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Original Research Article

A COMPARATIVE STUDY OF COGNITIVE FUNCTIONS IN BIPOLAR AND SCHIZOPHRENIC PATIENTS ON TREATMENT AND IN REMISSION WITH NORMAL CONTROLS

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Abstract

Background: Schizophrenia and bipolar mood disorders are major psychiatric illnesses, with cognitive impairments present in both. Neurocognitive dysfunction persists in patients with schizophrenia, even during the stable phases, suggesting an underlying pathology. This study aimed to assess and compare various domains of neurocognitive function in patients with bipolar disorder and schizophrenia during the remission period and in normal controls. **Material & Methods:** This cross-sectional comparative study was conducted over six months in departments other than psychiatry at the Government Rajaji Hospital, Madurai. The study used various scales, including the Hamilton Rating Scale for Depression, Young's Mania Rating Scale, Positive and Negative Syndrome Scale, neuropsychological tests such as the Digit Span, Rey Auditory Verbal Learning Test, Rey Complex figure Test, COWAT, Stroop test, general health questionnaire, and socioeconomic status scale. **Results:** This study found patients with schizophrenia and bipolar disorder were predominantly from rural backgrounds and had low socioeconomic status. Patients with schizophrenia had significantly lower scores on attention and executive function tests, as well as on all components of the Rey verbal learning test and the Rey-Osterie diagram. They also had lower scores in the digit forward task and Trial A, indicating poorer attention capacity. Patients with schizophrenia had lower scores in the controlled oral word association, delayed recall, and omission components of the Rey verbal learning test but not in the copy component of the Rey-Osterie diagram. **Conclusion:** Cognitive deficits in patients with bipolar disorder, schizophrenia, and schizophrenia in remission are similar but worse in patients with schizophrenia, with impaired executive function, verbal fluency, and visual memory.

INTRODUCTION

Schizophrenia and bipolar mood disorder are the two major psychiatric illnesses that curb the majority of the life years of affected individuals. Cognitive impairment in schizophrenia has been well studied. Evidence shows that these cognitive deficits are also present in bipolar disorder. Although medication addresses other dimensions of these illnesses, cognitive deficits remain unaddressed. It has been noted that several bipolar mood disorders and schizophrenia patients who have been treated for their predominant symptoms still do not lead an acceptable premorbid functional and social life. This observation raises the question of whether these patients have been truly treated for their illness or just the symptoms being treated.[1-4]

There is mounting evidence regarding the impairment of multiple cognitive areas during the active phase of bipolar disorder and the persistence of such impairment even during the euthymic phase after the active symptoms have been successfully treated. Euthymia was previously thought to be equivalent to recovery. However, recent trends have shown deficits in verbal and visual memory, complex problem-solving, verbal fluency, abstract concept formation, and attention set-shifting. Additionally, approximately thirty per cent of euthymic bipolar disorder patients are noticed to have difficulties in social and occupational

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functioning. The presence of these deficiencies (both cognitive and social), even during periods of normal mood, suggests an underlying pathology of bipolar disorder.[5-7] Psychiatric research has recently focused on the neurocognitive dysfunction in patients with schizophrenia. The persistence of neurocognitive dysfunction has been observed in patients with schizophrenia, even during the stable phase. Patients with schizophrenia perform systematically worse than those with affective disorders do.

Aim

This study aimed to assess and compare various domains of neurocognitive function in patients with bipolar disorder and schizophrenia during the remission period and in normal controls.

MATERIALS AND METHODS

A cross-sectional comparative study was conducted on 90 patients over six months in departments other than psychiatry at the Government Rajaji Hospital, Madurai. The study received approval from the institutional ethics committee before its initiation.

Inclusion Criteria

The study included patients aged between 18 and 45 years, with a minimum of 8 years of formal education, diagnosed with bipolar disorder or schizophrenia based on DSM-IV criteria and experiencing a remission period characterised by >4 months duration for bipolar disorder with Young Mania Rating Scale (YMRS) <7 and Hamilton Depression Rating Scale (HAMD) <7, or >6 months duration for schizophrenia with Positive and Negative Syndrome Scale (PANSS) <60. Patients should be on a single mood stabiliser for bipolar disorder or a single antipsychotic for schizophrenia with an illness duration of < 5 years and a history of no more than two episodes or exacerbations.

Exclusion Criteria

Patients with bipolar disorder, schizophrenia, schizophrenia, schizoaffective illness, major systemic illness, organic brain defects, neurological disorders, substance abuse, electroconvulsive treatment, intellectual capacity assessment, and a Mini-Mental State Examination score < 25 were excluded. Patients with YMRS and Hamilton Depression scores of ≥7, PANSS scores of ≥60, schizoaffective illness, absence of evidence for major systemic illness, organic brain defects, or neurological disorders, no history of substance abuse or dependence, and a Mini-Mental State Examination score of < 25.

The study used various scales, including the Hamilton Rating Scale for Depression, Young's Mania Rating Scale, Positive and Negative Syndrome Scale, neuropsychological tests such as the Digit Span, Rey Auditory Verbal Learning Test, Rey Complex figure Test, Animal Naming Test, COWAT, Stroop test, general health questionnaire, and socioeconomic status scale.

The digit span measures attention through Digit Forward and Digit Backward. The assessor reads the number of sequences to the subject, scoring each item as 0, 1, or 2 points. The Ry Auditory Verbal Learning Test (AVLT) measures auditory memory by presenting two lists with 15 words each. Words from list A were recited at a speed of one word per second for five trials, followed by immediate recall. The delayed recall score was obtained after 20 min. The recognition trial scores were Hit, while errors in missions were noted.

The Controlled Oral Word Association Test (COWAT) measures phonemic fluency by generating words based on phonetic similarity. The Animal Name Test (ANT) measures category fluency by regulating the content of words rather than phonetic similarity. The Stroop Test assesses the ease with which a perceptual set can be shifted to conjoin changing demands and suppress habitual responses. The Prefrontal areas are responsible for response inhibition. The Trail Making Test measures attention and cognitive flexibility by dividing the test into two parts: A and B. The subjects must draw lines connecting numbers in ascending order, and in Part B, they must alternate between numbers and letters in ascending order. The final score was the average number of new words generated over the three trials. The tests were designed to assess language proficiency and cognitive flexibility.

Statistical Analysis

The study used data collected from three groups: patients with bipolar disorder, patients with schizophrenia, and healthy controls. Central values and dispersion were calculated for each scale and sociodemographic variable. Chi-square and Student's t-tests were used for the categorical and numerical analyses, respectively. Data were analysed using the Statistical Package for the Social Sciences, version 10.0, for Windows. Statistical significance was set at $P < 0.05$. The study involved trials of list 'A', words in list 'B', and immediate recall of list 'A' words. The delayed recall score was obtained after 20 min. Hits were scored, and errors in omissions and commissions were noted.

RESULTS

The study included 90 patients divided into three groups: bipolar (30), schizophrenia (30), and control (30). There were no statistical differences between the groups regarding age and sex. [Table 1]

Compared to schizophrenia and bipolar patients, both groups were predominantly from rural backgrounds and had a low socioeconomic status. Most patients with schizophrenia were unemployed (86.7%) compared with bipolar patients, who were predominantly employed (60%), which showed a statistically significant difference. [Table 2]

Patients with bipolar disorder had significantly lower scores on attention and executive function

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tests than controls. There was a significantly lower score in the controlled oral word association test, but not in the definite fluency test, than in the controls. Patients with schizophrenia had significantly lower scores in all components of the Rey verbal learning test than controls. Patients had significantly lower scores in all components of the Rey-Osterie diagram than controls. [Table 3]

Patients with schizophrenia had significantly lower scores on tests of attention and executive function than controls. Patients had significantly lower scores on the animal naming and controlled oral word association tests than controls. Patients with schizophrenia had significantly lower scores during all the initial trials of the Rey verbal learning test and in the immediate and delayed recalls and omission components of the Rey verbal learning test compared to controls. Patients with schizophrenia had significantly lower scores in all components of the Rey-Osterie diagram than controls. [Table 4]

Patients had significantly lower scores in digit forward and trial A than bipolar patients, which shows their poorer attention capacity in schizophrenic patients. Patients with schizophrenia had significantly lower scores in the controlled oral word association test but not in categorical fluency when compared to bipolar patients. Patients with schizophrenia had significantly lower scores during the initial trials of the Rey verbal learning test and in the delayed recall and omission component of the same; when compared to bipolar patients, schizophrenia patients had significantly lower scores in immediate recall and delayed recall but not in the copy component of the Rey-Osterie diagram. [Table 5]

Table 1: Demographic data of the study

		Bipolar	Schizophrenia	Controls
Age (Mean)		32.57±6.956	32.43±5.322	32.90±5.726
Gender	Male	21	18	20
	Female	9	12	10

Table 2: Comparison of sociodemographic profiles between schizophrenia and bipolar patients

Variables		Schizophrenia (n)	Bipolar (n)	P-value
Education	<12 std	18	14	0.438
	>12 std	12	16	
Marital status	Unmarried	16	14	0.796
	Married	14	16	
Domicile	Rural	21	23	0.77
	Urban	9	7	
Occupation	UE	26	12	<0.001
	Employed	4	18	
Socio economic status	Low	29	26	0.35
	Mid	1	4	
	High	0	0	

Table 3: Comparison of attention and executive function, verbal fluency, verbal memory, and visual memory between bipolar and control subjects

		Bipolar	Controls	P-value
Digit span	Digit forward	6.27±1.617	6.47±1.167	0.585
	Digit backwards	3.27±1.760	4.77 ±1.104	< 0.001**
Stroop Colour Test	Stroop 1	83.53± 33.634	61.27± 10.130	0.001*
	Stroop 1 (error)	0.27 ±0.828	0.03 ±0.183	0.137
	Stroop 2	139.53± 49.963	103.57 ±12.235	< 0.001**
	Stroop 2 (error)	2.23± 4.987	.07 ±.254	0.021*
	Stroop 3	205.17± 66.740	196.33 ±32.238	0.516
	Stroop 3 (error)	6.43± 8.962	1.00 ±1.114	0.002*
Trail A & B	Trail A	90.00 ±27.264	85.67 ±29.641	0.558
	Trail B	230.70 ±67.265	144.83 ±42.439	< 0.001**
Word Fluency Test	Animals	9.87±3.082	11.17±2.306	0.069
	Fruits	9.20±2.091	9.77±2.897	0.389
COWAT		6.09±2.726	8.3±2.088	0.001*
Rey Verbal learning	T1	5.67±2.040	8.00±1.661	< 0.001**
	T2	7.33±2.426	8.43±1.612	0.043*
	T3	8.30±3.218	9.27±2.033	0.17
	T4	8.30±3.019	10.90±2.057	< 0.001**
	T5	9.53±3.003	12.73±1.741	< 0.001**
	B	4.40±1.976	5.57±1.960	0.025*
	IR A	7.50±2.898	10.63±1.450	< 0.001**
	DR A	6.90±3.428	9.40±1.522	0.001*
	H	12.23±2.373	13.57±1.194	0.008*
	O	2.77±2.373	1.47±1.224	0.010*
	C	1.03±1.426	.43±.728	0.045*
Rey- Osterieth	Rey O copy	32.73±6.685	35.70±.651	0.019*
	Rey O IR	23.73±9.329	33.00±2.435	< 0.001**
	Rey O DR	22.10±9.994	31.17±3.455	< 0.001**

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Table 4: Comparison of attention and executive function, verbal fluency, verbal memory, and visual memory between patients with schizophrenia and controls

		Schizophrenia	Controls	P-value
Digit span	Digit forward	5.20±1.562	6.47±1.167	0.001*
	Digit backwards	2.90±1.322	4.77±1.104	< 0.001**
Stroop Colour Test	Stroop 1	74.70±14.145	61.27±10.130	< 0.001**
	Stroop 1 (error)	.33±.661	.03±.183	0.020*
	Stroop 2	136.23±28.766	103.57±12.235	< 0.001**
	Stroop 2 (error)	1.90±2.369	.07±.254	< 0.001**
	Stroop 3	207.90±26.651	196.33±32.238	0.135
	Stroop 3 (error)	5.20±3.934	1.00±1.114	< 0.001**
Trail A & B	Trail A	121.93±51.997	85.67±29.641	0.002*
	Trail B	279.23±135.916	144.83±42.439	< 0.001**
Word Fluency Test	Animals	9.20±2.565	11.17±2.306	0.003*
	Fruits	8.77±2.128	9.77±2.897	0.133
COWAT		6.09±2.726	8.3±2.088	0.001*
Rey Verbal learning	T1	4.50±2.129	8.00±1.661	< 0.001**
	T2	5.40±2.111	8.43±1.612	< 0.001**
	T3	6.77±2.079	9.27±2.033	< 0.001**
	T4	7.53±2.446	10.90±2.057	< 0.001**
	T5	8.40±2.078	12.73±1.741	< 0.001**
	B	4.90±2.107	5.57±1.960	0.209
	IR A	6.87±2.488	10.63±1.450	< 0.001**
	DR A	4.60±2.920	9.40±1.522	< 0.001**
	H	10.20±2.538	13.57±1.194	< 0.001**
	O	4.80±2.538	1.47±1.224	< 0.001**
	C	.67±1.061	.43±.728	0.325
Rey- Osterieth	Rey O copy	33.93±2.625	35.70±.651	0.001*
	Rey O IR	14.07±5.433	33.00±2.435	< 0.001**
	Rey O DR	11.33±4.922	31.17±3.455	< 0.001**

Table 5: Comparison of attention and executive function, verbal fluency, verbal memory, and visual memory between bipolar and schizophrenic patients

		Bipolar	Schizophrenia	P-value
Digit span	Digit forward	6.27±1.617	5.20±1.562	0.012*
	Digit backwards	3.27±1.760	2.90±1.322	0.365
Stroop Colour Test	Stroop 1	83.53±33.634	74.70±14.145	0.19
	Stroop 1 (error)	.27±.828	.33±.661	0.732
	Stroop 2	139.53±49.963	136.23±28.766	0.755
	Stroop 2 (error)	2.23±4.987	1.90±2.369	0.742
	Stroop 3	205.17±66.740	207.90±26.651	0.836
	Stroop 3 (error)	6.43±8.962	5.20±3.934	0.493
Trail A & B	Trail A	90.00±27.264	121.93±51.997	0.004*
	Trail B	230.70±67.265	279.23±135.916	0.085
Word Fluency Test	Animals	9.87±3.082	9.20±2.565	0.366
	Fruits	9.20±2.091	8.77±2.128	0.43
COWAT		6.09±2.726	8.3±2.088	0.001*
Rey Verbal learning	T1	5.67±2.040	4.50±2.129	0.034*
	T2	7.33±2.426	5.40±2.111	0.002*
	T3	8.30±3.218	6.77±2.079	0.032*
	T4	8.30±3.019	7.53±2.446	0.284
	T5	9.53±3.003	8.40±2.078	0.094
	B	4.40±1.976	4.90±2.107	0.347
	IR A	7.50±2.898	6.87±2.488	0.367
	DR A	6.90±3.428	4.60±2.920	0.007*
	H	12.23±2.373	10.20±2.538	0.002*
	O	2.77±2.373	4.80±2.538	0.002*
	C	1.03±1.426	.67±1.061	0.263
Rey- Osterieth	Rey O copy	32.73±6.685	33.93±2.625	0.364
	Rey O IR	23.73±9.329	14.07±5.433	< 0.001**
	Rey O DR	22.10±9.994	11.33±4.922	< 0.001**

DISCUSSION

Our study showed no significant difference in the sex distribution among the three groups. The bipolar group had a mean duration of illness of 3.40±1.28 years, while the mean duration of illness in the schizophrenia group was 3.67 ± 1.12 years. The two groups had no significant difference in the mean duration of illness. The bipolar group performed poorly in all Rey Auditory Verbal Learning test components and Rey Osterieth's diagram. This is consistent with studies conducted by Balanza-Martinez et al. and Kieseppa et al., who showed that bipolar patients experienced deficits in verbal learning and memory, which persisted even during the remitted state.[3,8,9] The present study shows that

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euthymic bipolar patients have significant deficits in executive functioning and attention when compared to healthy normal individuals with similar profiles of age and premorbid intelligence. The results of this study correspond to the various cross-cultural studies on impairment in neurocognitive functions in bipolar disorder.[1]

For patients with long-standing bipolar disorder who are not in an acute psychotic state, Wilfred et al. and Savitz et al. found persistent neurocognitive difficulties.[10,12] The impairments were observed even when active symptoms were absent, while the severity and duration of illness were not found to have any effect on either cognitive domain. Some more studies showed that patients with bipolar disorder, both during acute and euthymic episodes, demonstrated cognitive deficits.8 Thus, it is apparent that all-important cognitive function domains are disrupted, including attention, memory, and executive function.[4] Martinez-Aran et al. state that Cognitive deficits and memory difficulties may have adverse consequences on the functional and psychosocial outcomes of bipolar patients.6 Neuropsychological functioning has been proposed to be the determinant of employment outcomes.

In the current study, except for Trial A, a statistical difference was observed in the poor performance of the schizophrenic group when compared with normal controls. Significantly, a smaller number of responses were given by the schizophrenic group in both phonological and categorical fluency. Both the immediate and delayed recall of words were significantly lower in the schizophrenic group. The schizophrenic group performed poorly in recalling the Rey Osterieth diagram. Trivedi et al. demonstrated that stable schizophrenic patients were specifically impaired in comparison to controls and euthymic subjects in continuous tasks (i.e. attention and concentration). However, euthymic subjects performed similarly to tightly matched normal controls on attention and concentration abilities.[12]

Patients with schizophrenia often have impaired spatial working memory, which is crucial for daily activities and social interaction. These cognitive impairments lead to frustration and poor social functioning. Impaired attention and immediate memory can also affect mathematical abilities, social skills, and medication dosage. Individuals with bipolar disorder and schizophrenia perform poorly in various aspects, with no significant differences in categorical fluency or verbal and visual memory. Trivedi et al. demonstrated that bipolar patients demonstrated an intermediary level of performance between schizophrenia and normal control in verbal memory and executive functions.[13] Altshuler et al. demonstrated that patients with schizophrenia on remission demonstrated a generalised impairment in cognitive functions across most domains compared with control subjects.5 In contrast, bipolar patients in remission were significantly impaired when compared with control subjects only in executive functioning and verbal memory domains.[15] It is clear from these results that schizophrenic patients perform systematically worse on cognitive measures than mood disorder patients, which is consistent with their generally poorer outcome.[13] The results also indicate that schizophrenia and mood disorders are quantitatively distinguishable in neuropsychological terms, given differences in obvious intellectual deterioration, profiles of cognitive deficits, and relations between cognitive performance and psychotic symptoms. Seidman et al. compared neurocognitive function in chronic schizophrenic patients with chronic bipolar patients and normal controls and found that patients with schizophrenia were considerably more impaired than controls in all neurocognitive functions, except for verbal fluency, and were significantly worse than patients with bipolar disorder in abstraction, perceptual-motor speed, and vigilance. Patients with bipolar disorder performed significantly poorly in declarative verbal memory compared to controls. They showed moderate-to-large effect size decrements on abstraction, perceptual-motor speed, and vigilance.[14]

Altshuler et al. analysed neurocognitive functions in 40 euthymic bipolar patients, 20 stable schizophrenia patients, and 22 no psychiatric disorder subjects. Both groups showed significant differences in neurocognitive function. Patients with schizophrenia showed more cognitive disruptions, whereas patients with bipolar disorder showed impairments in verbal memory and executive function. The study also found a subgroup with normal executive functions and a subgroup with significant deficits.[5] Schizophrenia patients with schizophrenia showed impaired planning, set-shifting, and problem-solving abilities, affecting their daily lives. This impairment is more pronounced in patients with schizophrenia than in those patients. The disorder may be linked to functional neuropathology in the lateral prefrontal cortex, which disrupts the extra-dimensional shifting stage, affecting both groups more than the bipolar group.[15]

In this study, the major confounding effect of psychotropic medications on neurocognitive function could not be ruled out. The majority of the cases were on atypical antipsychotic agents and mood stabilisers. Many of these compounds were also found in trihexyphenidyl. Numerous studies have demonstrated the negative effects of various drugs, including lithium, antipsychotics, and trihexyphenidyl, on neurocognitive function. Studies suggest that certain drugs, such as lithium, antipsychotics, and anticonvulsants, may not cause cognitive impairments, according to Goswami et al., Bilder et al., and Manji et al.[16-18] In most of the studies, this confounding effect of psychotropic drugs is present. It would be best to study drug-naïve patients with bipolar disorder and schizophrenia. However, this is not ethically

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possible, and drug-free patients do not represent the actual population.

CONCLUSION

Cognitive deficits do not depend on the patient's educational profile. Patients with bipolar disorder are better employed during the euthymic period than patients with schizophrenia. Impairment of executive function is observed in patients with bipolar disorder. Patients with bipolar disorder perform poorly in verbal fluency tests. Patients with bipolar disorder experience verbal and visual memory disturbances. Patients with schizophrenia in remission perform poorly on executive function tests. Verbal and visual memories are impaired in patients with schizophrenia. Patients with schizophrenia in remission have a deficiency in verbal fluency, and similar deficits are present in both patients with schizophrenia and bipolar disorder but are worse in schizophrenic patients.

Limitations

This study had several limitations, including drug disparity between bipolar and schizophrenia patients, a limited sample size, rigid inclusion criteria, and the halo effect. Patients with bipolar disorder were on mood stabilisers, while patients with schizophrenia were on antipsychotics, which can affect cognition. The study also had a rigid inclusion criterion, with only 30 participants in each group. The results were liable to fit the assessor's preconception, and an independent assessor could overcome this limitation in future studies. The validation of the Tamil version of the tests remains inadequate.

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