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Original Research Article.

To Compare and Analyze the Neurocognitive Functions in Patient Group, Their 1 St Degree Healthy Relative Group and Healthy Control Group

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ABSTRACT

Background: Cognitive deficits have been shown to be present in apparently healthy relatives of patients with bipolar disorder and thus they could be potential markers of familial vulnerability to bipolar disorder. The aim of this study to conduct the study on assessment of neurocognition in patients of Bipolar Affective Disorder (currently in Remission) and their 1st degree healthy relatives and healthy controls.

Material & Methods: This is a cross sectional study, which was conducted at the Mahatma Gandhi Hospital, Bhilwara, Rajasthan. After taking informed consent in 60 subjects, 30 patients 1st degree suitable matched healthy relative of BPAD patients and 30 subjects grossly matched healthy control also be taken for control group in this study.

Results: Our results showed that the demographic profile details in patient group and healthy relative group most of the subjects were male in both groups. The performance of patient group and healthy relative group on the test of cognitive functions such as attention/psychomotor speed processing (Trail Making Test A), there was statistically significant difference (P=0.0001***). The test of auditory verbal measure of simple span of attention (Digit Span Forward Test), test of working memory (Digit Span Backward Test), test of immediate verbal memory and learning (VL and MT) & test of visuospatial and visuoconstructional memory (VL & MT) were also statistical significant respectively in our study.

Conclusion: Patients of Bipolar Affective Disorder currently in remission phase performed poorly on measure of all domains of neurocognition like executive functions, working memory, verbal memory, visuospatial memory than healthy relatives.

Keywords: Bipolar Disorder, Trail Making Test A, Digit Span Forward & Backward Test, Verbal & Visual Learning And Memory Test.

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INTRODUCTION

Bipolar disorder (BD), formerly called manic depression, causes extreme mood swings that include emotional highs (mania or hypomania) and lows (depression). When one become depressed, he may feel sad or hopeless and lose interest or pleasure in most activities. When his mood shifts in the other direction, he may feel euphoric and full of energy. Mood shifts may occur only a few times a year or as often as several times a week.[1]

Bipolar Disorder is highly heritable; family members of patients with bipolar disorder are at high risk of bipolar disorder. Cognitive deficits have been shown to be present in apparently healthy relatives of patients with bipolar disorder and thus they could be potential markers of familial vulnerability to bipolar disorder.[2]

In order for a marker to be considered as a vulnerability marker (endophenotype), it must be associated with illness, must be present in asymptomatic patients, should be heritable, and must be served among unaffected relatives. Research over the past few years has revealed the presence of cognitive deficits in euthymic phase of bipolar disorder type 1. These cognitive deficits are independent of a mood state and have been proposed to a trait marker for BD. The first degree relatives of bipolar sufferers have been shown to have a 10-to 20-fold increase in the risk of developing BD themselves. Various domain of cognition can easily be measured and are the key factors affecting the subject's ability to function occupationally, socially and inter personally. The three cognitive domain of executive function, working memory and attentional abilities are considered to be the most important cognitive domain for daily functioning.[3]

A large proportion of bipolar disorder patients fail to regain the functioning even after resolution of major affective symptoms. The cognitive impairments have been found to persist in euthymic period, which can influence the psychosocial outcomes and explain the gap in clinical and functional recovery in a subgroup of patients.[4]

COGNITION IN BIPOLAR DISORDER

Attention

Attention refers to our ability to selectively and flexibly process some of the information in the environment at the expense of

other information. The attentional system of the human brain can be decomposed into several distinct mechanisms, including those responsible for selective attention, attentional shifting, and sustained attention.[5]

Executive Function

Executive function refers to a collection of higher-level psychological processes that enable the flexible organization of behavior, including planning, working memory, inhibitory control, strategy development, and attentional shifting.[6] These processes are intimately associated with the integrity of the prefrontal cortex. Specifically, executive control has been mapped to a lateral prefrontal system comprising the dorsolateral and ventrolateral prefrontal cortices.[7] Executive dysfunction may impact upon functional capacity, that is, patients' ability to complete everyday tasks and work-related activities, and it also impacts more broadly upon quality of life.

After going through various sources we could not find many studies on neurocognition in patients of bipolar affective disorder (currently in remission) and their first degree healthy relatives in our geographical area. So we have planned to conduct the study on assessment of neurocognition in patients of Bipolar Affective Disorder (currently in Remission) and their 1st degree healthy relatives and healthy controls.

MATERIALS & METHODS

It is a cross sectional study, which was conducted at the Mahatma Gandhi Hospital, Bhilwara, Rajasthan. After taking informed consent in 60 subjects, 30 patients 1st degree suitable matched healthy relative of BPAD patients and 30 subjects grossly matched healthy control also be taken for control group in this study.

Inclusion Criteria

1) Age between 18-60 years of both sex.
2) Patients of BPAD currently in remission phase of illness.
3) First degree healthy relatives of patients of BPAD.
4) Literate enough to read and understand the questionnaires.
5) Grossly socio demographically matched healthy control.

Exclusion Criteria

1. Substance abuse within past 6 months
2. History of head injury with any documented cognitive sequel or with loss of consciousness
3. Neurological disease or damage
4. Mental retardation
5. Medical illness that may significantly impair neurocongnitive function.
6. Participants who refused to give informed consent.

Digit Span Test

The Digit Span test is a measure of the storage component of working memory. The test is divided into two parts, Digit Span Forward and Digit Span Backward. The former requires participants to repeat a sequence of numbers in the order presented to them. If they are unsuccessful in recalling the numbers correctly a second trial, of the same amount numbers, is given. As the trials are completed the number of digits increases. The Digit Span Forward is primarily a measure of short-term auditory attention, which falls within the domain of Attentional Control. The Digit Span Backward task follows a similar pattern except the sequence of numbers must be repeated by the participant in the reverse order to that which is given. Digit Span Backward is a measure of working memory, which falls in the Cognitive Flexibility domain. The dependent variables derived from both Digit Span Forward and Digit Span Backward are based on the number of sequences correctly completed.[8]

Trail Making Test (TMT)

The Trail Making Test (TMT) is over 60 years old and is still one of the most commonly used neuropsychological tests.[9] The test consists of two parts.

Part A requires participants to consecutively connect circled numbers as fast as possible, which tests processing speed in the Information Processing domain. Part B requires participants to consecutively connect numbers and letters; here, the participant must alternate between the numbers and the letters, which provides a measure falling within the domain of Cognitive Flexibility.[10]

Verbal Learning and Memory Test (VL & MT)

The Hopkins Verbal Learning Test (HVLT; Brandt, 1991) was designed as a relatively brief test of verbal learning and memory to be used when more comprehensive memory assessment is not feasible or when serial testing is desired. It is composed of 12 items, organized into three semantic categories, and presented over three consecutive learning trials. Twelve distractor items (6 semantically related and 6 semantically unrelated) are interspersed with the 12 test items during subsequent immediate yes/no recognition testing.[11]

Visual Learning and Memory Test (VL & MT)

The test is a very basic analysis of what type of environment you prefer based upon your learning style: visual or auditory. The highly visual learner will enjoy the online environment; the highly auditory learner enjoys the traditional classroom setting. The results of this test will not indicate your ability to succeed in a certain environment. They only reflect the environment in which you are most comfortable. Everyone learns in a different way, so the specific methods that an individual prefer to study can vary from person to person.

RESULTS

Our results showed that the demographic profile details in patient group and healthy relative group most of the subjects were male in both groups. There was statistically no significant difference between both groups (p-value = 0.778). Most of them were married as compared to unmarried, difference was not statistically significant (p-value = 1.00). Most of subjects were farmer/clerical and unemployed in both groups. Difference was statistically insignificant with p-value 0.8424. Mostly patients were Hindu and there was statistically no significant difference found in religion (p-value 0.5536). Maximum families were nuclear in both groups and p-value was 0.432. Most of the subjects were rural domicile and minimum were urban domicile in all two groups (**table 1).**

The performance of patient group and healthy relative group on the test of cognitive functions such as attention/psychomotor speed processing (Trail Making Test A), there was statistically significant difference (P=0.0001***). The test of auditory verbal measure of simple span of attention (Digit Span Forward Test), test of working memory (Digit Span Backward Test), test of immediate verbal memory and learning (VL and MT) & test of visuospatial and visuoconstructional memory (VL & MT) were also statistical significant respectively in our study.

Table 1: Socio-demographic profile both groups

Variables		Patients group	Healthy related group	P-value
Gender	**Male**	22 (73.33%)	20 (66.66%)	0.778
	Female	8 (26.66%)	10 (33.33%)	
Marital status	**Married**	24 (80%)	25 (83.33%)	1.00
	Un-married	6 (20%)	5 (16.66%)	
Occupation	**Professional**	1 (3.33%)	2 (6.66%)	0.8424
	Farmer	16 (53.33%)	14 (46.66%)	
	Semiskilled	6 (20%)	8 (26.66%)	
	Unskilled	7 (23.33%)	6 (20%)	
Religion	**Hindu**	28 (93.33%)	29 (96.66%)	0.5536
	Muslim	2 (6.66%)	1 (3.33%)	
Family type	**Nuclear**	16 (53.33%)	19 (63.33%)	0.4321
	Joint	14 (46.66%)	11 (36.66%)	

Table 2: Comparison of patient group and healthy relative groups on neurocognitive test

Test	Patients group (N=30) Mean±SD	Healthy related group (N=30) Mean±SD	P-value
Trail making test a score	96.48 ±16.13	49.70±16.320	0.0001***
Digit span forward test score	4.13 ±0.43	5.00 ±0.698	0.0001***
Digit span backward test score	2.52 ±0.61	3.37 ±0.561	0.0001***
Verbal learning and memory test score	16.11 ±1.84	19.03±1.411	0.0001***
Visual learning and memory test score	13.70 ±1.61	16.85 ±1.713	0.0001***

DISCUSSION

In our study both groups were comparable on basis of sociodemographic variable. Maximum subjects were male (N = 42) and most of the subjects were married (N = 49) as compared unmarried. Mean age in all two groups range from 42 to 45 years. Maximum subjects were farmer/clerical (N = 30), most of the subject belonged to lower middle class socio-economic status.

Our findings of Trail making test-A are consistent with previous study Suwalska and Łojko[12] who claimed that patients in remission seem to be both affectively disturbed and cognitive impaired which may be a contributory factor to poor psychosocial outcome. Patients during affective episode show significantly lower performances on several measures (test) of attention, executive function, learning and verbal memory, and psychomotor speed. Doruk et al.[13] investigated cognitive function in the manic, depressed, and remission period of bipolar disorder by comparing with a healthy control group and found that attention, memory, and learning functions were worse in the manic and depressive patients than healthy controls or patients in remission. No difference was found between patients in remission and healthy controls. In our study, on comparing patient group with healthy relative group and control group on the test of auditory verbal measure of simple span of attention after applying digit span forward test. The results of our study are consistent with those of Sole et al. who reported that euthymic bipolar patients showed significantly lower performance a several measure of attention, learning and verbal memory, and executive function compared with healthy controls. Goswami et al.[14] tested attention, memory and executive function in euthymic patients with bipolar disorder and controls. Numerous other empirical studies have concluded that neurocognitive impairments are indeed evident in patients with euthymic BD compared to demographically matched healthy control.[15] For the present purposes, the results of interest in these studies are those related to the executive function deficit of the participants. In these studies, the most prominent test on which BD patients perform significantly more poorly than controls include the continuous performance test (CPT, which measure attentional impairment); the Digit Span Backward test (which measures working memory); and the Abstract Designs Self Ordered Pointing Task (which measures non-special executive working memory.[15] While medium-to-large effect sizes have been detected for measures of certain aspects of executive function (especially response-inhibition and setshifting tasks), not all executive functions are equally impaired in bipolar patients.[16] Verbal learning and memory deficits, for example, are frequently reported among euthymic bipolar patients. Robinson et al.[17] have also discussed about the potential overlap between executive functioning and verbal learning suggesting that executive deficits may affect memory performance.

Few studies have tried to account for very mild dysphoric or depressive symptoms in otherwise euthymic patients and found that even after statistically controlling for these subsyndromal symptoms, there was still impairment in visuospatial recognition memory, sustained attention, and executive function. It appears that euthymia is associated with at least some cognitive deficits despite carefully ruling out mood symptoms.[17]

CONCLUSION

Patients of Bipolar Affective Disorder currently in remission phase performed poorly on measure of all domains of neurocognition like executive functions, working memory, verbal memory, visuospatial memory than healthy relatives.

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