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Brain electrical activity in Newly diagnosed Generalized Anxiety Disorder: A Quantitative EEG analysis

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Abstract

Background: Generalized Anxiety Disorder (GAD) is one of the most common global mental disorders with negative impact on social life. Quantitative EEG can objectively estimate the anxiety status. Relatively increase beta activity along with decrease alpha activity is associated with GAD. **Objectives:** To evaluate power of all brain waves in female patients with GAD. **Methods:** This observational study was conducted on 20 female patients with GAD (age 20-40 years), For comparison, 20 healthy female volunteers of same age were enrolled as control. In this study, EEG was recorded for 3 minutes by placing electrodes on scalp according to 10-20 system. To assess brain electrical activities, the band power of delta, theta, alpha and beta brainwave was recorded from an EEG data acquisition device, EEG Traveler Brain Tech 32+ CMEEG -01, India. Power spectral analysis of EEG data was done by BT40 analysis software. Data were expressed as median (Inter Quartile Range). Statistical analysis was done by Mann-Whitney U test. **Results:** The significantly higher absolute power of beta was found in most of the

electrodes of prefrontal, frontal and temporal region as well as significantly lower power of alpha, theta and delta were found in all cortical regions in female GAD patients compared to healthy controls at baseline. **Conclusion:** This study concluded that GAD patients had high excitable state in most of cortical region associated with lack of relaxing ability.

Key words: EEG, GAD, brain waves, QEEG, anxiety, power spectral analysis

Introduction

Generalized Anxiety Disorder (GAD) is one of the most prevalent mental disorder around the world which affects patient's quality of life as well as disrupt daily activities.[1] According to American Psychiatric Association (APA), generalized anxiety disorders refer to chronic and severe anxiety with duration of at least 6 months which is beyond control. Diagnostic and Statistical Manual for Mental Disorder, 5th edition (DSM-V) describes it often associated with restlessness, lack of concentration, irritability, muscle tension, easily fatigued and sleep disturbance.[2] In every year GAD affects 6.8 million adults or 3.1% of the US population.[3] Women are twice affected than men. The peak age of GAD prevalence is in 3rd and 4th decade of life.[3] In Bangladesh National Mental Health Survey of Bangladesh, 2018-19 showed around 4.5% people are suffering from GAD.[4]

Conventionally the diagnosis and monitoring and treatment is relied on subjective assessment of symptoms of patients. But recent advancements of biotechnology facilitates, the identification of biomarkers that can be used for better understanding and its utilization for diagnostic accuracy and better monitoring and treatment. Recently quantitative EEG has been shown a promising tool to explore the status of brain activity specifically associated with different psychiatric illness.[5]

EEG is believed to reflect a variety of processes of the brain, especially the neocortex, in which our cognitive function and sensorimotor information are processed.[6] EEG data employed for diagnosis of neurological disorders are usually in qualitative nature. It can only identify the foci of abnormal brain activity at various location such as epilepsy.[7] But Power spectral analysis of EEG is widely used for quantitative analysis of brain wave in different clinics to estimate brain signal oscillations in regions of hemisphere to assess normal and abnormal cognitive process.[5,8]

Several previous studies suggested both too high beta and too low alpha in GAD patients estimating their anxious status by using quantitative EEG as a diagnostic tool for mental disorder.[9] Anxiety and alpha status of brain wave were significantly associated with each other and in anxiety state alpha power was extremely low.[10] While beta rhythms play an important role for clinical applications and differentiation of mental disorders. This wave is mostly associated with brain attentiveness and arousal state. Elevated beta power in GAD may suggest highest state of neuronal activity and hyperarousal state of brain. This significant value of beta power was observed in frontal, central, parietal and temporal region of brain.[8,11,12] Very little is known about power spectrum of EEG in GAD specially on lower frequency waves.

More details of involvement of each frequency band (delta, theta, alpha, beta) associated with cortical involvement in patients with GAD is required to comprehend the objective based

severity of GAD and monitoring the progress of therapy. For this purpose, the aim of this study was to evaluate the EEG power of all brain waves in GAD patients.

Methods

Study Design and setting:

This observational study was done in the year 2023 at the department of Physiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka to observe brain electrical activity in newly diagnosed GAD patients by assessing quantitative EEG.

Study participants

Twenty (20) newly diagnosed female GAD patients were enrolled from out-patient department (OPD) of Psychiatry, BSMMU. Age, sex, BMI and socio-economic status matched 20 apparently healthy subjects were selected as control. All the participants were free from medication that affect central nervous system. All of them were right-handed.

Sampling

Purposive sampling was adopted to select the patients as well as control subjects.

Exclusion criteria

All the participants were non-smoker, non-alcoholic. Women with pregnancy, lactational period, menstrual phase, hormonal contraceptive were also excluded. Participants were also non-diabetic, normotensive and no history of thyroid disorder.

Data collection

After taking history and informed written consent their demographic data of all participants were recorded. Thereafter, all of them were tested for handedness by Edinburgh Handedness Inventory (EHI) scale.[13,14] Then the detail procedure and preparation for EEG recording and the sessions were explained to them and requested to arrive at Noorzahan Begum Neurophysiology Lab in Department of Physiology, BSMMU, at 8-8:30 AM on a scheduled day for EEG recording. For the purpose of EEG recording, the subject was asked to finish their dinner by 9:00 pm and had a sound sleep in the previous night, so that they would not be fatigued or drowsy during the procedure. From previous night up to the time of test, they were requested to avoid consciously any physical or mental stress and avoid taking any sedatives or any other drugs that may affect central nervous system.[15] They were advised to wash their hair properly in the day before experiment to remove oiliness from the scalp with a mild non-fragrant shampoo and not to apply any sprays, antiperspirants or perfumes to their hair twelve hours prior to testing.[16] They were advised to have light breakfast in the morning without any caffeinated beverage such as tea, coffee or cola within 3 hours before the experiment.[17] They were also advised to dress up with clean clothes and they should not use any spray, perfumes or any cosmetics on their body. Upon their arrival subjects were provided with clean odorless gown to wear. Then they were allowed to sit in a cool and calm environment of lab for rest in a comfortable armchair for 10-15 minutes before actual EEG recording.

Laboratory setting

The laboratory environment was tightly controlled to minimize environmental influences on digital data recording device to ensure maximum possible error free quality data. The temperature of the laboratory was maintained at 23°C-25°C and lights were kept dim to ensure restriction of sunlight and noise from the surroundings.[16] Door lab was closed and no one was allowed to enter or leave the room during the test.

EEG Data recording

EEG 22 electrodes including the ground electrode were placed onto her scalp surface using conductive & adhesive EEG paste by international 10-20 system. EEG recording was done for total 3 minutes duration in eye closed condition for both groups.[18]

The recording of EEG measures was done by EEG (traveler) BrainTech32+ CMEEG-01(India) and analysis was done by the software Brain Tech 40+ Standard version 4.47a. A high pass filter was set at 1 Hz to reduce lower frequencies and a low pass filter was set at 35 Hz to ensure the signal is limited to the highest frequency of beta band.[19] The gain was set at 7.5 µv/mm. By default, Analog to digital (A/D) conversion was 24 bits, the notch filter was at 50 Hz, sampling rate was 1024 Hz (Clarity, India). Impedance was set at 5K Ohms.[20] Recorded EEG was displayed as brainwaves (analogue) in specific electrode on the window. Using Fast Fourier Transformation (FFT), this analogue signal was digitalized by default analogue to digital (A/D) converter. The software then generated frequency table with the power spectral parameter (absolute power) for each specific EEG frequency bands (delta, theta, alpha, and beta) which were recorded.

Statistical analysis

All data were checked for normal distribution by Shapiro Wilk test. Data were expressed as median (IQR). Statistical analysis was done using SPSS version 25. Data were found non normally distributed, non-parametric test Mann-Whitney-U test was done.

Results

In this study, similar general characteristics (Table I) of newly diagnosed female GAD and healthy control were observed. All the participants were right-handed.[13,14] The absolute power (μV^2) of each frequency band (delta, theta, alpha, beta) of EEG (GAD and control subjects) was recorded. Data were presented in table II, III, IV, V. Figure 1 showed topographical mapping of each frequency band. Our results showed significantly (p value<0.05) lower delta, theta, alpha power in most of the electrodes of all cortical regions compared to healthy control. But beta power was significantly higher in most of the electrodes in Prefrontal, frontal and temporal regions.

Table I : General characteristics of the subjects (N=40)

Parameters	GAD patients (n=20)	Healthy control (n=20)	P value
Age (years)	26.4 (12.25)	30.5 (4)	0.077
BMI (Kg/m2)	21.37 (8.25)	23.8 (9.25)	0.126
Pulse (mmHg)	79 (12.5)	76.5 (10)	0.667
SBP (mmHg)	118 (17.25)	120.5 (9.75)	0.267
DBP (mmHg)	82.5 (6.5)	74.5 (11.5)	0.061
SpO2(%)	97 (2)	97 (1)	0.302
Handedness(Score)	79 (6.5)	80 (8.75)	0.327

Data were expressed as median (IQR). Statistical analysis was done by Mann-Whitney U-Test. N-Total number of subjects; GAD- Generalized Anxiety Disorder; BMI- Body Mass Index; SBP- Systolic Blood Pressure; DBP- Diastolic Blood Pressure; SpO2- Saturation of peripheral Oxygen.

Table II : Absolute power (μV^2) of Delta wave in two groups at (N=40)

Cortical region	Electrode	GAD (n=20)	Control (n=20)	p value
Prefrontal	FP1	1.22 (2.89)	2.17 (0.53)	0.253
	FP2	1.49 (2.03)	2.15 (0.49)	0.072
	From above	1.44 (2.65)	2.16 (0.83)	0.028
Frontal	F7	0.76 (1.24)	1.71 (0.91)	0.007
	F3	0.65 (0.67)	0.91 (0.24)	0.054
	FZ	0.53 (0.48)	0.83 (0.32)	0.007
	F4	0.74 (0.47)	0.95 (0.62)	0.011
	F8	0.44 (0.84)	1.3 (1.44)	0.000
	CZ	0.34 (0.56)	0.77 (0.54)	0.006
	From above	0.62 (0.56)	0.98 (0.60)	0.000
Parietal	C3	0.32 (0.48)	0.59 (0.47)	0.007
	C4	0.34 (0.82)	0.67 (0.34)	0.108
	P3	0.62 (0.4)	0.98 (0.59)	0.000
	PZ	0.59 (0.76)	0.72 (0.23)	0.461
	P4	0.4 (3.39)	0.81 (0.44)	0.620
	From above	0.45 (0.68)	0.75 (0.42)	0.000
Temporal	T3	0.43 (0.32)	1.10 (0.52)	0.000
	T4	0.48 (0.65)	1.22 (0.98)	0.004
	T5	0.4 (0.75)	1.20 (1.10)	0.000
	T6	0.46 (0.52)	1.06 (0.51)	0.000
	From above	0.44 (0.57)	1.12 (0.78)	0.000
Occipital	O1	0.36 (1.31)	1.26 (0.61)	0.017
	O2	0.54 (0.67)	1.28 (0.59)	0.000
	From above	0.42 (0.77)	1.26 (0.58)	0.000

Data were expressed as median (IQR). Comparison of data between patient and control were done by Mann-Whitney U test. Here, N- Total number of subjects; n- Number of subjects in each group; GAD- Generalized Anxiety Disorder.

Table III: Absolute power (μV^2) of Theta wave in two groups at (N=40)

Cortical region	Electrode	GAD (n=20)	Control (n=20)	p value
Prefrontal	FP1	0.78 (0.78)	1.12 (0.42)	0.108
	FP2	0.85 (0.42)	1.02 (0.59)	0.165
		0.82 (0.67)	1.06 (0.44)	0.005
Frontal	F7	0.36 (0.26)	0.97 (0.40)	0.000
	F3	0.68 (0.79)	0.85 (1.05)	0.478
	FZ	0.61 (0.35)	0.88 (0.57)	0.076
	F4	0.68 (0.48)	0.82 (0.70)	0.096
	F8	0.45 (0.85)	0.95 (0.51)	0.018
	CZ	0.51 (1.24)	0.83 (1.04)	0.174
		0.52 (0.62)	0.88 (0.62)	0.000
Parietal	C3	0.47 (0.41)	0.83 (0.43)	0.013
	C4	0.37 (0.38)	0.68 (0.47)	0.023
	P3	0.65 (2.27)	0.93 (0.45)	0.183
	PZ	0.52 (0.78)	0.73 (0.42)	0.341
	P4	0.49 (0.85)	0.72 (0.50)	0.289
		0.48 (0.82)	0.77 (0.47)	0.000
Temporal	T3	0.42 (0.16)	0.91 (0.71)	0.000
	T4	0.56 (0.23)	0.89 (0.29)	0.002
	T5	0.51 (0.64)	0.92 (0.91)	0.003
	T6	0.75 (0.41)	0.86 (0.38)	0.165
		0.51 (0.44)	0.89 (0.30)	0.000
Occipital	O1	0.55 (0.53)	1.51 (1.16)	0.002
	O2	0.62 (0.79)	1.47 (1.13)	0.000
		0.55 (0.72)	1.51 (1.11)	0.000

Data were expressed as median (IQR). Comparison of data between patient and control were done by Mann-Whitney U test. Here, N- Total number of subjects; n- Number of subjects in each group; GAD- Generalized Anxiety Disorder.

Table IV : Absolute power (μV^2) of Alpha wave in two groups at (N=40)

Cortical region	Electrode	GAD (n=20)	Control (n=20)	p value
Prefrontal	FP1	0.79 (0.45)	3.13 (2.19)	0.000
	FP2	0.75 (0.44)	3.45 (2.16)	0.000
	From above	0.77 (0.46)	3.22 (2.09)	0.000
Frontal	F7	0.65 (0.94)	2.15 (1.33)	0.000
	F3	0.87 (0.55)	4.15 (3.4)	0.000
	FZ	0.6 (0.40)	4.46 (2.92)	0.000
	F4	0.65 (0.41)	3.76 (2.54)	0.000
	F8	0.82 (0.57)	2.58 (2.56)	0.000
	CZ	0.49 (1.24)	3.95 (3.07)	0.000
	From above	0.64 (0.54)	3.2 (3.03)	0.000
Parietal	C3	0.38 (0.39)	3.40 (3.22)	0.000
	C4	0.76 (1.34)	3.08 (2.58)	0.000
	P3	0.78 (0.52)	4.13 (1.66)	0.000
	PZ	0.84 (0.56)	4.66 (8.72)	0.000
	P4	0.84 (0.58)	7.90 (9.58)	0.000
	From above	0.76 (0.74)	3.92 (5.87)	0.000
Temporal	T3	0.51 (0.82)	2.12 (1.07)	0.000
	T4	0.65 (0.77)	2.44 (1.66)	0.000
	T5	0.83 (0.65)	5.75 (2.58)	0.000
	T6	0.76 (0.52)	5.67 (10.23)	0.000
	From above	0.73 (0.67)	2.85 (4.79)	0.000
Occipital	O1	1.46 (1.53)	10.56 (13.86)	0.000
	O2	1.23 (0.98)	7.41 (15.63)	0.000
	From above	1.40 (1.05)	10 (14.78)	0.000

Data were expressed as median (IQR). Comparison of data between patient and control were done by Mann-Whitney U test. Here, N- Total number of subjects; n- Number of subjects in each group; GAD- Generalized Anxiety Disorder.

Table V : Absolute power (μV^2) of Beta wave in two groups at (N=40)

Cortical region	Electrode	GAD (n=20)	Control (n=20)	p value
Prefrontal	FP1	1.78 (0.24)	1.01 (0.45)	0.000
	FP2	1.38 (2.37)	1 (1.01)	0.018
	From above	1.77 (1.80)	1.01 (0.74)	0.000
Frontal	F7	0.98 (0.74)	1.28 (1.01)	0.529
	F3	1.16 (0.84)	0.91 (0.24)	0.231
	FZ	1.24 (0.54)	0.78 (0.38)	0.005
	F4	1.12 (0.69)	0.95 (0.69)	0.327
	F8	1.6 (1.23)	0.81 (0.43)	0.000
	CZ	1.13 (0.62)	0.76 (0.52)	0.010
	From above	1.15 (0.72)	0.84 (0.43)	0.000
Parietal	C3	0.87 (1.52)	1.21 (1.02)	0.862
	C4	1.78 (1.8)	1.01 (0.94)	0.046
	P3	1.29 (0.54)	1.26 (0.51)	0.738
	PZ	1.01 (0.60)	0.99 (0.39)	0.820
	P4	1.55 (3.54)	1.33 (0.71)	0.046
	From above	1.33 (1.04)	1.20 (0.57)	0.106
Temporal	T3	1.7 (1.93)	1.64 (1.16)	0.947
	T4	2.24 (2.61)	1.21 (0.83)	0.030
	T5	1.96 (0.97)	1.58 (1.16)	0.002
	T6	1.86 (1.56)	1.23 (0.83)	0.007
	From above	1.91 (1.58)	1.44 (0.77)	0.000
Occipital	O1	2.26 (2.21)	1.89 (1.06)	0.044
	O2	1.62 (0.72)	1.88 (0.69)	0.698
	From above	1.87 (2.03)	1.87 (0.89)	0.197

Data were expressed as median (IQR). Comparison of data between patient and control were done by Mann-Whitney U test. Here, N- Total number of subjects; n- Number of subjects in each group; GAD- Generalized Anxiety Disorder.

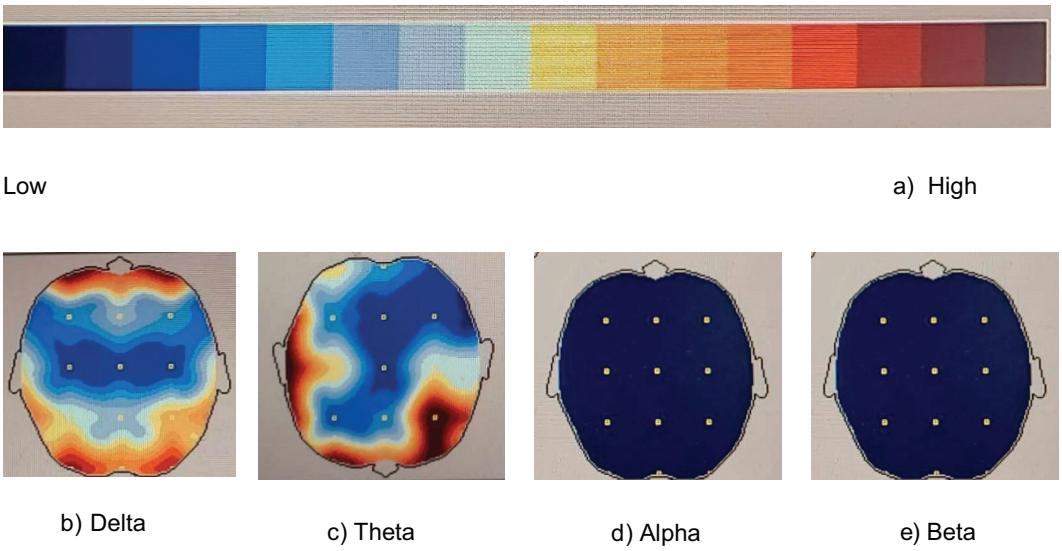

Figure 1: Topographical presentation of Absolute power (μV^2) in GAD group. a) a colour coded scale representing lower to higher absolute power value; b) delta; c) theta; d) alpha and e) beta wave

Discussion

In this study, all subjects were normotensive and their heart rate, oxygen saturation were within physiological limit.

The results of the current study depicted quantitative parameter (absolute power) of EEG in female patients with newly diagnosed GAD. This study showed lower alpha absolute power in almost all electrodes in all cortical regions and higher beta absolute power in GAD patients compared to healthy control in most of the electrodes in prefrontal, frontal and temporal regions. Similar to our result, Shen et al. found lower relative power of low frequency EEG wave (Theta and alpha1) in the frontal, temporal and central regions and higher relative power of high frequency EEG wave (alpha2 and beta) in frontal and temporal regions compared to healthy control.[21] Buchsbaum et al. found lower alpha and delta which was more marked in temporal region but similar beta in GAD patients compared to healthy control.[22] Remarkable proportion of beta frequency has also been reported in GAD.[12] Age related change of beta has also been reported in GAD patients. Older patients have been found with higher absolute power of beta compared to young patients. In our result, decrease alpha and delta was found in almost all region whereas increase beta in prefrontal, frontal and temporal regions. The pattern of these regional changes in our study suggests high alertness and increase vigilance and reduced sleepiness consistent with the psychological symptoms of GAD patients.[22]

Brain wave based behavioral physiology suggested that high power of alpha activity is correlated with concentration and memory. Low power of alpha is an indicator of high body tension and insomnia.[9] Moreover, cognitive performance is highly associated with alpha frequency. In particular, the decrease in alpha wave activity connects with reduced perception of calmness. Overall, the alpha waves are correlated with calmness, mental coordination, alertness, integration and learning condition of brain.[6,23]

Beta wave is mostly associated with brain attentiveness and arousal state. Elevated beta power may suggest highest state of neuronal

activity and indicator of severe anxiety and stress.[8,9,11,12]

Therefore in our GAD patients high beta and low alpha power is supporting their symptoms of restlessness, lack of concentration, highly excitable state of mind and lack of attention and relaxing capability.[1]

our study also revealed significantly lower absolute power of delta and theta in GAD patients compared to healthy control in almost all cortical regions of both hemispheres.

Visible dominance of Delta wave normally found in infants and sleeping adults and associated with very deep relaxation and refreshing of neurons.[24] Decreased delta wave leads to failure of the body as well as the brain to refresh and it also indicates inadequate sleep.[25]

Theta waves normally found in children than adults. These waves are also seen in emotional stress like frustration, during deep meditative state, drowsiness, daydreaming as well as creative thinking of subconscious mind. Theta wave is a marker of deep relaxation with low cortical excitation.[23,24] Decreased theta wave activity in most of the brain regions indicating absence of deep relaxed state.[24,26]

The results of delta and theta power in our study is related to the lack of relaxing ability and sleeplessness of GAD patients.

Conclusion

The results of the study conclude that high cortical excitability state was associated with GAD which was more marked in prefrontal frontal and temporal regions and GAD patients also lacks relaxing power and normal sleep state. Quantitative EEG can be used as a marker for anxious symptoms in GAD patients. Extent of regional involvement can predict severity of symptoms of GAD.

Ethical clearance

The ethical aspects of this study involving human subjects followed Helsinki (1964) ethical guideline and was first approved by departmental ethical and academic committee. It was then further reviewed and approved by Institutional Review Board (IRB) of BSMMU.

Conflict of interest There was no conflict of interest

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