

Cognitive Functioning In Bipolar Disorder

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ABSTRACT

BACKGROUND

Patients with bipolar disorder, cycle through episodes of mania, depression and euthymia, leading to dramatic fluctuations in energy, mood, social behaviour and cognitive functioning. It presents with dysfunctioning in cognition, particularly executive functioning, attention, processing speed, verbal learning and declarative memory. Cognitive dysfunctioning not only occurs in acute phase but also in remission phase. We compared the frequency and types of neurocognitive deficits and factors influencing them in individuals with Bipolar I disorder in euthymic state with healthy control.

METHODS

The study included 50 euthymic patients with bipolar I disorder and were compared with 50 healthy controls on cognitive functions. Diagnosis of bipolar disorder I was made following DSM IV TR criteria and current euthymic state was established by applying YMRS and HDRS scale. Neurocognitive performance was assessed on MMSE, Frontal Assessment Battery, Trail Making Test A and B. Statistical tests used were chi square test, ANOVA and Pearson's correlation using SPSS 20 software.

RESULTS

Patients with bipolar I disorder were found cognitively impaired in comparison to control group particularly in attention, working memory, and executive functioning. Factors affecting neurocognitive performance were early onset, age, duration of illness and number of episodes.

CONCLUSIONS

Our study suggests that Euthymic Bipolar I patients had significant frontal dysfunction and impairment in psychomotor speed, visual conceptualization and visuomotor tracking. Neuropsychological deficits in remission period impair socio-occupational functions which lead to poor compliance and more relapses. This highlights the need of routine assessment and early interventions even in euthymic stage.

KEYWORDS

Cognitive Functioning, Bipolar Disorder

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BACKGROUND

Bipolar disorder is a chronic and recurrent mental illness which presents with unusual mood shifts, decreased concentration and attention, such disturbances in cognition which can be measured by neuropsychological tests.¹ Cognitive impairments in bipolar disorder are independent of affected state, as they occur in all phases of illness, across all neuropsychological domains, even during remission phase.²⁻⁴

Cognitive dysfunctions are peculiar characteristics in bipolar disorder,⁵ particularly executive functioning (e.g. Inhibitory control), and attention, processing speed, verbal learning and declarative memory. All patients show clinical recovery in between affective episodes but only about one third recovers functionally during same period.⁶ Cognitive impairment in mood disorders influences individual's occupational functioning and thus hampers ability to maintain a normal social life. It also affects patient's insight, impairs compliance to the treatment, which may lead to further relapses. Better neurocognitive functioning improves chances of recovery. Therefore, even after adequate symptom control there is an intense need of developing interventions targeting cognitive impairments for improving recovery rates and quality of life in patients with bipolar disorder. The studies on neurocognitive deficits are mostly done in patients suffering from schizophrenia. There are very few studies about neurocognitive deficit in patients with bipolar disorder, especially in Indian population.⁷ Various studies have been conducted but most of them lacked comprehensible neuropsychological battery, there was no distinction between unipolar and bipolar state did not have control of mood state at the time of study.

To address these limitations, we have compared neurocognitive functions in a group of euthymic patients with Bipolar I Disorder, and a control group, on a battery of tests (Mini Mental Status Examination, Frontal Assessment Battery, Trail Making Test A and B).

METHODS

The present study was conducted in department of psychiatry of a tertiary teaching hospital after approval from institutional ethics committee. 50 patients suffering from bipolar disorder I currently in remission and 50 healthy controls were included in this study.

Clinical Assessment

Clinical state of individuals was assessed by a psychiatrist using a semi structured proforma for documenting which included socio- demographic data of patient, history of psychological symptoms, and thorough Physical examination findings. 50 patients were selected for the study, which fulfilled the DSM-IV TR criteria for Bipolar disorder I. Remission was assessed with scores of 8 or less on Hamilton Depression Rating Scale (H.D.R.S.)⁸ and 6 or less on Young's Mania Rating Scale (Y.M.R.S.).⁹ Inclusion criteria being cases

age 17-65 years, literate, euthymic at the time of interview, fulfilling DSM IV TR criteria of bipolar I disorder. Patients with coexisting other Psychiatric or neurological illness were excluded from the study. Neurocognitive Battery (Mini Mental Status Examination (M.M.S.E.),¹⁰ Frontal Assessment Battery (F.A.B.),¹¹ Trail Making Test¹²) were administered to bipolar I euthymic patients and were compared with 50 healthy controls.

Neuropsychological Measures

Following Neurocognitive Battery scales were used to find out neurocognitive profile of the patient. The task was given in same order to whole sample.

- Mini Mental Status Examination (M.M.S.E.): To assess overall neurocognitive function and the severity of cognitive impairment at a given point in time and to follow the course of cognitive changes in an individual over time, thus making it an effective way to document an individual's response to treatment.
- Frontal Assessment Battery: This is bedside battery to assess the prevalence and severity of a dys-executive syndrome affecting both cognition and motor behaviour. It consists of six subtests (score 0 to 3) each exploring functions related to the frontal lobes which include conceptualization and abstract reasoning, mental flexibility, motor programming and executive control of action, resistance to interference, self-regulation, inhibitory control and environmental autonomy. To assess the prevalence and severity of a dys-executive syndrome affecting both cognition and motor behaviour.
- Trail Making Test: To assess visual conceptualization and visuomotor tracking (involves motor speed and attention function). It consists of two parts: Trail making A and Trail making B.

Trail Making A- Subject was requested to draw lines to connect 25 consequently numbered circles which are randomly distributed. Time of completion noted in seconds.
Trail Making B- Subject was requested to draw lines to connect 25 consequently numbered and lettered circles by alternating between two sequences

Statistical Analysis

Data analysis was done with the help of SPSS Version 20. The tests used were the chi square test, ANOVA, and correlation was analysed using Pearson's correlation coefficient. Two - tailed 'p' value was obtained for all statistical analysis and score of $p \leq 0.05$ was considered as statistically significant.

RESULTS

All 3 groups were comparable in relation to age, gender, marital status, education and occupation.

Mini Mental State Examination (MMSE)

The mean MMSE score of euthymic Bipolar disorder I patients was 27.88 ± 2.455 as compared to 29.14 ± 0.756 in control group (Table 1). We observed that 6% (n=3) of the euthymic Bipolar disorder I patients had neurocognitive deficits on MMSE as compared to 0% (n=0) controls and this difference was statistically significant ($P=0.001$).

MMSE	Bipolar	Control
Mean	27.88	29.14
SD	2.455	0.756
Range	22-30	28-30
Table 1. Mini Mental State Exam (MMSE)		
ANOVA: $F = 7.430$, $df = 2,147$, $p = 0.001$, Significant		

Trail Making Test (T.M.T.)

TMT A- The mean time for completion of TMT-A for euthymic Bipolar disorder I patients was 70.68 ± 31.637 seconds as compared 39.48 ± 7.657 seconds in control group. (Table 2). 32% (n=16) euthymic Bipolar disorder I patients were found to be having neurocognitive deficit on TMT-A as compared to none of control.

	Bipolar	Control
Mean	70.68	39.48
SD	31.64	7.66
Range	25-151	25-50
Table 2. TMT A		
ANOVA: $F = 31.815$, $df = 2$, $p < 0.001$, Significant		

TMT B- The mean time for completion of TMT-B in euthymic Bipolar disorder I was 185.30 ± 78.239 seconds as compared 88.84 ± 8.321 seconds in control group. (Table 3)

TMT-B	Bipolar	Control
Mean	185.30	88.84
SD	78.24	8.32
Range	90-340	80-110
Table 3. TMT B		
ANOVA: $F = 44.605$, $df = 2$, $p < 0.001$, Significant		

Frontal Assessment Battery (F.A.B.)

The mean score on FAB of euthymic Bipolar disorder I group was 13 ± 2.89 as compared to 16.20 ± 1.25 for control group (Table 4). We found that 40% of euthymic Bipolar disorder I patients in our study had neurocognitive deficit on FAB as compared to 0% of control group.

FAB Test	Bipolar	Control
Mean	13.00	16.20
SD	2.89	1.25
Range	9-17	14-18
Table 4. FAB		
ANOVA: $F = 27.711$, $df = 2$, $p < 0.001$, Significant		

DISCUSSION

Bipolar I disorder presents with Cognitive impairment even in euthymic state. These deficits are considered as trait abnormalities. Executive functions, memory and tasks

involving mental flexibility and psychomotor speed are found to be specifically affected in patients with Bipolar disorder.¹³ Our findings suggest that euthymic Bipolar disorder I patients had significant cognitive impairment on MMSE. As compared to control group (Table 1). Impairment in visual conceptualization and visuomotor tracking (psychomotor slowing) on TMT-A was found in euthymic bipolar patients as compared to control. (Table 2). Other studies have also described that reduction in psychomotor speed continues during the euthymic period of Bipolar disorder.⁵ We observed that 24% (n=12) euthymic Bipolar disorder I patients were having neurocognitive deficits on TMT-B as compared to none of control group. (Table 3). Our findings are in compliance with other researchers who found impairment in executive functioning, visuomotorspeed, and alternative or divided attention in euthymic Bipolar disorder I than control.¹⁴

As a patient of Bipolar disorder, I performed poorly on Trail Making Test B; this indicates poor cognitive flexibility and set-shifting, which are parts of executive functioning. This reveals specific rather than generalized cognitive dysfunctioning which could represent trait or vulnerability marker. These findings are in consonance with some of the previous studies showing impairments of TMT-B in Bipolar Disorder I.¹⁵ Executive dysfunction has been seen in euthymic patients of Bipolar disorder I and is considered to be a potential vulnerability marker. FAB explores conceptualization and abstract reasoning, mental flexibility, motor programming and executive control of action, resistance to interference, self-regulation, inhibitory control and environmental autonomy. 40% of euthymic Bipolar disorder I patients in our study had neurocognitive deficit on FAB as compared to 0% of control group. Our findings are complementary to those of recent studies implicating impairment in executive functions,¹³ cognitive flexibility,¹⁶ ability to resist, interference and planning.¹⁷

Though in our study any imaging techniques was not used to support the results, but cognitive deficits can be explained on the basis of previous studies which correlates cognitive dysfunction with neuroanatomical deficits. The structural MRI studies by Videbech (1997) showed reduced volumes of thalamus and hypothalamus in Bipolar disorder I euthymic patients.¹⁸ Other studies on Bipolar disorder patients suggested that abnormalities in the fronto-subcortical neuroanatomic circuit are associated with impaired attention function,¹⁹ abnormalities of temporolimbic structures are associated with deficits in verbal memory and attention, poor psychomotor speed with white matter hyper intensities, impaired executive functions in Bipolar disorder I and Depression attributed to frontal lobe dysfunction. Also, there can be involvement of subcortical nuclei in cognitive processing, particularly working memory and planning future behaviour. Thus, we can conclude that specific neurocognitive dysfunctioning was found in patients of Bipolar disorder I currently in remission phase, which was validated by MMSE, TMT-A, TMT-B and FAB Various factors that influence cognitive functioning of euthymic bipolar I disorder patient are as follows: (Table 5).

Factors		MMSE	FAB	TMT-A	TMT-B
Age of Patient	Pearson Correlation	-0.478**	-0.584**	0.492**	0.643**
	Significance	p<0.001	p<0.001	p<0.001	p<0.001
Age of Onset	Pearson Correlation	-0.373**	-0.362**	0.275	0.461**
	Significance	0.008	0.010	0.054	0.001
Duration of Illness	Pearson Correlation	-0.310*	-0.480**	0.439**	0.478**
	Significance	0.029	0.000	0.001	0.000
Number of Total Episodes	Pearson Correlation	-0.173	-0.434**	0.313*	0.352*
	Significance	0.229	0.002	0.027	0.012
Number of Manic Episodes	Pearson Correlation	-0.208	-0.445**	0.356*	0.401**
	Significance	0.147	0.001	0.011	0.004
Number of Depressive Episodes	Pearson Correlation	-0.052	-0.312*	0.143	0.158
	Significance	0.719	0.027	0.322	0.273
Family History of Bipolar disorder	Pearson Correlation	0.088	-0.165	0.018	-0.037
	Significance	0.545	0.252	0.901	0.798
Table 5. Influence of Various Factors on Neurocognitive Profile of Euthymic Bipolar I Disorder Patient					
** = Correlation is significant at the 0.01 level (2-tailed).					
* = Correlation is significant at the 0.05 level (2-tailed).					

Age

With increasing age, performance on neurocognitive test gradually declines.

Duration of Illness

As duration of illness increases, neurocognitive functioning starts worsening. Other studies have also observed that progression in the course of illness was related to low performance on psychomotor speed, verbal memory, and overall cognitive dysfunctions.^{20,21}

Manic Episodes

With increase in the number of manic episodes, performance on MMSE and FAB decreases and time required to complete TMT-A, TMT-B increases. Decline in psychomotor speed with increase in number of manic episodes was suggested in previous studies.²⁰

Total Episodes

As the number of episodes increased performance on neurocognitive tests declined. Our finding is in accordance with various previous studies²⁰ which have demonstrated that cognitive dysfunction symptoms are more severe in bipolar patients who experience greater number of episodes.

Age of Onset

Earlier the age of onset, worse was the performance on neurocognitive domains.

Depressive Episode

We did not find any significant co-relation between numbers of depressive episodes and neurocognitive decline.

Our observations are similar to those of other researchers who have not found any significant co-relation between numbers of depressive episodes and neurocognitive decline.²¹ Multiple studies have shown that the severity of the relationship of depressive episodes with neurocognitive deficit is weaker than the relationship of manic episodes, which matches with our results.

CONCLUSIONS

Cognitive functioning of an individual is very important as it not only reflects patient's socio-occupational functioning and ability to live independently but also about insight of their illness and compliance to treatment. Adequate cognitive remediation at an early stage of illness might improve the outcome in bipolar illness. Therefore, development of interventions targeting cognitive impairments is imperative for improving recovery rates and quality of life in the patients suffering from bipolar disorder.

Limitations

The study was cross-sectional, whereas longitudinal follow-up might provide more information about cognitive dysfunction. A larger sample size would have allowed better analysis. Premorbid IQ of patients and control group was not measured. All the patients were on medications; so effect of medications on cognition cannot be ignored. The study was carried out in a tertiary hospital; so the results cannot be generalized.

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