Title: The Predictive Role of QEEG in Evaluation of Responsiveness of OCD Pa-Tients to Fluvoxamine

Authors: Mohammad Sayadnasiri[1], Mahta Moridian[1,*], Borzooyeh Naji[2]

1. *Department of Psychiatry, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran.*
2. *Institute for Cognitive Science Studies, Pardis, Tehran, Iran.*

***Corresponding Author**: Mahta Moridian, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran. Email: Mahta.Moridian@gmail.com

To appear in: **Basic and Clinical Neuroscience**

Received date: 2022/08/20

Revised date: 2023/07/24

Accepted date: 2023/09/04

Please cite this article as:

Sayadnasiri, M., Moridian, M., Naji, B. (In Press). The Predictive Role of QEEG in Evaluation of Responsiveness of OCD Pa-Tients to Fluvoxamine. Basic and Clinical Neuroscience. Just Accepted publication Jul. 10, 2023. Doi: http://dx.doi.org/10.32598/bcn.2023.4565.1

DOI: http://dx.doi.org/10.32598/bcn.2023.4565.1

Abstract

Introduction: It is not rare that an OCD patient does not response desirably to first chosen medication, and it may last up to one year to find the best treatment. According to the consequences of failed antidepressant therapy for OCD, any factor that can predict responsiveness, would be of high importance. We investigated potential predictive value of quantitative electroencephalography in the responsiveness of OCD patients to Fluvoxamine.

Methods: We included 40 medication free non-depressed OCD patients, assessed before intervention and six weeks after. Five minutes of opened eyes and closed eyes QEEG records were taken. The relative power of each frequency band was calculated for all electrodes. The patients received Fluvoxamine, 150-300 mg per day. We compared the waves between responders and non-responders, by univariate analyses and multivariate logistic regression.

Results: Responsiveness was correlated with normal relative powers in FP1, FP2, FZ and F3 and increased relative power in O1 in closed eyes condition and increased relative power of alpha in O1 and O2 and normal relative powers in FP1 and FP2 with open eyes. Unresponsiveness was correlated with increased theta in FP2, FZ and F3 and unincreased alpha in O1 with closed eyes and increased alpha in the O1 and O2 in opened eyes condition.

Conclusion: The electroencephalographic waves of medial-frontal area and occipital areas can be biomarkers to predict responsiveness to treatment with Fluvoxamine.

Keyword: Quantitative Electroencephalography, Obsessive-Compulsive Disorder, Responsiveness.

Introduction

Obsessive Compulsive Disorder is characterized by obsessive intrusive thoughts provoking fearful concerns and leading to rituals that seem to be protective. Although the content of obsessive symptoms may vary based on the cultural, ethnical and religious contexts, the whole frames have obvious similarities.[1] Lifelong prevalence of OCD has been estimated to be up to 2-3% in domestic studies.[2] A more recent study has presented the estimation of lifetime and annual prevalence equal as 2.3% and 1.2%, respectively.[3] Some investigators have calculated that around 10% of outpatients in psychiatric clinics are affected by OCD. Accordingly, OCD is the fourth most prevalent psychiatric disorder, after specific phobias, drug induced disorders and depressive disorders.[4]

Unfortunately, the data about costs about OCD are not updated recently. In 1995, DuPont et al, estimated the direct and indirect costs imposed by OCD, via human capital approach. The calculated total costs were 8.4 billion USD, equal to 5.7% of the estimated costs related to all of the mental disorders. The indirect costs that indicate the range of productivity that was lost by OCD patients, were estimated at $6.2 billion.[5] Recent studies stress on the huge amount of hidden costs imposed on payers, caused by un-effective treatment or misdiagnosis of OCD and due to care transition.[6]

For a comprehensive evaluation of burden imposed by OCD, we must remind the psychological pressure and financial costs imposed on their caregivers. It has been proven that although Obsessive Compulsive Disorder is less disabling than Depressive Disorders, their caregivers are more burdened and in need of higher levels of accommodation than the people who care of depressed patients.[7] Up to 75% of patients present the early symptoms before 25 and even in childhood, leading to huge disability-adjusted life years and imposed costs on families and health systems.[8]

According to highly variable features of this disorders, different therapeutic methods have been introduced so far, including psychological interventions (such as response prevention and mindfulness) and pharmacotherapy, or their combination.[9]

Based on the role of serotonergic system in the pathogenesis of OCD, selective serotonin reuptake inhibitors are among the most widely used drugs. Fluvoxamine is a member of this group that is chosen by many clinicians as the first choice in the treatment of OCD[10], and its efficacy has been approved by The United States Food and Drug Administration.[11]

Although usually the remission of symptoms, early after initiation of trial, is a promising signal for responsiveness, the outcomes of pharmaceutical interventions are routinely evaluated after 6 to 12 weeks.[12] The minimum time for the assessment of responsiveness to the first prescribed SSRI is 4 weeks, which would be expanded to 6 weeks for the evaluation of remission of symptoms.[13] Unfortunately, it is not rare that a patient does not response desirably to the first chosen medication[13], and in some cases it may last up to one year to achieve the best drug regimen,

as monotherapy or combination.[14-16] In addition to longer suffering that they experience, it has been estimated that about 26% of the patients who did not experience the ameliorative effects of firstly chosen drug, will refuse their treatment after two weeks[17], and this ratio increases up to 42% at 30th day.[18] According to the socioeconomical consequences of failed antidepressant therapy for OCD, any way that aids to predict responsiveness, would be of high clinical and financial importance.[19]

Digitalization of electroencephalography has made it possible to work on the correlation between characteristics of waves and other parameters, quantitatively. By Fourier Transform, any raw electroencephalographic data obtained of each point could be divided into categorized waves with specific frequency ranges, that each one has its own amplitude. Investigations to find any correlation between these detailed data and responsiveness to a specific treatment, or prognosis of a condition, is the topic of increasing number of studies on different psychiatric and neurologic disorders, such as, depression, drug dependency, psychosis, traumatic brain injuries, and disorders of consciousness. [20-25]

Considering all mentioned above, the investigators of this study decided to investigate potential predictive value of quantitative electroencephalographic features in the responsiveness of OCD patients to Fluvoxamine. There is no doubt that such a correlation, if proven, would be of high practical importance to design anticipatory models and individualized treatment plans, leading to diminished suffering of patients and burden on families and health systems.

Methods

This prospective study investigates the predictive power of electroencephalographic features in responsiveness of obsessive-compulsive disorder patients to fluvoxamine. We included 40 cases from Nezam Mafi University Clinic, University of Social Welfare and Rehabilitation Sciences, Tehran. Number of samples was calculated by 95% confidence and 80% of statistical power, based on the equation mentioned in the box no.1. All of the cases were visited by a board-certified psychiatrist and received diagnosis of OCD according to DSM-V, for the first time. All of them were medication free until the time of participation in our study. They were informed about the methods and purposes of the study, their right to quit at any time, and signed the consent form.

$$n = \frac{[Z^2_{(1-\frac{\alpha}{2})}.2P(1-P) + Z^2_{1-\beta}.P_A(1-P_A) + P_B(1-P_B)]}{\Delta^2}$$

$$\Delta = P_A - P_B \quad , \quad P = \frac{P_A + P_B}{2}$$

We applied Yale-Brown Obsessive-Compulsive Scale, Persian edition, for the assessment of severity of symptoms and responsiveness to treatment, at the beginning of study, and six weeks

after the initiation of treatment. This instrument which is scored by a clinician, includes 10 scales in likert system (from 0 to 4 aligned with the severity), ranging between 0 to 40 overall score. According to this scale, scores of 0 to 7, 8 to 15, 16 to 23, 24 to 31 and more than 31 indicate subclinical, mild, moderate, severe and very severe cases, respectively. Validity and reliability of this scale and its Persian version are proven to be desirable.[26, 27] We did not consider any minimum score of YBOCS for inclusion in the study, because we made our diagnosis clinically and the differences between pre and post treatment scores would be the data of comparison.

Quantitative electroencephalographies were obtained when patients had not used any medication with psychotropic effects for at least 72 hours, through the algorithms provided by American Clinical Neurophysiology Society and Pharmaco-EEG Guidelines.[28] The records were conducted by Nihon Konden EEG, Neurofac 1200 J/K, under direct observation of a neurologist. The electrodes were installed based on 10/20 montage system on O_2, O_1, T_5, T_6, P_3, P_4, P_2, T_4, T_3, C_3, C_4, C_2, F_8, F_7, F_4, F_3, F_2, F_{P2}, F_{P1} points in addition to reference and ground electrodes on auricles, and the impedances of each electrodes were checked and rechecked by an expert technician to not to be more than 10 KOhms. The Sensitivity was tuned on 7μV/mm, and low and high frequency filters (1 and 70 Htz) were activated. Notch filter (60 Htz) were also used if indicated. The recordings were performed between 9AM and 1PM, to diminish the effects of daily rhythms and feeding on the waves, in a semi-sitting position and awake, in a silent slightly enlighted room, kept away from hindering environmental stimuli. The obtained data were analyzed by Neuroguide software 2.3.8, that uses Fast Fourier Transform (FFT) for the assessment of waves. The primary Resting EEG with closed eye for 5 to 15 minutes was used to evaluate the electrode placements and potential artifacts, and abnormal cases including epileptical paroxysm and abnormal alpha waves were considered as exclusion criteria. Then the main records containing 5 minutes with opened eyes and 5 minutes with closed eyes were taken, for the principle analyses. The relative powers of each frequency range (alpha, beta, high beta, theta and delta) were calculated for all of the 19 electrodes. The frequencies were analyzed by the software of *NeuroGuide™ – Applied Neuroscience, Inc*.

After recording the electroencephalographs, the patients began to take Fluvoxamine, 150 to 300 mg per day, per os. Six weeks after treatment, provided that at least two weeks are passed since reaching the maximum dosage (based on clinical symptoms or therapeutic window), the patients were reinvestigated by Y-BOCS. In the analytic phase, the pre-intervention electroencephalographic waves were compared between responders and non-responders. Responders were defined as the reduction in the severity of symptoms by 50 percent or more. Also, age, gender and educational level were considered as potential confounding factors.

During medication period, the patients were assessed for any adverse effect at the end of the 1st, 2nd, 4th and 6th weeks.

Definition of Terms

Responder: The patients who experienced at least 50% reduction in the symptoms, based on the scores of YBOCS were considered as responders.

EEG frequency bands: The electroencephalic waves are categorized based on their frequencies: 1-3 Htz, 4-7 Htz, 8-12Htz and 13-25 Htz as Alpha, Theta, Alpha and Beta bands, respectively.

Z score: is defined as the difference between the scores of the examinee and normal population, described as standard deviation. In other words, Z score indicates that how much the patient's score is deviated from normal population.

Multivariate analysis: is the method of considering some electrodes that are next to each other as the indicator of electroencephalographic activity of that certain locus. These areas include: Left lateral by F_7, T_3 and T_5, Left medial by Fp_1, F_3, C_3, P_3 and O_1, Left anterior by Fp_1, F_7 and F_3, Left central by T_3 and C_3, Left posterior by T_5, P_3 and O1, Midline by Fz, Cz and Pz, Right lateral by F_8, T_4 and T_6, Right medial by Fp_2, F_4, C_4, P_4 and O_2, Right anterior by Fp_2, F_8 and F_4, Right central by T_4 and C_4, and Right posterior : T_6, P_4 and O_2. In multivariate analysis Z score is indicator of deviation from means among normal population.

Inclusion Criteria:

- Age between 18 and 65
- Diagnosis of obsessive-compulsive disorder based on DSM-V
- Volunteer attendance in the study

Exclusion Criteria:

- Severe somatic disorders (such as organ failures and endocrinological disorders)
- Neurological disorders (such as history of traumatic brain injury, epilepsy, cerebrovascular attacks, multiple sclerosis, and other degenerative disorders which may mimic obsessive symptoms.)
- Simultaneous suffering of Major Depressive Disorder, or psychotic features of any reason
- Usage of other psychotropic medications such as anti-convultants.
- Regular consumption of alcoholic drinks (more than 2-3 and 3-4 units/day in women and men, respectively)
- Regular smoking, more than 5 cigarettes per day or equal amount of other tobacco products
- Regular consumption of psychostimulants or opioids, at least 3 times a week
- Heavy drinking of caffeine drinks, more than 4 cups per day
- Patients with α- rhythm higher or lower than normal limits

Statistical Analyses:

To investigate the probable correlations, we firstly used univariate analyses including Pearson correlation and Chi square tests. Finally, multivariate logistic regression was performed for the

assessment of potential confounding factors. P-values less than 0.05 was considered as significant. All of these calculations were conducted by 22nd edition of Statistical Package for the Social Sciences (SPSS) software.

Results

Our study included 28 samples including 14 males and 14 females, with mean age of 34.9 ± 17.5. The mean duration of symptoms was 46.6 ± 11.6, with a wide range from 3 to 31 years. Six patients equal to 21.4% of cases had been educated to high school diploma, and 18 patients or 64.3% of samples had university degrees. The dosage of fluvoxamine prescribed for patients is mentioned in the table no. 1.

According to the definition of responsiveness to the treatment described above, table no.2 shows the rate of responsiveness based on different variables. The P values about different variables indicated that none of these confounding factors had led to significant difference.

Table no. 3 shows the correlations between different bands of electroencephalographic waves and responsiveness to fluvoxamine regimen. The details of the significant correlations between waves and loci including Fp1, Fp2, F2, F3, O1 and O2 are summarized in Table no.4 sorted by the p value, increasingly.

During the study, none of the cases experienced any serious adverse effect leading to interruption of pharmacotherapy.

Discussion

The results of our study showed that in closed eyes condition pre-intervention normal relative power of waves in FP1, FP2, FZ and F3 and increased Relative power of waves recorded from O1 are correlated with responsiveness to Fluvoxamine while increased theta wave in electrodes FP2, FZ and F3 and unincreased alpha waves from electrode O1 are correlated with unresponsiveness. In the electroencephalographic records obtained with opened eyes, increased relative power of alpha wave in electrodes O1 and O2 and normal relative power of waves in FP1 and FP2 where correlated with desirable responsiveness while increased alpha waves in the electrodes O1 and O2 were related with unresponsiveness to Fluvoxamine. Accordingly, the electroencephalographic waves recorded from medial-frontal area (specially left side) and occipital areas (specially left) can be utilized as biomarkers to predict responsiveness of OCD patients to treatment with Fluvoxamine.

Previous studies have shown that not only the antidepressant agents may alter the EEG waves, but also pre-interventional waves may also have predictive power about responsiveness to this medications and other therapeutic alternatives. Chronologically sorted, one the earliest outstanding studies working on the correlation between brain waves and OCD subtypes has been conducted by Prichep in 1993.[29] Among 27 patients with the diagnose of OCD following 12 weeks of treatment

with Fluvoxamine, Fluoxetine or Clomipramine, 16 patients expressed desirable outcomes. The responsiveness was correlated with higher relative power of alpha wave while non-responders showed higher theta waves, especially in temporal and frontal areas. Our results are compatible with findings of this study although more accurate localization and detection of an asymmetry of ways are two points of priority in our study.[30]

The next study was conducted by Cook in 1999. In this study 24 adult patients affected by major depressive disorder where categorized into concordant and discordant groups based on the assessment of QEEG cordance, a meassure for cerebral energy utilization. Although the both groups were clinically and historically similar before intervention, the concordant group experienced faster reduction in symptoms. The authors concluded that QEEG cordance can distinguish between depressed adults about responsiveness to Fluoxetine.[31] Cook and coauthors have reported their further studies on prefrontal activity measured by QEEG cordance and its early changes as predictor factor to distinguish between responders and non-responders to antidepressant agents such as Fluoxetine and Venlafaxine and in SSRIs non-responders going to initiate a new treatment by prescription of their psychiatrists. Compatible with the studies mentioned above, also prefrontal of cordance has been correlated with responsiveness to treatment.[32-34]

Tot reported the results of their study on 22 unmedicated OCD patients and showed that they have higher frequencies of slow wave bands and a lower frequency of alpha wave at frontotemporal region, in comparison with control group. They also found a significant correlation between increased slow wave and decreased beta activity at left frontal area during hyperventilation, in responders to SSRI agents and concluded that frontal lobe function had been better in this group, in comparison with non- responders.[35]

Another similar study has been conducted by Hansen in 2003 that shows that non-responsiveness to treatment with SSRI agent is related with excessive power of theta wave in frontal area while the responders show higher relative power of alpha wave in the same region. The pattern of change of brain waves and increased alpha is compatible with the results of our study but the anterior location of this change was not.[36]

Some other studies at this age have recorded similar changes in the electroencephalographic waves of OCD patients. Karadag et al and in 2003 has reported that the relative power of theta wave and power of alpha wave are significantly higher and lower in OCD patients, respectively in frontotemporal sites.[37]

Bucci and her team has also reported decreased power of alpha band and its negative correlation with time needed to complete neuropsychological tests about executive functions. They have suggested that hyperactivity of frontal networks in pathogenesis of OCD.[38]

At the same period of time some investigators have focused on such a correlation between responsiveness and electroencephalographic features in depressive disorder. In 2000, Knott and his team studied the brain waves in male patients affected by major depressive disorder before

being treated with Paroxetine for 6 weeks. The results of their study showed that pre-intervention lower power and frequency of beta waves in frontal area is correlated with better responsiveness to this medication. As increased beta wave indicates behavioral/affective activation, they concluded that hypoactivity of frontal cortex before treatment is predictive of more desirable outcome of treatment with SSRIs.[39]

In another study conducted in 2001, Bruder et al worked on the power of alpha waves in depressed patients, considering the negative correlation between its power and cortical activation and previous evidences about asymmetry of alpha wave in depression. Their sample included 34 depressed patients who responded to pharmacotherapy with Fluoxetine and 19 non- responder cases. Their study showed that although there was not a significant difference between overall alpha wave between two groups of responders and non-responders, they were different significantly about the alpha asymmetry, that was more prominent in eyes opened condition. According to the results, the responders showed more activation (lower alpha power) in their left hemisphere, in comparison with right side, while non-responders showed lower alpha waves in right hemisphere and less asymmetry. [40]

Later in 2008, Bruder has reported that higher alpha wave in occipital area in and alpha wave asymmetry are correlated with better responsiveness to Fluoxetine medication. In this study, after 12 weeks of treatment, the power and asymmetry of alpha wave did not alter. Hence, the investigators concluded that these differences are probably a family of trait indicating the subgroup of depressed patients, rather than a state dependent condition.[41]

In 2008, Bares and his team reported that in their sample that consisted of 12 responders and 13 non-responders depressed patients, decreased theta band QEEG cordance in frontal area after one week, is significantly related with responsiveness to 4 weeks of treatment with Venlafaxine.[42]

At the same year, Iosifescu et al investigated the changes in suicidal ideation during treatment with SSRIs and frontal electroencephalographic waves in depressed cases. They reported that worsening of suicidal ideation that had occurred in 11 percent of sample equal to 9 of 82 patients, was correlated with asymmetry of combined theta and alpha power in that region.[43]

The study conducted by Hunter and his team in 2010 on 72 major depressive patients showed that antidepressant treatment emergent suicidal ideation that happened in 13.5 percent of cases was correlated with a large temporary decrease of QEEG cordance in midline and right frontal area, 48 hours after initiation of treatment with Fluoxetine and Venlafaxine. [44]

Another study conducted by Hunter et all 2010 has categorized patients affected by major depressive disorder in 3 groups based on the pattern of changes of their symptoms along the time. In the intervention group of 94 cases that received Venlafaxine 62% were responder, 20% were non- responder and 17% were symptomatically volatile experiencing a fluctuating course of symptoms. They have investigated QEEG cordance, before intervention and after one week, and have shown that responsiveness to the treatment is correlated with higher degrees of decrease in

QEEG cordance in midline and right frontal area, in comparison with non- responders, but not volatile cases.[45]

The next study that is available in the literature is conducted by Ischedeck et al, based on the assumption of correlation between risk of anxiety and depressive disorder and electroencephalographic alpha wave. The investigators have assessed the power of lower alpha band (8 to 10 Hertz) in 20 patients affected by OCD comparison between 20 healthy control cases. The novelty of this study is recording the electroencephalographic waves during presentation of neutral, aversive and OCD related images. The reported asymmetry of lower alpha power in favour of left side in all of three conditions, did not exist in parietal areas as well as about higher alpha wave and theta and beta frequencies. They have concluded that their findings were supporting increased avoidance motivation in this disorder.[46]

Bares and his team have studied the predictive power of electroencephalographic features in 103 depressed cases who underwent treatment by SSRIs and SNRIs, 57 and 46 patients respectively. The parameters that they have investigated included alpha1, alpha2, theta power along with prefrontal theta cordance, frontal and occipital alpha1 and alpha 2 asymmetry, at pre-interventional stage and after 1 week. The only parameters that were found to be correlated with responsiveness to these groups of antidepressants were decreased prefrontal theta cordance and increased occipital alpha1 and alpha 2 asymmetry at first week, positively and negatively respectively. There was not any significant difference between the cases at baseline investigations, and the type of received medications did not alter these correlations too.[47]

The electroencephalographic features have not only been used to predict responsiveness to pharmacotherapy, but also some studies like what has been done by Metin et al in 2020 has assessed its correlation with responsiveness transcranial magnetic stimulation in OCD disorder. They have concluded that QEEG can be used as a determining factor in choosing the best treatment strategy approaching OCD patients.[48]

The higher alpha waves in occipital areas found in our study has been reported in some previous investigations such as Bruder's in 2008.[43] Our study has also showed that in closed eyes condition, existence of asymmetry between hemispheres and lower alpha in right occipital region is correlated with responsiveness to Fluvoxamine. Bruder has also reported such correlation in 2001[44], while Bares mentioned opposite findings in 2019[50], but both in depressed cases. The correlation between higher anterior theta and unresponsiveness has also been reported by Prichep and Hansen, as well as our study. [30, 36]

Conclusion

Conclusively, and considering all mentioned above, the results of our study, supported by previous literature, has shown that QEEG features especially occipital Alpha waves, and theta waves in frontal areas have desirable potency to be utilized as predictive biomarker about responsiveness of OCD patients to Fluvoxamine. Indeed integration of accessible biomarkers such as

electroencephalographic and neuroimaging data can lead to personalized treatment planning to patients; studies like ours are the pieces of the puzzle of algorithm that can make the railroad of choosing the best therapeutic alternative, hopefully minimizing the needed time to experience the ameliorative effect and maximizing effectiveness of therapy.

Limitations

There is no doubt that larger sample size could improve the significance of outcomes. Similar investigations on other routinely used medications and even comparisons between their efficacies may be of high practicality, that were far beyond of our study. Further studies with larger samples, and about different therapeutic alternatives, including medications and neuromodulation methods are suggested.

Conflict of interest

There is not any conflict of interest to declare. This project has been conducted by funding from university of social welfare and rehabilitation sciences.

Acknowledgment

Deep gratitude from authors to the staff psychiatry clinic and electroencephalography unit of Nezam Mafi University Hospital, for their kind cooperation and coordination.

References

1- Rajabi GhR. Validating of the Padua obsessive-compulsion inventory in freshman students of Shahid Chamran University of Ahvaz. The Quarterly Journal of Fundamentals of Mental Health 2007; 8(33): 43-52.
2- Salehi M, Salarifar M, Hadian M. The frequency pattern of compulsive disorder -OCD. Journal of New Cognitive Science 2003; 6 (2): 87-94.
3- (Mol Psychiatry. 2010 Jan; 15(1): 53–63. The Epidemiology of Obsessive-Compulsive Disorder in the National Comorbidity Survey Replication. A. M. Ruscio,1 D. J. Stein,2 W. T. Chiu,3 and R. C. Kessler3)
4- Kaplan, H. I. &Sadock, B. J. Synopsis of Psychiatry behavioral medicine, clinical psychiatry. 2003. (pp. 616-621).
5- Med Interface. 1995 Apr;8(4):102-9. Economic costs of obsessive-compulsive disorder R L DuPont 1 , D P Rice, S Shiraki, C R Rowland
6- https://www.businesswire.com/news/home/20210603005734/en/%E2%80%98Hidden%E2%80%99-OCD-Population-Costing-Payers-Employers-Billions-Annually
7- Psychosocial impact of obsessive-compulsive disorder on patients and their caregivers: a comparative study with depressive disorder. Ashis Vikas 1 , Ajit Avasthi, Pratap Sharan Psychiatry Clin Neurosci. 2012 Aug;66(5):432-41.
8- Sadock Bj, Sadock VA. Kaplan and Sadock's Comprehensive Textbook of Psychiatry. ninth ed. Lippincott Willliams and Wikins: Wolters Kluwer; 2009.
9- Sadock BJ, Kaplan HI, Sadock VA. Kaplan and Sadock's synopsis of psychiatry. 10th ed. Philadelphia:Lippincott Williams & Wilkins; 2007.
10- Fu CH, Steiner H, Costafreda SG. Predictive neural biomarkers of clinicalresponse in depression: a meta-analysis of functional and structuralneuroimaging studies of pharmacological and psychological therapies.Neurobiol Dis. 2013;52:75-83.
11- https://www.accessdata.fda.gov/drugsatfda_docs/label/2008/022235lbl.pdf
12- Fu CH, Steiner H, Costafreda SG. Predictive neural biomarkers of clinicalresponse in depression: a meta-analysis of functional and structuralneuroimaging studies of pharmacological and psychological therapies.Neurobiol Dis. 2013;52:75-83.
13- Trivedi MH, Fava M, Wisniewski SR, et al. Medication augmentationafter the failure of SSRIs for depression. N Engl J Med. 2006;354:1243-1252.
14- Rush AJ, Warden D, Wisniewski SR, et al. STAR*D: revising conventionalwisdom. CNS Drugs. 2009;23:627-647.
15- Rush AJ. Limitations in efficacy of antidepressant monotherapy. J ClinPsychiatry. 2007;68:8-10.
16- Keitner GI, Ryan CE, Miller IW, Norman WH. Recovery and major depression:factors associated with twelve-month outcome. Am J Psychiatry.1992;149:93-99.
17- Warden D, Trivedi MH, Wisniewski SR, et al. Predictors of attrition during initial (citalopram) treatment for depression: a STAR*D report. AmJ Psychiatry. 2007;164:1189-1197.
18- Olfson M, Marcus SC, Tedeschi M, Wan GJ. Continuity of antidepressanttreatment for adults with depression in the United States. Am J Psychiatry.2006;163:101-108.
19- Eduard Maron, David Nutt. Biological predictors of pharmacological therapies in anxiety disorders. Dialogues ClinNeurosci. 2015 Sep; 17(3): 305–317
20- J Affect Disord ٢٠١١ .Jan;128(1-2):41-8. An investigation of EEG, genetic and cognitive markers of treatment response to antidepressant medication in patients with major depressive disorder: a pilot study D Spronk 1 , M Arns, K J Barnett, N J Cooper, E Gordon
21- Am J Psychiatry ٢٠١٩ .Jan 1;176(1):44-56 .Electroencephalographic Biomarkers for Treatment Response Prediction in Major Depressive Illness: A Meta-Analysis. Alik S Widge 1 , M Taha

Bilge 1 , Rebecca Montana 1 , Weilynn Chang 1 , Carolyn I Rodriguez 1 , Thilo Deckersbach 1 , Linda L Carpenter 1 , Ned H Kalin 1 , Charles B Nemeroff 1

22- J Neuropsychiatry Clin Neurosci .Spring 2006;18(2):208-16.Variation in neurophysiological function and evidence of quantitative electroencephalogram discordance: predicting cocaine-dependent treatment attrition Sandy Venneman 1 , Andrew Leuchter, George Bartzokis, Mace Beckson, Sara L Simon, Melodie Schaefer, Richard Rawson, Tom Newton, Ian A Cook, Sebastian Uijtdehaage, Walter Ling

23- Schizophr Res ۲۰۱۴ .Mar;153(1-3):42-7.Can quantitative EEG measures predict clinical outcome in subjects at Clinical High Risk for psychosis? A prospective multicenter study Mirjam J van Tricht 1 , Stephan Ruhrmann 2 , Martijn Arns 3 , Ralf Müller 2 , Mitja Bodatsch 2 , Eva Velthorst 4 , Johannes H T M Koelman 5 , Lo J Bour 5 , Katharina Zurek 2 , Frauke Schultze-Lutter 6 , Joachim Klosterkötter 2 , Don H Linszen 4 , Lieuwe de Haan 4 , Anke Brockhaus-Dumke 7 , Dorien H Nieman 4

24- Clin EEG Neurosci ۲۰۱۸ .Jul;49(4):248-257.Quantitative EEG Parameters for Prediction of Outcome in Severe Traumatic Brain Injury: Development Study.Antti Tolonen 1 , Mika O K Särkelä 2 , Riikka S K Takala 3 4 , Ari Katila 3 4 , Janek Frantzén 4 , Jussi P Posti 3 4 , Markus Müller 4 , Mark van Gils 1 , Olli Tenovuo 3 4

25- Brain Topogr ۲۰۱۸ . Sep;31(5):848-862. Consciousness Indexing and Outcome Prediction with Resting-State EEG in Severe Disorders of Consciousness Sabina Stefan 1 , Barbara Schorr 2 3 , Alex Lopez-Rolon 4 , Iris-Tatjana Kolassa 3 , Jonathan P Shock 5 , Martin Rosenfelder 2 3 , Suzette Heck 4 , Andreas Bender 2 4

26- Rajezi Esfahani S, Motaghipour Y, Kamkari K, Zahiredin A, Janbozorgi M. Reliability and Validity of the Persian Version of the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS). IJPCP. 2012; 17 (4) :297-303

27- Rabiee M, Khorramdel K, Kalantari M, Molavi H. Factor Structure, Validity and Reliability of the Modified Yale-Brown Obsessive Compulsive Scale for Body Dysmorphic Disorder in Students. IJPCP. 2010; 15 (4) :343-350

28- Sinha SR, Sullivan L, Sabau D, San-Juan D, Dombrowski KE, Halford JJ, Hani AJ, Drislane FW, SteckerMM. American Clinical Neurophysiology Society Guideline 1: Minimum Technical Requirements for Performing Clinical Electroencephalography. JClinNeurophysiol. 2016 Aug; 33(4):303-7.

29- Psychiatry Res ۱۹۹۳ .Apr;50(1):25-32.doi: 10.1016/0925-4927(93)90021-9.Quantitative electroencephalographic subtyping of obsessive-compulsive disorder L S Prichep 1 , F Mas, E Hollander, M Liebowitz, E R John, M Almas, C M DeCaria, R H Levine

30- Psychiatry Res ۱۹۹۳ .Apr;50(1):25-32. Quantitative electroencephalographic subtyping of obsessive-compulsive disorderL S Prichep 1 , F Mas, E Hollander, M Liebowitz, E R John, M Almas, C M DeCaria, R H Levine

31- Psychiatry Res ۱۹۹۹ .Mar 22;85(3):263-73. Neurophysiologic predictors of treatment response to fluoxetine in major depressionI A Cook 1 , A F Leuchter, E Witte, M Abrams, S H Uijtdehaage, W Stubbeman, S Rosenberg-Thompson, C Anderson-Hanley, J J Dunkin

32- Semin Clin Neuropsychiatry ۲۰۰۱ . Apr;6(2):113-20. Prefrontal changes and treatment response prediction in depression I A Cook 1 , A F Leuchter

33- Neuropsychopharmacology. 2002 Jul;27(1):120-31. Early changes in prefrontal activity characterize clinical responders to antidepressants. Ian A Cook 1 , Andrew F Leuchter, Melinda Morgan, Elise Witte, William F Stubbeman, Michelle Abrams, Susan Rosenberg, Sebastian H J Uijtdehaage

34- J Psychiatr Res. 2005 Sep;39(5):461-6. Changes in prefrontal activity characterize clinical response in SSRI nonresponders: a pilot study. Ian A Cook 1 , Andrew F Leuchter, Melinda L Morgan, William Stubbeman, Barbara Siegman, Michelle Abrams
35- Can J Psychiatry. 2002 Aug;47(6):538-45. Association of QEEG findings with clinical characteristics of OCD: evidence of left frontotemporal dysfunction. Senel Tot 1 , Aynur Ozge, Ulkü Cömelekoğlu, Kemal Yazici, Nilgün Bal
36- Clin Electroencephalogr. 2003 Apr;34(2):70-4. Quantitative electroencephalography in OCD patients treated with paroxetine. Elsebet S Hansen 1 , Leslie S Prichep, Tom G Bolwig, E Roy John
37- Int J Neurosci. 2003 Jun;113(6):833-47. Quantitative EEG analysis in obsessive compulsive disorder. Filiz Karadag 1 , Nalan Kalkan Oguzhanoglu, Tülay Kurt, Atilla Oguzhanoglu, Figen Ateşci, Osman Ozdel
38- Clin Neurophysiol. 2004 Jun;115(6):1340-8. Executive hypercontrol in obsessive-compulsive disorder: electrophysiological and neuropsychological indices. Paola Bucci 1 , Armida Mucci, Umberto Volpe, Eleonora Merlotti, Silvana Galderisi, Mario Maj
39- Pharmacopsychiatry. 2000 Nov;33(6):201-5. Pre-treatment EEG and it's relationship to depression severity and paroxetine treatment outcome. V Knott 1 , C Mahoney, S Kennedy, K Evans
40- Electroencephalographic and perceptual asymmetry differences between responders and nonresponders to an SSRI antidepressant. Bruder GE, Stewart JW, Tenke CE, McGrath PJ, Leite P, Bhattacharya N, Quitkin FM. Biol Psychiatry. 2001 Mar 1;49(5):416-25.
41- Electroencephalographic alpha measures predict therapeutic response to a selective serotonin reuptake inhibitor antidepressant: pre- and post-treatment findings. Bruder GE, Sedoruk JP, Stewart JW, McGrath PJ, Quitkin FM, Tenke CE. Biol Psychiatry. 2008 Jun 15;63(12):1171-7.
42- Eur Psychiatry. 2008 Aug;23(5):350-5. Early reduction in prefrontal theta QEEG cordance value predicts response to venlafaxine treatment in patients with resistant depressive disorder. Martin Bares 1 , Martin Brunovsky, Miloslav Kopecek, Tomas Novak, Pavla Stopkova, Jiri Kozeny, Peter Sos, Vladimir Krajca, Cyril Höschl
43- Acta Psychiatr Scand. 2008 Apr;117(4):271-6. Pretreatment frontal EEG and changes in suicidal ideation during SSRI treatment in major depressive disorder. D V Iosifescu 1 , S Greenwald, P Devlin, R H Perlis, J W Denninger, J E Alpert, M Fava
44- Acta Psychiatr Scand. 2010 Dec;122(6):461-9. Brain functional changes (QEEG cordance) and worsening suicidal ideation and mood symptoms during antidepressant treatment. A M Hunter 1 , A F Leuchter, I A Cook, M Abrams
45- J Psychiatr Res. 2010 Jan;44(2):90-8. Antidepressant response trajectories and quantitative electroencephalography (QEEG) biomarkers in major depressive disorder. Aimee M Hunter 1 , Bengt O Muthén, Ian A Cook, Andrew F Leuchter
46- Psychophysiology. 2014 Jul;51(7):596-601. Altered frontal EEG asymmetry in obsessive-compulsive disorder. Moritz Ischebeck 1 , Tanja Endrass, Daniela Simon, Norbert Kathmann
47- Int J Psychophysiol. 2019 Sep;143:1-8. Early change of prefrontal theta cordance and occipital alpha asymmetry in the prediction of responses to antidepressants. Martin Bares 1 , Tomas Novak 2 , Premysl Vlcek 3 , Martin Hejzlar 4 , Martin Brunovsky 5
48- Clin EEG Neurosci. 2020 May;51(3):139-145. Use of EEG for Predicting Treatment Response to Transcranial Magnetic Stimulation in Obsessive Compulsive Disorder. Sinem Zeynep Metin 1 2 , Tugçe Balli Altuglu 3 , Baris Metin 1 4 , Turker Tekin Erguzel 3 , Selin Yigit 5 , Mehmet Kemal Arıkan 1 , Kasif Nevzat Tarhan

Dosage (mg)	Number of patients	Percent of patients
150	11	39.3
200	8	28.6
250	5	17.9
300	4	14.3
Sum	28	100

Table no. 1. Dosages of prescribed fluvoxamine

Variable		Non - Responder n(%)	Responder n(%)	P value
Age	Less than 30	4 (28.6)	4 (28.6)	0.9
	30 and more	10 (71.4)	10 (71.4)	
Gender	Male	8 (57.1)	6 (42.9)	0.45
	Female	6 (42.9)	8 (57.1)	
Education	Less than high school diploma	1 (7.1)	3 (21.4)	0.54
	High school diploma	3 (21.4)	3 (21.4)	
	University degree	10 (71.4)	8 (57.1)	
Dosage (mg)	150	6 (42.9)	5 (35.7)	0.34
	200	2 (14.3)	6 (42.9)	
	250	3 (21.4)	2 (14.3)	
	300	3 (21.4)	1 (7.1)	

Table no2. Demographic characteristics of samples

Electrode			Responder	Non-responder	
Fp1-EC		Normal	14(100)	7(50)	0/025
		Increased Theta	0	3 (21/4)	
		Increased Delta	0	2 (14/3)	
		Increased Theta and Delta	0	2 (14/3)	
	Increase Theta	Yes	0	3(21/4)	0/06
		No	14(100)	11(78/6)	
	Increased Delta	Yes	0	2(14/3)	0/14
		No	14(100)	12(85/7)	
	Increased Theta and Delta	Yes	0	2(14/3)	0/14
		No	14(100)	12(85/7)	
	Normal	Yes	14(100)	8(57/1)	0/006
		No	0	6(42/9)	
Fp2-EC		Normal	14(100)	8(57/1)	0/02
		Increased Theta	0	5 (35/7)	
		Increased Delta	0	1 (7/1)	
	Increased Theta	Yes	0	5(35/7)	0/01
		No	14(100)	9(364)	
	Increased Delta	Yes	0	1(7/1)	0/3
		No	14(100)	13(92/9)	
	Normal	Yes	14 (100)	8(57/1)	0/006
		No	0	6(42/9)	
F2-EC		Normal	14(100)	9(64/3)	0.04
		Increased theta	0	4 (28/6)	
		Increased theta and delta	0	1 (7/1)	
	Increased theta	Yes	0	4(28/6)	0/03
		No	14(100)	10(71/4)	
	Increased theta and delta	Yes	0	1(7/1)	0/3
		No	14(100)	13(92/9)	
	Normal	Yes	14 (100)	10(71/4)	0/03
		No	0	4(28/6)	
F3-EC		Normal	13(92/9)	8(57/1)	0/04
		Increased theta	0	5 (35/7)	
		Decreased theta	1(7/1)	0	
		Increased delta	0	1(7/1)	
	Increased theta	Yes	0	5(35/7)	0/01
		No	14(100)	9(364)	
	Decreased theta	Yes	1(7/1)	0	0/3
		No	13(92/9)	14(100)	
	Increased delta	Yes	0	1(7/1)	0/3
		No	14(100)	13(92/9)	
	Normal	Yes	13 (92/9)	9(64/3)	0/06
		No	1(7/1)	5(35/7)	
F 4		Normal	14(100)	12(85/7)	0/14

		Increased theta	0	2 (14/37)	
	Increased theta	Yes	0	2 (14/37)	
		No	14(100)	12(85/7)	0/14
	Normal	Yes	14(100)	12(85/7)	0/14
		No	0	2 (14/37)	
F7-EC		Normal	13(92/9)	11(78/6)	0/24
		Increased theta	0	1(7/1)	
		Decreased theta	1(7/1)	0	
		Increased delta	0	2(14/3)	
	Increased theta	Yes	0	1(7/1)	0/3
		No	14(100)	13(92/9)	
	Decreased theta	Yes	1(7/1)	0	0/3
		No	13(92/9)	14(100)	
	Increased delta	Yes	0	2 (14/37)	0/14
		No	14(100)	12(85/7)	
	Normal	Yes	13 (92/9)	11(78/6)	0/28
		No	1(7/1)	3(21/4)	
T3-EC		Normal	12(85/7)	13(92/9)	0/59
		Increased theta	1(7/1)	1(7/1)	
		Decreased theta	1(7/1)	0	
	Increased theta	Yes	1(7/1)	1(7/1)	0/98
		No	13(92/9)	13(92/9)	
	Decreased theta	Yes	1(7/1)	0	0/3
		No	13(92/9)	14(100)	
	Normal	Yes	12(85/7)	13(92/9)	0/54
		No	2(14/3)	1(7/1)	
T5-EC		Normal	13(92/9)	14(100)	0/3
		Increased Alpha	1(7/1)	0	
	Increased Alpha	Yes	1(7/1)	0	0/3
		No	13(92/9)	14(100)	
	Normal	Yes	13(92/9)	14(100)	0/3
		No	1(7/1)	0	
T6-EC		Normal	12(85/7)	14(100)	0/14
		Increased Alpha	2(14/3)	0	
	Increased Alpha	Yes	2(14/3)	0	0/14
		No	12(85/7)	14(100)	
	Normal	Yes	12(85/7)	14(100)	0/14
		No	2(14/3)	0	
C3-EC		Normal	12(85/7)	13(92/9)	0/59
		Increased theta	1(7/1)	1(7/1)	
		Decreased theta	1(7/1)	0	
	Increased theta	Yes	1(7/1)	1(7/1)	0/98
		No	13(92/9)	13(92/9)	
	Decreased theta	Yes	1(7/1)	0	0/3
		No	13(92/9)	14(100)	
	Normal	Yes	12(85/7)	13(92/9)	0/54
		No	2(14/3)	1(7/1)	
P2-EC		Normal	13(92/9)	14(100)	0/3
		Increased Alpha	1(7/1)	0	
	Increased Alpha	Yes	1(7/1)	0	0/3

		No	13(92/9)	14(100)	
	Normal	Yes	13(92/9)	14(100)	0/3
		No	1(7/1)	0	
P3-EC		Normal	11(78/6)	14(100)	0/06
		Increased Alpha	3(21/4)	0	
	Increased Alpha	Yes	3(21/4)	0	0/06
		No	11(78/6)	14(100)	
	Normal	Yes	11(78/6)	14(100)	0/06
		No	3(21/4)	0	
P4-EC		Normal	13(92/9)	14(100)	0/3
		Increased Alpha	1(7/1)	0	
	Increased Alpha	Yes	1(7/1)	0	0/3
		No	13(92/9)	14(100)	
	Normal	Yes	13(92/9)	14(100)	0/3
		No	1(7/1)	0	
O1-EC		Normal	6(42/9)	13(92/9)	0/01
		Increased Alpha	8(57/1)	1(7/1)	
	Increased Alpha	Yes	8(57/1)	1(7/1)	0/01
		No	6(42/9)	13(92/9)	
	Normal	Yes	6(42/9)	13(92/9)	0/01
		No	8(57/1)	1(7/1)	
O2-EC		Normal	8(57/1)	13(92/9)	0/07
		Increased Alpha	6(42/9)	1(7/1)	
	Increased Alpha	Yes	6(42/9)	1(7/1)	0/07
		No	8(57/1)	13(92/9)	
	Normal	Yes	8(57/1)	13(92/9)	0/07
		No	6(42/9)	1(7/1)	
Fp1-EO		Normal	13(92/9)	8(57/1)	0/04
		Increased Theta	0	4 (28/6)	
		Increased Delta	1 (7/1)	0	
		Increased Theta and Delta	0	2 (14/3)	
	Increase Theta	Yes	0	4(28/6)	0/09
		No	14(100)	10(71/4)	
	Increased Delta	Yes	1(7/1)	0	0/3
		No	13(92/9)	14(100)	
	Increased Theta and Delta	Yes	0	2(14/3)	0/14
		No	14(100)	12(85/7)	
	Normal	Yes	13(92/9)	8(57/1)	0/02
		no	1(7/1)	6(42/9)	
Fp1-EO		Normal	14(100)	10(71/4)	0/09
		Increased Theta	0	2 (14/3)	
		Increased Theta and Delta	0	2 (14/3)	
	Increase Theta	Yes	0	2(14/3)	0/14
		No	14(100)	12(85/7)	
	Increased Theta and Delta	Yes	0	2(14/3)	0/14
		No	14(100)	12(85/7)	
	Normal	Yes	14(100)	10(71/4)	0/03
		No	0	4(28/6)	
F 2		Normal	14(100)	12(85/7)	0/14

		Increased Theta	0	2(14/3)	
	Normal	Yes	0	2(14/3)	0/14
		No	14(100)	12(85/7)	
	Increased Theta	Yes	14(100)	12(85/7)	0/14
		No	0	2(14/3)	
F3-EO		Normal	12(85/7)	9(64/3)	0/09
		Increased theta	0	4 (28/6)	
		Increased delta	2 (14/3)	1(7/1)	
	Increased theta	Yes	0	4(28/6)	0/03
		No	14(100)	10(71/4)	
	Increased delta	Yes	2 (14/3)	1(7/1)	0/54
		No	12(85/7)	13(92/9)	
	Normal	Yes	12(85/7)	9(64/3)	0/19
		No	2 (14/3)	5 (35/7)	
F4-EO		Normal	14(100)	12(85/7)	0/14
		Increased theta	0	2 (14/37)	
	Increased theta	Yes	0	2 (14/37)	0/14
		No	14(100)	12(85/7)	
	Normal	Yes	14(100)	12(85/7)	0/14
		No	0	2 (14/37)	
F7-EO		Normal	11(78/6)	10(71/4)	0/82
		Increased theta	1(7/1)	2(14/3)	
		Increased delta	2(14/3)	2(14/3)	
	Increased theta	Yes	1(7/1)	2(14/3)	0/54
		No	13(92/9)	12(85/7)	
	Increased delta	Yes	2 (14/37)	2 (14/37)	1
		No	12(85/7)	12(85/7)	
	Normal	Yes	11(78/6)	10(71/4)	0/66
		No	3(21/4)	4 (28/6)	
F8-EO		Normal	14(100)	13(92/9)	0/3
		Increased delta	0	1(7/1)	
	Increased delta	Yes	0	1(7/1)	0/3
		No	14(100)	13(92/9)	
	Normal	Yes	14(100)	13(92/9)	0/3
		No	0	1(7/1)	
T3-EO		Normal	10(71/4)	12(85/7)	0/38
		Increased alpha	1(7/1)	1(7/1)	
		Decreased theta	2(14/3)	0	
		Increased delta	0	1(7/1)	
		Decreased delta	1(7/1)	0	
	Increased alpha	Yes	1(7/1)	1(7/1)	1
		No	13(92/9)	13(92/9)	
	Decreased theta	Yes	2(14/3)	0	0/14
		No	12(85/7)	14(100)	
	Increased delta	Yes	0	1(7/1)	0/3
		No	14(100)	13(92/9)	
	Decreased delta	Yes	1(7/1)	0	0/3
		No	13(92/9)	14(100)	
	Normal	Yes	10(71/4)	12(85/7)	0/35
		No	4(28/6)	2(14/3)	

T5-EO		Normal	11(78/6)	13(92/9)	0/24
		Increased alpha	2(14/3)	0	
		Decreased alpha	0	1(7/1)	
		Decreased delta	1(7/1)	0	
	Increased alpha	Yes	2(14/3)	0	0/14
		No	12(85/7)	14(100)	
	Decreased alpha	Yes	0	1(7/1)	0/3
		No	14(100)	13(92/9)	
	Decreased delta	Yes	1(7/1)	0	0/3
		No	13(92/9)	14(100)	
	Normal	Yes	11(78/6)	13(92/9)	0/28
		No	3(21/4)	1(7/1)	
T4-EO		Normal	13(92/9)	14(100)	0/3
		Increased theta	1(7/1)	0	
	Increased theta	Yes	1(7/1)	0	0/3
		No	13(92/9)	14(100)	
	Normal	Yes	13(92/9)	14(100)	0/3
		No	1(7/1)	0	
T6-EO		Normal	13(92/9)	14(100)	0/3
		Increased alpha	1(7/1)	0	
	Normal	Yes	1(7/1)	0	0/3
		No	13(92/9)	14(100)	
	Increased alpha	Yes	13(92/9)	14(100)	0/3
		No	1(7/1)	0	
C3-EO		Normal	12(85/7)	14(100)	0/14
		Decreased theta	2(14/3)	0	
	Decreased theta	Yes	2(14/3)	0	0/14
		No	12(85/7)	14(100)	
	Normal	Yes	12(85/7)	14(100)	0/14
		No	2(14/3)	0	
C4-EO		Normal	13(92/9)	14(100)	0/3
		Increased theta	1(7/1)	0	
	Increased theta	Yes	1(7/1)	0	0/3
		No	13(92/9)	14(100)	
	Normal	Yes	13(92/9)	14(100)	0/3
		No	1(7/1)	0	
P2-EO		Normal	11(78/6)	13(92/9)	0/12
		Increased alpha	3(21/4)	0	
		Decreased alpha	0	1(7/1)	
	Increased alpha	Yes	3(21/4)	0	0/06
		No	11(78/6)	14(100)	
	Decreased alpha	Yes	0	1(7/1)	0/3
		No	14(100)	13(92/9)	
	Normal	Yes	11(78/6)	13(92/9)	0/28
		No	3(21/4)	1(7/1)	
P3-EO		Normal	13(92/9)	13(92/9)	0/36
		Increased alpha	1(7/1)	0	
		Decreased alpha	0	1(7/1)	
	Increased alpha	Yes	1(7/1)	0	0/3
		No	13(92/9)	14(100)	

	Decreased alpha	Yes	0	1(7/1)	0/3
		No	14(100)	13(92/9)	
	Normal	Yes	13(92/9)	13(92/9)	1
		No	1(7/1)	1(7/1)	
P4-EO		Normal	13(92/9)	13(92/9)	1
		Increased alpha	1(7/1)	1(7/1)	
	Normal	Yes	1(7/1)	1(7/1)	1
		No	13(92/9)	13(92/9)	
	Increased alpha	Yes	13(92/9)	13(92/9)	1
		No	1(7/1)	1(7/1)	
O1-EO		Normal	4(28/6)	13(92/9)	0/0001
		Increased alpha	10(71/4)	1(7/1)	
	Normal	Yes	10(71/4)	1(7/1)	0/0001
		No	4(28/6)	13(92/9)	
	Increased alpha	Yes	4(28/6)	13(92/9)	0/0001
		No	10(71/4)	1(7/1)	
O2-EO		Normal	8(57/1)	13(92/9)	0/02
		Increased alpha	6(42/9)	1(7/1)	
	Normal	Yes	6(42/9)	1(7/1)	0/02
		No	8(57/1)	13(92/9)	
	Increased alpha	Yes	8(57/1)	13(92/9)	0/02
		No	6(42/9)	1(7/1)	

Table no 3. Characteristics of QEEG frequencies and responsiveness to Fluvoxamine based on electrode location and eyes openness.

Locus	Condition	Wave	Description	P value
O1	EO	Normal vs. increased alpha	Patients with normal waves in this locus significantly differ from patients with increased alpha wave in this locus in responsiveness to fluvoxamine.	0/0001
O1	EO	Normal	There is a direct correlation between normal waves in this locus and responsiveness to fluvoxamine.	0/0001
O1	EO	Increased alpha	There is an inverse correlation between alpha waves in this locus and responsiveness to fluvoxamine.	0/0001
Fp1	EC	Normal	There is a direct correlation between normal waves in this locus and responsiveness to fluvoxamine.	0/006
Fp2	EC	Normal	There is a direct correlation between normal waves in this locus and responsiveness to fluvoxamine.	0/006
Fp2	EC	Increased theta	There is an inverse correlation between increased theta waves in this locus and responsiveness to fluvoxamine.	0/01
F3	EC	Increased theta	There is an inverse correlation between increased theta waves in this locus and responsiveness to fluvoxamine.	0/01
O1	EC	Normal vs. increased alpha	Patients with normal waves in this locus significantly differ from patients with	0/01

			increased alpha wave in this locus in responsiveness to fluvoxamine.	
O1	EC	Normal	There is an inverse correlation between normal waves in this locus and responsiveness to fluvoxamine.	0/01
O1	EC	Increased alpha	There is a direct correlation between increased alpha waves in this locus and responsiveness to fluvoxamine.	0/01
Fp2	EC	Normal vs. increased theta and delta	Patients with normal waves in this locus significantly differ from patients with increased theta wave in this locus in responsiveness to fluvoxamine.	0/02
Fp1	EO	Normal	There is a direct correlation between normal waves in this locus and responsiveness to fluvoxamine.	0/02
O2	EO	Normal vs. increased alpha	Patients with normal waves in this locus significantly differ from patients with increased alpha wave in this locus in responsiveness to fluvoxamine.	0/02
O2	EO	Normal	There is a direct correlation between normal waves in this locus and responsiveness to fluvoxamine.	0/02
O2	EO	Increased alpha	There is an inverse correlation between alpha waves in this locus and responsiveness to fluvoxamine.	0/02
Fp1	EC	Normal vs. Increased Theta, Increased Delta, and Increased Theta and Delta	Patients with normal waves in this locus significantly differ from patients with increased theta, Increased delta, and Increased theta and delta waves in this locus in responsiveness to fluvoxamine.	0/025
F2	EC	Increased theta	There is an inverse correlation between increased theta waves in this locus and responsiveness to fluvoxamine.	0/03
F2	EC	Normal	There is a direct correlation between normal waves in this locus and responsiveness to fluvoxamine.	0/03
Fp1	EO	Normal	There is a direct correlation between normal waves in this locus and responsiveness to fluvoxamine.	0/03
F3	EO	Increased theta	There is an inverse correlation between increased theta waves in this locus and responsiveness to fluvoxamine.	0/03
F2	EC	Normal vs. Increased theta and Increased theta and delta	Patients with normal waves in this locus significantly differ from patients with Increased theta and Increased theta and delta waves in this locus in responsiveness to fluvoxamine.	0/04
F3	EC	Normal vs. Increased theta, Decreased theta and Increased delta	Patients with normal waves in this locus significantly differ from patients with Increased theta, decreased theta, Increased delta waves in this locus in responsiveness to fluvoxamine.	0/04
Fp1	EO	Normal, Increased Theta, Increased Delta and Increased Theta and Delta	Patients with normal waves in this locus significantly differ from patients with Increased Theta, Increased Delta and Increased Theta and Delta waves in this locus in responsiveness to fluvoxamine.	0/04

Table no 4. QEEG Variables with significant correlation with responsiveness to Fluvoxamine