working memory, including the Digit Span subtest from the Wechsler Adult Intelligence Scale – Third Edition (17), Trails Making Test parts A and B (18), and the Letter and Symbol Cancellation Task. The score on the latter task reflected speed (i.e., time in seconds) and accuracy (i.e., number of targets correctly identified), as indicators of total quality of performance (19). Finally, we employed the Wechsler Abbreviated Scale of Intelligence (20) to obtain an estimate of IQ.

2.5 Statistical Analysis

Group differences in demographic and clinical data were analyzed using Pearson's chi-square and t-tests for categorical and continuous variables, respectively. Group differences in neuropsychological test scores were determined by a multivariate analysis of covariance (MANCOVA), using mood measures administered at the time of testing (i.e., BDI-II and YMRS scores) and previous number of psychiatric hospitalizations as covariates. The tests were categorized into cognitive domains as measures of attention, visual memory, verbal memory, and executive functioning. Post-hoc between-subjects effects for individual measures were tested with ANCOVA, again covarying mood measure scores and number of prior hospitalizations. The analysis applied standardized Scaled Scores for the cognitive measures (mean = 50, standard deviation = 10; CVLT-II immediate and delayed recall and recognition scores had a mean of 0 and standard deviation of 1), with lower values representing poorer performance.

3. Results

3.1 Clinical and Demographic Variables

No group differences between the short and long-stay groups (Duration of stay in days: Mean=8.4, SD=2.3 and Mean=15.3, SD=2.1, respectively) were detected for age of onset for bipolar disorder, previous number of psychiatric admissions, number of psychiatric medications taken on the day of testing, and diagnostic subtype upon admission. Moreover, results showed no group differences for either depressive or manic symptoms, gender, marital status, age or years of education. Table 1 presents means, standard deviations, and test statistics of the clinical and demographic variables.

3.2 Cognitive Measures

Memory—Analysis detected significant group differences in visual memory (Wilks' Lambda, $F_{(7,30)}=3.95$, $p<0.01$), as measured by the Rey Complex Figure test. As Table 2 reveals, the analysis of between-subjects effects indicated more compromised performance in the group with longer hospital stay in the immediate recall ($p<0.02$) and recognition of the figure's parts ($p<0.05$). The analysis of delayed recall was marginally significant ($p<0.08$). The MANCOVA procedure for measures of verbal memory was significant (Wilks' Lambda, $F_{(7,30)}=2.9$, $p<0.01$). However, no significant group differences emerged for any of the specific verbal memory measures.

Executive Functioning—The MANCOVA procedure yielded highly significant group differences in measures of executive functioning. (Wilks' Lambda, $F_{(7,30)}=7.07$, $p<0.0001$). As Table 2 indicates, highly significant results emerged for the Stroop, Wisconsin Card Sorting Test, and COWAT (FAS). The group with the longer hospital stay performed significantly more poorly on these measures than the group with the shorter stay.

Attention, Working Memory and IQ—A MANCOVA procedure revealed no group differences on measures of attention and working memory (Wilks' Lambda, $F_{(7,30)}=1.78$, $p<0.13$). Similarly, no differences emerged in any of these measures on the tests of between-subjects effects. The MANCOVA procedure approached significance for IQ tests (Wilks' Lambda; $F_{(7,30)}=2.77$, $p<0.08$). However, no differences emerged in the comparison of the associated individual subtests.

4. Discussion

The results of the current investigation indicated a link between the duration of inpatient hospitalization and cognitive functioning at discharge in patients with bipolar disorder. Longer admission predicted more severe deficits in executive functioning, as indicated by more compromised performance on tasks tapping the ability to inhibit automatic responses (Stroop), retrieve verbal concepts without a categorical context (COWAT: FAS), and adjust the process of non-verbal concept formation in response to corrective feedback (WCST). The long-stay group also performed more poorly than the short-stay group on a visual memory task (Rey Complex Figure), a measure that is particularly sensitive to the adverse effects of executive dysfunction (i.e., deficits in the organization of complex information). This analysis may inform further speculation about whether a longer acute mood disturbance in bipolar disorder exacerbates deficits in executive functioning during early remission. Conversely, it is also possible that compromised cognitive functioning may in itself somehow impede recovery from an acute mood episode. The results of this study may also reflect the previously demonstrated association between illness severity and cognitive functioning in bipolar disorder (21,22,23,24,25), where more severe patients – identified here by longer hospital stay – exhibit greater cognitive dysfunction.

The reported association between hospital stay and cognitive functioning may be consistent with the notion of allostatic load. This notion was advanced by Kapczinski et al. (26) as a mechanism that may contribute to cognitive impairment in bipolar disorder. Allostatic load refers to the 'wear and tear' of the body and brain that results from the physiological exertion needed to adapt to environmental stress (27). Kapczinski et al. (26) proposed that the association between illness severity and cognitive impairment in bipolar disorder may be explained by an allostatic overload, where greater challenge or more intense emotional distress lead to more severe neurological damage and cognitive decline. In our sample, it is possible that patients who required a longer hospital stay also experienced a more stressful mood episode or greater acute allostatic load. Future research may explore whether a heavier

allostatic load (i.e. as indicated by physiological markers of stress) in discrete mood episodes impedes cognitive recovery in bipolar disorder during early remission.

The results of the current study carry potential implications for clinical care. Previous reports indicated that neurological abnormalities typically associated with frontal lobe and executive dysfunction impair psychosocial functioning (28). In particular, deficits in organization, planning, and problem-solving can seriously compromise patients' ability to negotiate demands of everyday life in unsupervised settings (3,29). Psychosocial functioning, in fact, has been found to correlate more with neuropsychological measures than with other clinical variables of bipolar disorder (2). The impact of cognitive deficits on psychosocial functioning may be important to consider at the time of discharge from inpatient care. Underestimating the extent of executive dysfunction in bipolar disorder patients requiring longer admissions can lead to discharge plans that do not fully facilitate recovery. Our results suggest that longer-stay patients may be especially vulnerable for impaired psychosocial functioning upon discharge. Thus, our findings highlight the importance of assessing the availability and sensitivity of social support networks, as part of effective discharge planning for patients who require longer admission.

Several limitations of the current study deserve mention. The assessment of cognitive functioning was conducted at one point in time. This methodological constraint limits conclusions about the direct contribution of a single episode of mood disturbance to cognitive decline in bipolar disorder. A follow-up assessment several months after discharge would allow for the examination of the degree of cognitive recovery in patients who reached a state of full remission. The current study employed statistical control over the impact of mild mood symptoms, which is less methodologically advantageous than a longitudinal design. In addition, depressive symptoms were assessed with self-report measures, which may be less accurate in bipolar patients who are recovering from acute disturbance. There is little concern, however, that patients experienced severe mood symptoms during the assessment, as the depression measures were cross validated with mental status notes from the medical chart, the structured diagnostic interview and clinician observations. At the same time, the inaccuracy in measurement may have increased variance due to error and decreased statistical power, as the BDI-II was used as a covariate. Error in measurement may have been further increased from having the same examiner administer both the mood measures and neuropsychological test battery. Possible examiner's expectations regarding the correlation between mood and test performance may have contributed to inaccuracies in measurement and decreased statistical power. It is also worthwhile noting that medications probably affected performance on testing; however, the naturalistic clinical setting in which the study was conducted did not allow us to control for medication type and doses. The sample size of the current study was relatively small, so an independent replication of results is warranted. In addition, the statistical analysis may have had limited power, and therefore may underestimate the presence of deficits in other cognitive domains such as verbal memory or attention.

Despite these limitations, the current study supports the larger notion that greater illness severity is associated with more severe cognitive dysfunction in patients with bipolar disorder. The current data indicate that longer duration of hospital stay is correlated with more severe deficits in executive functioning during the phase of early remission. These results illuminate the challenges bipolar disorder patients may face after discharge from a long inpatient admission, and underscore the need to develop better care for their outpatient recovery.

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Table 1

Clinical and demographic variables

Measures	Short Stay Group(n=21)		Long Stay Group(n=20)		t	Sig.
Continuous	Mean	SD	Mean	SD		
Education	14.5	2.71	15.1	1.45	-0.81	0.47
Age	34.4	12.92	37.9	12.51	-0.82	0.37
Onset	27.0	11.21	28.7	11.01	-0.55	0.62
Admissions	5.8	7.71	6.1	6.71	-0.14	0.81
YMRS	6.5	4.24	6.7	3.92	-0.59	0.96
BDI – II	7.7	3.27	7.8	3.56	-0.14	0.93
BHS	4.0	3.71	4.4	4.33	-0.33	0.74
Categorical	n		n		Chi Square	Sig.
Psychosis	6		11		2.94	0.09
Suicidality	4		6		0.66	0.41
Employed	12		7		2.02	0.15
Insurance type	H=6, P=4, M=7, O=3		H=5, P=2, M=11, O=3		2.29	0.51
Marital status	S=8, M=6, D=7		S=13, M=4, D=3		3.16	0.20
Aftercare	O=8, P=7, R=6		O=5, P=8, R=7		0.18	0.66
Medication class						
Lithium	14		11		0.58	0.44
Benzodiazepam	5		8		1.24	0.26
Neuroleptics	18		19		1.00	0.31
Anticonvulsant	12		8		1.20	0.27

Note: BDI=Beck Depression Inventory, BHS=Beck Hopelessness Scale, YMRS=Young Mania Rating Scale, Admissions=previous number of psychiatric admissions, Onset=age of first psychiatric admission for mood disturbance, Insurance type (H=HMO, P=PPO, M=Medicare, O=Other), Marital status (S=Single, M=Married, D=Divorced), Aftercare (O=Outpatient, P=Partial Hospital, R=Residential Treatment).

Table 2
Group Comparison of Scaled Scores of Visual Memory and Executive Functioning Measures

Test of Between-Subjects Effects				Means and Standard deviations of measures			
Measures	MD	MS	df	F	r	Short Stay Group(n=21) Mean	Long Stay Group(n=20) Mean
Visual Memory							
Rey-C	1.1	11.5	4.0	0.51	-0.06	30.9	29.8
Rey-I	12.2	408.6	4.0	3.35*	-0.42**	40.1	27.9
Rey-D	7.5	248.8	4.0	2.22	-0.28	33.4	25.9
Rey-R	9.1	329.7	4.0	2.59*	-0.31*	47.3	38.1
Executive Functioning							
FAS	10.3	372.6	4.0	3.81**	-0.36*	61.7	51.4
Animals	5.4	118.1	4.0	1.33	-0.28	48.7	43.2
Stroop-CW	9.6	302.6	4.0	3.85**	-0.39**	49.6	40.0
WCST-C	1.0	4.06*	4.0	2.02	-0.28	2.9	1.8
WCST-N	13.4	481.5	4.0	5.51***	-0.52***	45.9	32.4
WCST-P	4.3	105.4	4.0	2.43	0.09	43.3	39.9

Note: MD = Mean Difference (short-long), MS = Mean Square, SD = Standard Deviation, FAS = Controlled Oral Association Test, Stroop - CW = Color-Word Condition, WCST = Wisconsin Card Sorting Test (C = number of categories completed, N = non-perseverative errors, P = perseverative errors, r=correlation between cognitive measure and hospital stay.

* =P<0.05,

** = P<0.01=

*** =P<0.001.