Original Article

A Study of Neurocognitive Functioning in Euthymic Bipolar Patients with and without Alcohol Dependence

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Abstract

Introduction: Bipolar disorders are a large group of psychiatric disorders with signs and symptoms of pathological emotional disturbances.

Aim: The study aims to assess neurocognitive functioning in remitted bipolar individuals with and without a history of alcohol dependence and an average population.

Methods: A comparative study was conducted at the Institute of Mental Health Hospital Chennai. Informed consent was obtained from 99 patients after a proper explanation of the purpose and procedure of the study. A selection of two groups of patients with bipolar affective disorder, of which one group is with alcohol dependence, while the other is without prior history of alcohol dependence.

Results: The mean age of subjects in the cases Group A is 32.2 years. The mean age of subjects in cases Group B is 33.5 years. The mean age of subjects in control is 33.8 years. In addition, the duration of illness of bipolar disorder significantly negatively correlated with performance on measures of perseverative error and total error of executive function and Hits 1 and 2 of N Back test of bipolar subjects with alcohol non-dependent. In alcohol dependent group, the number of episodes of mania significantly correlated with poor performance on measures of attention, executive function, and verbal memory of bipolar subjects of alcohol dependent.

Conclusion: The lifetime duration of bipolar illness adversely affects neurocognition. This relationship between this impairment and to lifetime duration of illness raises the possibility that early diagnosis and treatment could reduce the degree of neurocognitive impairment.

Key words: Alcohol, Bipolar, Memory, Neurocognitive, Psychiatric disorders

INTRODUCTION

Bipolar disorders are a large group of psychiatric disorders with signs and symptoms of pathological emotional disturbances, present over weeks to months, that represent a marked decline in a person's activities of daily living and tend to recur, often periodically or cyclically.[1] The

prevalence of bipolar disorder is approximately 1% in the general population and studies have shown that the lifetime prevalence of bipolar disorders may be around 5%. In Bipolar disorders, a patient is said to be euthymic when the Hamilton Depression Scale score is below 7 and the Young Mania Rating Scale score is below 6 for 3 consecutive monthly assessments just before neuropsychological testing.[2]

Bipolar disorders are often associated with other comorbid disorders. Lifetime psychiatric comorbidity in bipolar disorders is 50–70%. The comorbidities associated with bipolar disorders are substance use disorders, anxiety disorders, personality disorders, and attention-deficit hyperactivity disorder. These comorbidities affect the course, severity, treatment response, and disease outcome.

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In addition, there is a strong association between bipolar disorders and alcohol dependence. Hence, there is a high prevalence of alcohol dependence in bipolar disorders, which might be due to the emotional instability leading to increased consumption of alcohol.[3] The severity of alcohol use-related disorders in bipolar patients is more disabling and has a damaging effect on the course of bipolar disorders. Therefore, the course of illness in patients with bipolar disorders and comorbid alcohol dependence may be very severe, and their long-term recovery is also poor.

Cognition includes attention, memory, language, orientation, praxis, executive function, judgment, and problem-solving. Hence, cognition disorders can affect personal, occupational, and social functioning.[1] In bipolar disorders, cognitive impairments in several domains are present not only during acute mood episodes such as manic, hypomanic, and depressive episodes but also during euthymic periods.[4] Neuropsychology research shows that significant cognitive impairment persists into euthymic periods, especially in patients with multiple episodes.[3] Some studies show that there is a significant cognitive impairment in domains such as attention, executive function, immediate memory, and verbal and visuospatial declarative memory in euthymic bipolar patients.[5]

In alcohol-related disorders, cognitive deficits in abstract reasoning, non-verbal learning, and perceptual-motor abilities may occur and slow to resolve the deficits in skills involving processing memory, problem-solving, and new learning ability. In bipolar disorder patients with comorbid alcohol dependence, cognitive deficits occur in executive functions and verbal memory. This deficit is more severe in patients with bipolar disorders and comorbid alcohol dependence.[6] Neuropsychological deficits associated with both bipolar disorders and alcohol dependence contribute to impairment of greater severity in patients who have bipolar disorder with comorbid alcohol dependence. The cumulative cognitive deficits contributed by bipolar disorder and alcohol dependence may lead to a severe cognitive impairment that interferes with the patient's recovery and overall functional ability.[4]

Many studies have demonstrated cognitive impairment in depressive, manic, or hypomanic episodes.[7] Studies about cognitive impairment in bipolar patients in the euthymic state with alcohol dependence are limited. Therefore, the purpose of this study is to evaluate cognitive functioning in euthymic bipolar individuals with and without alcohol dependence.

Aim
The aim of the study was to assess neurocognitive functioning in remitted bipolar individuals with and without a history of alcohol dependence and normal population.

MATERIALS AND METHODS

A comparative study was conducted at the Institute of Mental Health Hospital Chennai.

Study Period
Informed consent was obtained from 99 patients after a proper explanation of the purpose and procedure of the study.

Inclusion Criteria
The following criteria were included in the study:

Group 1: Subjects between the ages 20 and 55 years who are diagnosed to have Bipolar affective disorder and alcohol dependence as per ICD 10, who have been euthymic for at least 3 consecutive months, and who have been identified as alcohol dependent should be abstinent for 3 consecutive months at the time of interview. Group 2: Subjects between the ages 20 and 55 years, diagnosed with the bipolar affective disorder as per ICD-10 and without prior history of alcohol abuse or dependence, and who have been euthymic for at least 3 consecutive months. Group 3: Subjects aged 20–55 years and normal population.

Exclusion Criteria
The following criteria were excluded from the study:

All groups with a history of head injury and loss of consciousness for more than 1 h, H/o seizure disorder, H/o other psychiatric disorder, and H/o comorbid physical conditions.

To collect data regarding their characteristics such as name, age, sex, marital status, and education, using a patient questionnaire. Furthermore, collect disease-related information-duration of illness, number of episodes, duration of treatment etc. collected from the patients. YMRS and HAMD are to be administered to confirm euthymia in both groups.

Administration of neuropsychological tests in both groups to assess three domains of neurocognition, that is, Wisconsin card sorting test for executive functions; Digit Span Backwards and Digit Span Forwards for Attention, N back test for verbal memory.

The Independent t-test and Mann–Whitney U test, and Fisher's test were used to analyze sociodemographic data. In addition, Spearman's correlation coefficient is used to compare the course of illness and cognitive function.

RESULTS

The mean age of subjects in the cases Group A is 32.2 years. The mean age of subjects in cases Group B s 33.5 years. The mean age of subjects in control is 33.8 years.

In education, three groups have predominantly completed higher secondary education. In comparing occupation between groups, there is no statistical significance between Groups A and B ($P = 0.44$). However, there is significance in comparing Group A and the controls ($P = 0.01$) and between Group B and the controls ($P = 0.01$). In comparing married status between groups, there is no statistical significance between Groups A and B ($P = 0.67$) and B and C ($P = 0.15$). However, there is significance in comparing Group B and the controls ($P = 0.05$) [Table 1].

In Group A, the mean age of onset of alcohol use is 17.1 years and the mean duration of alcohol use is 12.6. There is no significant difference in the onset and duration of illness and depressive episodes between groups, but significance in manic episodes. On comparison of all parameters between bipolar alcohol-dependent (Group A) and bipolar alcohol-non-dependent (Group B) was not statistically significant. Still, when both groups were compared with the control group, they were statistically significant [Table 2].

The age of onset of bipolar illness is not significantly correlated with performance on measures of attention, executive function, and verbal memory of bipolar alcohol-dependent subjects.

The duration of illness of bipolar disorder significantly negatively correlated with performance on measures of attention, perseverative error, conceptual response, and total error of executive function and Hits 1 and 2 of N Back test of bipolar subjects with alcohol-dependent. In addition, the duration of illness of bipolar disorder significantly negatively correlated with performance on measures of perseverative error and total error of executive function and Hits 1 and 2 of N Back test of bipolar subjects with alcohol non-dependent [Table 3].

In alcohol dependent group, the number of episodes of mania significantly correlated with poor performance on measures of attention, executive function, and verbal memory of bipolar subjects of alcohol dependent.

In the alcohol-non-dependent group, the number of episodes of mania significantly correlated with poor performance on measures of attention, executive function, and verbal memory of bipolar subjects with alcohol-non-dependent [Table 4].

Table 1: Distribution of patients characteristics in the study

Parameters	Groups		
	Alcohol dependent (%)	Alcohol non-dependent (%)	Control (%)
Education			
Illiterate	4 (10.3)	0	0
Primary	5 (12.8)	6 (15)	0
Secondary	7 (17.9)	5 (12.5)	4 (20)
Higher sec	15 (38.5)	14 (35)	10 (50)
Diploma/IT	5 (12.8)	3 (7.5)	1 (5)
Graduate	3 (7.7)	12 (30)	5 (25)
Occupation			
Unemployed	13 (33.3)	11 (27.5)	1 (5)
Unskilled	6 (15.4)	9 (22.5)	11 (55)
Semi-skilled	4 (10.3)	1 (2.5)	0
Skilled/Farmer	11 (55)	12 (30)	3 (15)
Clerical/shop owner	3 (7.7)	2 (5)	0
Semi-profession	0	1 (2.5)	4 (20)
Professional	2 (5.1)	4 (10)	1 (5)
Married status			
Married	14 (35.9)	18 (45)	13 (65)
Unmarried	22 (56.4)	20 (50)	5 (25)
Separated	3 (7.7)	2 (5)	2 (10)

Table 2: Mean parameters of the study

Parameters	Group A	Group B	*P*-value
Onset of illness	24.8±3.8	25.5±4.3	0.44
Duration of illness	7.3±2.7	7.9±4.0	0.43
Manic episodes	5.8±3.9	3.3±2.1	0.001
Depressive episodes	0.4±1.0	0.3±0.8	0.59

Parameters	Group A	Group B	Control	*P*-value
Digit span forwards	5.5±0.9	5.3±1.1	6.9±0.7	0.48
Digit span backwards	3.3±0.7	3.3±0.8	4.5±0.5	0.96
Digit span test total standard score	91.7±8.1	89±8.8	102.1±3.0	0.15
WCST total error	88.6±8.0	89.2±10.4	106.1±6.4	0.76
WCST perseverative error	86.4±8.4	86.5±11.6	116.5±16.8	0.97
Non-perseverative error	97.1±5.8	96.9±7.4	93.3±3.5	0.91
WCST conceptual response	84.8±13.0	87.8±8.2	100.3±3.9	0.23
N back 1 hits	5.8±1.6	5.1±1.9	8±0.7	0.08
N back 2 hits	3.7±1.7	3.2±2.1	6.9±0.9	0.31
N back 1 error	3.8±1.9	3.2±1.6	1.1±0.8	0.36
N back 2 error	5.8±2.1	5.4±1.7	2.2±0.9	0.11

Table 3: Correlation of duration of illness for Group A and B

Parameters	Group A	P-value	Group B	P-value
Digit forwards	−0.605	<0.001	−0.173	0.29
Standard score	−0.469	0.002	−0.013	0.93
Total error	−0.690	<0.001	−0.377	0.01
Perseverative error	−0.503	0.001	−0.317	0.04
Non-perseverative error	−0.015	0.92	−0.198	0.22
Conceptual response	−0.690	<0.001	−0.173	0.29
N back 1 hits	−0.555	<0.001	−0.398	0.01
N back 2 hits	−0.633	<0.001	−0.367	0.02
N back 1 error	−0.015	0.92	0.130	0.42
N back 2 error	0.092	0.57	0.119	0.47

Table 4: Correlation of manic episodes for Group A and B

Parameters	Group A	*P*-value	Group B	*P*-value
Digit forwards	−0.553	<0.001	−0.475	0.002
Standard score	−0.452	0.005	−0.497	0.001
Total error	−0.629	<0.001	−0.564	<0.001
Perseverative error	−0.537	<0.001	−0.529	<0.001
Non-perseverative error	0.078	0.63	−0.063	0.70
Conceptual response	−0.618	<0.001	−0.570	<0.001
N back 1 hits	−0.611	<0.001	−0.566	<0.001
N back 2 hits	−0.482	0.002	−0.644	<0.001
N back 1 error	0.393	0.013	0.14	0.38
N back 2 error	0.305	0.05	0.11	0.50

DISCUSSION

In our study, the mean age of subjects among the three groups was 32–33 years, and there were no significant differences between the two groups in educational status. On comparing the occupational status of alcohol-dependent and non-dependent bipolar subjects, predominantly alcohol-dependent bipolar subjects were unemployed, whereas the alcohol-non-dependent bipolar subjects were mostly employed. Kumar et al.[8] study show that bipolar patients with substance use were predominantly unemployed.

In our study, bipolar patients with alcohol dependence were predominantly unmarried, consistent with Kumar et al.[8] study. However, Chaudhury et al.[9] demonstrated that bipolar patients with alcohol dependence are predominantly married. This study revealed that attention, executive functions, and verbal memory are impaired in both alcohol-dependent and non-dependent bipolar groups when compared to controls (P < 0.001). There is no significant difference between the two groups of bipolar subjects.

Von Gorp et al.[3] study reveals that only the bipolar group with alcohol dependence shows significantly worse performance than alcohol non-dependent and controls on measuring frontal lobe functioning. The author explains that it might be caused by the direct effects of alcohol on bipolar subjects who are alcohol dependent and due to which they have a more malignant form of bipolar disorder. Sanchez-Moreno et al.[10] studies of comparison between the neurocognitive functioning of bipolar patients with a history of alcohol abuse or dependence and without such history showed that cognitive dysfunction is more strongly associated with bipolar disorder than with a history of alcohol dependence or abuse. Bipolar patients with a history of alcohol abuse or dependence have greater difficulty in inhibitory control due to higher impulsivity.

Robinson and Ferrier[11] also demonstrated poor performance in executive functions, particularly interference. Levy et al.[12]

also showed severe impairment in executive functions in bipolar disorder with alcohol dependence regardless of the euthymic state. Similar findings were demonstrated by Marshall et al.,[13] who showed poorer performance of conceptualization in bipolar disorder with alcohol use. In our study, the subjects in the bipolar disorder group with alcohol dependence had young onset of alcohol use (17.1 years), and the mean duration of alcohol use was 12.6 years. Strakowski et al.[14] suggested that bipolar subjects with a young onset of alcohol use would present more frequent episodes and a worse course of bipolar disorder.

In our study, there were no significant differences while comparing the age of onset of illness between alcohol-independent bipolar subjects and alcohol-dependent bipolar subjects. Furthermore, there was a significant negative correlation while comparing the duration of illness and the number of episodes of bipolar disorder with bipolar subjects with and without alcohol dependence. This explains that when the duration of illness of bipolar disorder increases, performance in cognitive domains decreases. Alcohol-dependent bipolar subjects have more cognitive impairment (Attention, total error, preservative error, conceptual response of executive function, and Hits 1 and 2 of N Back Test) than non-alcohol-dependent bipolar subjects (total error, preservative error of executive function, and Hits 1 and 2 of N Back Test) on correlating with a duration of illness.

Our results explained that several manic episodes negatively correlated with cognitive performances in alcohol-dependent and non-dependent bipolar groups. This finding suggests that the aggregate duration of illness/episodes has more effect on cognitive function. In addition, Von Gorp et al.[3] demonstrated that longer duration of illness and number of episodes of mania significantly correlated with poorer performance on measures of executive function. However, no significant differences were seen in depressive episodes between these two groups.

Karry et al.[15] demonstrated that there were no differences in cognitive functions between bipolar patients with >10 years of duration of illness compared to those with <10 years of illness. Denicoff et al.[6] suggest a relationship between a greater number of episodes, a longer duration of illness, and poorer neurocognitive functioning in subjects with bipolar disorder. Zubieta et al.[16] and Winokur et al.[17] suggest that neurocognitive impairment in dually diagnosed subjects may be associated with the severity of the bipolar disorder. In addition, mood episodes of greater severity and duration have been independently associated with poor neurocognitive functioning and cooccurring substance use disorder.

CONCLUSION

There is an increased number of manic episodes in alcohol-dependent bipolar patients. Euthymic bipolar subjects have impaired function on attention, executive function, and verbal memory. However, there is no statistically significant impairment of cognitive function in euthymic bipolar subjects with alcohol dependence. The lifetime duration of bipolar illness adversely affects neurocognition. This relationship between this impairment and to lifetime duration of illness raises the possibility that early diagnosis and treatment could reduce the degree of neurocognitive impairment.

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