



Obsessive-compulsive disorder (OCD) is associated with increased electroencephalographic (EEG) delta and theta oscillatory power but reduced delta connectivity

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ABSTRACT

Obsessive-Compulsive Disorder (OCD) is a mental health condition causing significant decline in the quality of life of sufferers and the limited knowledge on the pathophysiology hinders successful treatment. The aim of the current study was to examine electroencephalographic (EEG) findings of OCD to broaden our understanding of the disease. Resting-state eyes-closed EEG data was recorded from 25 individuals with OCD and 27 healthy controls (HC). The 1/f arrhythmic activity was removed prior to computing oscillatory powers of all frequency bands (delta, theta, alpha, beta, gamma). Cluster-based permutation was used for between-group statistical analyses, and comparisons were performed for the 1/f slope and intercept parameters. Functional connectivity (FC) was measured using coherence and debiased weighted phase lag index (d-wPLI), and statistically analyzed using the Network Based Statistic method. Compared to HC, the OCD group showed increased oscillatory power in the delta and theta bands in the fronto-temporal and parietal brain regions. However, there were no significant between-group findings in other bands or 1/f parameters. The coherence measure showed significantly reduced FC in the delta band in OCD compared to HC but the d-wPLI analysis showed no significant differences. OCD is associated with raised oscillatory power in slow frequency bands in the fronto-temporal brain regions, which agrees with the previous literature and therefore is a potential biomarker. Although delta coherence was found to be lower in OCD, due to inconsistencies found between measures and the previous literature, further research is required to ascertain definitive conclusions.

1. Introduction

Obsessive-compulsive disorder (OCD) is a mental health disorder characterized by unwanted and intrusive thoughts (obsessions), often leading to compulsions such as repetitive behaviors, mental acts, or rigidly applied rituals (Richter et al., 2003). With a lifetime prevalence of 1–3%, OCD has been classified as a mental health condition causing significant reduction in the quality of life of sufferers (Angelakis et al., 2015). First-line treatments for OCD, including Selective Serotonin Reuptake Inhibitors (SSRIs) and cognitive behavioral therapy are found to have poor success rates (Taylor et al., 2012). This inadequacy has motivated investigators to study the underlying pathophysiology of OCD

in the hope of identifying better suited therapeutic approaches.

Resting-state electroencephalographic (EEG) studies have shown that individuals with OCD show significant differences in brain electrical activity compared to healthy controls (HC) (Perera et al., 2019). Although differences in the power of neural oscillations within all frequency bands have been reported in the previous literature, reports of delta, theta and alpha differences are the most common. Several studies have noted increased resting fronto-temporal delta (Tot et al., 2002; Molina et al., 1995) and theta (Kamaradova et al., 2016; Koprivová et al., 2011; Karadag et al., 2003) power in OCD groups compared to HC. However, there are inconsistencies between the studies examining alpha activity, with reports of both power increases (Ischebeck et al., 2014;

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Bolwig et al., 2007) and decreases (Karadag et al., 2003; Pogarell et al., 2006).

Identification and analysis of brain oscillatory activity involves transforming the EEG data to frequency or time-frequency domain. Power in the frequency spectrum reflects both oscillatory activity and irregular, asynchronous, aperiodic firing of neurons or assemblies of neurons and exhibits a 1/f-like power spectrum, where power (amplitude) decreases as a function of frequency (He, 2014). When measuring oscillatory power, it is imperative to correct for this non-oscillatory activity to avoid confounding estimates of power, obscuring differences in oscillatory activity between bands, and creating false differences where none exist. Therefore, detecting the rhythmicity of brain oscillations needs to be an additional consideration when interpreting measures of oscillatory power. Additionally, it is important to perform between-group analyses of the 1/f slope and intercept parameters as these may better represent the neural activity at lower frequencies and may also be functionally and behaviorally relevant (Donoghue et al., 2020).

Functional connectivity (FC) refers to various measures of how neural activity of one brain region relates to activity in another (Nentwich et al., 2020). Several studies have reported altered connectivity in OCD when compared to HC. Many of these studies have reported decreased connectivity in alpha and beta frequency bands (Choi et al., 2021; Olbrich et al., 2013; Tan et al., 2019, 2022; Velikova et al., 2010; Yazdi-Ravandi et al., 2018), while one study reported decreased global field synchronization of frontal EEG in the delta band (Özçoban et al., 2018). Furthermore, it has been hypothesized that the pathophysiology of OCD may be attributed to defective structure and function of the cortico-striato-thalamo-cortical (CSTC) circuit, resulting in poor FC between these regions (Gan et al., 2017). However, the substantial heterogeneity between data collection parameters, EEG pre-processing methods and the utilized connectivity measures makes it difficult to interpret these results.

A principal aim of the current study was to investigate the differences in EEG power spectra in all frequency bands between OCD and HC groups. The primary hypothesis was that individuals with OCD would show increased oscillatory power in delta and theta frequency bands. Additionally, exploratory hypotheses were that there would be between-group differences in functional connectivity and 1/f parameters. Although several previous studies have investigated power spectral differences between OCD and HC groups, this is the first to account for the 1/f non-oscillatory activity and to use a cluster-based permutation method to account for multiple comparisons. Furthermore, this is the first study to compare and report findings of 1/f parameters between OCD and HC groups. The FC analysis was performed in adherence to a recently published checklist (Miljevic et al., 2021) designed to standardize connectivity analyses and to our knowledge, this is the first OCD FC study to conform to these standards.

2. Material and methods

2.1. Participants

Male and female participants aged between 18 and 65 years were recruited through internet and poster advertisements and doctor referrals from the state of Victoria, Australia. The required sample size was calculated using Cochran's formula (supplemental materials S1) (Kotrlík and Higgins, 2001). The clinical trial was conducted as per the latest version of the Guidelines for Good Clinical Practice (Dixon, 1999). Following verbal and written explanation of the nature of all involved procedures, informed written consent was obtained from each participant. All participants were reimbursed for their participation in the trial. The study received ethics approval from Monash Health Human Research Ethics Committee and was registered on the Australian New Zealand Clinical Trials Registry (ANZCTR).

The OCD group comprised individuals diagnosed with OCD

according to the International Classification of Diseases – 10th revision (WH Organization, 1993) or DSM-IV/V (American Psychiatric Association, 2013). Symptom severity was assessed utilizing the Yale-Brown Obsessive Compulsive Scale (YBOCS) (Goodman et al., 1989). Additionally, the Beck Anxiety Inventory (BAI) (Beck et al., 1988) was used to assess the level of anxiety and the Quick Inventory for Depressive Symptoms – Self Report (QIDS-SR) (Rush et al., 2003) was used to assess the level of concurrent depression. A Mini International Neuropsychiatric Interview (MINI) (Sheehan et al., 1998) was performed to verify the OCD diagnosis and exclude other major mental health disorders. Exclusion criteria for the OCD group included scoring <17 on the YBOCS, presence of an unstable medical/neurological disorder and being diagnosed with another mental health condition other than depression and anxiety. Participants were included regardless of their medication status but were required to be on a stable dose for at least 6 weeks prior to the study. Clinical data obtained from the patient group included age of OCD onset, illness duration, medication history, presence of comorbidities (depression and anxiety) and symptom severity.

Healthy control data was obtained from individuals who have never been diagnosed with a mental health or neurological disorder. Other exclusion criteria for the HC group included currently being on psychoactive medication and previous concussion or head injury with loss of consciousness for more than 10 min. HC participants also underwent a MINI to exclude significant mental health conditions including OCD. While we did not administer the YBOCS to the HC participants, none of them endorsed any of the OCD-related items in the MINI.

2.2. EEG recording

EEG recording took place in a laboratory with constant levels of lighting and background noise from air conditioning. The participants were seated upright on a padded, comfortable chair and requested to close their eyes, try to stay awake and relaxed during the recording period. Prior to recording, participants were provided with an explanation of the procedure and its safety along with instructions to minimize muscle and eye movements that may affect the recording. All participants underwent 3 min of EEG recording at rest with eyes closed.

The EEG data was collected using the actiCHamp amplifier (Brain Products GmbH, Munich, Germany) with the BrainVision software (version 1.21.0303) and 64 Ag/AgCl electrodes embedded within an EasyCap (Hersching, Germany) based on the international 10–20 system. Out of these, 63 electrodes were used (supplemental materials S2) and CPz was excluded due to being the reference electrode. All recordings were made at a sampling rate of 1000 Hz with the ground placed at AFz. A transparent electro-gel was injected onto the scalp to reduce impedance, which was kept below 5 k Ω . No online band-pass or notch filtering was applied during the recording.

2.3. EEG pre-processing

Raw, continuous EEG data was pre-processed using the RELAX pipeline (Bailey et al., 2022) implemented within MATLAB (The MathWorks Inc, 2022), which utilizes functions from EEGLAB (Delorme and Makeig, 2004) and fieldtrip (Oostenveld et al., 2011). This pipeline initially applied a 4th order acausal Butterworth bandpass filter from 1 to 80 Hz and a second order acausal Butterworth notch filter from 47 to 53 Hz. Following this step, several measures were taken to identify and reject bad electrodes. The initial removal of noisy electrodes occurred through the “findNoisyChannels” function of the PREP EEG pre-processing pipeline (Bigdely-Shamlo et al., 2015). Thereafter, electrodes were marked for rejection based on 1) extreme outlying amplitudes (Alday and van Paridon, 2021); 2) extremely improbable voltage distributions; 3) extreme drift; 4) extreme kurtosis; and 5) muscle activity (Fitzgibbon et al., 2016). Overall, the rejection of a maximum of 20% of electrodes was accepted. If more than 20% were marked for removal, electrodes were ranked based on the number of epochs

showing extreme artifacts and only the worst 20% were removed. The same measures were applied subsequently to mark extreme periods to be excluded from further analysis. The resultant data was then subjected to three sequential multiple Wiener filter (MWF) cleaning steps (Somers et al., 2019) to address the following artifacts: 1) Muscle activity: low-power log-frequency slopes of more than -0.59 were classified as epochs affected by muscle activity; 2) Blink artifacts: following bandpass filtering using a fourth order Butterworth filter from 1 to 25 Hz, pre-specified blink affected electrodes were selected and voltages were averaged within 1 s epochs. Blinks were flagged at time points where the averaged voltage exceeded the upper quartile plus thrice the inter quartile range of the distribution of all voltages in these pre-specified electrodes. The 800ms period surrounding each blink flag was marked as artifacts for further cleaning; 3) Horizontal eye movements and drift: Periods of selected lateral electrodes affected by horizontal eye movement showing voltages greater than twice the median absolute deviation (MAD) from the median of their overall amplitude, with a similar opposite voltage movement in the electrode on the opposite side of the head were classified as horizontal eye movements (Rogasch et al., 2017). Epochs with an amplitude greater than 10 times MAD from the median of all electrodes were considered to be affected by drift (Nolan et al., 2010) and marked as artifacts for further analysis. The resultant data was average re-referenced using the PREP method (Bigdely-Shamlo et al., 2015) before performing Independent Component Analysis (ICA) using fastICA (Hyvarinen, 1999). Artifactual components were detected using ICLabel (Pion-Tonachini et al., 2019) and only these components were cleaned with wavelet enhanced ICA (wICA) (Castellanos and Makarov, 2006). Continuous data was then reconstructed back into the scalp space and previously rejected electrodes were spherically interpolated to obtain a full set of electrodes for each participant.

2.4. Detection of better oscillations with eBOSC

Following the initial pre-processing, data was further processed using an extended version (eBOSC) (Kosciessa et al., 2020) of the Better OSCillation (BOSC) method (Whitten et al., 2011). This method was designed to detect the arrhythmic, non-oscillatory portion of the EEG signal (1/f activity). In BOSC, duration (D_T) and power (P_T) thresholds are calculated by modelling the known background power spectrum. Thus, at a given frequency, BOSC detects increases in power above P_T of a specific minimum duration D_T , thereby removing non-repeating rises in spectral amplitude. In eBOSC, rhythm detection benchmarks are derived using simulations to further characterize rhythmicity. During the eBOSC process, 1s of data from bilateral edges were zero-padded to avoid edge artifacts and continuous data was segmented into 4s epochs with no overlap. The output of eBOSC includes the results of the time-frequency analysis as well as the specific time points of rhythmic episodes and this information was utilized in spectral analysis methods. Furthermore, the slope and intercept of the 1/f spectrum were also analyzed to identify any differences between HC and OCD groups.

2.5. Power spectral analysis

For spectral analysis, frequency bands were defined as: delta (0.5–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), beta (12–30 Hz) and gamma (30–45 Hz). The wavelet time-frequency transformation table and the detected rhythmic episodes were obtained from the eBOSC output, and the power of each band was computed after removing the background 1/f activity. The output of periods showing oscillatory activity within each frequency band was separately time averaged for OCD and HC groups and cluster-based permutation was applied to the resultant data. The fieldtrip function “ft_prepare_neighbours” was used to find channel neighbors for spatial clustering using triangulation (Oostenveld et al., 2011). At least 2 neighboring electrodes were required to show significance to be included in a significant cluster. A family-wise error rate (FWER) was estimated by sampling and permuting the null distribution

using the Monte Carlo method. A two-tailed independent sample *t*-test was used to evaluate the between-group differences. The cluster alpha (critical value used for thresholding the sample-specific *t*-statistics) was set at 0.05 and the number of permutations was set at 50000. Hypothesis testing was performed for delta, theta, and alpha bands, while beta and gamma bands were analyzed as exploratory analyses. The results of all primary hypothesis-driven analyses were controlled for experiment-wise multiple comparisons using a false discovery rate (FDR).

2.6. Functional connectivity analysis

FC analysis was performed adhering to a recently published EEG connectivity checklist that was developed to standardize FC studies while ensuring optimal connectivity assessment (Miljevic et al., 2021). The debiased estimator of the weighted phase lag index (d-wPLI) and the coherence connectivity measures were separately used to compute the connectivity matrices based on the multi-taper Fourier spectral estimate. Both connectivity measures provide a value between 0 and 1 for each electrode pair, where higher values indicate higher connectivity.

Statistical analysis was performed using the Network-Based Statistic (NBS) which uses non-parametric permutation testing and controls for FWER using mass univariate testing at each connection (Zalesky et al., 2010). The number of iterations performed for permutation testing was 10000 and the primary threshold was set at $p_t = 0.05$. If a significant network was identified, the primary threshold was adjusted based on the recommendations of the NBS manual (Zalesky et al., 2010); a range of thresholds were experimented where liberal thresholds (e.g., $p_t = 0.05$) produced topologically extended results and conservative thresholds (e.g., $p_t = 0.001$) produced strong, topologically focal results. The identified networks were visualized using the BrainNet Viewer (Xia et al., 2013).

As suggested in the checklist, continuous EEG data was segmented into 6s epochs, but the number of epochs was limited to the <50 category due to the short total duration of recording (the only non-optimal study parameter for d-wPLI). Re-referencing was performed with robust common average reference and all types of artifacts were addressed through the RELAX pre-processing pipeline. When our methods were applied to the checklist, a total score of 5 and 4.5 were achieved for d-wPLI and coherence measures (Supplemental Table 1), indicating high and moderate study quality, respectively.

2.7. Regression analysis between symptom severity and oscillatory power/connectivity

A within-group linear regression was performed between the YBOCS and oscillatory power of each frequency band at each channel. Additionally, following a reviewer's request, we performed exploratory within-group linear regressions between the QIDS-SR, BAI and oscillatory power of each frequency band at each channel. A regression was also performed for each channel pair in any networks identified through the FC analysis. Bonferroni correction was used to account for multiple comparisons. These analyses provide information of any associations between the oscillatory power/connectivity measures and the OCD symptom severity.

3. Results

3.1. Demographic and clinical data

The study sample comprised 25 OCD and 27 HC participants. The Demographic characteristics and clinical data are summarized in Table 1. No significant differences were observed between OCD and HC participants in any demographic variables.

Table 1
Demographic and clinical characteristics of participants.

Variable	OCD (n = 25)			HC (n = 27)			Test statistic (<i>p</i> -val)
	Mean	SD	n	Mean	SD	n	
Demographic Characteristics							
Gender (M/F)			12/ 13			9/ 18	$\chi^2 = 1.14$, $p = 0.29$
Age (years)	36.24	13.06	25	31.22	10.66	27	$t = 1.52$, $p = 0.13$
Handedness (R/L)			21/ 4			26/ 1	$\chi^2 = 2.22$, $p = 0.14$
Marital status (S/M)			20/ 5			21/ 6	$\chi^2 = 0.04$, $p = 0.85$
Clinical Characteristics							
Age at onset (years)	24.64	9.90	25				
Duration of illness (years)	11.60	9.98	25				
YBOCS (total)	28.00	3.82	25				
YBOCS - obsessions	13.88	1.81	25				
YBOCS - compulsions	14.12	2.39	25				
BAI	17.04	8.92	24 ^a				
QIDS-SR	10.17	4.94	24 ^a				
Medication status (Y/N)			19/ 6 ^b				

Note.

OCD – Obsessive Compulsive Disorder, HC – Healthy Control, SD – Standard Deviation, M – Male, F – Female, R – Right, L – Left, S – Single, M – Married, YBOCS – Yale-Brown Obsessive Compulsive Scale, BAI – Beck Anxiety Inventory, QIDS-SR – Quick Inventory of Depressive Symptoms-Self Report, Y – on medications, N – off medications, SSRI – Selective Serotonin Reuptake Inhibitor, SNRI – Serotonin-Norepinephrine Reuptake Inhibitor.

^a BAI and QIDS-SR scores for one participant were unavailable due to a data collection issue.

^b If Y, type of medication (n = number of participants on the medication): SSRI (n = 14), Antipsychotics (n = 7), SNRI (n = 2), Clomipramine (n = 1), Sodium valproate (n = 1), Lithium (n = 1).

3.2. Power spectral analysis

Three clusters were identified through cluster-based permutation; two for the delta band (Cluster 1: $p = 0.0065$, cluster statistic = $84.81 \pm$

0.0007; Cluster 2: $p = 0.046$, cluster statistic = 26.38 ± 0.002) and one for theta ($p = 0.041$, cluster statistic = 44.46 ± 0.002). The topographical plots indicated that the OCD group had significantly higher power than HC in these frequency bands, in the regions highlighted by the clusters (Fig. 1). Delta clusters were concentrated around the left fronto-temporal and the right parietal regions and the theta cluster was found at the left fronto-temporal and parietal regions. Upon controlling for multiple comparisons using FDR, only the first delta cluster was found to be significantly different ($p = 0.0357$). No significant clusters were found between OCD and HC groups in the alpha ($p = 0.14$, cluster statistic = 14.6 ± 0.003), beta and gamma bands.

There were no significant differences between the OCD and HC groups for the intercept and slope parameters of the 1/f spectrum in any of the channels (Supplemental Fig. 1).

3.3. Functional connectivity

One significant network in the delta band was identified using the coherence measure (Fig. 2). Following the adjustment of the primary threshold to the conservative value of $p_c = 0.0038$, 21 nodes and 26 edges remained in the network ($p = 0.049$, network statistic = 3.13), indicating that the connectivity was significantly lower in the OCD group. Supplemental Table 2 shows the unique connections identified within this network and the corresponding regions of interest. It is evident that multiple differences between groups in the strength of connections exist between the bilateral frontocentral and frontal electrode groups. No statistically significant differences in functional connectivity were identified between OCD and HC groups with the d-wPLI method. No other frequency bands had networks that were found to be significantly different between OCD and HC groups.

3.4. Regression analysis

Statistically significant associations were absent between the YBOCS and oscillatory power in all frequency bands following Bonferroni correction within the regression analysis. However, the QIDS-SR (slope = 0.308, $p = 0.03$) and BAI (slope = 0.294, $p = 0.038$) were found to be positively correlated with increasing oscillatory power in the delta band. Furthermore, although a negative trend was identified between YBOCS and coherence connectivity (slope = -0.009 , $p = 0.057$), the values were not statistically significant. Similarly, there were no significant associations between QIDS-SR, BAI and coherence connectivity.

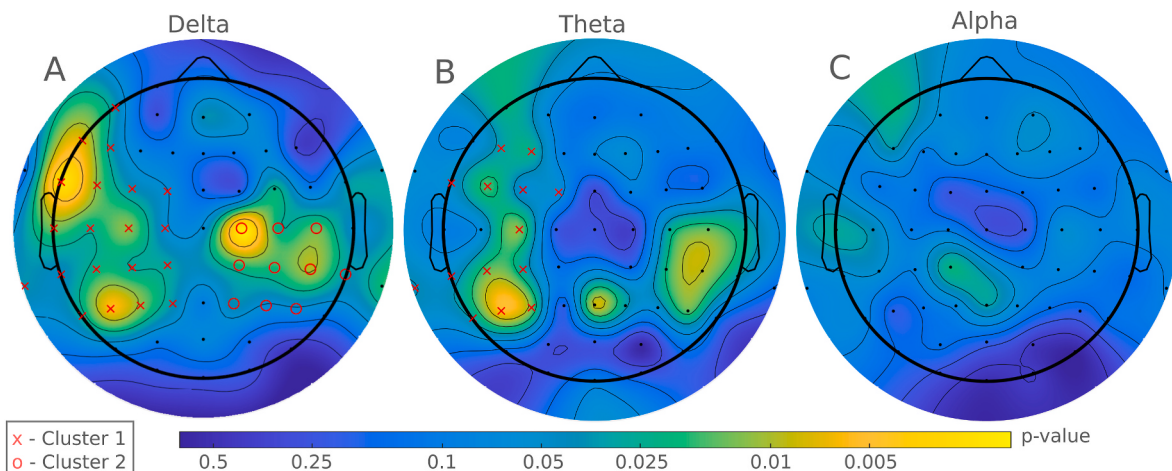


Fig. 1. Topographical Plots Illustrating Spectral Power Differences Between OCD and HC Groups Using the Cluster-Based Permutation Method

Note. A) OCD groups showed significantly higher delta band power than HC in two significant clusters. Cluster 1 in the left fronto-temporal, parietal region (AF7, F5, F7, FC1, FC3, FC5, C1, C3, C5, T7, TP7, TP9, FT7, CP1, CP3, CP5, P1, P3, P5, P7), and Cluster 2 in the right parietal region (C2, C4, C6, CP2, CP4, CP6, P2, P4, P6, TP8). B) OCD groups showed significantly higher theta band power than HC in one cluster in the right fronto-temporal and parietal regions (F3, F5, FT7, FC1, FC3, FC5, TP7, TP9, P3, P5, P7, C3, CP3, CP5). C) No significant difference in band power was noted in the alpha band.

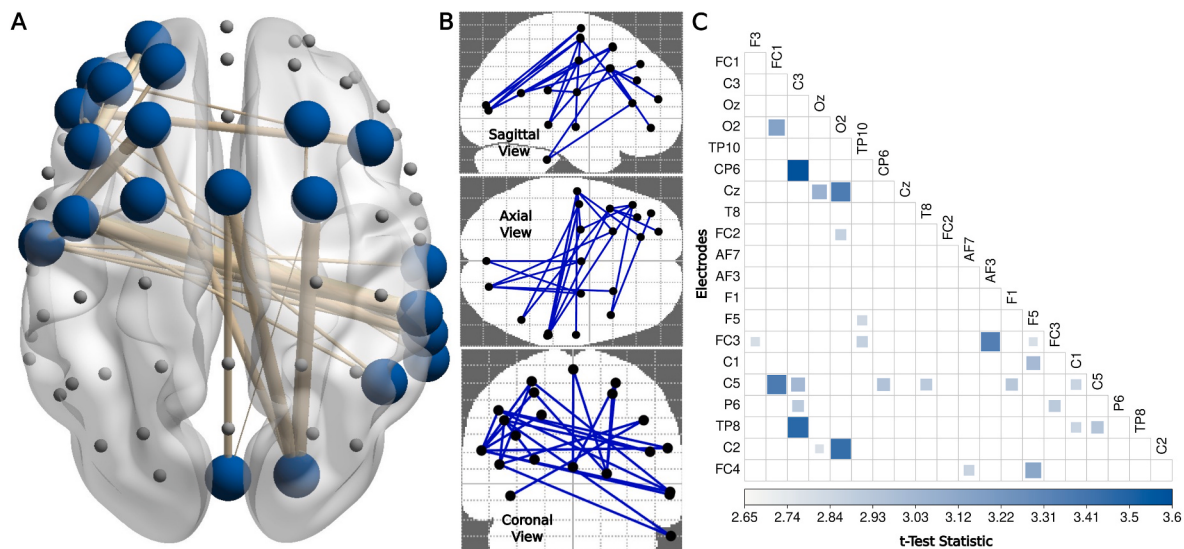


Fig. 2. Network-Based Analysis of Functional Connectivity in OCD with Coherence Connectivity Measure.

Note. A) Output of the BrainNet Viewer illustrating the identified connectivity network in the delta band. The nodes and weighted links indicate brain areas and the magnitude of the reduction in connectivity in the OCD group when compared to HC, with larger link weightings indicating a larger magnitude of reduced connectivity in the OCD group. B) Depiction of the connectome in three different views C) Connectivity matrix indicating the pairs of electrodes included in the identified network.

Supplemental figures 2, 3 and 4 present further details on the regression analysis.

4. Discussion

EEG power spectral and functional connectivity findings in OCD populations have largely been inconsistent across previous studies. Therefore, we investigated spectral power changes between OCD and HC groups. Our study attempted to address these inconsistencies by adhering to better methodology involving a comprehensive EEG pre-processing pipeline and controlling for $1/f$, non-oscillatory activity. Furthermore, the current study analyzed the parameters of the $1/f$ slope for the first time in an OCD sample. We also performed an exploratory analysis of network-based functional connectivity changes in OCD.

Power spectral findings of the current study showed that the OCD group had significantly higher power in the delta and theta bands in comparison to HC in several clusters of electrodes. The delta clusters were concentrated around the left and right fronto-temporal and parietal regions, while the theta cluster was in the left fronto-temporal region. These findings agree with several previous studies that reported increased delta and theta powers in these same regions in OCD (Tot et al., 2002; Molina et al., 1995; Kamaradova et al., 2016; Koprivová et al., 2011; Karadag et al., 2003; Pogarell et al., 2006; Velikova et al., 2010; Desarkar et al., 2007a; Kuskowski et al., 1993; Locatelli et al., 1996; Perros et al., 1992; Prichep et al., 1993), and supports the theory that OCD is associated with pathological hyperactivation of the frontal brain networks (Yoshimura et al., 2019). However, two studies reported deficits in delta (Hansen et al., 2003) and theta (Min et al., 2011) power in OCD when compared to HC.

OCD is known to be associated with significant reductions in cerebral blood flow (CBF) in the fronto-temporal brain regions (Lucey et al., 1995). Insufficient rates of CBF, leading to poor cortical grey matter oxygen uptake, has been found to be correlated with increased slow EEG frequencies (Ingvar et al., 1976). Additionally, as postulated by Michel et al. the increase in the power of slow frequency oscillations in the frontal regions could be due to over-activation of frontal slow wave generators causing excessive delta and theta powers (Michel et al., 1992). Therefore, frontal slow wave generators being activated due to low frontal CBF may explain the raised slow wave oscillatory power in

OCD. Moreover, our findings of excessive frontotemporal slow wave activity may indicate pathological hyperactivation of the frontal control network, causing an inability to inactivate the frontotemporal “action” network to switch to the default “rest” network (Leon et al., 2014). Furthermore, the presence of excessive frontal slow wave activity has also been reported in other mental health conditions including social phobia (Sachs et al., 2004), depression (Bailey et al., 2018) and schizophrenia (Lavoie et al., 2012). Additionally, increased frontal delta activity has been reported in individuals with Alzheimer’s disease and mild cognitive impairment (Babiloni et al., 2006). As depression is a common comorbidity of OCD (Fineberg et al., 2005), this finding may be an indicator of underlying depression, rather than OCD.

Although several previous studies reported increased (Ischebeck et al., 2014; Bolwig et al., 2007; Desarkar et al., 2007a; Prichep et al., 1993; Hansen et al., 2003) and decreased (Karadag et al., 2003; Pogarell et al., 2006; Locatelli et al., 1996; Min et al., 2011; Drake et al., 1996; Simpson et al., 2000; Bucci et al., 2004) alpha power in OCD groups when compared to HC, the current analysis did not find any differences in the alpha band. It has been reported that individuals with OCD who respond to SSRIs showed excess alpha power, while non-responders showed excess theta power (Hansen et al., 2003). The OCD sample recruited in this study comprised largely of non-responders to SSRIs, which might explain this finding. Furthermore, OCD is known to have significantly higher complexity of information processing when compared to HC, as evaluated by fractal dimensions (Yazdi-Ravandi et al., 2021), which might explain the contradicting findings in some frequency bands.

There is limited literature available relating to EEG connectivity in OCD. The present study reported no differences in connectivity using the d-wPLI measure and significantly decreased functional connectivity using coherence, in a network comprising frontocentral, temporal and parietal nodes in the delta band. However, these results must be interpreted cautiously as coherence may find strong spuriously increased connectivity due to its vulnerability to volume conduction (Vinck et al., 2011). One previous study reported a similar observation, where global field synchronization in the delta band was found to be lower in OCD in comparison to HC (Özçoban et al., 2018). Similarly, a resting-state magnetoencephalography (MEG) study reported decreased connectivity in the delta and theta bands in the OCD group when compared to HC

(Koh et al., 2018). A recent EEG study reported that OCD is associated with deterioration of the Salience Network, accompanied by a failure of the Default Mode Network to deactivate (Thirioux et al., 2022). Impaired FC between these brain regions, as seen in our study, may lead to poor cross-network interactions, and this is known to give rise to clinical symptoms of self-control and attentional deficits that are seen in OCD (Krönke et al., 2020).

The most significant electrode pairs of the identified network correspond to frontal, temporal and central brain regions (Supplemental Table 2), which are closely related to the CSTC circuit (Arikan et al., 2022). Therefore, our finding of reduced connectivity within this circuit is in agreement with the CSTC circuit dysfunction theory of OCD (Gan et al., 2017). Furthermore, alterations of functional nature in OCD, such as neurotransmitter dysfunctions (Nikolaus et al., 2010) and structural grey matter deformities (Radua and Mataix-Cols, 2009) may explain the decreased connectivity findings of OCD. Literature suggests that synchronous brain oscillations in slow frequencies are crucial for cognitive and motivational processes of attention, memory, perception, planning and decision-making (Abramovitch and Cooperman, 2015; Menzies et al., 2008; Sauseng and Klimesch, 2008), all of which are known to be impaired in individuals with OCD. Therefore, impaired functional connectivity in the slow frequency bands may underpin the clinical symptoms of OCD.

In contrast, several clinical and experimental studies have suggested that network synchronization is enhanced within the theta band in OCD and other conditions associated with impaired conflict monitoring (Cavanagh et al., 2011; Voon et al., 2017). Moreover, this finding was inversely correlated with OCD symptom severity, whereby OCD symptom provocation was associated with decreased theta synchronization (Rappel et al., 2018). Furthermore, another study reported significantly higher fronto-occipital theta coherence, indicating dysfunction of subcortical circuitry in OCD (Desarkar et al., 2007b). However, our connectivity analyses did not find significant between-group differences in theta connectivity. This may have been due to inadequate sample size.

Animal and human studies suggest that dysfunction of the CSTC circuit with reduced FC between the brain regions of this circuit may underpin the clinical symptoms of OCD (Posner et al., 2014; Graybiel and Raucht, 2001). Furthermore, within the CSTC circuit, theta and alpha oscillations seem to play a crucial role in maintaining FC (Buzsáki and Draguhn, 2004). In this context, it can be hypothesized, subject to verification, that oscillatory abnormalities in these frequency bands, as reported in individuals with OCD, may be related to or reflect the disruption of coordinated network activity, and thereby lead to clinical symptoms of OCD.

The current study reported no significant differences in the 1/f parameters (slope and intercept) between OCD and HC groups, which potentially indicates that OCD is a condition that exhibits altered oscillatory power, but not alterations to 1/f parameters. Several previous studies have reported 1/f parameter changes in bipolar disorder (Timpe, 2020), attention deficit hyperactive disorder (Robertson et al., 2019) and age-related variations (Pathania et al., 2022). It has been reported that the 1/f slope and offset parameters are functionally relevant to excitation/inhibition balance (Medel et al., 2020) as well as neural firing strength/rate (Voytek and Knight, 2015). The lack of similar findings in our study may be due to OCD being a condition in which these are unaffected.

4.1. Limitations and future directions

The current study has several limitations. While the total sample size was sufficient to identify group-level differences as per the sample size calculation (supplementary S1), inclusion of additional participants would have increased the statistical power and therefore enabled subgroup comparisons to examine potential mediating effects of demographic or clinical variables which may influence EEG. For instance, controlling for mediating effects of medication status may be useful as

the recruited OCD participants were not drug naïve, and were on different classes of medications which may influence EEG activity.

The resting EEG data was collected over a total duration of 3 min, which resulted in a smaller number of epochs than is optimal for connectivity analysis (Miljevic et al., 2021). However, the extent of the influence of epoch number is not established, and the other parameters of our study met the optimal recommendations for connectivity analysis. A principal limitation of the d-wPLI method is its relative insensitivity to true connectivity findings when the coherency phase lies close to 0 or 180, phases at which coherence performs better at identifying true connectivity changes. However, coherence may produce false connectivity results due to its vulnerability to volume conduction (Vinck et al., 2011). Therefore, the findings of the current study should be interpreted cautiously. Furthermore, EEG connectivity studies for OCD are scarce in the literature and therefore, further connectivity analyses of OCD that adhere to the checklist and recommendations (Miljevic et al., 2021) are essential.

The regression analysis of the current study did not show a significant association between increasing OCD symptom severity and reduced connectivity in the delta band. However, a negative trend was identified and the inadequate power may be due to the sample size insufficiency, relative to the variability of the data (Schönbrodt and Perugini, 2013). An alternative explanation could be that the significant oscillatory power and connectivity findings may be present even with low OCD severity.

Although there were no significant associations between OCD severity and EEG findings, we found a significant positive association between the QIDS-SR/BAI and delta band power. This may indicate that the comorbid depressive and anxiety symptoms are more predictive of the EEG pattern than OCD symptoms. However, these analyses were exploratory in nature and not controlled for multiple comparisons. Furthermore, these were self-report, brief measures and therefore, more reliable assessment tools should be used in future studies to arrive at definitive conclusions.

It has been reported that deep brain stimulation (DBS) may be effective in reducing clinical severity of treatment-resistant OCD (Wu et al., 2021). Furthermore, a recent study (Sildatke et al., 2022) found that DBS of the anterior limb of the internal capsule and nucleus accumbens modulated neural activity by reducing medial frontal theta activity and the error-related negativity (ERN; the ERN is known to be altered in OCD, compared to HC (Perera et al., 2022)). Therefore, future OCD studies using other brain stimulation techniques could incorporate pre-to post-treatment EEG analysis to further explore the neuromodulatory effects of these therapies.

The current study is the first to incorporate the eBOSC pipeline in the EEG processing to account for 1/f non-oscillatory activity in an OCD study. Future EEG studies of OCD should also use a similar method in their analyses to validate these results. Due to the poor efficacy and the resultant non-adherence to medications, treating OCD with alternative novel modalities such as non-invasive brain stimulation is becoming popular (Perera et al., 2021). The findings of the current study and other power spectral/connectivity studies may be used to determine parameters for future brain stimulation studies.

4.2. Conclusions

OCD is a mental health condition causing significant disability and the poor understanding of its pathophysiology has made it difficult to establish a definitive treatment. This study aimed to further the current knowledge of the disease by performing EEG power spectral and functional connectivity analyses. Our findings suggest that OCD is associated with raised oscillatory power in the delta and theta frequency ranges in fronto-temporal regions, while no differences were noted in the alpha band. The connectivity findings with the d-wPLI measure showed no differences between groups while a significantly reduced functional connectivity was found in the delta band using the coherence measure.

These findings encourage future research to further explore oscillatory power and connectivity measures as potential biomarkers for OCD.

Declaration of competing interest

In the last 3 years PBF has received equipment for research from Medtronic Ltd, Neurosoft, Nexstim and Brainsway Ltd. He has served on scientific advisory boards for Magstim and LivaNova and acted as a founder and board member for TMS Clinics Australia and Resonance Therapeutics. All other authors report no biomedical financial interests.

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The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. This study was approved by the Monash Health Human Research Ethics Committee (Reference: RES-20-0000-265A).

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jpsychires.2023.05.026>.

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