

ORIGINAL PAPER: RESEARCH ARTICLE

Cognitive functions among bipolar affective disorder patients with and without comorbid alcohol dependence syndrome

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Abstract

Background: A complex relationship exists between Bipolar Affective Disorder and comorbid Alcohol dependence. This has crucial clinical implications such as increase in the frequency and severity of episodes of bipolar illness and also increased risk of suicide. Both Bipolar Affective Disorder and Alcohol Dependence syndrome are characterised by cognitive impairments with both domains of memory and executive function being adversely affected. **Aim:** The current study aims to explore the deleterious effect of comorbid Alcohol dependence in Bipolar Affective Disorder on cognitive functions. **Methods:** A total of 140 patients (70 having BPAD with Alcohol dependence syndrome and 70 having BPAD without Alcohol dependence syndrome) were included in this study and their cognitive functions were assessed. **Results:** Patients with both BPAD and ADS have generally poorer cognitive function compared to those with BPAD only, especially in areas of mental flexibility, programming, and inhibitory control. Overall frontal lobe function is more impaired in BPAD patients with alcohol dependence. Cognitive functions like processing speed and mental adaptability are more adversely affected by alcohol dependence in BPAD patients. **Conclusion:** The current study highlights the intriguing correlation between BPAD and Alcohol dependence which has significant implications for clinical practice and future research.

Keywords: Bipolar Affective Disorder, Comorbidity, Cognitive dysfunction

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INTRODUCTION

Bipolar affective disorders are a class of complex episodic psychiatric condition. It is characterized by unusual swings in the mood and activity level of the patient. The severe symptoms of bipolarity lead to many adverse consequences like poor academic achievements, unemployment, harm to self and others, break in relationship etc. However, with proper treatment and support, many people with BPAD can lead full and productive lives^{1,2}. Research indicates that 50% to 70% of individuals with BPAD experience lifetime psychiatric comorbidities^{3,4}. These comorbidities include anxiety disorders”, “substance use disorders” and “personality disorders. The presence of comorbid conditions in BPAD patients affects the severity, treatment response, and overall outcome of the disorder. Substance use disorders are particularly prevalent among persons with BPAD. This comorbidity is more prevalent in males and is associated with both Bipolar I and II disorders⁵. The use of alcohol, drugs, or other substances can exacerbate the symptoms of BPAD and complicate treatment. Substance use can lead to increased mood swings, more severe depressive or manic episodes, and a higher risk of suicide. Individuals with BPAD may use substances as a way to self-medicate their symptoms, but this often leads to a worsening of their condition.

Individuals with BPAD are at an increased risk of engaging in substance misuse, particularly with alcohol. This heightened risk is due to multiple factors, including the use of substances as a form of self-medication to alleviate the symptoms of BPAD⁶. Substance misuse can serve both as a symptom and a coping mechanism for those with BPAD, leading to a complex and intertwined relationship between the two conditions⁷. The prevalence of dependence and abuse of substance is significantly higher in individuals with BPAD compared to those with unipolar depression and schizophrenia, underscoring the unique challenges faced by this population^{8,9}. Alcohol use exacerbates the severity of BPAD, complicates its onset, progression, and treatment, and negatively influences the prognosis^{10,11}. Patients with BPAD and comorbid AUD often experience significant distress and disability, which increases the overall healthcare burden. These individuals typically have longer hospital stays and a higher incidence of suicidal attempts. Furthermore, they exhibit poor adherence to treatment regimens and show less favourable responses to de-addiction programs, resulting in a poorer overall prognosis^{12,13,14}. Cognitive impairments are common in both BPAD and substance use disorders, with deficits particularly evident in areas such as memory and executive functions. The co-occurrence of BPAD and SUD further exacerbates these cognitive impairments, leading to poorer overall cognitive performance^{15,16}. Tackling these cognitive deficits is crucial for enhancing the quality of life and functional outcomes for individuals with BPAD and co-occurring substance use disorders. Memory impairments are common in individuals with BPAD and can be further exacerbated by substance use. These impairments can affect both short-term and long-term memory, making it difficult for individuals to retain and recall information. Addressing memory impairments in treatment can help improve cognitive functioning and overall outcomes^{17,18}. Executive functioning deficits are also common in individuals with BPAD and can be further exacerbated by substance use. These deficits can affect an individual's ability to plan, organize, and complete tasks, leading to difficulties in daily functioning. Addressing executive functioning deficits in treatment can help improve cognitive functioning and overall outcomes¹⁹. Individuals with BPAD often experience attention and concentration challenges, which can be worsened by substance use. These challenges can hinder their ability to focus and accomplish tasks, resulting in struggles with daily activities. Addressing attention and concentration difficulties in treatment can help improve cognitive functioning and overall outcomes¹⁹.

METHOD

The aim of the study was to compare the cognitive functions in patients with Bipolar affective disorder with and without alcohol dependence syndrome. The study was approved by the institutional ethics committee and it was ensured that the research would not harm the patients' current treatment or functioning in any way. A total of 140 cases (70 cases of Bipolar affective disorder with alcohol dependence syndrome and 70 cases of Bipolar affective disorder without alcohol dependence syndrome) were included in the study. The cases of BPAD with ADS were classified as Group A and the cases of BPAD without ADS were classified as Group B. The assessment tools used were:-

Alcohol use disorder identification test (AUDIT): It is a 10-item screening tool developed by the WHO to assess alcohol consumption, drinking behaviours, and alcohol-related problems. It helps identify individuals at risk of alcohol use disorder, guiding early intervention efforts.

Severity of Alcohol Dependence Questionnaire (SAD-Q): It is a 20-item self report tool designed to measure the severity of alcohol dependence. It assesses physical withdrawal symptoms, affective disturbance, and the frequency of heavy drinking, helping to guide treatment decisions.

Frontal Assessment Battery (FAB): This is a short cognitive test that evaluates executive functions associated with the frontal lobe. It consists of six tasks, assessing abilities like conceptualization, mental flexibility, motor programming, and inhibitory control, useful in diagnosing frontal lobe dysfunctions.

Digit symbol substitution test (DSST): The "DSST" is a neuropsychological assessment used to measure processing speed, attention, and working memory. It involves matching symbols to numbers according to a key within a specific time limit, and is often used in cognitive evaluations for conditions like dementia or brain injury.

Stroop word colour test: It is a psychological test that measures cognitive flexibility, selective attention, and processing speed. It involves naming the color of the ink a word is printed in, rather than reading the word itself, challenging the ability to suppress automatic responses and manage interference.

Verbal N back test: This is a cognitive task used to assess working memory and executive function. Participants are required to monitor a sequence of verbal stimuli and indicate when the current stimulus matches one presented "n" steps earlier, with varying levels of difficulty based on the value of "n".

Duration of study: March 2023 to February 2024.

Place of study: Silchar Medical College Hospital, Silchar, Assam, India.

Informed consent and ethics committee clearance taken.

STATISTICAL ANALYSIS: Analysis of data collected was on the basis of descriptive statistics. Figures, charts and tables were placed wherever required by using Microsoft Excel 2016.

RESULTS

Table A-1: DISTRIBUTION AND COMPARISON OF AGE BETWEEN GROUP A & GROUP B

Comparison of Age between Groups						
Group	N	Mean	Median	SD	Minimum	Maximum
Group A	70	37.5	37.0	8.91	21	55
Group B	70	34.4	35.0	8.41	18	55

Age Distribution of Groups			
Age Groups	Group A	Group B	Total
16-25 Years	5 3.6 %	13 9.2 %	18 12.8 %
26-35 Years	28 20.0 %	26 18.6 %	54 38.6 %
36-45 Years	20 14.3 %	26 18.6 %	46 32.9 %
46-55 Years	17 12.1 %	5 3.6 %	22 15.7 %

- The mean age for BPAD + ADS (Bipolar Affective Disorder with Alcohol Dependence Syndrome) is slightly higher at 37.5 years compared to 34.4 years for BPAD only.
- The median age is similar in both groups, with a slight difference (37.0 for BPAD + ADS and 35.0 for BPAD).
- The 26-35 age group has the highest proportion of individuals in both BPAD+ADS and BPAD groups, indicating this is the most common age range for the disorders.
- There is a notable difference in the 46-55 age group, with a higher percentage in the BPAD + ADS group (12.1%) compared to the BPAD group (3.6%).
- The 16-25 age group shows a small proportion in both groups, with BPAD+ADS at 3.6% and BPAD at 9.2%.
- The above table suggests that while BPAD can present in younger individuals, the combination of BPAD with ADS is more common in mid-adulthood, particularly in the later years, which may indicate a progression of the disorder or an increased likelihood of developing comorbid alcohol dependence as patients age.

TABLE NO- B-1 SHOWS THE ALCOHOL DEPENDENCE IN BPAD WITH ADS GROUP

History of Alcohol Dependence in Group A (N=70)					
	Mean	Median	SD	Minimum	Maximum
Age Of Onset Of Alcohol Use	21.1	21.0	3.49	15	29
Duration Of Alcohol Use	16.4	15.0	7.60	3	33
Audit Score	23.3	24.0	3.14	18	32
SADQ Score	39.2	38.0	6.84	28	56

- **Age of Onset and Duration of Alcohol Use:** The mean age of onset of alcohol use is 21 years, with a mean duration of alcohol use being approximately 16 years.

Inference: Patients with BPAD + ADS tend to develop alcohol dependence early, which can lead to long-term alcohol use.

- **Audit and SADQ Scores:** High scores on the AUDIT (mean = 23.3) and SADQ (mean = 39.2) suggest severe alcohol dependence among GROUP A.

Inference: The severity of alcohol dependence is significant in the BPAD + ADS group, contributing to more complex clinical outcomes

SERIES C: TABLE NO C-1 TO C-4 SHOWS THE COMPARISON OF THE VARIOUS COGNITIVE FUNCTIONS BETWEEN BPAD WITH ADS AND BPAD WITHOUT ADS GROUP

Table C-1: COMPARISON OF SCORES OF FRONTAL ASSESSMENT BATTERY BETWEEN GROUP A & GROUP B

Comparison of Frontal Assessment Battery between Groups								
Variables	Group	Mean	Median	SD	Minimum	Maximum	t value	p value
Similarities (Conceptualisation)	Group A	2.00	2.00	0.590	1	3	-2.285	0.024
	Group B	2.23	2.00	0.594	1	3		
Lexical Fluency (Mental Flexibility)	Group A	1.73	2.00	0.635	1	3	-2.916	0.004
	Group B	2.00	2.00	0.450	1	3		
Motor Luria (Programming)	Group A	1.81	2.00	0.728	1	3	-2.534	0.012
	Group B	2.11	2.00	0.671	1	3		
Conflicting Instructions (Sensitivity To Interference)	Group A	2.09	2.00	0.583	1	3	-0.291	0.772
	Group B	2.11	2.00	0.578	1	3		
Go-no-go (Inhibitory Control)	Group A	1.26	1.00	0.793	0	3	-2.695	0.008
	Group B	1.60	2.00	0.710	0	3		
Prehension Behaviour (Environmental Autonomy)	Group A	2.09	2.00	0.654	1	3	-1.539	0.126
	Group B	2.24	2.00	0.550	1	3		

Scores of FAB denotes:

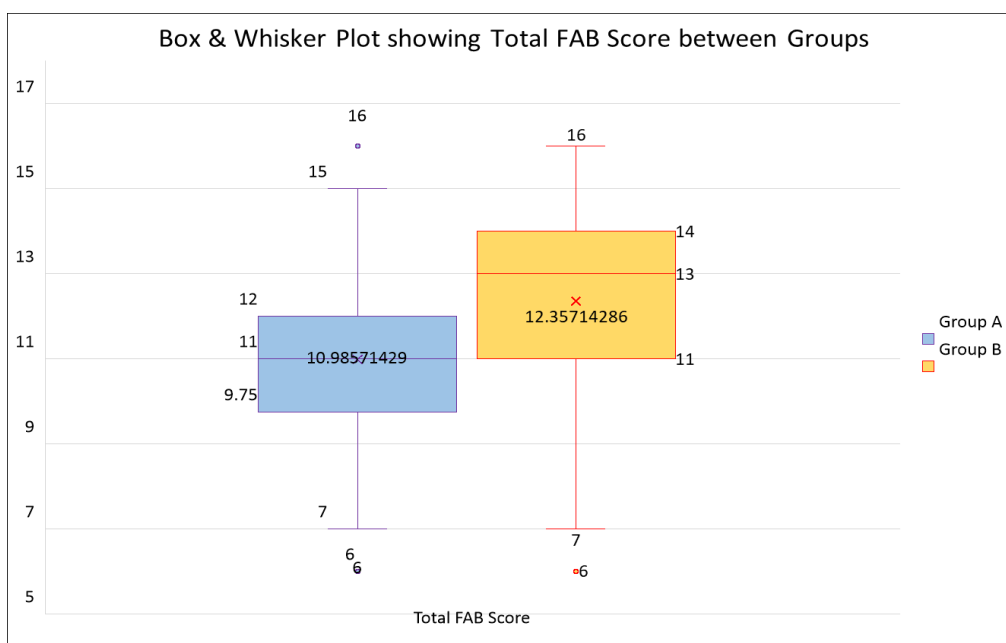
1. **Similarities (Conceptualization)**: Significant difference ($p = 0.024$) between the two groups, with BPAD having a higher mean score.
2. **Lexical Fluency (Mental Flexibility)**: BPAD group shows significantly better performance ($p = 0.004$).
3. **Motor Luria (Programming)**: BPAD group has significantly higher scores ($p = 0.012$).
4. **Go-no-go (Inhibitory GROUP B)**: Significant difference ($p = 0.008$) indicates poorer inhibitory GROUP B in the BPAD + ADS group.
5. **Prehension Behavior (Environmental Autonomy)**: No significant difference ($p = 0.126$).

Inference: Patients with both BPAD and ADS have generally poorer cognitive function compared to those with BPAD only, especially in areas of mental flexibility, programming, and inhibitory GROUP B. Alcohol dependence may impair conceptualization in BPAD patients. Comorbid alcohol dependence negatively affects executive function in BPAD patients.

Table C-2: COMPARISON OF TOTAL SCORES OF FRONTAL ASSESSMENT BATTERY BETWEEN GROUP A & GROUP B

Comparison of Frontal Assessment Battery between Groups								
Variables	Group	Mean	Median	SD	Minimum	Maximum	t value	p value
Total Score Of Frontal Assessment Battery	Group A	10.99	11.00	2.275	6	16	-3.535	<.001
	Group B	12.36	13.00	2.316	6	16		

Fig C-1: BOX & WHISKER PLOT SHOWING COMPARISON OF TOTAL FAB SCORE BETWEEN GROUP A & GROUP B



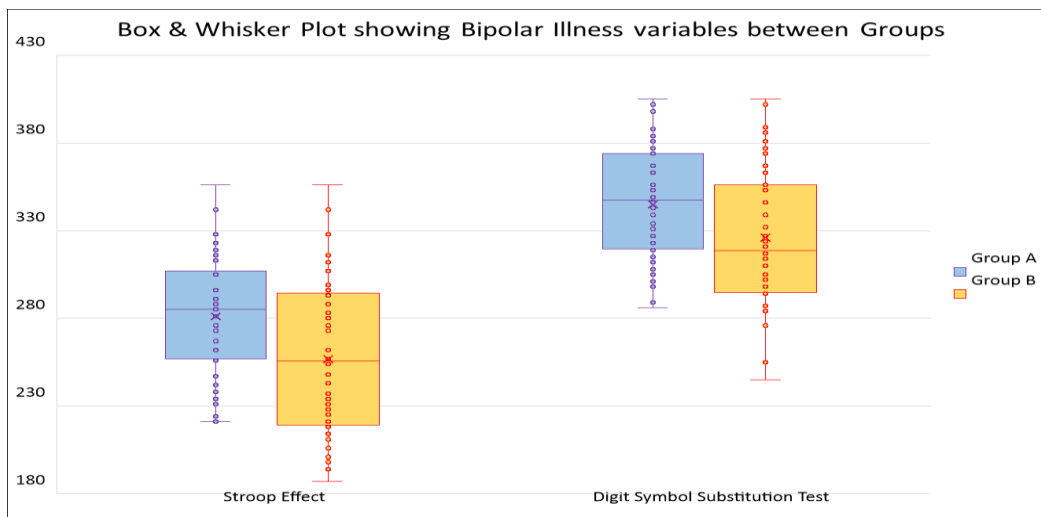
Total FAB Score:

- The BPAD + ADS group has a significantly lower total FAB score compared to the BPAD group ($p < 0.001$).
- **Inference:** Overall frontal lobe function is more impaired in BPAD patients with alcohol dependence.

Table C-3: COMPARISON OF SCORES OF STROOP EFFECT AND DSST BETWEEN GROUP A & GROUP B

Comparison of Frontal Assessment Battery between Group								
Variables	Group	Mean	Median	SD	Minimum	Maximum	t value	p value
Stroop Effect In Seconds	Group A	281	285	31.6	221	356	3.85	<.001
	Group B	257	256	42.5	187	356		
Digit Symbol Substitution Test In Seconds	Group A	345	348	31.7	286	405	3.23	0.002
	Group B	326	319	36.9	245	405		

Fig C-2: BOX & WHISKER PLOT SHOWING COMPARISON OF STROOP EFFECT & DIGIT SYMBOL SUBSTITUTION TEST IN SECONDS BETWEEN GROUP A & GROUP B

**Stroop and Digit Symbol Substitution Tests:**

- The BPAD + ADS group performs worse on both tests, with significant differences ($p < 0.001$ for Stroop; $p = 0.002$ for Digit Symbol Substitution).
- **Inference:** Cognitive functions like processing speed and mental flexibility are more adversely affected by alcohol dependence in BPAD patients.

Table C-4: COMPARISON OF SCORES OF VERBAL N BACK TEST BETWEEN GROUP A & GROUP B

Comparison of Frontal Assessment Battery between Groups								
	Group	Mean	Median	SD	Minimum	Maximum	t value	p value
N1 Back Hit	Group A	7.66	8.00	0.679	7	9	0.3834	0.702
	Group B	7.61	8.00	0.644	7	9		
N1 Back Error	Group A	1.91	2.00	0.913	0	3	-0.4640	0.643
	Group B	1.99	2.00	0.909	0	3		
N2 Back Hit	Group A	6.64	7.00	0.933	5	8	1.2815	0.202
	Group B	6.46	7.00	0.774	5	8		
N2 Back Error	Group A	3.93	4.00	1.231	1	6	0.0713	0.943
	Group B	3.91	4.00	1.139	1	6		

Variables:

- N1/N2 Back Hit/Error: Scores related to performance on working memory tasks.

Significant Findings:

- N1 Back Hit/Error: No significant difference between groups ($p > 0.05$).
- N2 Back Hit/Error: Again, no significant differences found.

Inference:

- There is no substantial difference in working memory performance between patients with BPAD and those with both BPAD and ADS.

DISCUSSION

Significant differences were observed between the two groups—Bipolar Affective Disorder (BPAD) patients with comorbid Alcohol Dependence Syndrome (ADS) and those without—across various domains, including sociodemographic variables and cognitive functions.

Alcohol Use Patterns: Our results indicate that the mean age of onset of alcohol use in the BPAD + ADS group is 21 years, with a mean duration of alcohol use of approximately 16 years. This suggests that patients with BPAD + ADS typically develop alcohol dependence at a relatively young age and sustain long-term alcohol use. This early onset and prolonged duration of alcohol dependence among BPAD patients is consistent with findings from studies like those by ²⁰Boaz et al (2007) and ²¹Shan et al. (2011). High scores on the AUDIT (mean = 23.3) and SADQ (mean = 39.2) reflect severe alcohol dependence in the BPAD + ADS group. The severity of alcohol dependence, as indicated by these scores, contributes to more complex clinical outcomes and challenges in managing BPAD. These findings are supported by research from ²²Lee et al. (2015), who demonstrated that high AUDIT (23.8) and SADQ scores (37.6) correlate with severe alcohol dependence and more complicated clinical presentations. Our results are also consistent with Indian studies such as that by ²³Pary et al. (2017), which reported high levels of alcohol dependence in BPAD patients with comorbid alcohol use disorders.

Cognitive Functions 1. Frontal Assessment Battery (FAB): The comparison of FAB scores revealed that the BPAD group had higher mean scores in conceptualization ($p = 0.024$), mental flexibility ($p = 0.004$), and programming ($p = 0.012$), indicating better performance in these areas compared to the BPAD + ADS group. The BPAD + ADS group demonstrated poorer inhibitory control ($p = 0.008$) but no significant difference in environmental autonomy ($p = 0.126$). These findings suggest that alcohol dependence negatively impacts cognitive functions, especially in areas such as mental flexibility and inhibitory control, which are crucial for executive functioning. This aligns with studies like those by ²⁴Naik et al. (2021) and ¹⁷Adhikari et al. (2023), which report that substance use exacerbates cognitive impairments in bipolar disorder patients, particularly affecting executive functions.

2. Total FAB Score: The BPAD + ADS group had a significantly lower total FAB score compared to the BPAD group ($p < 0.001$), indicating more impaired overall frontal lobe function. This supports the notion that comorbid alcohol dependence leads to more severe cognitive deficits in BPAD patients. Similar findings are reported by ²⁴Naik et al. (2021) (mean = 29.02, $t = 0.361$, $p < 0.001$) and the Digit Symbol Substitution Test ($p = 0.002$), reflecting poorer processing speed and mental flexibility. These results underscore the detrimental effect of alcohol dependence on cognitive functions such as processing speed and cognitive flexibility. Indian research by ²⁴Naik et al. (2021) (for Stroop effect: mean = 34.88, $t = 5.432$, p further impairs cognitive functions related to processing speed and executive control in bipolar disorder patients. 4. Verbal N-Back Test: No significant differences were observed in working memory performance between the BPAD and BPAD + ADS groups ($p > 0.05$ for both N1 and N2 Back Hit/Error). This suggests that comorbid alcohol dependence does not significantly affect working memory in this sample. This is somewhat inconsistent with studies by ²¹Shan et al. (2011), which indicate that working memory can be impacted by substance use disorders, although the extent may vary based on the sample and methods used.

Conclusion

The BPAD WITH ADS group was younger and displayed severe alcohol dependence, with early onset and prolonged duration of alcohol use, consistent with prior studies. This severity is reflected in higher scores on the AUDIT and SADQ scales, highlighting the challenges in managing this dual diagnosis. The BPAD WITH ADS group also demonstrated significant impairments in frontal lobe functions, processing speed, and cognitive flexibility, as indicated by lower scores on the Frontal Assessment Battery (FAB), Stroop Test, and Digit Symbol Substitution Test (DSST). These cognitive deficits were more pronounced with longer illness duration and extended alcohol use, suggesting a compounding effect of alcohol on cognitive decline in BPAD patients.

The study's findings highlight the complex interplay between Bipolar Affective Disorder (BPAD) and Alcohol Dependence Syndrome (ADS), with significant implications for clinical practice and future research.

AUTHOR CONTRIBUTIONS

SKM: Definition of intellectual content, data acquisition, manuscript preparation, guarantor; **KN:** Design, clinical studies, statistical analysis, manuscript editing, guarantor; **HD:** Design, clinical studies, statistical analysis, manuscript editing, guarantor; **AB:** Concepts, data analysis, manuscript review, guarantor.

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