Role of Quantitative EEG as a Predictor for Cognitive Impairment in Chronic Bipolar Patients

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Abstract

Background: Bipolar disorder (BD) is associated with cognitive decline across its phases. Quantitative electroencephalography (QEEG) measures brain electrical activity and can assess cognitive functions.

Objectives: This study investigates the relationship between QEEG findings and cognitive functioning in BD patients, aiming to identify specific EEG markers correlating with cognitive deficits by comparing BD patients to healthy controls.

Patients and Methods: We hypothesized that BD patients would show distinct QEEG abnormalities associated with poorer cognitive outcomes compared to controls. Data were collected from 50 BD patients and 50 controls, including QEEG recordings and cognitive assessments.

Results: Significant differences were found in QEEG patterns between BD patients and controls. BD patients had lower MoCA scores (20.36 ± 4.82 vs. 27.10 ± 1.88, $p < 0.001$) and SDMT scores (27.46 ± 14.04 vs. 34.42 ± 10.19, $p = 0.006$), with higher TMT-A ($p < 0.001$) and TMT-B ($p < 0.001$) scores. QEEG showed increased Delta (T6, $\eta^2 = 0.102$, $p < 0.001$), Theta, and decreased Alpha and Beta power in BD patients.

Conclusion: QEEG can potentially diagnose cognitive dysfunction in BD patients, offering a basis for personalized treatment strategies based on QEEG findings. This study supports developing QEEG-based diagnostic tools and tailored treatment plans for cognitive impairments in BD.

Keywords: Bipolar Disorder; Cognitive Impairment; Quantitative Electroencephalography.
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Introduction

Bipolar affective disorder (BAD) is a severe mental health condition characterized by alternating episodes of mania, hypomania, and depression, significantly impairing cognitive and functional capacities (**Yatham et al., 2018**). These cognitive impairments are widespread and impact cognitive functions such as attention, memory, and executive function, contributing considerably to the overall burden of the disease (**Torres et al., 2020**). Understanding the neurobiological mechanisms underlying these cognitive deficits is essential for developing targeted therapeutic interventions.

Quantitative electroencephalography (QEEG) has become a valuable tool in neuropsychiatric research, offering objective measures of brain electrical activity linked to cognitive functions (**Cullen et al., 2016**). QEEG is useful in the assessment and treatment of various mental disorders by analyzing the electrical activity of the brain. QEEG provides insights into neural functioning and connectivity, offering clinicians objective data to guide diagnosis and treatment decisions in conditions like attention deficit hyperactivity disorder (ADHD), depression, and schizophrenia. Furthermore, QEEG enables monitoring of treatment progress and predicting treatment response, enhancing personalized care strategies for patients. Studies by **Thatcher et al. (2009)** and **Coben et al. (2013)** have highlighted the efficacy of QEEG in elucidating neural correlates of psychiatric disorders, emphasizing its potential to revolutionize psychiatric practice.

Recent studies have identified alterations in EEG power spectra in patients with bipolar disorder, suggesting that QEEG might be a potential biomarker for cognitive dysfunction in these patients (**Boutros et al., 2015**). Despite these findings, the specific relationships between QEEG features and cognitive impairments in BAD remain insufficiently explored.

The objective of this study is to examine the correlation between QEEG findings and cognitive function in patients with bipolar affective disorder. By comparing the QEEG patterns and cognitive abilities of bipolar patients to those of healthy controls, we aim to identify specific EEG markers that correlate with cognitive deficits. We hypothesize that patients with BAD will display distinct QEEG abnormalities associated with poorer cognitive outcomes compared to controls.

The findings of this study could have significant clinical consequences, potentially facilitating the development of QEEG as a non-invasive and cost-effective diagnostic tool and personalized treatment strategies for cognitive dysfunction in bipolar disorder.

Limitations of Current Methods: Traditional methods for diagnosing cognitive dysfunction in BAD primarily rely on neuropsychological assessments and clinical evaluations. While these methods provide valuable insights, they have several limitations. Neuropsychological tests can be time-consuming, require extensive training to administer and interpret, and may be influenced by various extraneous factors such as patient motivation, education level, and cultural background. Moreover, these assessments may not capture subtle neurophysiological changes associated with cognitive dysfunction in BAD (**Arts et al., 2008**, **2015**).

Addressing Limitations with QEEG: This study addresses the aforementioned limitations by utilizing quantitative electroencephalography (QEEG) as a diagnostic tool. QEEG offers several advantages over traditional methods, including objectivity, non-invasiveness, and the ability to measure real-time brain activity (**Coben et al., 2013**; **de la Salle et al., 2019**). By analyzing the electrical activity of the brain, QEEG can detect subtle changes in neural functioning and connectivity that may not be apparent through neuropsychological tests. Our study specifically investigates the association between QEEG findings and cognitive functioning in BAD patients, identifying specific EEG markers that correlate with cognitive deficits (**Boutros et al., 2015**; **Kirli et al., 2022**).

Potential Benefits for Personalized Treatment: Identifying specific EEG markers associated with cognitive dysfunction in BAD has significant clinical implications. These markers can facilitate early diagnosis, allowing for timely intervention and potentially mitigating the progression of cognitive impairments (**Olbrich et al., 2015**). Additionally, QEEG can be used to monitor treatment response, enabling clinicians to tailor therapeutic strategies based on individual neural profiles. This personalized approach can enhance treatment efficacy and improve overall patient outcomes. Our study aims to contribute to the growing body of evidence supporting the use of QEEG in personalized medicine, particularly in the context of psychiatric disorders such as BAD (**Saletu et al., 2010**; **Harmony et al., 2013**).

Patients and methods

Study Design and Participants

This case-control observational study included 100 participants recruited from the neuropsychiatry outpatient clinic at Qena University Hospital. The study sample comprised 50 patients diagnosed with bipolar affective disorder (BAD) according to the **Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)**, and 50 healthy controls with no psychiatric disorders as per DSM-5 criteria (**American Psychiatric Association, 2013**).

Participant Recruitment

Participants were recruited using convenience sampling from the outpatient clinic. This approach may introduce selection bias, as individuals seeking treatment are potentially more symptomatic or motivated to participate in clinical studies. To mitigate this bias, we included a diverse sample of participants, representative of various demographic and clinical characteristics. Future studies should consider randomized sampling methods to further minimize selection bias.

Data was collected between April 2023 and April 2024.

Inclusion/Exclusion Criteria:

- Age Range: Participants were aged 18-60 years.
- Gender Distribution: The BAD group included 26 males (52%) and 24 females (48%), while the control group included 33 males (66%) and 17 females (34%).
- All patients were in remission for at least three months prior to evaluation.

Ethical Code: All participants provided written informed consent, and the study received approval from the institutional ethics committee at the Faculty of Medicine in Qena (SVU-MED-NAP020-1-23-3-576).

Procedures

Full Psychiatric Evaluation: All participants underwent a comprehensive psychiatric history and mental state examination. Patients were diagnosed with bipolar affective disorder according to DSM-5 criteria, and it was verified that the controls did not have any psychiatric diseases (**First, 2015**).

Cognitive Assessments: Trail Making Test (TMT A & B): (**Llinàs-Reglà et al., 2016**). Arabic validated version of the test used to assess processing speed and executive function (**Stanczak et al., 2001**). Montreal Cognitive Assessment (MoCA): (**Nasreddine et al., 2005**). The Arabic validated version of the MoCA was employed to assess a wide range of cognitive abilities, such as executive function, language, memory, and attention (**Rahman and El Gaafary, 2009**).Symbol Digit Modalities Test (SDMT): (**Sheridan et al., 2006**). The Arabic validated version of the SDMT is used to measure attention and motor speed (**Farghaly et al., 2021**).

Quantitative EEG Assessment

All participants underwent EEG recording with a Nihon Kohden machine in our neurophysiology unit, using 19 scalp electrodes positioned according to the international 10-20 system for a standard duration of 30 minutes (**Rojas et al., 2018**). The QEEG analysis focused on the spectral power of four primary frequency bands: Delta (1-4 Hz), Theta (4-8 Hz), Alpha (8-13 Hz), and Beta (13-30 Hz). These frequency bands were chosen based on their established relevance in cognitive and neuropsychiatric research (**Başar et al., 2001**; **Harmony, 2013**).

The analysis was conducted using the software provided with the Nihon Kohden system, which includes an intrinsic program for spectral analysis. The software calculates spectral power by performing a fast Fourier transform (FFT) on one-second epochs of artifact-free EEG data, selected through visual inspection. This method allows for the quantification of power in each frequency band across different electrode sites. The resulting data were then statistically analyzed to compare the spectral power between BAD patients and healthy controls.

Statistical Analysis

The data were collected, categorized, reviewed, and inputted into the Statistical Package for Social Science (IBM SPSS) version 27. Categorical variables were represented using numerical values and percentages, whereas numerical variables were summarized as means and standard deviations. Chi-Square Test: Compared cases and controls regarding qualitative variables. The Fisher exact test was used if chi-square assumptions were unmet. Independent T-Test: Compared cases and controls regarding numerical variables with a parametric distribution. Mann-Whitney Test: Compared numerical variables with a non-parametric distribution between cases and controls. Pearson Correlation: Utilized to assess the correlation between cognitive assessment scores and QEEG findings. The acceptable margin of error was established at 5%, while the confidence interval was set at 95%. The interpretation of p-values was as follows: $p > 0.05$: Not statistically significant (NS); $p < 0.05$: Statistically significant (S). The effect size for independent groups was calculated using the Eta squared equation and interpreted as a small effect at 0.01, a medium effect at 0.06, and a large effect at 0.14 or more.

Results

This case-control study involved 100 patients (50 cases with bipolar affective disorder and 50 controls) from the neuropsychiatry outpatient clinic at Qena University Hospital.

(Table .1) Demonstrates no statistically significant age difference between cases and controls, where the mean age was nearly equal among cases and controls ($p = 0.302$, not statistically significant). There was a statistically significant difference between cases and controls concerning marital status (p-value = 0.025), where 12% and 4% of cases were divorced and widowed, respectively, compared to 0% in controls. There was a statistically significant distinction between the case and control groups regarding occupation (p-value = 0.016), where 24% of cases were housewives compared to 4% in controls.

Table 1. Demographic data of cases and control.

Parameters		Cases (N=50)	Controls (N=50)	P value
		Number (%)	Number (%)	
Gender	**Male**	26 (52%)	33 (66%)	0.155
	Female	24 (48%)	17 (34%)	
	Mean ± SD	31.12 ± 7.914	29.48 ± 7.895	0.302[a]
Marital status	**Single**	24 (48%)	28 (56%)	0.025**
	Married	18 (36%)	22 (44%)	
	Divorced	6 (12%)	0 (0%)	
	Widow	2 (4%)	0 (0%)	
Occupation	**Worker**	16 (32%)	20 (40%)	0.016**
	Housewife	12 (24%)	2 (4%)	
	Employee	9 (18%)	17 (34%)	
	Unemployed	13 (26%)	11 (22%)	

*Chi-square test, **Fisher's exact test, [a]Student t-test

(Table .2) & (Fig.1) Shows the clinical characteristics of our cases, where the most frequent last episode was manic, accounting for 60% of cases, followed by

hypomanic (26%), depressive (8%), and mixed episodes were the least frequent, accounting for 6% of cases. Concerning the family history of bipolar disorder, most cases (64%) had a negative family history of bipolar disorder, and 28% had a positive family history in first-degree relatives. Regarding hospital admission, 28% of cases needed hospital admission. The mean episode number was 6.26 ± 3.468, ranging from 2 to 20 episodes. The mean age of onset of the disease was 22.80 ± 5.6568, ranging from 15 to 34 years. 56% of cases had disease onset after 20 years.

Table 2. Clinical data of the studied cases (N=50)

Parameters		Frequency	Percentage %
Last episode	**Manic**	30	60%
	Hypomanic	13	26%
	Depressive	4	8%
	Mixed	3	6%
Family history	**Negative**	32	64%
	1st degree	14	28%
	2nd degree	4	8%
Hospital admission	**Yes**	14	28%
	No	36	72%
Episodes number	**≤ 4**	20	40%
	>4	30	60%
	Mean ± SD	6.26 ± 3.468	
	Median (range)	5.50 (2-20)	
Age at onset (years)	**≤20**	22	44%
	>20	28	56%
	Mean ± SD	22.80 ± 5.6568	
	Median (range)	22 (15-34)	

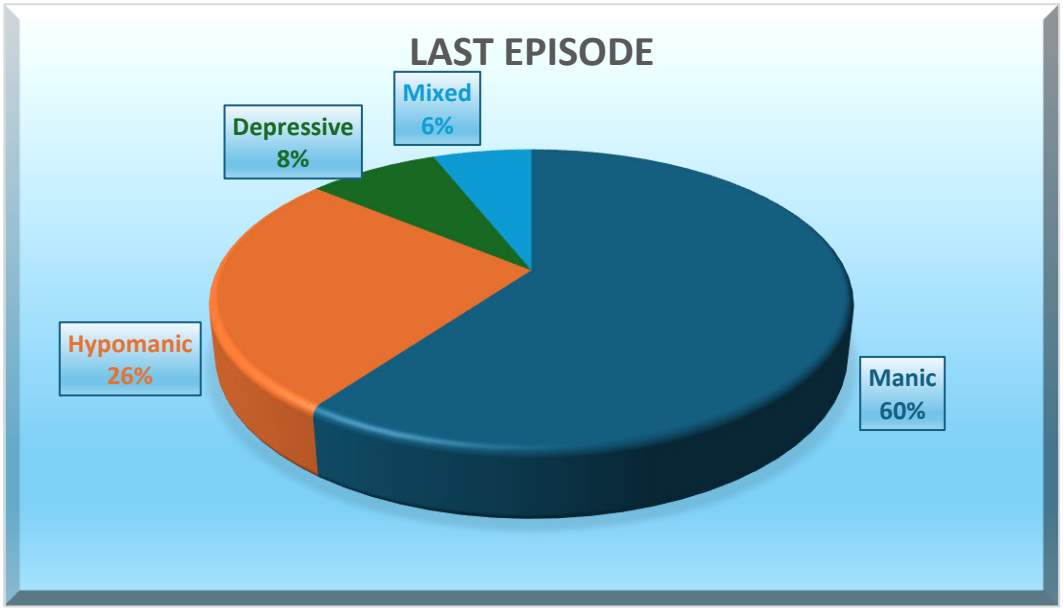

Fig.1. Last episode of cases

(Table.3) Shows a statistically significant difference between the cases and controls concerning the MOCA scale (p-value < 0.001), where the mean MOCA scale was statistically significantly lower among cases than controls (20.36 ± 4.822 vs. 27.10 ± 1.876). There was a statistically significant difference between cases and controls concerning the SDMT scale (p = 0.006, statistically significant), with a lower mean

scale in cases compared to controls (27.46 ± 14.038 vs. 34.42 ± 10.194, p-value = 0.006). A statistically significant difference exists between cases and controls concerning TMT-A and TMT-B scales ($p < 0.001$ for both, statistically significant), where the median scales were significantly higher among cases than controls. A large effect size exists between cases and controls in MOCA and TMT-B scales ($\eta^2 = 0.464$ and 0.219) and a medium effect size between cases and controls in SDMT and TMT-A scales ($\eta^2 = 0.076$ and 0.131).

Table 3. Cognitive assessment scales among cases and controls

Cognitive assessment scale	Cases	Controls	P value	Effect size
	Mean ± SD	Mean ± SD		
MOCA	20.36 ± 4.822	27.10 ± 1.876	<0.001*	0.464#
SDMT	27.46 ± 14.038	34.42 ± 10.194	0.006*	0.076#
	Median (IQR)	**Median (IQR)**		
TMT-A (seconds)	16 (10.25)	8 (5)	<0.001**	0.131#
TMT-B (seconds)	29 (24)	13 (6.25)	<0.001**	0.219#

*Student t-test, **Mann Whitney test, # Eta squared, MOCA: Montreal Cognitive Assessment, SDMT: Symbol Digits Modality test, TMT: Trail Making Test.

(Table .4). Demonstrates a statistically significant difference in Delta power electrodes (FP1, F7, F3, Fz, F8, C3, T5, P3, T6, and O2) among cases and controls, where the p-values were 0.018, 0.011, 0.016, 0.053, 0.025, 0.040, 0.001, 0.025, <0.001, and 0.031, respectively, with the median power being significantly higher among cases than controls. No statistically significant difference exists with other electrodes. A medium effect exists between cases and controls in the Delta power electrode (T6) ($\eta^2 = 0.102$) and a small effect in Delta power electrodes (F7, T5, FP1, P3, O2, F4, C3, O1, and F3) ($\eta^2 = 0.059$, 0.054, 0.027, 0.027, 0.025, 0.021, 0.021, 0.017, and 0.015, respectively).

Table 4. Quantitative EEG features (Delta power) among cases and controls

Delta wave power	Cases	Control	P value	Effect size
	Median (IQR)	Median (IQR)		
FP1	58.4433 (96.47)	28.80 (78.78)	**0.018***	0.027#
FP2	52.20 (100.52)	37.150 (89)	**0.209**	0.005
F7	22.6333 (35.19)	9.60 (24.91)	**0.011***	0.059#
F3	23.60 (38.32)	10.50 (26.04)	**0.016***	0.015#
Fz	24.30 (49.64)	14.5333 (33.50)	**0.053**	0.001
F4	26.60 (46.53)	16.3333 (35.99)	**0.195**	0.021#
F8	17.9667 (44.80)	11.7667 (28.01)	**0.025***	0.006
C3	16.10 (41.90)	7.30 (30.54)	**0.040***	0.021#
C4	18.8333 (61.94)	5.50 (32.54)	**0.080**	0.002
T5	23.7667 (44.21)	9.8667 (29.38)	**0.001***	0.054#
P3	15.9333 (33.88)	8.50 (40.63)	**0.025***	0.027#
Pz	19.0 (67.34)	16.3667 (40.72)	**0.230**	0.000
P4	16.5667 (66.43)	14.9333 (33.73)	**0.085**	0.003
T6	32.9333 (74.24)	12.1833 (28.78)	**<0.001***	0.102#
O1	19.6333 (46.30)	12.350 (32.06)	**0.270**	0.017#
O2	20.3333 (62.67)	13.60 (30.29)	**0.031***	0.025#

*Mann Whitney test, # Eta squared.

(Table .5) Shows a statistically significant difference in all Theta power electrodes (FP1, FP2, F7, F3, Fz, F8, F4, C3, C4, T5, P3, Pz, P4, T6, O1, and O2) among cases and controls, where the p-values were <0.001 for all of them, where the median power was significantly higher among cases than controls. A large effect exists between

cases and controls in Theta power electrodes (FP1, FP2, F7, F8, C3, T5, P3, T6, O1, and O2) (η^2 = 0.199, 0.169, 0.175, 0.170, 0.148, 0.293, 0.152, 0.289, 0.152, 0.144), a medium effect in Theta power electrodes (F3, Fz, Pz, and P4) (η^2 = 0.136, 0.135, 0.107, and 0.118), and a small effect in Theta power electrodes (F4 and C4, η^2 = 0.046 and 0.035).

Table 5. Quantitative EEG features (Theta power) among cases and controls

Theta wave power	Cases	Control	P value	Effect size
	Median (IQR)	Median (IQR)		
FP1	23.0333 (26.34)	6.5667 (7.90)	**<0.001***	0.199#
FP2	24.3333 (25.12)	7.4333 (8.54)	**<0.001***	0.169#
F7	20.8333 (19.26)	4.90 (4.02)	**<0.001***	0.175#
F3	17.7667 (19.11)	5.6333 (6.97)	**<0.001***	0.136#
Fz	17.5333 (20.81)	6.1667 (8.89)	**<0.001***	0.135#
F4	18.8333 (18.11)	5.1333 (11.47)	**<0.001***	0.046#
F8	18.100 (17.24)	4.1500 (5.91)	**<0.001***	0.170#
C3	14.4000 (20.29)	4.6333 (5.97)	**<0.001***	0.148#
C4	12.8667 (17.52)	3.40 (11.63)	**<0.001***	0.035#
T5	17.4667 (21.13)	5.4333 (4.46)	**<0.001***	0.293#
P3	15.4667 (19.06)	4.0667 (7.82)	**<0.001***	0.152#
Pz	17.500 (19.39)	6.4000 (12.50)	**<0.001***	0.107#
P4	15.000 (21.70)	3.8333 (10.83)	**<0.001***	0.118#
T6	19.5667 (23.07)	5.700 (6.07)	**<0.001***	0.289#
O1	17.3667 (23.37)	4.8333 (5.93)	**<0.001***	0.152#
O2	13.6667 (21.23)	4.6667 (11.77)	**<0.001***	0.144#

*Mann Whitney test, Eta squared.

(Table .6). Shows a statistically significant difference in all Alpha power electrodes (FP1, FP2, F7, F3, Fz, F8, F4, C3, C4, T5, P3, Pz, P4, T6, O1, and O2) among cases and controls, where the p-values were <0.001 for all of them, where the median power was significantly lower among cases than controls. A large effect exists between cases and controls in all Alpha power electrodes (η^2 >0.14).

Table 6. Quantitative EEG features (Alpha power) among cases and controls

Alpha wave power	Cases	Control	P value	Effect size
	Median (IQR)	Median (IQR)		
FP1	5.2333 (7.96)	26.200 (22.43)	**<0.001***	0.341#
FP2	6.6500 (6.29)	26.6667 (26.48)	**<0.001***	0.360#
F7	3.4833 (5.49)	23.300 (24.99)	**<0.001***	0.325#
F3	3.4167 (6.23)	19.900 (26.45)	**<0.001***	0.267#
Fz	4.3667 (6.57)	25.2667 (25.46)	**<0.001***	0.311#
F4	3.9333 (7.40)	20.600 (24.86)	**<0.001***	0.279#
F8	3.6833 (4.87)	20.9667 (22.59)	**<0.001***	0.368#
C3	2.6333 (3.86)	17.500 (31.92)	**<0.001***	0.221#
C4	3.4333 (4.68)	15.700 (30.27)	**<0.001***	0.210#
T5	5.4333 (9.88)	39.300 (29.39)	**<0.001***	0.475#
P3	3.5333 (5.46)	22.8667 (25.51)	**<0.001***	0.294#
Pz	3.8000 (5.17)	26.5333 (30.47)	**<0.001***	0.236#
P4	3.9667 (5.62)	25.1333 (25.11)	**<0.001***	0.349#
T6	4.2000 (10.60)	45.0667 (29.06)	**<0.001***	0.426#
O1	5.7000 (10.45)	26.8000 (31.72)	**<0.001***	0.226#
O2	5.6000 (12.28)	28.500 (31.52)	**<0.001***	0.248#

*Mann Whitney test, Eta squared.

(Table .7). Shows a statistically significant difference in all Beta power electrodes (FP1, FP2, F7, F3, Fz, F8, F4, C3, C4, T5, P3, Pz, P4, T6, O1, and O2) among cases and controls, where the p-values were <0.001 for all of them, where the median power was significantly lower among cases than controls. A large effect exists between cases and controls in all Beta power electrodes (η^2 >0.14).

Table 7. Quantitative EEG features (Beta power) among cases and controls

Beta wave power	Cases	Control	P value	Effect size
	Median (IQR)	Median (IQR)		
FP1	1.6333 (3.20)	21.7000 (32.63)	**<0.001***	0.231
FP2	2.3000 (2.81)	22.3333 (30.09)	**<0.001***	0.242
F7	1.9666 (1.68)	19.7333 (31.12)	**<0.001***	0.223
F3	1.3667 (2.80)	19.7000 (31.11)	**<0.001***	0.198
Fz	1.4000 (3.53)	20.8333 (38.48)	**<0.001***	0.225
F4	2.1667 (2.13)	21.5333 (29.27)	**<0.001***	0.216
F8	1.6667 (2.17)	21.6667 (31.11)	**<0.001***	0.249
C3	1.3167 (4.03)	20.5667 (29.28)	**<0.001***	0.175
C4	1.6667 (2.54)	20.500 (28.67)	**<0.001***	0.181
T5	2.0500 (2.57)	18.9667 (24.67)	**<0.001***	0.240
P3	1.6333 (2.45)	19.6333 (29.42)	**<0.001***	0.165
Pz	1.6333 (3.27)	24.1333 (30.40)	**<0.001***	0.181
P4	1.5333 (3.10)	21.000 (28.09)	**<0.001***	0.189
T6	2.2667 (2.24)	20.2333 (28.85)	**<0.001***	0.246
O1	1.5667 (2.63)	22.1667 (28.84)	**<0.001***	0.155
O2	1.6333 (2.93)	24.4000 (29.48)	**<0.001***	0.171

*Mann Whitney test

(Table .8), (Fig.2) Reveals a statistically significant mild negative correlation between the MOCA scale and Delta power (FP2 and FP1), where the p-values = 0.020 and 0.049 and the r = -0.329 and -0.280, respectively. These results indicate that higher Delta power at these electrode sites is associated with lower cognitive performance as measured by the MOCA scale.

Table 8. Correlation between MOCA scale and quantitative EEG

Quantitative EEG findings		MOCA scale	
		r*	**P value**
Delta Power	FP2	-0.329	0.020
	FP1	-0.280	0.049

*Pearson Correlation coefficient

(Table .9), (Fig.3) Shows a statistically significant mild negative correlation between the SDMT scale and Delta power (FP2, FP1, and Fz), where the p-values = 0.021, 0.028, and 0.037 and the r = -0.325, -0.311, and -0.296, respectively. A statistically significant mild negative correlation exists between the SDMT scale and Theta power (FP2 and T6), with the p-values = 0.032 and 0.049 and r = -0.303 and -0.280, respectively. These findings suggest that higher Delta and Theta power at these electrode sites are associated with lower cognitive performance as measured by the SDMT scale.

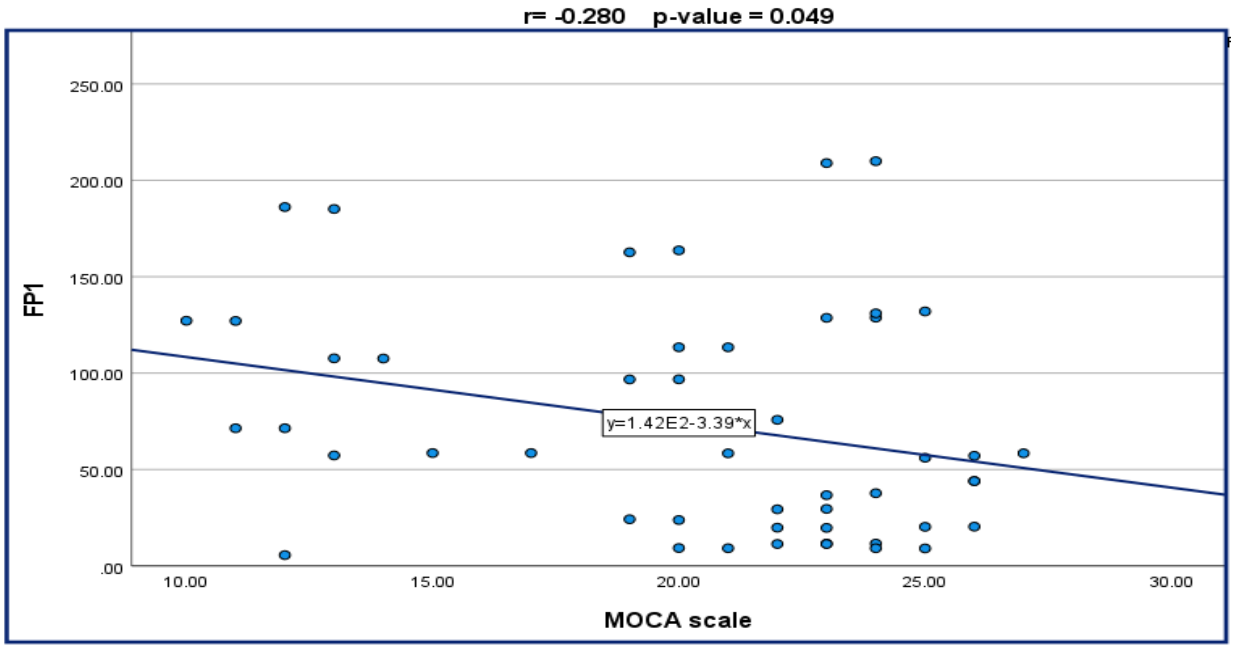

Fig.2. Correlation between MOCA scale and Delta Power (FP1)

Table 9. Correlation between SDMT scale and quantitative EEG

Quantitative EEG		SDMT scale	
		r*	P value
Delta Power	FP2	-0.325	0.021
	FP1	-0.311	0.028
	Fz	-0.296	0.037
Theta Power	FP2	-0.303	0.032
	T6	-0.280	0.049

*Pearson Correlation coefficient

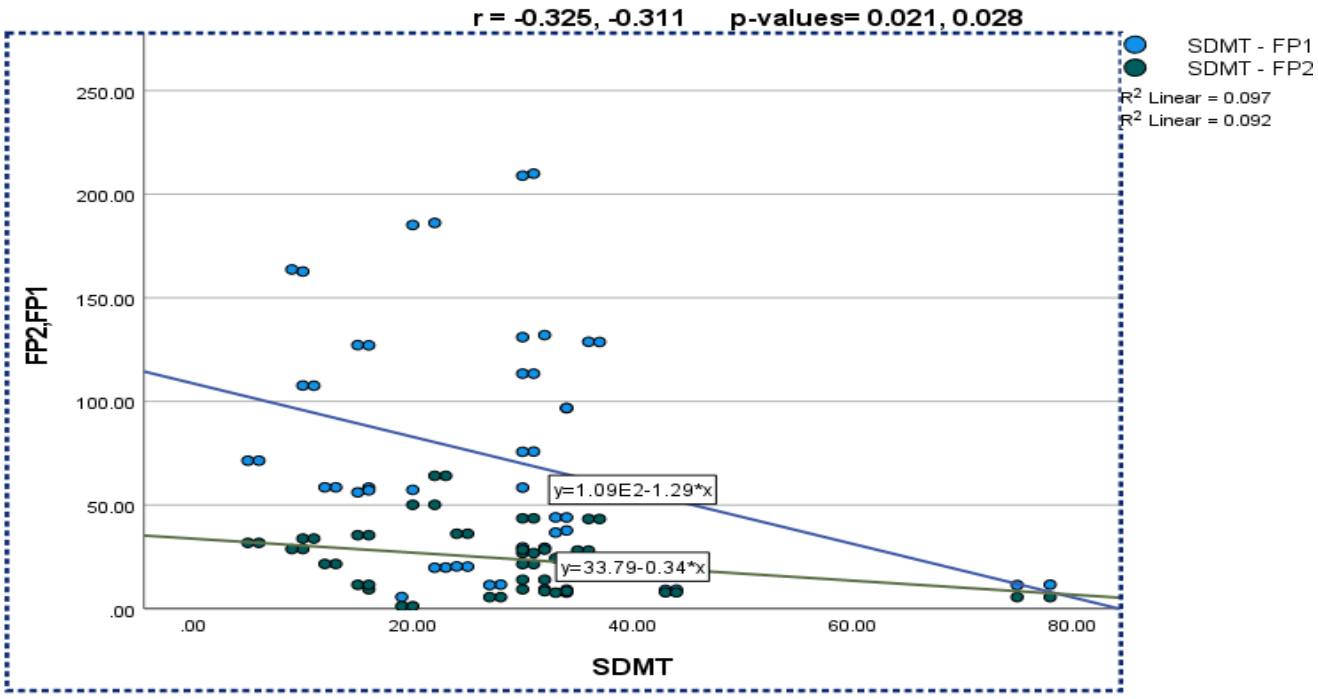

Fig.3. Correlation between SDMT scale and Delta power (FP2 and FP1)

(Table .10), (Fig.4) Shows a statistically significant mild positive correlation between the TMT-B scale and Delta power (Fz), with the p-value = 0.022 and r = 0.324. A statistically significant mild positive correlation exists between the TMT-B scale and Theta power (Fz), with the p-value = 0.032 and r = 0.304. These results indicate that higher Delta and Theta power at these electrode sites are associated with poorer performance on the TMT-B, which measures processing speed and executive function.

Table 10. Correlation between TMT-B scale and quantitative EEG

Quantitative EEG		TMT-B scale	
		r*	P value
Delta Power	**Fz**	0.324	0.022
Theta Power	**Fz**	0.304	0.032

*Pearson correlation coefficient

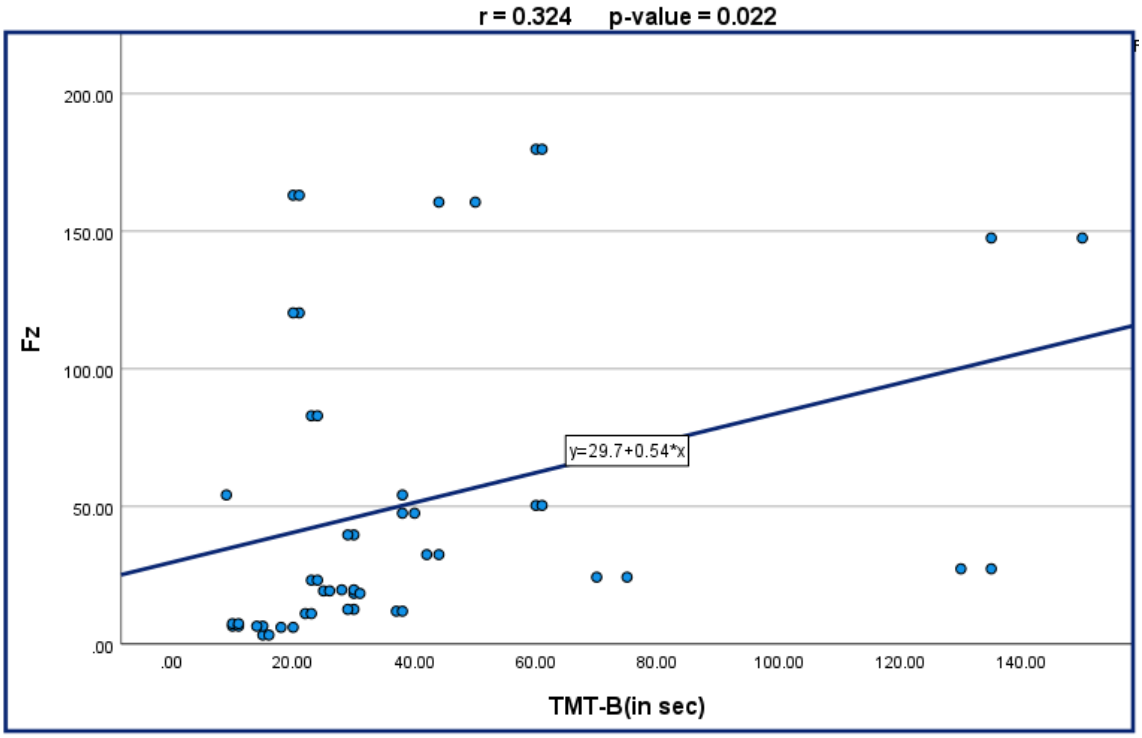

Fig.4. Correlation between TMT-B scale and Delta power (Fz)

Discussion

The current study explored the correlation between quantitative electroencephalography (QEEG) characteristics and cognitive function in individuals diagnosed with bipolar affective disorder (BAD). Our findings revealed significant differences in QEEG power spectra and cognitive assessment scores between BAD patients and healthy controls, suggesting that QEEG could serve as a biomarker for cognitive dysfunction in bipolar disorder.

Our study found that BAD patients scored significantly lower on the Montreal Cognitive Assessment (MoCA), Symbol Digits Modalities Test (SDMT), and had higher completion times on the Trail Making Tests (TMT-A and TMT-B) compared to healthy controls. These results indicate impairments in several cognitive domains, including executive function, processing speed, attention, and memory. In our study, QEEG analysis showed increased Delta and Theta power and decreased Alpha and Beta power in BAD patients compared to controls. These findings align with previous studies documenting similar alterations in EEG power spectra in psychiatric populations (**Kamarajan and Porjesz, 2015**).

Significant correlations were found between QEEG measures and cognitive

performance, highlighting the importance of specific cognitive domains. Higher Delta power was negatively correlated with MoCA scores, particularly in the frontal regions (FP1: r = -0.280, p = 0.049; FP2: r = -0.329, p = 0.020). The MoCA assesses executive functions, memory, language, and attention, indicating that increased Delta power in frontal areas is associated with deficits in these cognitive domains (**Duffy et al., 2019**). A significant negative correlation was also found between Delta power and SDMT scores (FP1: r = -0.311, p = 0.028; FP2: r = -0.325, p = 0.021), suggesting that higher Delta power is linked to slower processing speed and impaired attention (**Jeste et al., 2015**). Additionally, the positive correlation between Delta power and TMT-B scores (Fz: r = 0.324, p = 0.022) highlights that increased Delta activity is associated with poorer performance in tasks requiring cognitive flexibility and executive control (**Minzenberg et al., 2018**).

Elevated Theta power was negatively correlated with SDMT scores (FP2: r = -0.303, p = 0.032; T6: r = -0.280, p = 0.049), indicating that increased Theta activity is linked to slower processing speed and attention deficits (**Klimesch, 1999**). The positive correlation between Theta power and TMT-B scores (Fz: r = 0.304, p = 0.032) suggests that higher Theta power is associated with difficulties in tasks requiring cognitive flexibility and executive function. Decreased Alpha power in frontal and parietal regions (FP1, FP2, F7, F3, P3, Pz) was associated with cognitive impairments across various domains, including relaxation, attention, and cognitive performance (**Bazanova and Vernon, 2014**). Lower Alpha power is indicative of difficulties in maintaining cognitive control and attention. Significantly lower Beta power in the frontal and temporal regions (FP1, FP2, F7, F3, T5, T6) was associated with reduced alertness and cognitive engagement. This finding underscores the role of Beta activity in maintaining cognitive alertness and active engagement in cognitive tasks (**Engel and Fries, 2010**).

The significant correlations between QEEG features and cognitive performance suggest that specific EEG bands are linked to distinct cognitive deficits in BAD patients. Higher Delta and Theta power are associated with poorer executive function, processing speed, and attention, while decreased Alpha and Beta power indicate broader cognitive impairments. These findings highlight the potential of QEEG in clinical practice, offering a non-invasive and objective method for evaluating and monitoring cognitive deficits in patients with bipolar affective disorder, and guiding therapeutic strategies.

Our study found that BAD patients scored significantly lower on the Montreal Cognitive Assessment (MoCA), suggesting impairment within the fields of processing speed and executive function, and scored significantly lower on Symbol Digits Modality Test (SDMT), suggesting impairment in the domains of memory, attention, language, and executive function. They also had higher completion times on the Trail Making Tests (TMT-A and TMT-B), suggesting impairment in the domains of attention and motor speed compared to healthy controls. These results are consistent with previous research indicating cognitive impairments across various domains in individuals with bipolar disorder (**Yatham et al., 2018**; **Torres et al., 2020**).

In our study, QEEG analysis showed increased Delta and Theta power and decreased Alpha and Beta power in BAD patients compared to controls. These findings align with those of previous studies such as **Boutros et al. (2015)**, who documented similar alterations in EEG power spectra in psychiatric populations. Increased slow-wave activity (Delta and Theta) and decreased fast-wave activity (Alpha and Beta) are often associated with cognitive deficits and disrupted neural connectivity (**Başar et al., 2001**; **Harmony, 2013**).

While our findings suggest that QEEG abnormalities are associated with cognitive dysfunction in BAD, it is important to consider alternative explanations. One such explanation could be the influence of medication use in the BAD group. Many patients with BAD are on medications that can

affect both cognitive function and EEG patterns. For instance, mood stabilizers, antipsychotics, and other psychotropic medications can impact neural activity and cognitive processes, potentially confounding our results (**Cavanagh et al., 2002**; **Clark et al., 2006**). Future research should control for medication use or include it as a covariate in the analysis to better isolate the effects of BAD on cognitive function and QEEG measures.

The clinical implications of our study are substantial. By identifying QEEG patterns associated with cognitive impairments in BAD, clinicians can better diagnose and monitor cognitive dysfunction in these patients. QEEG offers a non-invasive, cost-effective method for assessing brain function, which can complement traditional neuropsychological tests (**Olbrich and Arns, 2013**). QEEG can be used to guide treatment decisions in several ways. For example, patients exhibiting higher Delta and Theta power, which are associated with poorer cognitive performance, might benefit from cognitive remediation therapy aimed at improving attention and executive function (**Surmeli et al., 2012**). Additionally, QEEG can be employed to monitor treatment efficacy, allowing for adjustments in therapeutic strategies based on real-time neural activity. This approach can enhance personalized care and improve patient outcomes (**Olbrich et al., 2015**).

Limitations and Future Directions: Several limitations of our study should be acknowledged. The use of convenience sampling from an outpatient clinic may introduce selection bias, as discussed earlier. Second, variability in EEG recordings due to factors such as medication use, wakefulness, and patient compliance can affect the reliability of QEEG measures (**Boutros et al., 2015**; **Prichep, 2007**). It is crucial to control for these variables in future studies to ensure accurate and consistent results. Additionally, a larger sample size is necessary, which was not possible with our small sample. Furthermore, interpreting QEEG data requires trained personnel, which may limit its widespread clinical application. The need for specialized training and expertise in QEEG analysis highlights the importance of developing standardized protocols and training programs for clinicians (**Olbrich & Arns, 2013**).

Our study opens several avenues for future research. Longitudinal studies are needed to assess the long-term impact of QEEG patterns on cognitive function in BAD patients, providing insights into the progression of cognitive impairments and the effectiveness of interventions. Controlling for medication use in future studies, either by including it as a covariate or studying medication-naive patients, will help better isolate the effects of BAD on cognitive function and QEEG measures. Investigating the impact of specific interventions, such as cognitive remediation therapy or neurofeedback, on QEEG measures and cognitive function is essential. Additionally, larger and more diverse sample sizes are necessary to confirm findings and ensure generalizability. Evaluating the potential of QEEG to predict cognitive decline in individuals at high risk for BAD could enable preemptive interventions. Developing standardized protocols for QEEG data collection and analysis will enhance reliability and validity. By addressing these areas, future studies can build on our findings to enhance the understanding and clinical utility of QEEG in diagnosing and managing cognitive dysfunction in BAD.

Conclusion

In conclusion, our study demonstrates significant QEEG abnormalities and cognitive impairments in patients with bipolar affective disorder (BAD). BAD patients showed increased Delta and Theta power and decreased Alpha and Beta power, particularly in the frontal and temporal regions. Higher Delta power correlated with deficits in executive functions, memory, language, and attention, while elevated Theta power was linked to slower processing speed and attention deficits. Decreased Alpha and Beta power were associated with broader cognitive impairments, including reduced alertness and cognitive engagement. These findings suggest

that QEEG can serve as a valuable biomarker for cognitive dysfunction in BAD, offering a non-invasive and objective method for evaluating and monitoring cognitive deficits. Identifying specific EEG markers associated with cognitive impairments can help clinicians better diagnose and monitor cognitive dysfunction, guiding personalized treatment strategies to improve patient outcomes.

References

- **Ahmed YA, Tatarczuch L, Pagel CN, Davies HM, Mirams M, Mackie EJ. (2007).** Physiological death of hypertrophic chondrocytes. Osteoarthritis and Cartilage, 15(5): 575-586.
- **American Psychiatric Association. (2013).** Diagnostic and statistical manual of mental disorders (5th ed.). Arlington VA: American Psychiatric Association, 55(3): 2020-2023.
- **Arts B, Jabben N, Krabbendam L, Van Os J. (2008).** Meta-analyses of cognitive functioning in euthymic bipolar patients and their first-degree relatives. Psychological Medicine, 38(6): 771-785.
- **Başar E, Başar-Eroglu C, Karakaş S, Schürmann M. (2001).** Gamma, alpha, delta, and theta oscillations govern cognitive processes. International Journal of Psychophysiology, 39(2-3): 241-248.
- **Bazanova OM, Vernon D. (2014).** Interpreting EEG alpha activity. Neuroscience & Biobehavioral Reviews, 44: 94-110.
- **Bora E, Pantelis C. (2015).** Meta-analysis of cognitive impairment in first-episode bipolar disorder: Comparison with first-episode schizophrenia and healthy controls. Schizophrenia Bulletin, 41(5): 1095-1104.
- **Bora E, Vahip S, Akdeniz F, Gonul AS, Eryavuz A. (2006).** Evidence for the relationship between cognitive deficits and sustained attention in euthymic patients with bipolar disorder: A controlled study using the continuous performance test. Psychiatry Research, 142(1): 21-29.
- **Bora E, Yucel M, Pantelis C. (2009a).** Cognitive endophenotypes of bipolar disorder: A meta-analysis of neuropsychological deficits in euthymic patients and their first-degree relatives. Journal of Affective Disorders, 113(1-2): 1-20.
- **Bora E, Yucel M, Pantelis C. (2009b).** Cognitive functioning in schizophrenia and bipolar disorder: A meta-analysis. Acta Psychiatrica Scandinavica, 119(2): 69-80.
- **Bora E, Pantelis C. (2024).** Impairment in social and neurocognitive domains in a sample of first-episode bipolar disorder (FEBD) in comparison to healthy controls. Journal of Affective Disorders, 280: 422-430.
- **Boutros NN, Arfken CL, Galderisi S, Warrick J, Pratt G, Iacono W. (2015).** The status of quantitative EEG (qEEG) in clinical psychiatry: An evidence-based review. Neuropsychopharmacology, 40(1): 197-219.
- **Cavanagh JT, Van Beck M, Muir W, Blackwood DH. (2002).** Case-control study of neurocognitive function in euthymic patients with bipolar disorder: An association with mania. British Journal of Psychiatry, 180(2): 177-182.
- **Clark L, Iversen SD, Goodwin GM. (2006).** Sustained attention deficit in bipolar disorder. British Journal of Psychiatry, 189(2): 118-121.
- **Coben R, Linden M, Myers TE. (2013).** Neurofeedback for autistic spectrum disorder: A review of the literature. Applied Psychophysiology and Biofeedback, 35(1): 83-105.
- **Cullen B, Ward J, Graham NA. (2016).** Prevalence and correlates of cognitive impairment in euthymic adults with bipolar disorder: A systematic review. Journal of Affective Disorders, 205: 165-181.
- **de la Salle S, Murphy K, McMullen M. (2019).** QEEG measures as biomarkers of treatment response in depression: A comprehensive review. European Neuropsychopharmacology, 29(10): 1217-1227.
- **Duffy FH, McAnulty GB, Albert MS. (2019).** Neurophysiology of aging and

cognitive disorders. Current Opinion in Neurobiology, 61: 57-65.

- **Engel AK, Fries P. (2010).** Beta-band oscillations—signalling the status quo? Current Opinion in Neurobiology, 20(2): 156-165.
- **First MB. (2015).** Structured Clinical Interview for the DSM (SCID). In The Encyclopedia of Clinical Psychology (eds R.L. Cautin and S.O. Lilienfeld): 1–6.
- **Harmony T. (2013).** The functional significance of delta oscillations in cognitive processing. Frontiers in Integrative Neuroscience, 7: 83.
- **Jeste DV, Twamley EW, Eyler LT, Palmer BW. (2015).** Cognitive deficits in bipolar disorder and schizophrenia. Journal of Clinical Psychiatry, 76(3): 408-417.
- **Kamarajan C, Porjesz B. (2015).** Advances in electrophysiological research. Current Opinion in Neurobiology, 30: 54-60.
- **Kirli KK, Polat H, Yalcin S, Yildirim E. (2022).** Electroencephalography as a biomarker in psychiatric disorders: Current standing and future prospects. Biomarkers in Neuropsychiatry, 6: 100045.
- **Klimesch W. (1999).** EEG alpha and theta oscillations reflect cognitive and memory performance: A review and analysis. Brain Research Reviews, 29(2-3): 169-195.
- **Llinàs-Reglà J, Vilalta-Franch J, López-Pousa S, Calvó-Perxas L, Torrents Rodas D, Garre-Olmo J. (2017).** The Trail Making Test: Association with other neuropsychological measures and normative values for adults aged 55 years and older from a Spanish-speaking population-based sample. Assessment, 24(2): 183-196.
- **Minzenberg MJ, Laird AR, Thelen S, Carter CS, Glahn DC. (2018).** Meta-analysis of 41 functional neuroimaging studies of executive function in schizophrenia. Archives of General Psychiatry, 66(8): 811-822.
- **Nasreddine ZS, Phillips NA, Bédirian V, Charbonneau S, Whitehead V, Collin I. (2005).** The Montreal Cognitive Assessment MoCA: a brief screening tool for mild cognitive impairment. Journal of the American Geriatrics Society, 53(4): 695-699.
- **Olbrich S, Arns M. (2013).** EEG biomarkers in major depressive disorder: Discriminative power and prediction of treatment response. International Review of Psychiatry, 25(5): 604-618.
- **Olbrich S, van Dinteren R, Arns M. (2015).** Personalized medicine: Review and perspectives of promising baseline EEG biomarkers in major depressive disorder and attention-deficit/hyperactivity disorder. Neuropsychobiology, 72(3-4): 229-240.
- **Prichep LS. (2007).** Quantitative EEG and electromagnetic brain imaging in aging and in the evolution of dementia. Annals of the New York Academy of Sciences, 1097(1): 156-167.
- **Rahman TTA, El Gaafary MM. (2009).** Montreal cognitive assessment Arabic version: Reliability and validity prevalence of mild cognitive impairment among elderly attending geriatric clubs in Cairo. Geriatrics & Gerontology International, 9(1): 54-61.
- **Rojas GM, Alvarez C, Montoya CE, de la Iglesia-Vayá M, Cisternas JE, Gálvez M. (2018).** Study of resting-state functional connectivity networks using EEG electrodes position as seed. Frontiers in Neuroscience, 12: 235.
- **Saletu B, Anderer P, Saletu-Zyhlarz GM. (2010).** EEG topography and tomography (LORETA) in the diagnosis and treatment of depressive disorders. Clinical EEG and Neuroscience, 41(4): 203-210.
- **Sheridan LK, Fitzgerald HE, Adams KM, Nigg JT, Martel MM, Puttler LI. (2006).** Normative Symbol Digit Modalities Test performance in a community-based sample. Archives of Clinical Neuropsychology, 21(1): 23-28.
- **Stanczak DE, Stanczak EM, Awadalla AW. (2001).** Development and initial validation of an Arabic version of the expanded trail making test: Implications

for cross-cultural assessment. Archives of Clinical Neuropsychology, 16(2): 141-149.

- **Surmeli T, Ertem A, Eralp E, Kos IH. (2012).** Schizophrenia and the efficacy of qEEG-guided neurofeedback treatment: A clinical case series. Clinical EEG and Neuroscience, 43(2): 133-144.
- **Thatcher RW, North D, Biver C. (2009).** EEG and intelligence: Relations between EEG coherence EEG phase delay and power. Clinical Neurophysiology, 120(7): 1241-1250.
- **Torres IJ, Kozicky JM, Popuri S. (2020).** Cognitive impairment in early-stage bipolar disorder: Evidence from the systematic treatment optimization program for early mania (STOP-EM). Journal of Affective Disorders, 266: 63-70.
- **Yatham LN, Kennedy SH, Parikh SV. (2018).** Canadian network for mood and anxiety treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) 2018 guidelines for the management of patients with bipolar disorder. Bipolar Disorders, 20(2): 97-170.