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Dysfunctional brain circuitry in obsessive–compulsive disorder: Source and coherence analysis of EEG rhythms

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ABSTRACT

Background: Morphological and functional studies suggested involvement of several cortical and subcortical circuitries in patients with obsessive–compulsive disorder (OCD). The aim of the present study was to investigate networks involved in OCD pathophysiology, using power (coupling of EEG bands, low-resolution electromagnetic tomography—LORETA) and coherence analysis in drug naïve patients.
Method: EEG was obtained from 37 drug-naïve patients with OCD and 37 age- and sex-matched controls. Resting EEG was recorded from 29 scalp channels. Coupling (ratio and correlation) between low and high frequencies was analyzed on Fz. For each frequency band, LORETA current density distribution, intra-hemispheric and inter-hemispheric coherence analysis were computed.
Results: OCD had increased current density for delta in the insula and for beta in frontal, parietal and limbic lobes. OCD also had decreased inter-hemispheric coherence and reduced coupling between delta and beta frequencies.
Conclusions: In OCD, increased frontal beta is consistent with previous evidence of frontal dysfunction. Hyperactivity of insular delta sources, together with rhythms decoupling and reduced interhemispheric alpha coherence are consistent with additional involvement of cortico-subcortical functional connections. Combined use of power and coherence analysis may provide functional measures on different levels of involvement of cortico-subcortical circuits in neuropsychiatric disorders.

Introduction

Obsessive–compulsive disorder (OCD) is considered as a manifestation of recurrent cortico-subcortical processing deficit. Among the described five functional cortico-striato-thalamo-cortical loops (Affifi and Bergman, 2005), imaging studies in OCD showed abnormalities in related structures such as orbito-frontal (OF), lymbic and dorsolateral prefrontal (DLPF) loop pathways (Saxena et al., 1999; Alptekin et al., 2001; van den Heuvel et al., 2005; Russell et al., 2003; Valente et al., 2005; Fitzgerald et al., 2000; Cannistraro et al., 2004).

The integrity of thalamo-cortical and cortico-cortical circuits may be investigated by means of the analysis of EEG oscillatory activity, mainly EEG power and coherence.

Several studies have investigated EEG power in OCD (John and Prichep, 2006), with conflicting results, reporting excess alpha and beta activity in the central channels (Prichep et al., 1993), increased delta and decreased alpha (Locatelli et al., 1996; Bucci et al., 2004) or decrease of both delta and beta (Kuskowski et al., 1993). Recent functional imaging techniques based on quantitative EEG *allow* 3-D presentation of EEG current source densities (low-resolution electromagnetic tomography—LORETA, Variable resolution electromagnetic tomography-VARETA). Using these methods, increased beta in the region of cingulate gyrus was found in OCD compared with controls (Sherlin and Congedo, 2005). Increased alpha activity in the thalamus, corpus striatum, orbito-frontal and temporoparietal regions has been reported in OCD patients responders to SSRI (Bolwig et al., 2007), while a lower frontal beta activity was associated with a better treatment response (Fontenelle et al., 2006). One of the main confounding factors when interpreting resting EEG analysis in neuropsychiatric disorders is the effect of psychoactive drug treatment on EEG. In fact, one study was not restricted to drug-free patients (Sherlin and Congedo, 2005) and the other only included patients responders to SSRI (Bolwig et al., 2007).

Whether changes in EEG power are mainly a result of changes in cortical arousal or linked also with changes in deeper structures is still a matter of debate. Some authors have suggested that slow (delta and theta) oscillations are EEG correlates of processes influenced by subcortical activity, whereas fast (alpha and beta) oscillations are generated within cortical networks (Robinson, 1999; Knyazev and Slobodskaya, 2003; Neuper and Pfurtscheller, 2001, View Record in Scopus, Cited By in Scopus (117)). In accordance with this view, it has

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been suggested that coupling between slow and fast frequencies could provide information about subcortical–cortical communication (Knyazev and Slobodskaya, 2003). This hypothesis might be supported by the findings of a link between brain oscillations and behaviour, as well as between brain oscillations and biochemical changes. Moreover, substances known to change cortico-subcortical communication lead also to changes in the coupling of EEG bands (Schutter and van Honk, 2004; van Peer et al., 2008).

EEG coherence is a measure for phase consistency (as a function of frequency) between two EEG signals. It has been considered as an indicator of functional cortico-cortical connections (Thatcher et al., 1986) and reflects the competition between functional segregation and integration between specific brain regions (Nunez et al., 1999). A previous study on EEG coherence in OCD reported increased fronto-occipital theta coherence in the right hemisphere (Desarkar et al., 2007).

It may be hypothesized that the combined rather than separate use of power and coherence analyses might allow a more complex exploration of structures and oscillatory networks playing a role in the pathophysiology of OCD. Moreover, it is also important to exclude that some EEG changes are related to drug treatment and not to the presence of OCD per se. The aim of the present study was to search for neurophysiological correlates of cortico-subcortical processing, using analysis of coherence and power (current source density and coupling between frequency bands) in drug naïve OCD patients. The novel elements of the present work in comparison with previous LORETA studies concern: (i) the selection of patients (a relatively large group without co-morbid diseases and never medicated for OCD symptoms); (ii) combination of LORETA method with two other QEEG approaches (EEG coherence analysis and coupling of EEG rhythms).

Methods

Subjects

Data from 37 patients with OCD (male 15, mean age 31 ± 10.5) were analyzed and compared with data from 37 age and sex matched control healthy subjects (mean age 31.5 ± 10.5). The diagnosis of OCD was made by a certificated psychiatrist, according to DSM IV (American Psychiatric Association, 1994). The selection of participated patients was made following next steps:

The Structured Clinical Interview for DSM IV was used to determine axis I diagnosis. Including criteria was primary diagnosis of OCD according DSM IV. Excluding criteria were: (i) co-morbid DSM IV axis I disorders; (ii) specific medical or neurological conditions that would interfere with evaluation the results of the study (Tourette syndrome, hyperactivity, organic mental diseases, mental retardation, history of psychosurgery, history of epilepsy); (iii) previous or current psychoactive medication. Therefore, all patients were naïve to medications and underwent EEG recording before starting any psychiatric treatment. Their scoring on the Yale-Brown Obsessive Compulsive Scale (Goodman et al., 1989) was: mean total score = 27.8, SD = 4.7, range = 20–40; mean obsessions subscale score = 14.4, SD = 2.2, range = 9–20; and mean compulsions subscale score = 13.2 SD = 3.7, range = 2–20). After complete description of the study to the subjects, written informed consent was obtained to participate in the study, which was approved by the local ethics committee.

EEG recording

Twenty-nine channel EEG with binaural reference was recorded with scalp electrodes mounted on an elastic cap (Electro-cap International, Eaton, OH) according to the 10-20 international system of electrode placement, with additional electrodes placed along the longitudinal axis. The EEG signal was amplified (Synamps Amplifiers, Neuroscan Inc., Herndon, VA), filtered (DC to 50 Hz), and digitized (250 Hz sampling frequency). Bipolar recordings of the electrooculogram and of the EMG from the extensor pollicis brevis (EPB) muscle were obtained to detect eye movement or failure to relax. The data were obtained from a period of 5 min at rest, with the eyes closed.

EEG analysis

During off-line analysis, EEG segments with artifacts were removed by visual inspection of the raw data. At least 70 artifact-free (after rejection of epochs with eye movement, other artifacts or failure in muscle relaxation in the EMG) 2-s epochs were obtained for each subject. The average absolute power and coherence with steps of 1 Hz for each of the 29 monopolar derivations was computed. Then, power and coherence values were averaged for the classical frequency bands: delta (1–3 Hz), theta (4–7 Hz), alpha (8–12 Hz), beta 1 (13–18 Hz), beta 2 (19–21 Hz) and beta 3 (22–30 Hz) according to previous EEG studies using LORETA (Isotani et al., 2001; Gianotti et al., 2007), since each band provides information on different cortico-cortical and cortico-subcortical circuits (Robinson, 1999; Knyazev and Slobodskaya, 2003; Teipel et al., 2009).

LORETA analysis

Power data from each frequency band were used for calculation of current source density using standard LORETA procedure (Pascual-Marqui et al., 1994). Results were computed for the cortical areas of the Talairach probability atlas (Talairach and Tournoux, 1988), with a spatial resolution of 7 mm (2394 voxels). According to LORETA method, statistical group comparison was performed using non-parametric statistical analysis (unpaired *t*-test).

Coherence analysis

For each band, inter-hemispheric and intra-hemispheric coherence were computed from a total of 16 selected electrode pairs. Intra-hemispheric coherence was calculated from 8 electrode pairs, distributed in 4 regions: frontal (left: FP1-F3; right: FP2-F4), centro-parietal (left: C3-P3; right: C4-P4), temporal (left: T3–T5; right: T4–T6) and occipital (left: F3-O1; right: F4-O2). For calculation of inter-hemispheric coherence, other 8 electrode pairs, distributed also in frontal (FP1–FP2, F3–F4, F7–F8), centro-parietal (C3–C4, P3–P4), temporal (T3–T4, T5–T6) and occipital (O1–O2) regions were used. For coherence data, mixed Factorial ANOVA designed for repeated measures (1st level—two factors: intra-hemispheric/ inter-hemispheric; 2nd level—4 regions and 3rd level—6 bands) was applied for detection of group effects, with post-hoc comparisons using unpaired *t*-test.

Coupling between slow and fast rhythms

In order to reduce the number of variables, power in beta frequencies was averaged within the 13–30 Hz interval. Coupling between slow (delta and theta) and fast (beta) frequencies was calculated for each group using the following parameters:

- delta/beta and theta/beta power ratio on Fz
- ratio values were used for intergroup comparison (independent samples *t*-test, two-tailed)
- power values in low (delta, theta) and high (beta) frequencies, measured on Fz were tested for within-group correlation between them (Spearman's correlation test) according to previously reported methods (Schutter and van Honk, 2004).

Results

Source analysis—LORETA

At source analysis of brain rhythms using LORETA, OCD showed significant increase of current source density compared with