ORIGINAL ARTICLE

COGNITIVE FUNCTIONS IN BIPOLAR AFFECTIVE DISORDER CURRENT EPISODE DEPRESSION

Neha Sayeed[1], Amool Ranjan Singh[2]

[1]Associate Professor in Clinical psychology, Central Institute of Psychiatry, Kanke, Ranchi 834006
[2]Professor in Clinical Psychology, Ranchi Institute of euro-Psychiatry & Allied Sciences, Kanke, Ranchi 834006

ABSTRACT

The study focusses on cognitive functions in bipolar affective disorder (BAD) patients currently in depression.The study was conducted on 60 BAD patients current episode depression and 60 normal controls. BAD patient fulfilling the inclusion and exclusion criteria was taken up for the study. Apart from recording their socio-demographic and clinical details, all subjects were rated on the Hamilton Depression Rating Scale (Hamilton, 1960) and the Young Mania Rating Scale (Young et al., 1978) and Global assessment of functioning scale (DSM-IV, 1992). Then the appropriate psychological tool was applied for assessing the cognitive functions. Similar procedure was applied for the normal controls, except that General Health Questionnaire-12 was applied in this group. Bipolar affective disorder patients, current episode depression had greater deficits on cognitive functioning than normal controls in all domains except in attention, concentration and recent memory.

Keywords : cognitive, bipolar, depression.

Early research suggested that bipolar patients in acute depressive or manic states demonstrate disproportionate impairment on tests of cognitive functioning. Not surprisingly, this findings have been confirmed in cross-sectional studies that evaluate groups of patients in euthymic or active mood states and compare their neuropsychological performance to each other and/or to healthy individuals. A number of test-retest studies evaluating patients in symptomatic and asymptomatic mood states also support the idea that cognitive performance worsens in the midst of a depressive or manic state. In mania, patients demonstrate widespread neuropsychological impairment that includes broad deficits in sustained attention (both inattention and impulsivity), memory recall and recognition (verbal and non-verbal), executive function, judgment and decision making (Pradhan et al., 2008). These findings implicate global dysfunction in multiple brain systems, including dorsal and ventral prefrontal brain regions in mania. Although some of the deficits subside or diminish with symptomatic resolution, other impairments persist into the euthymic state. In a depressive state, patients with bipolar disorder also show preferential decline in attention, concentration, memory, psychomotor speed and visual-spatial function, and again, these cognitive impairments improve with resolution of the depressive episode (Bora et al, 2009).

Corresponding Author :
Dr. Neha Sayeed (Ph.D, M.Phil) Associate Professor in Clinical psychology, Central Institute of Psychiatry, Kanke, Ranchi 834006
e-mail : neha.s.cip@gmail.com
Contact : 9709228860
Conflict of interest : None
Any funding : None

Numerous studies have suggested that cognitive limitations in bipolar disorder primarily affect attention, memory, and executive functioning. Implicated in compromised executive domain functioning are the structures of the frontal lobe, especially the dorsolateral prefrontal cortex. This area of the brain is involved in attentional set-shifting, planning, working memory, problem solving, and temporal sequencing of information. Disrupted organization and execution of plans occurs when there is damage to this region. In addition, especially in mania, there is poor performance on measures of sustained attention associated with compromised parietal and frontal lobe functioning. Attention has been associated with many regions of the brain, including the prefrontal cortex, thalamus, anterior cingulate, and structures that are linked by "frontostriatal loops" that relate to the modulation and generation of affect (Malhi et al., 2004).

The effect of severity of depression on neurocognitive task performance has been measured in many studies by examining the correlation between Hamilton depression scores (Hamilton, 1960) and neurocognitive task scores. Findings have, however, been conflicting (Rush et al., 1983). Correlation may be sensitive to patient selection because Hamilton scores may be confounded by whether severe scores are associated with more endogenous patterns of symptoms. The finding that subjects with depression were impaired on verbal recall while performing normally on verbal recognition suggested that patients with depression generally had difficulty with 'effortful' as compared to 'automatic tasks (Weingartner et al., 1981; Cohen et al., 1982; Roy-Byrne et al., 1983). Based on correlation findings alone, the authors hypothesized that both the motor and cognitive impairments seed in depression could be secondary to an underlying motivational deficit, rather than arising in their own right. Similarly, Bazin et al., (1984) proposed that the dissociation between explicit (impaired) and implicit (intact)memory tasks seen in patients with depression (Hertel & Hardin, 1990; Denny & Hunt, 1992; Bazin et al., 1994; Danion et al., 1995; Ilsley et al., 1995) was also a result of the greater effort required for the former and the more automatic performance of the latter.

METHODOLOGY

It was a cross sectional hospital based study and purposive sampling was used. The study was conducted in psychiatry based hospitals in Ranchi city i.e. Central institute of Psychiatry (CIP) and Ranchi Institute of Neuropsychiatry and Allied Sciences (RINPAS) Kanke, Ranchi. Bipolar affective disorder current episode depression, who have been diagnosed by ICD-10, DCR criteria (WHO) and have been attending OPD of CIP and RINPAS. The sample comprised of 60 patients from BAD current episode depression (30 males and 30 females) and 60 normal controls (30 males and 30 females). Study aimed to see the cognitive functioning in BAD current episode depression in comparison to normal controls. The study was part of doctorate thesis passed through ethical committee RINPAS, Ranchi.

Subjects of either gender aged between 18 and 45 years, diagnosed as bipolar Affective Disorder, current episode depression, ICD-10, DCR (WHO) criteria, scored < 17 on Hamilton Depression Rating Scale and having 5+ years of formal education were included in study. Subjects having any major medical, organic or psychiatric disorder, with substance dependence or harmful use (except nicotine), who had received ECT in the past six months, with any visual or hearing impairment were excluded from the study. Normal controls who scored three or above on GHQ-12, having no history of psychiatric illness in their family (first degree relatives),with no substance dependence or harmful use (except nicotine) and no visual or hearing impairment were included in study.

Other than socio-demographic data sheet specially prepared for the study following tools were used :

a. **Young Mania Rating Scale (YMRS, Young et al., 1978) :** The scale has 11 items and is based on the patient's subjective report of his or her clinical condition over the previous 48 hours.

There are four items that are graded on a 0 to 8 scale (irritability, speech, thought content, and disruptive/ aggressive behavior), while the remaining seven items are graded on a 0 to 4 scale.

b. Hamilton Depression Rating Scale (HAM-D, Hamilton, 1960) : HAM-D, is a multiple choice questionnaire that clinicians may use to rate the severity of a patient's depression. The questionnaire rates the severity of symptoms observed in depression such as low mood, insomnia, agitation, anxiety and weight loss.

c. General Health Questionnaire-12 (GHQ-12, Jacob, 1997) : The General Health Questionnaire is a widely used screening instrument. It detects a wide range of psychological disorders, mainly the anxiety/depression spectrum, and has been shown to be a valid and reliable instrument across cultures.

d. **Global Assessment of Functioning Scale (GAF, DSM-IV) :** Overall functioning status will be assessed using the Global Assessment of Functioning scale (GAF, DSM-IV). The original GAF instructions call for rating symptoms or functioning.

e. Wisconsin Card Sorting Test (WCST; Heaton, 1981) : The WCST, a measure of prefrontal cortical function (executive functions, abstract conceptual skills, concept formation, cognitive flexibility, working memory), consist of four stimulus cards and 128 response cards that depict figures of varying forms (crosses, circles, triangles or starts), colours (red, blue, yellow or green) and numbers of figures (one, two, three or four). As the task is usually administered, the four stimulus cards with the following characteristics are placed before the subject in left to right order : one red triangle, two green stars, three yellow crosses and four blue circles. The client is then handed a deck of 64 response cards and instructed to match each consecutive card from the deck with one of the four stimulus cards, whichever one the subject thinks it matches. The client is told only whether each response is right or wrong and is never told the correct sorting principle or category. Once the client has made a specified number of consecutive correct matches to the initial sorting principles (i.e.colour), the sorting principle is changed to form or number without warning, requiring the client to use the examiner's feedback to develop a new sorting strategy. The WCST proceeds in this manner through a number of shifts in set (i.e. sorting principle) among the three possible sorting categories (colour, form and number) (Heaton et al., 1993). The WCST yields several scores which potentially can be examined such as categories completed, number of errors, perseverative responses/errors, conceptual level response and failure to maintain set. The WCST has been standardized and norm for use with children, adolescents, and adults ranging from 6½ through 89 years of age. Clients should have normal or correct vision and hearing sufficient to adequately comprehend the instruction and to visually discriminate the stimulus parameters of colour, form and number.

f Trail-making Test A and B (Reitan, 1958) : It is measure of visual conceptual and visual motor tracking skills focusing on divided attention, ability to shift and mental flexibility and motor function. Reitan (1958) added this popular test, originally part of the Army Individual Test Battery (1944) to the Halstead Battery. It requires the connection, by making pencil lines, between 25 encircled numbers randomly arranged on a page in proper order (Part-A) and of 25 encircled numbers and letters in alternating order (Part-B). The test has two forms: the Children (Intermediate) form and the Adult Form. The intermediate form is used for children 9 through 14 years of age. The adult form is used from age 15 years and older. Rapid performance in Part-A appears to be dependent primarily on efficiency of visual scanning and psychomotor speed. The alternation between two sequences in part-B (going from 1 to A, A to 2, 2 to B and so on) is

thought to require executive control, specifically flexibility of thinking and a greater demand on working memory. Numerous investigators have found that BD patients have slower performance on this task than do normal (e.g., Jones, Tham, Hawkins, Ferrier and Mojtabai).

g. **Controlled Word Association Test (CWAT; Ruff et al., 1996) :** Consisting of the FAS test and the Category/Animal/Food Naming Test. It is a brief and sensitive measure of executive cognitive dysfunction. There are two commonly used forms of the test, one using the letters F, A and S and the other using C, F and L. An important component of executive function is the generation of responses appropriate to a given set of stimulus conditions. Measures of verbal and non-verbal fluency provide a means of evaluating the ability to produce responses which comply with a set of constraints yet differ from one another. Fluency tests are timed so that focused attention and response generation is necessary for adequate performance. COWAT is perhaps the most widely used fluency task (also known as the 'FAS' test). In the COWAT, the subject is asked to say as many words as he/she can think of, beginning with the letters F, A & S (some authors substitute the letters C, F and L) during three respective one minute trails. The primary score obtained from COWAT is the total number of words generated. A performance on COWAT is thought to reflect subject's ability to generate and utilize an efficient strategy which is thought to exemplify the aspects of 'organized search', a component of executive function (Welsh, 1990).

h. **Memory scale of PGIBBD (Pershad and Wig, 1977) :** An Indian adaptation of the Wechsler Memory Scale. The PGI memory scale is part of the PGI battery of brain dysfunction, developed at PGIMER, Chandigarh, India. It includes 10 subtests, standardized on adult subjects in the age range of 20-45 years.

i **n-Back test (Kirchner, 1958) :** The n-back task is a Continuous Performance Task. The subject was presented with a sequence of stimuli, and the task consists of indicating when the current stimulus matches the one from n-steps earlier in the sequence.

The study was conducted on 60 BAD patients current episode depression (30 males and 30 females) and 60 normal controls (30 males and 30 females). Subjects fulfilling the inclusion and exclusion criteria was taken up for the study. Apart from recording their socio-demographic and clinical details, all subjects were rated on the Hamilton Depression Rating Scale (Hamilton, 1960) and the Young Mania Rating Scale (Young et al., 1978) and Global assessment of functioning scale (DSM-IV, 1992). Then the appropriate psychological tool was applied for assessing the cognitive functions. Similar procedure has to be applied for the normal control which are 60 (30 males and 30 females), except General Health Questionnaire-12 was applied in this group.

STATISTICAL ANALYSIS

The statistical analysis was done with the help of statistical package for social sciences-22 (SPSS-22). Data of category variable has been described using number and percentage and data of continuous variable has been described using mean and standard deviation. In socio-demographic data, the Chi-square test was used for analysis of categorical variable and t-test was used for analysis of continuous variable. To test the null hypothesis (the groups did not differ in terms of cognitive functions), the comparison between two groups was done using t-test. The comparison between three groups was done using one way ANNOVA with post hoc Bonferroni.

Table 1 : Table showing the comparison of BAD current episode depression and Normal control on Socio-Demographic variables

Variable		BAD current episode depression (N-60) n(n%)	Normal Control (N-60) n(n%)	χ^2	p
Age groups	18-27	25(41.7)	19(31.7)	2.144	0.341
	28-35	25(41.7)	33(55)		
	36-45	10(16.7)	8(13.3)		
Sex	Female	30(25)	30(25)	0.001	1
	Male	30(25)	30(25)		
Education	5-10	22(18.3)	15(12.5)	1.943	0.390
	11-15	26(21.7)	30(25)		
	16 & above	12(10)	27(22.5)		
Marital Status	Married	32(26.7)	28(23.3)	1.637	0.200
	Unmarried	25(20.8)	35(29.2)		
Religion	Hindu	44(36.7)	34(28.3)	3.663	0.050
	Others	16(13.3)	26(21.7)		
Occupation	Employed	20(16.7)	31(25.8)	4.126	0.040
	Unemployed	40(33.3)	29(24.2)		
Socio-economic status	Lower	9(7.5)	6.7(17)	2.166	0.331
	Middle	50(41.7)	35.8(93)		
	Higher	1(.8)	10(7.5)		
Habitat	Rural	35(29.2)	27(22.5)	2.166	0.331
	suburban	20(16.7)	27(22.5)		
	Urban	5(50)	6(5)		

Table shows distribution and comparison of sex, age groups, marital status, occupation, religion, education, habitat, past psychiatric history, past medical illness, family, family medical illness, birth and development history, premorbid personality and substance dependence. Chi-square test was applied. There were 36.7% Hindu in the experimental group and 28.3 Hindu in control group and 13.3 and 21.7 in other than Hindu in the two groups respectively. Past psychiatric history was present in 18.3 in experimental group and no history was present in control group. The control group did not differ significantly on the above mentioned socio-demographic variables other than religion, occupation.

Table 2 : Table showing comparison of BAD current episode depression and Normal control on HAM-D and YMRS

VARIABLE	BAD current episode depression (N-60) M±SD	Normal Control (N-60) M±SD	t	p
HAM-D	10.38±2.66	1.03±1.44	23.893	0.001*
YMRS	1.11±1.32	0.33±0.70	4.003	0.001*

Table 2 shows comparison between Hamilton rating scale for depression and young mania rating scale scores in experimental and control groups. There was significant difference in the two groups in both the variables. Mean score in Ham-D were10.38±2.66 in experimental group and 1.03±1.44 in control group. Mean score in YMRS was 1.11±1.32 in experimental group and .33±.705 in control group.

Table 3 : Table showing functioning in BAD current episode depression on GAF

VARIABLE GAF	BAD current episode depression (N-60) n%	M±SD
30-21	1 (0.8)	6.483±1.321
40-31	2(1.7)	
50-41	12(10.0)	
60-51	14(11.7)	
70-61	17(14.2)	
80-71	11(9.2)	
90-81	3(2.5)	

Table shows frequency distribution in Global assessment of functioning in BPAD current episode depression. Here we see that maximum subjects falls in the range of 70-61 score and minimum on 30-21 score. The mean score is 6.48 and standard deviation of 1.32.

Table 4 : Table showing comparison of BAD current episode depression and Normal control on cognitive functioning tests

Variable	BAD current episode depression (n=60) M ± SD	Normal Control (n=60) M ± SD	t	P
WCST TA	128±0.001	117.51±16.4	4.951	0.001
WCST CR	58.95±15.37	77.18±9.88	7.72	0.001
WCST ER	68.08±15.71	40.18±17.26	9.25	0.001
WCST CC	1.95±1.419	4.4±1.55	9.07	0.001
WCST PR	45.45±21.16	20.13±9.88	8.39	0.001
WCST PE	37.71±16.93	17.93±8.63	8.06	0.005
WCST NPE	32.35±17.92	23.25±16.55	2.88	0.001
WCST CLR	37.96±19.12	63.08±12.32	8.55	0.001
Wcst FC	42.76±44.61	17.75±9.16	4.25	0.001
n-Back	22.2±8.09	28.48±4.07	5.37	0.001
Remote memory	5.46±1.09	5.98±0.12	3.62	0.001
Recent memory	4.80±0.73	5.0±0.01	2.11	0.036
Mental Balance	2.21±0.82	2.95±0.21	6.65	0.001
Attention & Concentration	6.33±1.50	6.93±1.44	2.22	0.028
Delayed recall	6.5±2.48	8.4±3.18	3.64	0.001
Immediate recall	7.06±2.57	10.21±2.91	6.27	0.001
Similarity	4.35±2.38	4.5±0.70	0.46	0.641
Dissimilarity	7±4.012	13.21±1.64	11.10	0.001
Visual retention	3.56±1.35	4.65±0.75	5.42	0.001
Recognition	7.75±2.04	8.9±1.87	3.20	0.002
COWAT test	9.26±5.14	13.71±8.35	3.51	0.001
Trail A(time)	88.53±48.62	29.85±18.74	8.72	0.001
Trail B(time)	178.48±102.96	40.28±19.22	10.22	0.001
Trial A(error)	2.08±2.3	0.28±0.64	5.81	0.001
Trial B(error)	4.81±7.36	0.33±0.60	4.69	0.001

Table 4 shows comparison of experimental groups and control groups on WCST where there was significant difference between the two groups. The groups differed significantly on total time taken, error responses, perseverative responses, perseverative errors, conceptual level response and first category completed, n-back test, PGI-MS, COWAT test Trail A & B.

Table 5 : Correlation of clinical correlates with cognitive functioning in BPAD current episode depression.

Variable		GAF	HAM-D	YMRS
Cognitive Functions		(N=60)		
		p		
WCST	Correct response	-0.069	0.061	-0.041
	Error	0.053	-0.031	0.099
	Perseverative response	0.143	0.019	0.136
	Perseverative error	0.172	-0.053	0.105
	Non-perseverative error	-0.027	-0.073	-0.106
	Conceptual level response	-0.104	0.062	0.013
	No of category completed	0.058	-0.022	-0.087
	Trials to complete first category	0.059	-0.002	-0.010
PGI-Memory Scale	Remote	0.427**	-0.045	-0.131
	Recent	0.049	0.023	0.164
	Mental balance	0.120	0.016	-0.193
	Attention-concentration	0.105	-0.257*	-0.291*
	Delayed	-0.095	0.648	0.892
	Immediate	0.155	-0.185	-0.231
	Retention of similar pairs	0.187	-0.005	-.0222
	Retention of dissimilar pairs	0.086	0.098	-0.213
	Visual retention	0.308*	-0.174	-0.338**
	recognition	-0.143	-0.172	-0.182
n-back test	Correct response	0.124	-0.109	0.132
CWAT test	No. of correct response	0.223	-0.026	-0.119
Trial A	Time taken	-0.254*	0.085	-0.001
	Error made	-0.180	0.033	0.267*
Trial B	Time taken	-0.247	-0.001	0.241
	Error made	-0.008	0.285*	0.196

*P<0.05 (2 tailed) **P<0.01 (2 tailed)

Table 5 shows Pearson correlation which assesses neuropsychological variables which were associated with global or psychosocial functioning and depressive and manic features. It shows the correlation of clinical correlates with cognitive functioning in BPAD current episode depression where Global assessment of functioning is positively correlated with remote memory and negatively with Trial making A. HAM-D is negatively correlated with errorin trail B, & attention concentration. YMRS is negatively correlated with attention.

DISCUSSION

Analysis of socio-demographic data obtained from the Bipolar current episode depression and Normal control in the present study indicate that the groups did not differ significantly in their age, sex, education, marital status, and residence. However the groups did differ in their religion, occupation, family psychiatric history significantly. While the cause of bipolar disorder is not known, it occurs most often in people who have relatives with the disorder. This cognitive impairment in bipolar illness may be stable characteristics of the illness and in the long run can cause considerable impairment in psychosocial and occupational functioning.

Analysis of relevant clinical variables shows that there was significant difference in the two groups in both the variables. Mean score in HAM-D were 10.38+2.66 in experimental group and 1.03+1.44 in control group. The subjects with BPAD current episode depression may have : low mood with difficulty concentrating; lack of energy with slowed thinking and movements; changes in eating and sleeping patterns; feelings of hopelessness, helplessness, sadness, worthlessness or guilt; or thoughts of suicide. Mean score in YMRS was 1.11+1.32 in experimental group and 0.33+.705 in control group. Here we too see that the mean scores in HAM-D is many times the mean score of YMRS, which shows that patients are in the current episode depression, but have some manic features which could not be diagnosed mania. The Bipolar Disorder is difficult to detect using self report measures (Laje et al, 2002). One of the reasons could be the difficulty in recognizing the hypomanic or sub-hypomanic features by the patient as they do not cause substantial impairment. YMRS was used essentially in order to rule out symptomatic manic patients from the study sample. However, significant differences in YMRS and HAM-D ratings between two groups could have become a relevant variable, as residual mood symptoms have been found to have an impact on cognitive functioning (Clark et al., 2002).

Bipolar disorder is associated with a significant impairment of overall functioning at work, social and family levels, even during periods of sustained and substantial remission (Poongothai, 2009). The BPAD group was assessed on Global assessment of functioning with GAF scale where we see that the BAD group fall maximum i.e. 14.2 % on the group of 70-61 which shows patients have some mild symptoms or have some difficulties in social occupational or school functioning, but generally functioning pretty well and has some meaningful interpersonal relationship. Moderate symptoms was seen 11.7 % of BAD current episode depression which shows that moderate difficulty in social, occupational and school functioning and only in 0.8% behaviour was influenced by delusions or hallucinations or serious impairment in communication and judgement. In 14.2%, some mild symptoms was seen but generally functioning pretty well and has some meaningful interpersonal relationship. The correlation of clinical correlates was seen with cognitive functioning in BAD current episode depression where findings suggest that Global assessment of functioning is positively correlated with remote memory and negatively with Trail making A. Bipolar subjects with low general functioning are more cognitively impaired than highly functioning patients, particularly with regard to verbal memory tests (Dickerson et al., 2004; Martinez-Aran et al., 2007), vigilance or sustained attention skills (Clark et al., 2002), and executive tasks. Memory deficits were also associated with poor psychosocial functioning. Bonnin et al. (2010) showed, in a prospective study, that certain cognitive factors (such as verbal memory) and depressive symptoms were significant predictors of long-term functionality, confirming the findings of these earlier transverse studies.In recent years, there has been increased interest in the study of factors implicated in the psychosocial maladjustment of bipolar disorder. The variables studied, however, are mainly clinical or neuropsychological (verbal memory, executive functions, sustained attention), despite the growing evidence that cognitive deficit is not only an individual but also an interpersonal and social variable.

The study aims to address neuropsychological functioning across bipolar illness in current episode of depression and todetermine relationships among clinical features, neuropsychological performance, and psychosocial functioning with the control group. A poorer performance was observed in bipolar group regarding clinical expression, executive function & memory in relation to the healthy comparison subjects (Martinez-Aran etal., 2004). People with major depression have mild-to-moderate impairments in cognitive performance compared to healthy norms (Harvey, 2011). So, according to the first hypothesis that significant difference is found in almost all areas between the

two groups except in attention, concentration and recent memory is seen in this study. HAM-D, that is depression, is negatively correlated with error in trail B, & attention, concentration. Most research on neurocognitive function in depression has found that depressed individuals tend to have worse performance relative to non-depressed comparison groups on a number of neuropsychological measures (Zakzanis et al, 1998), with the most consistent deficits occurring in the areas of processing speed (Sheline et al, 2006); effortful tasks involving selective attention, response inhibition, and performance monitoring (i.e. executive functions) (Palmer et al. 1995). YMRS, that is manic symptoms in BPAD current episode depression, is negatively correlated with attention (George et al, 1997).

Overall, in this study patients performed significantly worse than controls on all trials of WCST, PGI-MS, n-Back test, Trial A & B and COWAT test. The findings brought to notice that BAD patients gave poor results in comparison with normal control. Poor performance on TMT can be attributed to psychomotor slowness and deficits in visual scanning (Heaton et al., 1991). The normal group performed better than the clinical group. This could be due to impairment in the ability to focus, sustain, and execute the task. Bora et al. (2009) found marked deficits in executive-function and verbal learning.Particular significance has been attached to the cognitive deficits as they have been linked to the intensity of the disease process, and are persistent despite psychiatric symptom reduction and have been linked to psychosocial and competitive employment status (e.g., Martinez-Aran et al., 2004).

CONCLUSION

It may therefore be concluded from the present study that bipolar affective disorder patients having current episode depression have greater deficits on cognitive functioning than normal controls in all domains except in attention, concentration and recent memory. There were some limitations of the study. As neuropsychological tests require basic education, illiterate participants were not included in the study. This was a time bound study, so only 60 samples were taken in each group. Since this was a cross-sectional study, it has not focused upon the longitudinal aspects of neuropsychological profile. Future research can focus on similar study whichcan be replicated with patients endophenotype for a closer look at the etiology of the cognitive deficits.

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