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ORIGINAL ARTICLE

Decreased global field synchronization of multichannel frontal EEG measurements in obsessive-compulsive disorders

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Abstract Global field synchronization (GFS) quantifies the synchronization level of brain oscillations. The GFS method has been introduced to measure functional synchronization of EEG data in the frequency domain. GFS also detects phase interactions between EEG signals acquired from all of the electrodes. If a considerable amount of local brain neurons has the same phase, these neurons appear to interact with each other. EEG data were received from 17 obsessive-compulsive disorder (OCD) patients and 17 healthy controls (HC). OCD effects on local and large-scale brain circuits were studied. Analysis of the GFS results showed significantly decreased values in the delta and full frequency bands. This research suggests that OCD causes synchronization disconnection in both the frontal and large-scale regions. This may be related to motivational, emotional and cognitive dysfunctions.

Keywords Global field synchronization · EEG · Obsessive-compulsive disorders · Functional connectivity

1 Introduction

Obsessive-compulsive disorder (OCD) is a neuropsychiatric disease defined by repetitive, intrusive disturbing thoughts and mental acts and behaviours that are triggered by these thoughts. OCD is the tenth most common neuropsychiatric disease in the world. OCD is a frequently abrasive severe disorder that is observed approximately 2% of the population [51].

In the past, several EEG research studies were performed to propose a quantitative biomarker for diagnosing OCD by applying fundamental signal processing tools, such as estimation of absolute and relative powers for specified frequency bands [8, 48], computation of current source density by using LORETA [53] and calculation of the Fourier spectra by independent component analysis using LORETA [28], for eyes-closed EEG data collected from patients in a resting state. In recent years, advanced signal processing tools have become attractive for estimating entropy-based EEG complexity to provide insight into resting state electrophysiological dysfunctions in OCD [3].

Impaired memory functions were also investigated in association with average event related potential (ERP) in alpha band activity to understand the relationship between memory and symptoms of OCD in references [45, 46]. In the present study, global field synchronization (GFS) has been applied to a multichannel resting state surface EEG series to observe the functional and regional abnormalities originating from drug naive patients with OCD. EEG synchronization refers to the dependencies of two or more recordings collected from

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different locations on the scalp surface. Mutual information (MI) [18], coherence function [44] and cross correlation [42] are well known, and basic synchronization quantities proposed to measure inter-hemispheric dependency of two channel EEG series in several domains, such as the statistical, spectral and time domain, respectively. Time domain dynamical hemispheric interdependence measurement called synchronization likelihood [4] and frequency domain linear and nonlinear estimators, called Granger causality [5], and permutation conditional MI [36] have also been applied to EEG measurements to extract meaningful features for EEG classification in cognitive disorders because synchronous oscillations in EEG frequency bands may play an important role in various aspects of cognitive functioning.

The frequency domain global synchronization level over simultaneously recorded multiple EEG series was first quantified by the method of omega complexity (OC) presented in reference [55]. In the following years, conceptually similar frequency domain global synchronization estimators called GFS [24], global synchronization index (GSI) [11, 31] and global coupling index (GCI) [56] were assessed for estimation of functional connectivity between several brain processes in distinct frequency bands to compare controls and patients with varying degrees of cognitive decline or disconnection syndromes, such as Alzheimer's disease (AD), without assumptions about the spatial location of brain activities. Koenig et al. applied GFS to an EEG series to observe the variability of phase synchronization by means of functional brain connectivity in schizophrenia, and decreased functional connectivity was found with decreased theta frequency band activity [24]. In subsequent studies, GFS was used in diagnoses to detect electrophysiological differences between patients with AD and mild cognitive impairment (MCI) and controls [25]. Similar to schizophrenia, both AD and MCI cause a decrease in GFS values. Previously, GFS values were found to be positively correlated with both Mini-Mental Status Examination (MMSE) and Clinical Dementia Rating (CDR) scores [47]. Effect of neuropsychiatric disorders on cognitive functions was examined in many papers such as significant relationships were found between theta phase coherence and working memory process, successful episodic encoding [52], memory span [27] and meditation [32]. In a schizophrenia study, lower global synchronization was detected in the theta band related to working memory (WM) dysfunctions [24]. Many alpha phase studies have shown that these oscillations reflect significant information regarding sensory semantic (long term) memory [19, 20] and attentional process [54, 58]. Several OCD studies have found that the amplitude and phase of alpha events are related to oscillations coupling during WM [46]. Beta band activity has been linked to motor control and attentional top-down processing [9]. Beta band activation coupling has been linked to abnormal behavioural and cognitive changes such as Parkinson disease (PD) [7, 13]. Phase coherence in the beta-3 band has been linked to stimulus selection, attention [14], multisensory and sensorimotor integration, movement, memory and conscious awareness, and it reflects cortical activation [40] in addition to this decreased phase coupling was found in schizophrenia patients [30].

The aim of the present study is to use GFS, which was commonly found to be capable of measuring the degree of cognitive decline [24–26, 38, 47], in discriminating OCD from controls.

To our knowledge, GFS assessment has not been used previously for estimation of frequency-based EEG synchronization in both regional and global levels to observe the electroencephalographic abnormalities of relationships between functional connectivity and cognitive deficits originating from OCD. The method and implementation, in addition to the experimental paradigm, are provided in the following sections.

2 Data collection

Surface EEG series were collected from voluntary patients and age-matched controls at the Uskudar University Neuropsychiatry Health Practice and Research Centre. All voluntary participants signed a form of written consent. The guidelines of the Helsinki Declaration were obeyed, and the research protocol was approved by the university ethics committee. Inclusion criteria of healthy control (HC) volunteers are non-smoking, right-hand use, lacking a history of epilepsy and stroke and not to use medication. Patients with a history of traumatic head injury in addition to neurological and bipolar disorders, as well as alcoholics and left-handedness, were excluded from the study. All patients had never received psychiatric treatment in clinics; the demographic information of these drug-naive patients is listed in Table 1. The neuropsychiatric diagnostic tools used for diagnosis of OCD were the DSM-4 [41], the Yale-Brown Obsessive-Compulsive Scale (Y-BOCs) with the severity range of 0–40 [16], the 17 item Hamilton Depression Rating Scale (H-17) with the range of 0–51 [57] and the Beck Anxiety Inventory (BAI) score [6]. Data from 19-channel EEG series were recorded from participants via a Neuroscan Synamps II (Neuroscan Products, Compumedics, USA) recording system including a quick cap in accordance with the international 10–20 electrode placement. The recording room was light controlled and sound attenuated. EEG data were sampled at a frequency of 250 Hz. The analogue-to-digital converter was 16-bit. The impedance values of the Ag/AgCl surface electrodes were maintained at less than 5 kΩ. To remove artefacts originated from eye blinks (EOG signals) or body movements, values were rejected with levels of 50 μVolt peak-to-peak. Both vertical and horizontal bipolar EOG signals were measured by

Table 1 The demographic and clinical characteristics of the patients. (*F* female, *M* male, *o* obsession, *c* compulsion, *s* score, *d1* and *d2* refer the duration from the appearance of initial symptoms in years and obvious symptoms in months, respectively)

Sex	Age	os	cs	Y-BOCs	H-17	BAI	d1	d2
F	26	11	12	23	5	5	2	12
M	28	12	13	25	9	10	5	10
F	28	15	18	23	26	22	5	8
M	42	6	8	14	9	11	2	11
M	48	9	15	24	10	20	18	1
M	23	11	12	23	14	11	5	24
F	22	13	2	15	19	18	11	8
M	29	14	2	16	8	11	11	36
F	31	9	6	15	20	18	6	12
M	22	7	5	12	20	27	0.5	6
F	33	8	1	14	22	10	15	72
F	28	11	5	16	10	15	0.5	6
F	24	9	10	19	14	17	11	120
M	28	10	11	21	10	10	22	12
M	23	11	12	23	14	11	5	24
F	32	12	14	34	22	32	4	32
F	32	9	9	18	17	33	26	48

using electrodes, which were placed inferior to the right eye and to the left and right outer acanthi of the eyes. A band pass filter (0.5–70 Hz) was applied to raw data in Scan Edit 4.3 software. Power-line interference of 50 Hz was suppressed by a notch filter. Finally, muscle artefacts were carefully eliminated by an expert technician.

3 Methods

Eyes-closed EEG series of 3 min were collected from 17 controls and 17 patients with OCD. Each sweep was segmented by a constant window of 2 s and then GFS was computed for each segment (90 segments in each sweep of 3 min with a sampling frequency of 250 Hz). The mean value of the GFS values, which were estimated for all segments in the whole sweep, was computed. Particular EEG frequency band activities (BA) were defined as follows [29]:

- Delta BA, 1.5–6.0 Hz
- Theta BA, 6.5–8.0 Hz
- Alpha-1 BA, 8.5–10.0 Hz
- Alpha-2 BA, 10.5–12 Hz
- Beta-1 BA, 12.5–18 Hz
- Beta-2 BA, 18.5–21.0 Hz
- Beta-3 BA, 21.5–30 Hz

3.1 Global field synchronization

GFS was proposed in [24] as a nonlinear analysis approach, which produces a number between 0 and 1 depending on the level of functional EEG synchronization over all recording placements on the scalp surface in the frequency domain. High GFS values refer the high EEG synchronization; lower GFS values refer the low EEG synchronization. The numeric value, obtained by assessing GFS for multi-channel EEG series, can be concluded to measure the degree of cognitive deterioration. Moreover, we can understand the neural network in the brain in either local or larger scales when GFS is applied to EEG frequency bands. The algorithm of GFS is graphically pictured in Fig. 1.

The conventional FFT method has some disadvantages in multichannel data analysis. Spectral analysis obtained by using conventional FFT leads to bias due to the dependency of the results on a reference point. Additionally, variability of reference selection causes many problems, such as confirmative statistical analysis. Therefore, FFT dipole approximation has been proposed to overcome these problems [33]. This approximation was found to be relatively more useful in comparison with the conventional spectral analysis FFT method [12].

FFT-based spectra of the EEG series at each recording channel are represented by a vector in a complex plane. The phase of the signal can be determined with respect to the

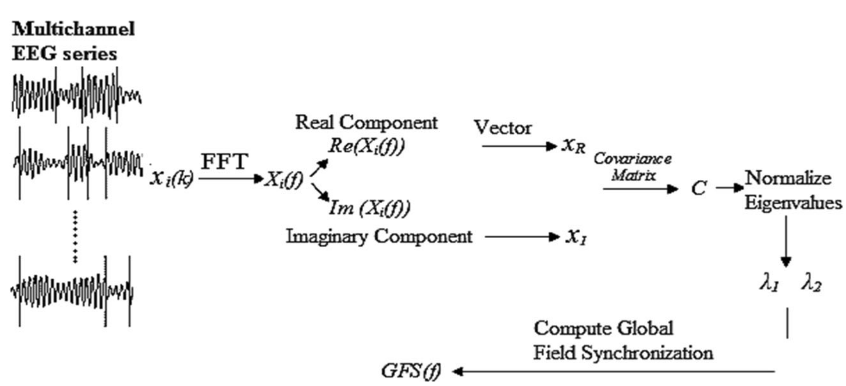

Fig. 1 The algorithmic steps in performing the method of GFS

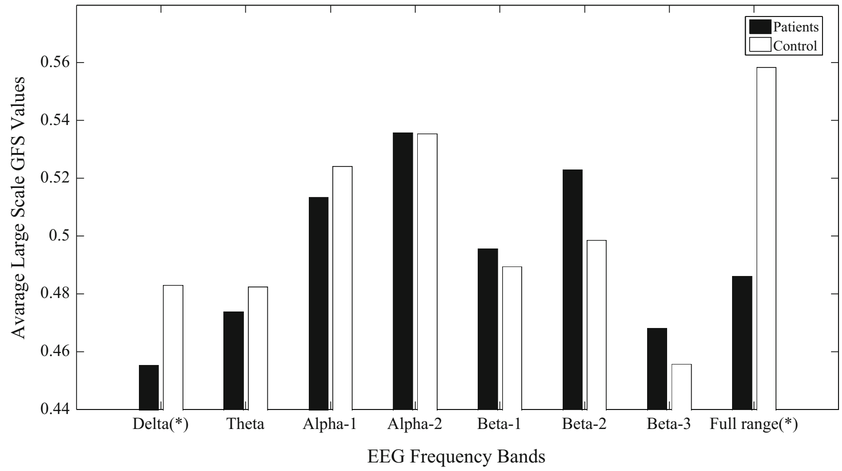

Fig. 2 Mean interval of GFS values in patients with OCD and healthy individuals in each EEG frequency and at 19 recording locations. (*) indicates *p* values < 0.01

direction of the vector for each EEG frequency band activity. Coefficients of real and imaginary parts in the complex plane are denoted by points in two-dimensional Cartesian coordinates. Then, the GFS method can be used to quantify the phase synchronization of the EEG series data at all scalp locations by inspecting whether the endpoints of the vectors lie on a straight line. The reference electrode is shown as the origin of the system, and the measurement electrode is represented by the point. Then, PCA is applied to all the points for an estimation of the phase-locking degree of the EEG series at all recording electrodes. If there is a common phase between these signals, the vectors would lie on a straight line and have small angles with the x-axis. However, if there is no common phase between recording channels, endpoints of the vectors would be circular. To quantify the shape of the cloud in the complex plane, a two-dimensional PCA was applied by fitting an elliptical formed bivariate Gaussian distribution where the ratio of the principal axes corresponds to the ratio of the PCA eigenvalues. The ratio of the resulting two eigenvalues defines GFS value.

$$\mathrm{GFS}(f) = \frac{\left|E_{(f)1} - E_{(f)2}\right|}{E_{(f)1} + E_{(f)2}} \qquad (1)$$

where $E_{(f)1}E_{(f)1}$ and $E_{(f)2}$ are two eigenvalues obtained by using PCA at a particular frequency band activity denoted by *f*. When the distribution of the complex vectors can be explained by a single principal component, the resulting value is equal 1. The higher GFS values indicate the increased functional connectivity over all recording electrodes. In contrast, the lower GFS values indicate decreased functional connectivity, i.e. the absence of a common phase [24–26].

In the present study, GFS values were calculated in 2-s EEG epochs at each recording electrode and were averaged separately for the following frequency band activities within each participant: delta (1.5–6.0 Hz), theta (6.5–8.0 Hz), alpha-1 (8.5–10.0 Hz), alpha-2 (10.5–12.0 Hz), beta-1 (12.5–18 Hz), beta-2 (18.5–21.0 Hz), beta-3 (21.5–30.0 Hz) and full range (1–70 Hz).

4 Results

In the present study, GFS was applied to 19-channel eyes-closed surface EEG series data collected from 17 patients with OCD and 17 controls to observe the difference between patients and controls by means of phase synchronization at specific frequency band activities. The coefficients estimated by using conventional FFT were shown in the complex plane.

The GFS values were determined for OCD patients and healthy control (HC) volunteers. The values were computed

Table 2 Group mean values and standard deviation of GFS in the seven frequency bands and full frequency range

Frequency bands Frequency range in Hz	Delta 1.5–6.0	Theta 6.5–8.0	Alpha-1 8.5–10.0	Alpha-2 10.5–12.0	Beta-1 12.5–18.0	Beta-2 18.5–21.0	Beta-3 21.5–30.0	Full range 0.5–70
Patients' GFS value	0.4552	0.4738	0.5134	0.5357	0.4955	0.5230	0.4681	0.4860
Std. deviation	0.02904	0.05652	0.08814	0.09492	0.05532	0.08972	0.05260	0.03424
Control group's GFS value	0.4829	0.4824	0.5240	0.5354	0.4895	0.4985	0.4557	0.5584
Std. deviation	0.03395	0.04834	0.06465	0.06734	0.04825	0.06289	0.02549	0.06975
p value (1-tailed *t* test)	*0.008*	0.317	0.3455	0.496	0.369	0.182	0.193	*0.0005*

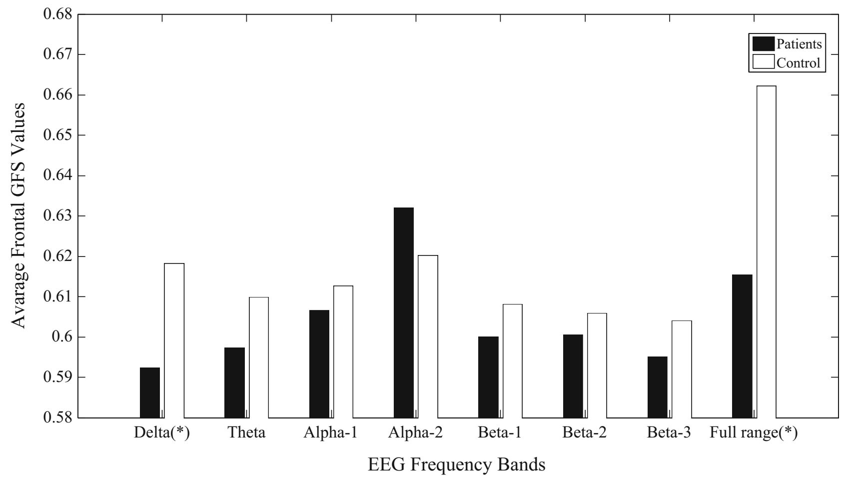

Fig. 3 Mean interval of GFS values in patients with OCD and healthy individuals in each EEG frequency band at various frontal locations. (*) indicates p values < 0.01

separately for each frequency band and differed significantly between the groups in the delta band ($p < 0.05$) and full band ($p < 0.01$). However, no significant difference was found in the other frequency bands. Large-scale GFS values of HC and OCD patients were measured as shown in Fig. 2. The values were computed using all channels averaged for each EEG frequency band (delta, 1.5–6 Hz; theta, 6.5–8.0 Hz; alpha-1, 8.5–10 Hz; alpha-2, 10.5–12 Hz; beta-1, 12.5–18 Hz, beta-3, 21.5–30 Hz). Independent sample t tests were used to compare the OCD patient and HC for each frequency bands. GFS values for large-scale brain analysis and group statistical analysis results are shown in Table 2.

It is known that OCD causes EEG dysfunctions in the frontal lobe [10, 49]. Therefore, we have examined the method of GFS for both the 19 electrode placements and the frontal scalp locations.

The results obtained for patients and controls with respect to the five EEG frequency band activities over the frontal scalp locations are summarised in Fig. 3. Independent sample t tests were used to compare patients with controls by means of GFS depending on the particular frequency band activity. Statistically significant differences between patients and controls were observed with respect to the delta band activity (with $p < 0.001$) and full EEG frequency range (with $p < 0.05$). GFS values for frontal lobes and group statistical analysis results are shown in Table 3. There are six electrodes on the frontal site: Fp1, Fp2, F7, F3, F4 and F8.

This result indicates that OCD causes changes in functional brain synchronization in the slow frequency bands.

5 Discussion

In the present study, the usage of GFS to estimate functional EEG synchronization by means of phase in OCD has been presented. The results show that OCD causes decreased GFS values in several frequency band activities such as delta, theta, alpha-1, as well as the EEG full band for the entire scalp surface. Particularly, loss of functional connectivity by means of phase synchronization was found in patients with OCD at frontal locations in delta, theta, alpha-1, beta-1, beta-2 and beta-3 activities at full band range.

Our results are similar to previous results that indicate decreased GFS in neuroleptic-naive patients with schizophrenia [24–26, 47]. Moreover, our recent findings are also consistent with earlier EEG synchronization works, including different signal processing methods used to understand the mechanism of OCD [34, 53]. We have focused on synchronization analysis of EEG frequency band activities because the literature

Table 3 Group mean values and standard deviation of GFS (frontal) in the seven frequency bands, full frequency range

Frequency bands Frequency range in Hz	Delta 1.5–6.0	Theta 6.5–8.0	Alpha-1 8.5–10.0	Alpha-2 10.5–12.0	Beta-1 12.5–18.0	Beta-2 18.5–21.0	Beta-3 21.5–30.0	Full range 0.5–70
Patients' GFS value (frontal)	0.5923	0.5973	0.6066	0.6319	0.6001	0.6006	0.5951	0.6154
Std. deviation	0.01389	0.01262	0.02847	0.04639	0.01660	0.02105	0.02380	0.02581
Control group's GFS value (frontal)	0.6182	0.6099	0.6127	0.6202	0.6082	0.6059	0.6040	0.6622
Std. deviation	0.01532	0.02983	0.03564	0.03875	0.02380	0.02626	0.02063	0.05013
p value (1-tailed t test)	*0.00005*	0.059	0.2925	0.2145	0.130	0.259	0.125	*0.001*

indicates that synchronous brain oscillations in slow frequency bands provide important information about both motivational and cognitive processes (memory, attention, perception, decision-making and planning) [1, 39, 50].

Neuroimaging studies analyse both PET and fMRI slices for estimation of brain dynamics and detection of the location generated delta band activity. In these studies, it was reported that the subcortical centres generating delta band activity are in both the medial prefrontal cortex and the orbitofrontal cortex [2, 17, 21–23, 35, 43].

EEG methods such as synchronization, complexity analysis, etc. are used only for exclusion of the comorbid disease (for instance depression with OCD) with obsessive-compulsive symptoms in clinical practise. In treatment or therapeutic use of EEG methods is very limited. This study was shown that global field synchronization analysis (GFS) values may be used as biomarker for OCD, and it can be used also for monitoring course of disease and treatment. GFS studies are shown that synchronization power is important marker for diagnosis of neuropsychiatric diseases.

In future work, we plan to compare the performance of those global synchronization metrics as follows: OC, GFS, GSI and GCI in detecting the severity of OCD. In addition, we will investigate the relationship between interneuronal synchronization and the degree of EEG complexity within a short time interval.

6 Conclusions

Some of the investigations on OCD effects on the brain sites have shown important patterns. Neuropsychological tests indicated that OCD causes functional dysfunctions on frontal lobe [10], neuroimaging studies also support these findings [49]. One of our results is decreased synchronization on frontal site is consistent with this study.

EEG synchronization level of OCD patients was investigated, and the level was found low for delta and full frequency range. Loss of phase synchronization would have relevance with functional connectivity. The major findings of the present study are that the loss of synchronization in delta band and functional connectivity of the brain changes with OCD. Studies using low resolution brain electromagnetic tomography (LORETA) have founded delta activity at maximum level in medial prefrontal cortex and orbito-frontal cortex [2]. In addition to this, investigations with fMRI have detected abnormal and dysfunctional activity in orbito-fronto striatal networks of OCD patients [39] and fronto-subcortical network dysfunctional causes a loss of functional connectivity in the brain [2, 15, 35, 37]. Our results that functional connectivity and desynchronization in delta band for frontal and global site are also consistent with previous findings.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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