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Standardized low-resolution electromagnetic tomography in obsessive–compulsive disorder—A replication study

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HIGHLIGHTS

- We compared resting state EEG in 50 obsessive–compulsive patients and 50 controls.
- In patients, increased delta activity was found in the cingulate gyrus.
- Delta is related to dopamine release and reward processing in the ventral striatum.

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ABSTRACT

Previous EEG source localization studies in obsessive–compulsive disorder (OCD) reported ambiguous results. The reason probably lies in different OCD samples included in the studies – obsessive–compulsive subjects selected based on a psychopathology questionnaire (the Symptom Checklist – Revised), drug-naïve OCD cases or patients with a long-term disorder. This study was conceived as a replication of our previous research on OCD population coming to treatment in Prague Psychiatric Centre [9]. We included 50 OCD patients (8 drug-free and 42 medicated with SSRIs) and 50 healthy controls. All subjects were different from those enrolled in the previous study. Resting state EEG was analyzed in 8 frequency bands as well as with 1 Hz frequency resolution using the standardized low-resolution electromagnetic tomography (sLORETA). In OCD, sLORETA indicated low-frequency power excess at 2 and 3 Hz in the cingulate gyrus with maximal *t*-values in Brodmann area 24. The low-frequency activity was unrelated to the severity of clinical symptoms and illness duration but delta power in the right orbitofrontal cortex positively correlated with age of OCD onset. Our results confirm previous finding of the low-frequency excess in the cingulate gyrus in OCD and document the essential role of delta frequencies. Delta activity in the cingulate gyrus is negatively associated with reward-signalling dopamine release in the ventral striatum and increases in states connected with a need for reinforcement. Thus, delta activity could reflect a repetitive need to perform compulsive behaviour in OCD patients.

1. Introduction

Obsessive–compulsive disorder (OCD) is a relatively common neuropsychiatric condition with a lifetime prevalence of more than 2% in general population [16] marked by recurrent intrusive thoughts (obsessions) and/or repetitive behaviours (compulsions). Although OCD pathophysiology is not fully understood, there is a wide-spread agreement on the key role of aberrant functioning or imbalanced interactions in fronto-striatal circuits [2]. The traditional orbitofronto-striatal model including orbitofrontal cortex, ventral striatum, ventral pallidum and mediodorsal thalamus has recently been challenged by a two-network model including orbitofronto-striatal as well as dorsolateral prefronto-striatal loop [12]. However, evidence from performance monitoring [5] and resting state EEG source localization studies [9,18,20] stressed the role of the cingulate gyrus in this disorder. Inverse solution techniques such as low-resolution electromagnetic tomography – LORETA [14,13] demonstrated increased low-frequency as well as beta EEG activity in OCD subjects at rest in this structure. Sherlin and Congedo [18] reported increased amount of beta activity in the cingulate gyrus in obsessive–compulsive subjects (the lower frequency of the beta band, the more anterior its location within the cingulate gyrus). Elevated resting-state beta activity in the cingulate gyrus was later reported also by Velikova et al. [20]. On the other hand, the largest study in this area found increased

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low-frequency activity (2–6 Hz) in the medial frontal cortex, especially anterior cingulate gyrus in OCD [9]. Higher pre-treatment delta in anterior cingulate and/or similarly localized pre-treatment beta were related to a worse treatment response to SSRIs [6] and/or cognitive behavioural therapy [10]. On the other hand, pre-treatment high beta in middle to posterior cingulate gyrus and adjacent areas was positively related to a better response to cognitive-behavioural therapy [10].

Thus, the results of EEG source localization studies are only partially overlapping. They consistently support the role of the cingulate gyrus in OCD but they report abnormalities at low as well as at high frequencies. As discussed in [9] the reason could be due to heterogeneity of OCD, especially to a different obsessive–compulsive population included in EEG studies. Sherlin and Congedo [18] included eight obsessive–compulsive subjects based on a psychopathology questionnaire (the Symptom Checklist – Revised), Velikova et al. [20] included 37 drug-naïve OCD cases and the largest previous study [9] comprised 50 OCD patients who had been suffering from OCD in average for 12.5 years and usually were previously treated.

The aim of this replication study was to compare EEG sources in a different sample of OCD patients from Prague Psychiatric Centre and a different sample of healthy controls. We tested the difference between EEG sources in OCD patients and healthy controls as well as the relationship between EEG activity and clinical variables (age of OCD onset, illness duration and symptom severity).

2. Materials and methods

2.1. Subjects

Fifty right-handed patients diagnosed with OCD according to ICD-10 [22] and DSM-IV [1] criteria were included in the study. Eleven patients had comorbid diagnosis based on ICD-10 (social phobia – 3, mixed anxiety and depressive disorder – 3, panic disorder – 1, generalized anxiety disorder – 1, mental anorexia – 1, dysmorphophobia – 1, personality disorder – 1). Eight patients were drug-free, forty-two patients were medicated with SSRIs. In our previous study we also included drug-free and SSRIs medicated patients and demonstrated that the increased level of low-frequency activity found in OCD was not due to medication use [9]. Medication status was stable for at least one month prior to the study. All patients participated in the 6-week cognitive-behavioural therapy programme, however, EEG was recorded at the beginning of the treatment, in the first week after admission. Therefore cognitive-behavioural therapy did not affect the results of this study.

The demographic and clinical data are summarized in Table 1. The study was approved by the local Ethical committee and all subjects signed informed consent.

2.2. EEG recording and analysis

EEG was recorded during eyes-closed resting state on a Brainscope differential amplifier (Unimedis Ltd., Czech Republic) against the AFz reference. The signal was obtained from 19 scalp locations according to the international 10–20 system using an ECI electrocap (Electro-Cap International, Inc., Eaton, USA) with a sampling rate of 250 Hz. For more details see [9].

Artefacts were removed in EureKa software (NovaTechEEG, Inc., Mesa, Arizona, USA) and if necessary, continuous muscle artefacts were removed as independent components using ICoN software (http://sites.google.com/site/marcocongedo/software/nica). Before analysis, all data were filtered between 1 and 45 Hz, re-referenced against the average reference montage and resampled at 128 Hz for comparability with our older data.

Data analysis was performed by the standardized low-resolution electromagnetic tomography – sLORETA [13], an inverse solution technique estimating the intracranial distribution of electrical activity (current density) in the cortex based on a three shell spherical head model co-registered with Talairach coordinates [19]. In our study we used the LORETA-Key software (Key Institute for Brain-Mind Research, Zurich, Switzerland) and the sLORETA transformation matrix. We obtained current density estimates in 2394 cortical voxels of 7 mm × 7 mm × 7 mm.

Absolute and relative current density was computed in 8 frequency bands delta (2–3.5 Hz), theta (4–7.5 Hz), alpha1 (8–10 Hz), alpha2 (10.5–12 Hz), beta1 (12.5–18 Hz), beta2 (18.5–21 Hz), beta3 (21.5–32 Hz) and gamma (32.5–44 Hz) as well as in 1 Hz frequency bins (2–44 Hz). Data were log-transformed, smoothed with a 14 mm spatial moving average filter and the absolute current density power was normalized. Groups comparisons and correlations with clinical variables were performed on a voxel-wise basis in the MHyT software (NovaTechEEG, Inc.) by means of randomization-permutation statistics. All bands were treated simultaneously in the t-between two-sided max-statistics test guaranteeing that the family-wise type I error did not exceed the nominal level (0.05).

3. Results

3.1. Demographic and clinical data

The two groups did not differ in age, sex, handedness and education level (Table 1). Clinical data (age of OCD onset, illness duration and score at the Yale-Brown Obsessive–Compulsive Scale – Y-BOCS) were available in 40 patients. The mean Y-BOCS score was 21.4 indicating marked psychopathology. Mean age of OCD onset was 20 years and patients had been suffering from OCD for almost 11 years on average.

3.2. EEG sources in OCD patients and healthy controls

In OCD patients compared with healthy controls we found an increased amount of normalized absolute delta power in the anterior and middle cingulate (Fig. 1). The highest t-values were located in Brodmann area (BA) 24. In 1 Hz resolution analysis the difference between OCD patients and healthy controls was found at 2 and 3 Hz (Table 2). t-Values at 4, 5 and 6 Hz in the same region were higher in OCD than in controls, however, statistical significance was not reached even in one-sided test or in single-band testing.

3.3. Medication, gender and comorbid anxiety disorders

Drug-free and medicated patients did not show differences in the mean normalized absolute delta power in the region with significantly increased delta activity in OCD compared to healthy controls ($t = 0.09$, $p = 0.932$). Moreover, medication dosage (the imipramine equivalent of SSRI according to [3]) was not related to the amount of delta activity in this region ($\rho = 0.029$, $p = 0.854$).

EEG source comparison of subjects with and without comorbid anxiety disorder as well as comparison of male and female patients did not yield significant results ($p > 0.05$).

3.4. Correlations with clinical variables

As clinical data were available in 40 OCD patients, correlations with clinical variables were performed only in this OCD subgroup. Normalized absolute delta activity in the right orbitofrontal cortex (BA 11 and 47) was positively related with age of OCD onset ($r \geq 0.51$, $p < 0.05$, Fig. 2). However, no relationship was