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The characteristics of a discrete mood episode, neuro-cognitive impairment and re-hospitalization in bipolar disorder

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Abstract

This longitudinal study examined characteristics of a discrete mood episode that predict re-hospitalization for bipolar disorder, highlighting associated cognitive dysfunction as a potential mechanism linking episode severity and relapse. Eighty-two inpatients meeting DSM-IV-TR diagnostic criteria for bipolar I disorder completed the study. Twenty-two of the patients were readmitted to the hospital within 3 months of discharge. The study compared these patients to the remaining 60 patients who were not readmitted to the hospital during this period. Patients were compared on several factors related to the severity of the mood episode and the course of illness more generally. Analysis also compared the groups on measures of mood and neuro-cognitive functioning, assessed 24–48 hours before initial hospitalization discharge. Re-hospitalized patients had longer initial hospital stays ($t = -3.10$, $p < 0.01$), higher rates of psychosis while in the hospital (Chi square=5.1, $p < 0.02$), and lower GAF scores on discharge ($t = 2.37$, $p < 0.05$). The groups did not differ in age of illness onset or number of previous psychiatric hospitalizations. With respect to neuro-cognitive functioning, analysis indicated poorer performance for re-hospitalized patients on measures of executive functioning (Wilks' Lambda, $F(7, 71) = 9.0$, $p < 0.001$), IQ (Wilks' Lambda, $F(2, 76) = 5.06$, $p < 0.01$), and memory (Wilks' Lambda, $F(6, 72) = 4.19$, $p < 0.001$). Trends in the expected direction emerged for attention/working memory tests (Wilks' Lambda, $F(7, 71) = 1.79$, $p < 0.10$). Results highlight features of a discrete mood episode associated with increased rates of re-hospitalization. This study observed connections among episode severity, cognitive dysfunction at hospital discharge and re-hospitalization.

Keywords

bipolar disorder; relapse; cognitive dysfunction

1. Introduction

Bipolar disorder (BD) affects about 2% of the world population, representing the sixth leading worldwide cause of psychosocial disability, morbidity, and suicide (Murray & Lopez, 1996). Over the past 15 years, a large volume of studies have shown that patients with BD suffer from significant impairment in cognitive functioning compared to healthy controls (Basso et al., 2002; Kurtz & Gerraty, 2009; Sánchez-Morla, 2009). Although cognitive dysfunction in BD manifests most severely during episodes of acute mood

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disturbance (Martinez-Aran et al., 2004a), debilitating deficits often persist into periods of euthymia (Martinez-Aran et al., 2004b; Torres et al., 2007). Linger cognitive dysfunction in asymptomatic patients has led to theories about possible chronic neurological impairment in BD (Kurtz & Gerraty, 2009; Martinez-Aran, 2004b; Marvel & Paradiso, 2004).

Current theories of cognitive dysfunction in BD emphasize neurodegenerative factors. The neurodegenerative hypothesis suggests that the excessive stress associated with chronic mood disturbance leads to progressive neurological damage and impairment (Goodwin et al., 2008; Kapczinski et al., 2008). Support for the neurodegenerative hypothesis comes from the robust link consistently found between illness severity (i.e., number and duration of mood episodes; number of psychiatric hospitalizations) and cognitive dysfunction (Cavanagh et al., 2002; Clark et al., 2002; Basso et al., 2002; Kurtz & Gerraty, 2009; Robinson et al., 2006; Sánchez-Morla et al., 2009; Torres et al., in press). Thus, the recurrence of mood disturbance potentially carries neuro-toxic effects and lead to cognitive decline over the course of illness (Kapczinski et al., 2008).

Additional accounts of cognitive dysfunction in BD point to the potential involvement of neuro-developmental processes (Terry et al., 2009; Torres et al., in press). Recent studies found significant deficits in sustained attention, learning, memory, nonverbal reasoning and executive function very early in the course of BD (Kolar et al., 2006; Pavuluri et al., 2009; Robinson et al., 2006; Terry et al., 2009). It is therefore possible that certain cognitive deficits in BD emerge during neuro-development, and grow progressively worse over the course of illness. Taken together, the neuro-developmental and neuro-degenerative models provide a trait-like account of the cognitive dysfunction observed in asymptomatic patients with BD.

With the current theoretical emphasis on trait-like factors, “state” factors that may contribute to cognitive impairment in BD receive less attention. In particular, certain characteristics of a discrete mood episode might affect the degree of cognitive dysfunction patients experience during early remission (Frangou et al., 2005; Jaeger et al., 2007; Jud et al., 2008; Segal et al., 2006). In two recent studies, length of hospital stay (Levy et al., 2009) and psychosis (Levy & Weiss, 2008) were correlated with cognitive functioning at discharge from inpatient care, beyond the predictive value of clinical factors related to the general course of illness. These preliminary results suggest that a more severe mood episode may be associated with greater cognitive impairment during early remission. On the physiological level, the pace of neurological recovery from acute mood disturbance may depend in part on the severity and duration of the episode, beyond the severity of the illness more generally.

The investigation of neuro-cognitive recovery from a discrete mood episode may carry important implications for patient-care, especially at the time of discharge from the hospital. Whereas cognitive impairment likely remains inconspicuous in the custodial environment of the inpatient unit, it may quickly overwhelm patients as they attempt to negotiate the functional demands of less-supervised environments post-discharge (Dion et al., 1988; Jaeger et al., 2007; Keck et al., 2008; Levy et al., 2008; Winokur et al., 1993). Facing increasing functional demands with cognitive impairment may intensify residual symptoms, and undermine stability. There is some evidence that residual symptoms during early remission from an acute mood episode may be more predictive of relapse in BD than factors related to the course of illness more generally (Judd et al., 2008). Thus, a more severe mood episode and poorer neuro-cognitive functioning at hospital discharge may predispose patients to greater mood instability during early affective remission and eventually lead to relapse (Levy et al., 2008; Levy & Weiss, 2008; Levy et al., 2009).

The current investigation examined this hypothesis. The study explored clinical and cognitive differences between patients who were readmitted to the hospital within 3 months after discharge and patients who maintained outpatient level of care during the same period. Re-hospitalization was hypothesized to be associated with a more severe mood episode (psychosis, longer duration of hospital stay, more severe residual mood symptoms), beyond factors related to the general course of illness (i.e. previous number of hospitalizations, age of illness onset), and with poorer neuro-cognitive functioning at the time of discharge.

2. Method

2.1 Subjects

One hundred and three inpatients at McLean Hospital who met DSM-IV-TR diagnostic criteria for bipolar I disorder signed informed consent for the study. All of these participants were admitted to the hospital due to an acute mood disturbance. Sixteen participants failed to complete the initial assessment before discharge. Five additional participants withdrew from the study after discharge. Of the remaining 82 participants (age range: 18–59), 53% were men, and 23% indicated an affiliation with a minority group. Fifty-four percent of participants were single, 27% were married, and 19% were divorced.

In the entire sample (n=82), 22 participants were readmitted to the hospital within 3 months of discharge. In this group, 15 participants were re-hospitalized for an acute mood disturbance and 7 participants were readmitted to a unit that specialized in the treatment of substance use disorders. Among the 60 participants who were not re-hospitalized, 14 met diagnostic criteria for alcohol dependence in the past year, and 7 reported abuse or dependence for multiple drugs, including alcohol. None of the participants required a detoxification protocol upon admission to the initial hospitalization. Additional demographic and clinical variables are summarized in Table 1.

2.2 Inclusion/Exclusion Criteria

All of the participants in this study were adults (age ≥ 18) with a diagnosis of bipolar I disorder. None of the participants received electroconvulsive therapy during the 12 months prior to admission, nor presented with a history of neurological illness or injury. To control for the possible effects of severe mood symptoms on test performance, inclusion criteria further required a Beck Depression Inventory – Second Edition (BDI-II) score < 15 (Dozois et al., 1998) a Beck Hopelessness Scale (BHS) score < 10 (Beck et al., 1974) and a Young Mania Rating Scale (YMRS) score < 15 (Young et al., 1978).

2.3 Diagnosis and Procedure

Treating clinicians on the hospital unit referred potential participants for the study, based on the inclusion/exclusion criteria described above. Patients who expressed interest in the study were approached by a member of the research team for a detailed explanation of the study's procedure and informed consent. The initial evaluation consisted of an administration of the Structured Clinical Interview for DSM-IV – Part I (First et al., 1994). At this time, researchers also obtained further clinical information to confirm the diagnosis from both the medical record and from consultation with the attending psychiatrist and treatment team. In this process, the research team gathered data about psychiatric and medical history, as well as recent symptoms and psychosocial functioning. GAF scores were obtained from the discharge note, generated by the 4 attending psychiatrists on the unit. Additional information was gleaned from available records of prior hospitalizations, and documented reports from family members and outpatient mental-health workers. Participants were scheduled for assessment only after the treatment team on the unit determined sufficient stability for discharge. On the day of testing, no active psychotic symptoms were noted by examiners. In

addition, no psychotic symptoms were reported in the medical chart since the time participants were scheduled for testing. Trained examiners administered the mood measures and a neuropsychological battery 24 to 48 hours before discharge. The examiners were blind to group assignment during testing and scoring. After discharge, the treatment team maintained telephone contact with participants monthly to verify status of care.

2.4 The Neuropsychological Battery

The neuropsychological battery included measures with well-documented norms and satisfactory estimates of reliability and validity. The battery assessed 5 areas of cognitive functioning: executive functioning, IQ, attention and working memory, verbal memory, processing of complex visual material and visual memory.

Executive Functioning

- 1 Trail Making Test (TMT), Parts A and B (Corrigan et al., 1987; Gaudino et al., 1995; Spreen & Strauss, 1998). TMT A measures visual scanning and sequencing, requiring participants to draw a line between consecutive numbers printed on a page as fast as they can. TMT B measures planning, sequencing, and the ability to shift cognitive set. On TMT Part B, patients draw a line connecting 25 encircled letters and numbers in an alternating sequence (i.e., 1-A-2-B). Results are reported in a ratio score between TMT B and TMT A to form an index for executive control related to set-switching (Arbuthnott and Frank, 2000).
- 2 Controlled Oral Word Association Test (COWAT) - FAS letters format, and Animal Naming Task (Tombaugh et al., 1999). The test measures phonemic and semantic fluency, requiring participants to retrieve as many words as they can that begin with F, A and S, and the names of as many animals as they can in 60 seconds.
- 3 Stroop Color-Word Interference Test (Golden et al., 2002). This test assesses inhibition of dominant or over-learned responses in favor of responses that are more relevant to task demand. Participants are asked to name the color of the ink of words that verbally label the name of a different color (e.g., the word GREEN written in blue ink).
- 4 Wisconsin Card Sorting Test (WCST) – 64 Card Version (Heaton et al., 2003). This is a test of non-verbal concept formation, cognitive flexibility and ability to benefit from feedback. Participants are asked to match a target card to 1 of 4 alternatives, while receiving corrective feedback. After 10 consecutive correct matches, the rule shifts without announcement and participants need to accommodate their strategy accordingly. A review (Greve, 2001) of studies comparing the 64-card and full versions of the WCST concluded that there is a solid case for the comparability of the two tests, and for the clinical utility of the WCST-64. The review noted that, although the WCST-64 has reliable and valid psychometric properties and a substantial normative basis, the comparability of the tests has not yet been fully established across all types of populations.

IQ

- 5 Wechsler Abbreviated Scale of Intelligence (WASI) - Vocabulary and Block Design subtests (Wechsler, 1999). The WASI was designed as an abbreviated measure for estimating IQ, derived from the Wechsler Adult Intelligence Scale – Third Edition (WAIS-III). There is evidence for satisfactory correlations of summary scores between WASI and WAIS-III in non-patient populations

(Wechsler, 1999); although, an increase in measurement error of IQ has been observed in samples that included people with dementia and neurological illness (Axelrod, 2002). Changes in the psychometric properties of the WASI in people who suffer from bipolar disorder is currently unknown.

With respect to the test components, the Vocabulary subtest requires participants to provide definitions for words on a scale of gradual difficulty. On the Block Design subtest, participants manipulate colored blocks to match an integrated design, which does not portray the outline of the single pieces. The score is determined by accuracy and speed of execution.

Of note, the current study was not designed to produce an estimate of a Full Scale IQ because we expected to observe a verbal/performance split in impaired patients. In addition, the study strived to minimize cognitive fatigue during testing by an economical choice of subtests. On the verbal side, we included the Vocabulary subtest because it carries the largest loading on g factor. On the performance side, Block Design was preferred over Matrix Reasoning (which is technically required for calculating Full scale IQ on the WASI) because of its well-documented sensitivity to neurological impairment, which relates to executive dysfunction. (Lezak, 2009).

Attention and working Memory

- 6 Digit Span subtest from the Wechsler Adult Intelligence Scale – Third Edition (Wechsler, 1997). This is a test of auditory attention span and working memory. Participants are required to repeat a string of digits forward and then backward.
- 7 Letter and Symbol Cancellation Task (Spreen & Strauss, 1998). This is a test of visual scanning, where participants are required to mark specified symbols or letters with a pencil at maximum speed.

Verbal Memory

- 8 California Verbal Learning Test II – Short Form (Delis et al., 1999). This is a list-learning task, consisting of 9 words, which is administered over the course of 4 acquisition trials, followed by an immediate and 20-min. delayed recall of the words.
- 9 Logical Memory from Wechsler Memory Scale-R (Wechsler, 1987). This test assesses memory of the gist and details of stories that are read to subjects.

Processing of complex visual material and visual memory

- 10 Rey Complex Figure test (Meyers & Meyers, 1995). In this test, participants are required to copy a complex visual design and then reproduce it from memory after a short and long delay.

2.5 Statistical Analysis

Cognitive data were analyzed with Multivariate Analysis of Variance (MANCOVA) on PASW-18. This procedure was repeated 5 times for the different cognitive domains outlined above, and employed psychosis, duration of hospitalization, and GAF scores as covariates. The same covariates were applied in post-hoc analyses of between-subjects effects for individual measures. Experimentwise type I error for multiple comparisons was controlled with Rom's (1990) procedure. Scores for cognitive measures included Standard Scores, based on normative data (mean = 50, SD = 10; California Verbal Learning Test II, immediate and delayed recall and recognition scores all had means of 0 and a SD of 1; Digit Span scores had a mean of 10 and a SD of 3; TMT scores converted from a standard normal distribution to T scores, based on $T=50+/- 10Z$). In all tests, lower values reflected poorer

performance. To analyze group differences in demographic and clinical data, we employed Pearson's chi-square as well as t-tests for categorical and continuous variables, respectively.

3. Results

3.1 Clinical and Demographic Variables

Table 1 reveals similarities and differences between the groups with respect to demographic and clinical variables. The groups did not differ in terms of age, age of illness onset, education, employment or formal disability status, nor were they distinct with regard to number of prior hospitalizations, diagnostic subtype or number of psychiatric medication taken on the day of testing. However, several key group differences were observed. Participants who were readmitted had been initially hospitalized approximately three days longer than those who were not ($p < 0.01$). In addition, participants who were re-hospitalized also obtained lower GAF scores from the discharging psychiatrists; the mean group difference was 3 points ($p < 0.05$). Finally, whereas 40% of the group that maintained outpatient level of care experienced psychosis, that rate for the re-hospitalized group was approximately 68% (Chi-square=5.1, $p < 0.24$). No other significant differences emerged in clinical and demographic variables. Based on these analyses, the multivariate analysis of group differences on cognitive measures employed duration of hospital stay, GAF scores and psychosis as covariates.

3.2 Cognitive Measures

Executive Function—Neuro-cognitive assessment was performed 24–48 hours before hospital discharge. The multivariate procedure yielded highly significant group differences in measures of executive functioning (Wilks' Lambda, $F(8,70) = 5.14$, $p < 0.001$). As Table 2 indicates, the MANCOVA procedure revealed poorer performance for participants who were re-hospitalized on tests that assess planning and shifting of cognitive set (TMT B/A), phonemic fluency (FAS), inhibition of over-learned or automatic responses (Stroop), and the ability to detect and adapt to changes in rules according to corrective feedback (WCST). No differences emerged on the word reading (mean=40.56/37.3, $SD=11.4/11.7$, $t=1.13$ $p < 0.26$) or color naming (mean=39.1/37.50, $SD=11.0/11.8$, $t=1.11$ $p < 0.39$) components of the Stroop test between non-rehospitalized/rehospitalized patients, respectively. In addition, no group differences emerged in set losses on WCST (re-hospitalized group mean = 1.14, non-rehospitalized group mean = 1.10, $t=0.14$, $p < 0.8$).

IQ, Attention and Working Memory—Significant group differences emerged on the measure of IQ (Wilks' Lambda, $F(2,76) = 5.06$, $p < 0.01$). The post-hoc procedure indicated that whereas patients who were re-hospitalized performed significantly worse on Block Design ($MS=308.4$, $df=4$, $F=2.84$ $p < 0.029$), no such differences emerged on Vocabulary ($MS=192.7$, $df=4$, $F=1.99$ $p < 0.10$).

Although marginally significant group differences emerged on measures of attention and working memory on the omnibus multivariate procedure (Wilks' Lambda, $F(5,73) = 1.79$, $p < 0.55$), the ANCOVA tests for differences on individual measures highlighted a significant difference on the unstructured cancellation subtests for both symbol ($p < 0.01$) and letter ($p < 0.04$), with the re-hospitalized group exhibiting poorer performance.

Memory—The multivariate procedure revealed significant group differences for measures of both verbal and visual memory (Wilks' Lambda, $F(6,72) = 4.19$, $p < 0.001$). As Table 3 reveals, the ANCOVA procedure indicates poorer performance for re-hospitalized participants on delayed auditory recall for stories ($p < 0.03$), and on immediate recall of a word-list ($p < 0.05$). All other subtests show a similar trend with significance levels ranging

from 0.08 to 0.12. Significant differences emerged more consistently for memory and processing of complex visual material (Wilks' Lambda, $F(4,74) = 5.64$, $p < 0.001$). Re-hospitalized participants performed more poorly on all subtests of the Rey Complex Figure Task (including copy, immediate recall, delayed recall and yes/no recognition of the figure's parts).

4. Discussion

The current study explored clinical and cognitive differences between patients with BD who maintained outpatient status 3 months after discharge from the hospital and patients who were readmitted to an inpatient unit during this period. Group differences emerged on measures marking the severity of the discrete mood episode (i.e., length of hospital stay, psychosis, GAF scores on discharge), but not on measures related to the general course of illness (i.e., age of onset and number of previous psychiatric hospitalizations). Participants who were re-hospitalized suffered from a more severe mood episode leading to the hospitalization. They also performed more poorly on various neuropsychological measures at discharge. The cognitive differences remained significant after controlling for length of hospital stay, psychosis, and GAF scores. Thus, re-hospitalization was associated with the severity of the discrete mood episode and the degree of cognitive impairment during early remission.

The current results are consistent with earlier work showing that markers of episode severity correlate with levels of cognitive impairment at the time of hospital discharge (Levy et al., 2009). The replication of this finding further supports the hypothesis that a more severe mood episode predicts greater cognitive dysfunction during early mood remission. However, the data offer no insight into possible neurological accounts for this association. From a broader perspective on the course of illness, various markers of illness severity in general, and psychosis in particular, are related to both cognitive dysfunction and readmission (Milkowitz, 1992; Martinez-Aran et al., 2008; Tohen et al., 2000). It is therefore possible that the co-variances among these factors also emerge in the context of a discrete mood episode: patients who suffered a recent episode of psychosis might be more likely to experience greater cognitive deficits and become more vulnerable to relapse.

In the current study, group differences in cognitive functioning were evident in a variety of domains, especially in executive functioning (effect sizes ranged from .72 to 1.25). The large differences between the groups on measures of visual processing/visual memory (i.e., the Rey Complex Figure tests) and Block design (e.g. a measure of fluid intelligence) may also be attributed to disturbances in executive functioning (Somerville et al., 2000). In BD, disturbances in executive functioning have been tied to difficulties in accomplishing ordinary tasks (Bell-McGinty et al., 2002; Gildengers et al., 2007; Martinez-Aran et al., 2007; Mur et al., 2007; Mitchell & Miller, 2008; Royall et al., 2004). Executive functions have been described as crucial to performing tasks of daily living (Bonnín et al., 2010; Martinez-Aran, et al., 2007; Sanchez-Moreno, 2009; Torres, 2008) and important to the quality of life of patients (Brissos et al., 2008a, 2008b). In addition, research has shown that executive functioning is involved in both behavior and emotion regulation as well as social competence (Riggs et al., 2006; Zelazo & Cunningham, 2007). A number of recent investigations reported that adverse life events and disruption in social rhythm, including difficulties in psychosocial functioning, predicted relapse in persons with BD (Altman et al., 2006; Cohen et al., 2004; Hosang et al., 2010a, 2010b; Johnson et al., 2008; Kim et al., 2007; Malkoff-Schwartz et al., 2000; Post et al., 2006; Sylvia et al., 2009). Thus, problems with executive function may compromise the ability to meet functional and social demands of daily living, and potentially lead to relapse and re-hospitalization.

Several limitations of the current study deserve mention. The sample size is relatively small, and may only offer preliminary results that require replication. In the context of a naturalistic observation, the study did not control for the effects of medications, although groups did not differ with respect to the number of medications taken on the day of testing. The duration of hospitalization may have been affected by confounding factors, leading to premature discharge of patients with longer hospital stays. Recent substance use and SUD more generally may have also affected both test performance and readmission; however, the groups did not differ in ratios of participants who suffered from SUD co-morbidity. In addition, we were unable to determine inter-judge reliability for GAF scores generated by the attending psychiatrist on the unit, as the scores applied to different patients. Despite the longitudinal nature of the study, conclusions about cause and effect are limited. The current study reported no measurement of cognitive and clinical variables post-discharge, and did not control for various additional factors that can account for relapse. To consolidate conclusions, future longitudinal research should assess patients' stress levels, substance use, sleep patterns, family functioning, and ability to meet the demands of daily living at multiple points in time following hospital discharge. Future investigations should also examine patients' capacity for emotional regulation in relation to both executive functioning and vulnerability to relapse. Such measurement would permit clearer causal pathways to be drawn between cognitive impairment, functional and emotional regulation difficulties, and changes in BD symptoms. Despite these limitations, this longitudinal study suggests that characteristics of a discrete mood episode predict cognitive functioning during early remission and re-hospitalization.

Finally, the results of the current study carry implications for patient care. Patients who are admitted to the hospital with psychosis, require longer hospital stay to stabilize, receive lower GAF scores, and suffer from significant cognitive impairment at discharge may be at higher risk for re-hospitalization. These patients may be of greater need for a highly supervised post-discharge environment and on-going supportive services. The severity of the mood episode and level of cognitive functioning while in the hospital may inform clinical decisions regarding patient-care post-discharge. For screening purposes, a brief executive battery may be a parsimonious approach to cognitive evaluation upon hospital discharge in routine clinical practice. Future research may attempt to form normative data for episode duration, lingering residual symptoms, and patterns of cognitive deficits during early remission from a mood episode. This information may be useful for making forward prediction of relapse.

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Group comparisons of clinical and demographic variables

Table 1

Variable	Patients stable at 3 months follow up (n=60)		Patients relapsed by the 3 months follow up (n=22)		t	P Value	Effect size: Cohen's d
Continuous	Mean	SD	Mean	SD			
Education	14.5	2.2	13.7	2.1	1.4	0.14	
Age	38.4	11.6	39.9	12.7	-0.49	0.62	
Onset	25.8	9.1	26.9	9.1	-0.44	0.61	
Admissions	5.8	6.1	6.1	4.1	-0.23	0.81	
P. Admission	4.4	3.1	4.0	3.2	0.37	0.71	
YMRS	6.2	3.6	7.5	3.6	-1.40	0.16	
BDI - II	8.0	3.0	8.9	3.3	-1.19	0.23	
BHS	4.2	3.4	4.6	3.8	-0.56	0.57	
Hospital Stay	10.8	2.8	13.6	4.7	-3.1	0.002***	.82
GAF	59.8	5.4	56.8	3.9	2.37	0.02*	.59
Categorical	n	n	Chi Square	p			
Psychosis	24	15	5.1	0.02			
Diagnostic subtype	Manic=38 Mixed=13 Depressed=9	Manic=15 Mixed=5 Depressed=2	0.48	0.78			
Disability	42	17	0.22	0.51			
Employment	26	9	0.39	0.84			
Medication type							
Lithium	32	9	0.99	0.31			
Benzodiazepine	12	5	0.73	0.78			
Neuroleptic	38	17	1.4	0.23			
Anticonvulsant	28	11	0.07	0.78			
Anticholinergic	3	0	---	---			

Note: BDI=Beck Depression Inventory, BHS=Beck Hopelessness Scale, YMRS=Young Mania Rating Scale, Admissions=previous number of psychiatric admissions, P. Admissions=number of years past from previous admission (n=66), Onset=age of first psychiatric admission for mood disturbance. Hospital Stay=duration of admission in days, GAF=Global Assessment of Functioning (from the medical record).

* P<0.05,

*** P<0.01=

P<0.001.

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Table 2
Group Comparison of Scaled Scores of Attention/Working Memory and Executive Functioning Measures

Test of Between-Subjects Effects				Means and Standard deviations of measures			
Measures	MD	MS	df	F	Sig.	Mean	SD
Attention/Working Memory							
CT-SS	4.7	131.2	4.0	0.88	0.47	40.1	11.7
CT-SU	7.6	342.5	4.0	3.3**	0.01	41.1	10.9
CT-LS	2.9	164.4	4.0	1.31	0.27	42.4	10.0
CT-LU	6.6	294.7	4.0	2.66*	0.04	41.5	11.4
Digit Span	1.2	10.9	4.0	2.14	0.83	8.5	2.4
Executive Functioning							
TMT-B/A	0.62	1.61	4.0	4.4**	0.003	2.03	0.47
FAS	9.5	481.9	4.0	2.9*	0.02	50.7	12.9
Animals	3.1	158.0	4.0	2.1	0.08	44.1	8.6
Stroop-CW	9.6	521.8	4.0	7.7***	0.0001	43.3	8.7
Stroop-INT	8.9	432.9	4.0	5.3***	0.001	45.2	10.0
WCST-C	1.2	6.45	4.0	4.16**	0.004	2.0	1.33
WCST-N	10.6	462.5	4.0	5.25***	0.001	39.4	9.6
WCST-P	6.0	253.4	4.0	3.78***	0.007	41.7	7.8
						35.7	9.8

Note: MD = Mean Difference, MS = Mean Square, SD = Standard Deviation, CT = Cancellation Test (SS=Symbol Structured, SU=Symbol unstructured, LS=Letter Structured, LU=Letter Unstructured), TMT=Trails Making Test (B/A=ratio of raw score in seconds), FAS/Animals = Controlled Oral Association Test, Stroop (INT = Interference, CW=color word condition), WCST = Wisconsin Card Sorting Test (C = number of categories completed – raw score, N = non-perseverative errors, P = perseverative errors), Sig. = Significance level (p value),

* P<0.05,

** P<0.01=

*** P<0.001.

Table 3

Test of Between-Subjects Effects				Means and Standard deviations of measures						
				Patients stable at 3 months follow up			Patients relapsed by 3 months follow up			
Measures	MD	MS	df	F	Sig.	Mean	SD	Mean	SD	Effect size: Cohen's d
Verbal Memory										
LM-I	6.0	169.1	4.0	1.87	0.12	42.8	9.6	36.8	8.7	
LM-D	7.4	240.8	4.0	2.83 [*]	0.03	42.7	9.7	35.3	6.9	.82
CVLT-AQ	6.3	207.7	4.0	2.15	0.08	40.4	10.1	34.1	8.4	
CVLT-I	0.9	3.86	4.0	2.46 [*]	0.05	-0.7	1.3	-1.6	1.0	.73
CVLT-D	0.7	2.22	4.0	1.99	0.10	-1.0	1.0	-1.7	1.1	
CVLT-REC	0.5	3.05	4.0	2.14	0.08	-0.9	1.2	-1.4	1.0	
Visual Memory										
Rey-C	3.7	104.3	4.0	5.13 ^{***}	0.001	30.8	3.9	27.1	6.3	.80
Rey-I	8.1	334.7	4.0	3.26 ^{**}	0.01	37.3	9.9	29.2	10.5	.81
Rey-D	7.1	365.4	4.0	3.44 ^{**}	0.01	32.4	10.4	25.3	10.5	.68
Rey-REC	9.2	410.9	4.0	3.73 ^{**}	0.008	40.5	10.9	31.3	9.0	.88

Note: MD = Mean Difference, MS = Mean Square, SD = Standard Deviation, LM = Logical Memory (I = Immediate Recall, D = Delayed Recall), CVLT=California Verbal Learning Test (AQ=Acquisition, I=Immediate recall, REC=Recognition), Rey (C=copy, I=Immediate, D=Delayed Recall, REC=Recognition), Sig. = Significance level (P value),

^{*}P<0.05,
$$^{**} P<0.01=$$

P<0.001.