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EEG source analysis in obsessive–compulsive disorder

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HIGHLIGHTS

- 50 obsessive -compulsive (OCD) patients and 50 healthy controls analyzed for EEG sources.
- OCD showed elevated low-frequency activity mainly in the medial frontal cortex.
- The findings are of interest for new therapeutic interventions, e.g. neurofeedback.

ABSTRACT

Objective: The goal of this study was to assess the activity of intracortical EEG sources in patients with OCD.
Methods: We compared resting state EEG from 50 OCD patients and 50 matched controls using standardized low-resolution electromagnetic tomography (sLORETA) and normative independent component analysis (NICA). Data were analyzed with 1 Hz frequency resolution. Group ICA was used to separate seven independent components from the control group data. The resulting weights and norms served to derive the same components from the OCD group and to compare their power with controls.
Results: In OCD, sLORETA indicated low-frequency power excess (2–6 Hz) in the medial frontal cortex, whereas group ICA showed increased low-frequency power in a component reflecting the activity of subgenual anterior cingulate, adjacent limbic structures and to a lesser extent also of lateral frontal cortex.
Conclusions: Both methods provided evidence for medial frontal hyperactivation in OCD.
Significance: Our study is the first to use normative ICA in a clinical sample and indicates its potential utility as a diagnostic tool. The findings provide consistent results based on EEG source localization in OCD and are of practical interest for therapeutic interventions.

1. Introduction

Obsessive–compulsive disorder (OCD) is a common neuropsychiatric disorder marked by recurrent intrusive thoughts (obsessions) and repetitive behaviours (compulsions) with a prevalence of 2–3% (Karno et al., 1988). Neuroimaging studies provide evidence for the involvement of cortico-striatal circuits in OCD pathophysiology (Aouizerate et al., 2004). The traditional and most widely accepted model, supported by a large body of scientific evidence, postulates a hyperactive orbitofronto-striatal circuit including orbitofrontal and cingulate cortex, ventral striatum, ventral pallidum, mediodorsal thalamus, hippocampus and amygdala (Menzies et al., 2008a). However, accumulating evidence from various methodological approaches suggests that OCD is mediated by more widely distributed neural networks including also dorsal brain regions such as dorsolateral prefrontal cortex (Gu et al., 2008; Remijnse et al., 2006; van den Heuvel et al., 2005), parietal cortex (Menzies et al., 2008b) or cerebellum (Nabeyama et al., 2008; van den Heuvel et al., 2009). A recent multimodal review and meta-analytic study by Menzies et al. (2008a) proposed a more comprehensive OCD model including two relatively segregated fronto-striatal networks: affective orbitofronto-striatal loop and dorsolateral prefronto-striatal loop which also includes parietal and lateral prefrontal cortex and subserves spatial and attentional functions. Aberrant functioning and imbalanced interactions between fronto-striatal networks might explain clinical OCD symptoms and neuropsychological deficits such as excessive perception of error (Ullsperger and von Cramon, 2006), abnormal

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reward processing (Remijnse et al., 2006), cognitive and behavioural inflexibility (Gu et al., 2008) and difficulty to inhibit prepotent responses (Roth et al., 2007).

Electroencephalographic (EEG) studies based on quantitative analysis reported abnormalities registered at frontal or frontotemporal electrode sites in OCD (e.g. Karadag et al., 2003; Pogarell et al., 2006; Prichep et al., 1993). However, only limited attention has been paid to the localization of generators of the aberrant EEG activity in OCD. EEG sources have been investigated in relation to treatment response (Bolwig et al., 2007; Fontenelle et al., 2006) and in subjects with obsessive–compulsive symptoms (Sherlin and Congedo, 2005) and recently also in drug naïve obsessive–compulsive patients (Velikova et al., 2010). All studies using low-resolution electromagnetic tomography in OCD (Fontenelle et al., 2006; Sherlin and Congedo, 2005; Velikova et al., 2010) reported significant results in anterior cingulate (ACC). In addition, abnormal ACC functioning in OCD has been supported by evoked-potential EEG research that revealed an enhanced error-related negativity (ERN) in OCD patients. ERN is generated after erroneous response or in conflict situations and reflects activity of the performance monitoring system in OCD (Endrass et al., 2008). Its source has been localized near to dorsal ACC (Dehaene et al., 1994) using electrophysiological inverse solution methods as well as simultaneous EEG and fMRI recording (Debener et al., 2005). Functional magnetic resonance studies confirmed the overactivity of the performance monitoring system in OCD and its link with ACC and medial frontal cortex hyperactivation (Fitzgerald et al., 2005; Ursu et al., 2003). It has been hypothesized that an overactive performance monitoring system generates a feeling that something is wrong or not just right and triggers compulsive behaviour, thus providing a possible explanation how brain abnormalities translate in clinical symptoms of OCD (Maltby et al., 2005).

Our study aimed to compare resting state current density power in intracortical sources between OCD patients and control subjects as well as between unmedicated patients and patients medicated with selective serotonin reuptake inhibitors (SSRIs). To address this issue we used two different methods of EEG analysis: standardized low-resolution electromagnetic tomography (sLORETA) and normative independent component analysis (NICA) recently described by Congedo et al. (2010). sLORETA (Pascual-Marqui, 2002) is a widely used inverse solution technique that estimates the intracranial distribution of electrical activity in the cortex based on a head model. ICA is a data-driven (i.e. model-free) technique widely used to decompose the multivariate EEG signal into sources as independent as possible (Congedo et al., 2008; Onton et al., 2006). The assumption of EEG source independence is consistent with the fact that the cortex is organized into functionally distinct areas and that neighbouring and highly connected regions (e.g. via corpus callosum) are likely to fire in synchrony (Onton et al., 2006). Physical and statistical principles supporting the use of decomposition methods based on second-order statistics for EEG data have been reviewed in Congedo et al. (2008).

Whereas sLORETA focuses on voxel by voxel analysis without searching for relationships between them, ICA separates the signal based on its intrinsic relationships. For example, sLORETA may identify abnormal power in a cluster containing a number of independent sources that ICA would split into several components. On the other hand ICA would group correlated sources into the same components, even if they are distant in space from each other. The two methods provide complementary information and their application on the same data may provide a more comprehensive and consistent view, especially considering a high sample size as in this study.

2. Methods

2.1. Subjects

Fifty in-patients diagnosed with OCD according to ICD-10 (World Health Organisation, 1992) and DSM-IV (American Psychiatric Association, 1994) criteria and 50 healthy controls matched for age, sex and handedness were included in the study (Table 1). Exclusion criteria involved concurrent severe or chronic medical disease, substance abuse, mental retardation, organic mental disorder, lifetime history of psychosis, mood disorders, severe head injury and neurosurgery. In addition, controls were required to have no history of any mental disorder. At the time of EEG recording, 20 patients were drug-free and 30 were using SSRIs medication. The medication status was stable for at least 4 weeks prior to the study. Besides the diagnosis of OCD, the rationale to include both SSRIs medicated and drug-free patients was the presence of marked clinical symptoms that could possibly be reflected in EEG. At the same time, the drug-free subgroup served as a reference group allowing a control of the effect of the SSRIs medication. Clinical data in the patient group included age of OCD onset, illness duration and symptom severity (Table 1). Symptom severity was assessed using the Yale–Brown Obsessive–Compulsive Scale (Y-BOCS) (Goodman et al., 1989). The level of general anxiety was measured with the Hamilton Anxiety Rating Scale (HAMA) (Hamilton, 1959). The study was carried out in accordance with the Declaration of Helsinki and written informed consent was obtained from all subjects.

Table 1
Demographic and clinical characteristics of the groups of subjects.

Sample characteristics	OCD ($N = 50$)		Controls ($N = 50$)		OCD-DF ($N = 20$)		OCD-SSRIs ($N = 30$)		Stat. test	OCD vs. controls	OCD-DF vs. controls	OCD-SSRIs vs. controls	OCD-DF vs. OCD-SSRIs
	Mean	SD	Mean	SD	Mean	SD	Mean	SD		p	p	p	p
Demographic													
Age (years)	29.2	5.0	28.4	5.6	28.4	4.7	29.1	5.3	Wilcoxon	0.319	0.303	0.533	0.781
Sex (men:women)	20:30	NA	23:27	NA	7:13	NA	13:17	NA	Chi-square	0.545	0.401	0.816	0.556
Handedness (right:left)	48:2	NA	48:2	NA	19:1	NA	29:1	NA	Chi-square	1.000	0.852	0.879	0.768
Clinical													
Y-BOCS (n = 38)	19.4	8.0	NA	NA	16.4	7.6	21.0	7.9	t-test	NA	NA	NA	0.092
Obsessions	9.8	3.4	NA	NA	9.4	3.6	10.0	3.3	t-test	NA	NA	NA	0.576
Compulsions	9.8	5.0	NA	NA	7.5	4.4	11.0	5.0	t-test	NA	NA	NA	0.040
HAMA (n = 35)	12.7	6.0	NA	NA	12.7	5.0	12.7	6.5	t-test	NA	NA	NA	0.979
Age of onset (years)	16.9	7.2	NA	NA	18.1	6.9	16.1	7.4	t-test	NA	NA	NA	0.406
Illness duration (years)	12.5	7.9	NA	NA	11.2	8.8	13.3	7.4	t-test	NA	NA	NA	0.402

Abbreviations: Y-BOCS, Yale–Brown Obsessive–Compulsive scale; SD, standard deviation; DF, drug-free; SSRIs, selective serotonin reuptake inhibitors; NA, not applied/not applicable.