

Working Memory Impairment in Euthymic State of Bipolar Disorder

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Abstract

Introduction: Cognitive deficits in bipolar disorders persist after the subsidence of active symptoms. This study was carried out to assess the working memory of patients with bipolar disorder in euthymic state.

Material And Method: Forty euthymic bipolar patients attending a tertiary care mental hospital with equal number of matched controls in terms of age, sex and education were included in the study. Working memory assessments was done using WAIS-III digit span subtest.

Results: The mean of total digit span test for case group was 8.48 ± 2.04 similarly it was 10.33 ± 2.32 for the controls. The result showed that the mean digit span of cases and control groups are significantly different (p value of < 0.01). The Pearsons correlation between the clinical variables and working memory test in euthymic bipolar patients (case group) was found that the total score for digit span test was negatively correlated with all other clinical variables However, this correlation was found to be non-significant.

Conclusion: The working memory impairment persists in remitted bipolar disorder patients and this may represent underlying trait abnormality not the state abnormality.

Keywords: Bipolar Disorder, Mania, Euthymic state, Memory Disorder

INTRODUCTION

Bipolar disorders are common, recurrent and debilitating illness characterized by fluctuations in mood.^{1,2} Bipolar disorder has been reported as being the sixth leading cause of disability worldwide in terms of global health burden.³ The lifetime prevalence of bipolar disorder is estimated to be between 1.0 to 5%.⁴ It has been found that patients with bipolar disorder in a euthymic state experience difficulties in various domains of social, cognitive and occupational functioning.^{5,6} A study by Thompson et al., found that euthymic bipolar clients have a deficit in their ability to monitor the contents of working memory.⁷ Another study found that the bipolar patients in remission seems to be both affectively disturbed and have impaired

working memory.⁸ study have shown subtle deficits were present in attention and working memory during euthymic period of bipolar illness but those deficits weren't statistically significant.⁹ Study of neuro-cognitive performance in the euthymic phase of bipolar disorder have demonstrated a perseveration of neuro-cognitive impairment in a number of areas like impairment in the domains of motor speed, as well as verbal learning, and several measures of memory (verbal, visual and working memory).¹⁰ Research has also demonstrated impairment in higher cognitive functioning including working memory during remission phase of bipolar disorder as demonstrated by performance on the Wisconsin card sorting test.¹¹

This study was carried out to assess the working memory of patients with bipolar disorder in euthymic state.

MATERIAL AND METHOD

A descriptive cross-sectional analytical study was carried out in Mental Hospital, Lagankhel, Lalitpur from January 2016 to December 2016 after obtaining ethical approval from Institutional review board-National Academy of Medical Sciences. Written informed consent was obtained from patient and controls for enrollment. Purposive sampling method was opted. First forty people stabilized on medication of age 20 to 60 years with DSM-5 diagnosis of bipolar affective disorder were recruited from outpatient department. Illness characteristics were derived from patients and their relatives via interview along with reviewing hospital medical records. Patients taking benzodiazepines; patients with any other co-morbid psychiatric, medical or neurological conditions; patient with history of co-morbid substance use and history of ECT in the past 6 months were excluded from the study. Euthymia was defined as score of <7 on the 17-item Hamilton Depression Rating Scale (HAM-D17)⁷ and a score of <7 on the Young Mania Rating Scale (YMRS) on the day of study.¹² For the control group, 40 people matched on individual basis with euthymic bipolar patients for age, gender and years of education were recruited from non relative friends of the patient, staffs working at the mental hospital or students volunteering at the mental hospital with no current or past history of any Psychiatric disorder. Absence of psychopathology was concluded after evaluation from two consultant psychiatrists and if agreed that the control subject is free from any psychiatric morbidity. Controls were excluded if they had past history of psychiatric illness, family history of affective and or psychotic disorders in the first degree relatives, had history of traumatic brain injury or any other medical or neurological condition and/or history of psychoactive substance use. A semi structured self designed questionnaire was suitably designed after 10% of respondents pretesting to collect information regarding the demographic variables in both groups. Assessment of socioeconomic status was done

by using Kuppuswamy's socioeconomic status scale for Nepal.¹³

Neuropsychological measures to assess working memory on participants was done with the digit span subtest from the WAIS-III.¹⁴ The test was administered to assess the working memory. The task was given in same order to whole sample.

Statistical analysis was conducted using the statistical package for social sciences, version 20.0. Data were first examined to see if they fulfilled the assumptions for parametric test. Variables fulfilling these assumptions were analyzed by t-test. Data not fulfilling the assumptions of parametric analysis were analyzed non-parametrically with chi-square test. P values were reported. Descriptive measures like mean, standard deviation were used. To study the impact of illness on digit span test correlations were calculated using Pearson's method.

RESULT

There was no significant group difference across age and educational status among both groups (Table 1). On YMRS and HAM-D17 clinical rating scales patients exhibited more scores compared to controls which were significant (Table 2). The mean digit span of the cases and control groups are significantly different (Table 3). Total score for digit span test (working memory test) non-significantly correlated with all clinical variables: age of onset, total duration of illness, total number of episodes, number of hospitalizations, total number of previous ECT and duration since last episode (Table 4).

Table 1: Mean Age & Education Of Cases & Controls

	Case	Control	t-stat	p-value
N	40	40		
Mean age (in years)	33.75	34.08	-0.153	0.879
Std. Deviation	9.47	9.57		
Std. Error Mean	1.50	1.51		
Mean education (in years)	8.70	8.70	0.000	1.000
Std. Deviation	4.09	4.09		
Std. Error Mean	0.65	0.65		

Table 2. Mean of Clinical variables in the euthymic bipolar (case) and control group

Characteristic	Case		Control		t-stat	p-value
	Mean	SD	Mean	SD		
Age Onset (in years)	21.85	6.81	NA	NA	NA	NA
Total duration of illness (in years)	11.96	8.03	NA	NA	NA	NA
Total number of episodes	3.73	2.21	NA	NA	NA	NA
Duration since last episode (in months)	27.70	25.78	NA	NA	NA	NA
Number of hospitalization	1.95	1.83	NA	NA	NA	NA
Total number of previous ECT	0.88	2.09	NA	NA	NA	NA
Intensity of manic symptoms [YMRS Score]**	1.80	1.14	0.55	0.71	5.888	<0.001
Intensity of depressive symptoms [HAM_D Score]**	4.30	1.02	2.30	0.94	9.134	<0.001

**The mean YMRS score and the mean HAM-D score of the case and control groups are significantly different (p<0.001)

Table 3. Working memory test performance in euthymic bipolar patients (case) and healthy (control) group

Digit span	Case		Control		t-stat	p-value
	Mean	SD	Mean	SD		
Digit forward score	4.90	1.26	5.75	1.21	-3.076	0.003
Digit backward score	3.58	1.06	4.58	1.32	-3.740	<0.001
Total score for digit span test	8.48	2.04	10.33	2.32	-3.785	<0.001

Table 4. Correlations between clinical, psychosocial variables and working memory tests in euthymic bipolar patients (case group)

Pearson's Correlation	Age of Onset	Total duration of illness	Total number of episodes	Number of hospitalizations	Total number of previous ECT	Duration since last episode (in months)
Total score for digit span test Vs Other variables	-0.146	-0.159	-0.158	-0.138	-0.088	0.215
p-value	0.368	0.328	0.329	0.395	0.589	0.184

DISCUSSION:

The case group performed poor compared to healthy control group on digit span subtest and the difference in the performance was statistically significant and the total score for digit span subtest was non-significantly correlated with all other clinical variables of illness. This study finding is similar to the findings of similar previous studies.^{13,15} This finding supports that there is working memory deficits in the euthymic bipolar patients. As there was no significant co-relation between the clinical variables and working memory test performance, this impairment of working memory may be a trait abnormality i.e antecedent predisposed biological process rather than a state abnormality i.e. status of clinical manifestation in patients. However the effects of persistent subclinical mood symptoms on working memory performance couldn't be ruled out. This deficit also reflects that there may be disruption in frontal lobe circuits in BPAD clients that remains persistent in euthymic state of illness.¹⁶ However during the study, all the patients were on medication and combined pharmacotherapy in these patients which made difficulty in establishing their real impact on working memory. However, working memory deficits can't only be justified by medication as there is controversy regarding the effect of mood stabilizers. Several studies have found impairment in memory whereas others have reported no change in cognitive functions.¹⁷⁻²⁰ Similarly effects of antipsychotic medication on working memory also exist. Some studies report that it cause the memory deficits.²¹ However there are reports of improvement of cognitive functions using atypical antipsychotics in schizophrenia and less information is available for BPAD patients.¹ Such deficits of working memory in euthymic state along with impaired cognitive functions in healthy first degree relative of bipolar probands as shown by study done by Schulze KK et al.²² may represent the endophenotypic marker of genetic vulnerability. We admit that we have many limitations in this work. We conducted the study with small sample size and the euthymic patients were on medication so, the results can't be generalized. Longitudinal studies are required to follow up the course of working memory deficits.

CONCLUSION:

Patients with BPAD are impaired in working memory status and this deficit persists beyond the symptomatic recovery of an episode which may lead to poor social outcome. Mood stabilizer should be used at adequate dose and duration for remitting persistent subclinical mood symptoms and this step may decrease working memory deficit state in euthymic phase of illness and enhance the inter-episode recovery.

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CONFLICT OF INTEREST: None

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