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Symptom-specific EEG power correlations in patients with obsessive–compulsive disorder

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Abstract

Neurophysiological studies in patients with obsessive–compulsive disorder (OCD) consistently revealed frontal alterations of cortical activity but otherwise showed inhomogeneous results, conceivably due to variable subgroups with diverse pathomechanisms involved. The aim of this study was to investigate quantitative electroencephalography (EEG) in patients with OCD as compared to healthy controls and to correlate neurophysiological data with clinical variables. EEGs were digitally recorded from 18 unmedicated patients (8 male, mean age 32.4±11.8 years, Yale–Brown Obsessive–Compulsive Scale (Y-BOCS) 15.3±7.9) and 18 matched healthy controls, and analysed quantitatively. The mean frequency of EEG background activity and absolute power in delta, theta, alpha and beta frequency bands were calculated. Mean frequency of background activity was significantly lower in patients as compared to controls (−1.44/s, $p<0.01$), predominantly for the frontal electrode positions. Power spectra revealed increased delta- and decreased alpha-/beta-power in the group of patients ($p<0.05$, patients vs. controls). Correlation analyses showed significant positive correlations of EEG-power with the Y-BOCS sub-scores "obsessions", and negative correlations with the sub-scores "compulsions" (Spearman's correlations, $r_s=+0.48$ to $+0.70$, and -0.47 to -0.6, respectively, $p<0.05$). The data provide evidence of a dysfunction of frontal cortical activity in patients with OCD. The opposite correlations of neurophysiological data and clinical features, i.e. obsessions and compulsions, are suggestive of pathophysiological differences based on the presence of the respective cardinal symptoms of OCD.

Keywords: Obsessive–compulsive disorder; OCD; Obsessions; Compulsions; Quantitative electroencephalography; qEEG; EEG power spectra

1. Introduction

Obsessive–compulsive disorder (OCD) is a chronic condition characterized by the presence of recurrent and often disabling obsessions and compulsions, experienced as intrusive and inappropriate (Stein, 2002). Nowadays there is growing evidence for a neurobiological basis of OCD (Insel, 1992; Stein, 2000). Functional neuroimaging studies with PET, SPECT, or fMRI (Baxter et al., 1988; Machlin et al., 1991; Hollander et al., 1995; Breiter et al., 1996; Saxena et al., 1998; Saxena and Rauch, 2000) support the involvement of the frontal–subcortical circuitry including orbitofrontal hyperactivity.

Functional alterations of cortical activity have also been shown in neurophysiological studies. Early EEG studies in patients with OCD, simply based on visual inspection, have reported a higher rate of abnormal patterns with unspecific slow wave abnormalities (Pacella et al., 1944) and a diffuse non-specific theta-activity (Insel et al., 1983). Although most of the more recent quantitative EEG studies revealed abnormalities predominantly in frontal and frontotemporal regions (Jenike and Brotman, 1984; Prichep et al., 1993; Kuskowski et al., 1993; Locatelli et al., 1996; Karadag et al., 2003), the reported changes were not homogeneous and were partly conflicting. The observations comprised reductions in absolute delta and beta power with a corresponding increase in relative alpha

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Table 1
Demographics and clinical characteristics of the study population: patients with obsessive–compulsive disorder (OCD) and matched healthy controls (HC); clinical scores (Clinical Global Impression/CGI, Hamilton Depression Rating Scale/HAM-D, Beck Depression Inventory/BDI, Yale–Brown Obsessive–Compulsive Scale/Y-BOCS) of the patient group; data presented as mean±S.D. or *n*, where applicable

	OCD	HC
n	18	18
Sex (female/male)	10/8	10/8
Age (years)		
Mean±S.D.	32.4±11.8	33.3±11.3
Range	17–57	21–60
Disease duration (years)		
Mean±S.D.	9.0±5.2	
Range	1.5–22	
CGI	4.9±2.0	
HAM-D	7.2±4.9	
BDI	12.6±8.2	
Y-BOCS	15.3±7.9	
Sub-scores:		
– Obsessions	8.4±6.2	
– Compulsions	6.8±4.9	

power (Kuskowski et al., 1993), or an increase in relative delta– but a decrease in relative alpha – power (Locatelli et al., 1996). Using the neurometrics method, other groups were able to differentiate OCD subgroups, characterized by the pattern of EEG power topography, in terms of the patients' responses to serotonin reuptake inhibitors (Prichep et al., 1993; Hansen et al., 2003). OCD subtypes, defined either clinically by the individual constellation of symptoms or with respect to treatment response, might be a consequence of different pathophysiological patterns, leading to variable and sometimes inconsistent neurophysiological findings.

Therefore, the aim of this study was to assess quantitative EEG parameters in patients with OCD compared to healthy controls, and to investigate, whether there are electrophysiological differences between the patients according to their clinical presentation in terms of the cardinal features "obsessions" and "compulsions".

2. Methods

The study was reviewed and approved by the local ethics committee of the Ludwig–Maximilians–University of Munich and was carried out in accordance with the Declaration of Helsinki. All subjects gave written informed consent for participation in this study, after the design and the procedures had been fully explained.

2.1. Subjects

We investigated 18 inpatients (10 female, 8 male) with obsessive–compulsive disorder (OCD), free of any additional psychiatric (axis I) or medical illnesses, diagnosed by experienced psychiatrists according to DSM-IV and ICD-10 criteria during hospitalization in the Psychosomatic Hospital Windach. The patients were compared with 18 age- and sex-matched healthy controls, mainly recruited from medical students and hospital personnel, who were free of any previous or current neuropsychiatric disorders, exposure to psychotropic medication, or a family history of neurological or psychiatric diseases.

The overall severity of the disease was estimated by the Clinical Global Impression Score (CGI). Signs and symptoms of OCD were clinically rated with the Yale–Brown Obsessive–Compulsive Scale (Y-BOCS) (Goodman et al., 1989b,c), additional depressive symptoms were assessed with the Hamilton Rating Scale for Depression (HAM-D, 17-item version; Hamilton, 1960) and the Beck Depression Inventory (BDI; Beck et al., 1961).

All study participants were right-handed according to the Edinburgh-Handedness Scale (Oldfield, 1971). At the time of the EEG-recordings, both patients and controls were free of any medication with a drug free period of at least 2 weeks prior to the study.

2.2. EEG data acquisition and analysis

For EEG recording, the patients were seated in a sound-attenuated, electrically shielded room in a reclining chair with eyes closed (wakeful-resting condition). Electrodes were placed via electrocaps according to the 10/20 system with Cz as reference and Fpz as ground electrode. Additional electrodes (above the left eye and at the left ocular canthis) were used to record the electrooculogram (EOG) simultaneously. Impedances of all electrodes were below 10 kΩ throughout the session. EEG recordings were obtained during 5 min eyes closed, resting condition using a computerised 19-channel acquisition system (brain electrical signal topography (BEST)) through amplifiers with bandpass from 0.16 to 70 Hz (50 Hz notch filter), digitized at a sample rate of 256 Hz, and were digitally stored for further processing and analysis off-line. Visual inspection for artifact detection was performed off line subsequently by two independent investigators. Any epochs with generalised or local biological or technical artifacts (e.g. muscle activity, electrode artifacts, eye movements/blinks) were identified and excluded. Furthermore, the subjects' wakeful–resting condition during recording was controlled for by the exclusion of any EEG epochs indicating somnolence or reduced alertness, which was

Table 2
Differences in absolute EEG power [μV^2] (OCD patients minus healthy controls) for the respective frequency bands: presentation of mean differences and of the significant differences per electrode position ($^{\dagger}p<0.05$, $^{\ddagger}p<0.01$)

	Delta	Theta	Alpha1	Alpha2	Beta1	Beta2	Beta3
F3-C3	$4.52^{\ddagger}$				$-2.44^{\dagger}$		
F4-C4	$6.59^{\dagger}$				$-2.14^{\ddagger}$	$-1.79^{\dagger}$	
F7-T3				$-4.17^{\ddagger}$	$-2.38^{\ddagger}$		
F8-T4	$8.54^{\dagger}$		$4.13^{\dagger}$	$-3.44^{\dagger}$	$-2.70^{\ddagger}$	$-2.55^{\dagger}$	
T3-T5	$2.64^{\dagger}$			$-30.08^{\ddagger}$	$-5.49^{\ddagger}$		
T4-T6				$-23.81^{\ddagger}$	$-5.03^{\ddagger}$	$-2.87^{\dagger}$	
C3-P3	$2.20^{\ddagger}$			$-18.41^{\ddagger}$	$-3.23^{\ddagger}$	$-1.60^{\dagger}$	
C4-P4				$-15.50^{\ddagger}$	$-2.64^{\ddagger}$		
P3-O1	$2.31^{\dagger}$			$-16.39^{\dagger}$	$-3.53^{\ddagger}$	$-2.16^{\dagger}$	
P4-O2	$2.05^{\ddagger}$			$-14.00^{\dagger}$	$-3.12^{\ddagger}$	$-1.62^{\dagger}$	
Mean	$3.87^{\dagger}$	−0.03	8.94	$-13.42^{\dagger}$	$-3.27^{\dagger}$	$-2.13^{\dagger}$	−0.68

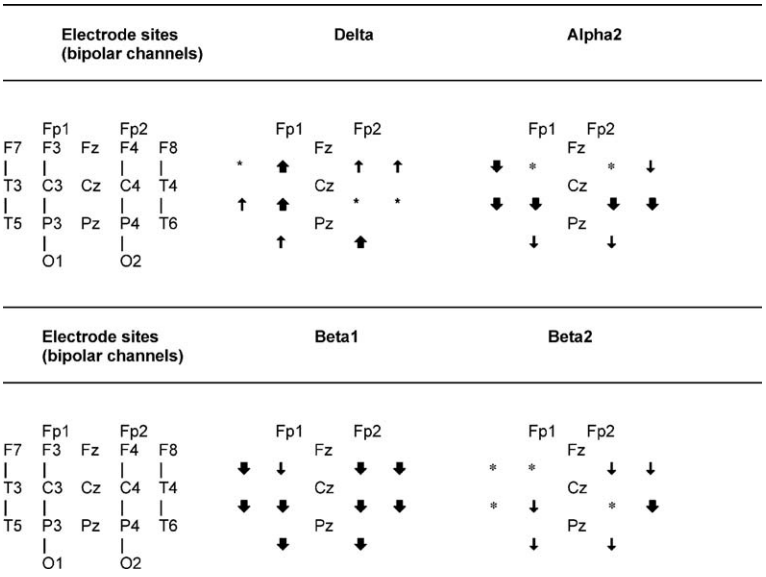

Fig. 1. Significance maps (patients with OCD vs. healthy controls) for absolute EEG power of bipolar channels according to the approximate topography of electrode positions (10/20 system) and bipolar channels. ↓: $p<0.05$, ⬇: $p<0.01$, power decreased in patients with OCD vs. controls. ↑: $p<0.05$, ⬆: $p<0.01$, power increased in patients vs. controls.

defined by the presence of the subjects' regular occipital background activity in less than 50% of the epochs. For this procedure the EEG were stepwise screened in 2 s segments by the two raters. The artifact-free, alertness-controlled data were processed by bipolar transformation (F3-C3, F4-C4, C3-P3, C4-P4, P3-O1, P4-O2, F7-T3, F8-T4, T3-T5, T4-T6) and segmentation into 2-s epochs. At least 20 segments were required from each subject for fast Fourier transform (FFT) and frequency-/power-spectral analysis. FFT allows to quantify the power of brain electric activity as recorded from the single electrodes (or bipolar derivations) and averaged for the total of the EEG segments. For each of the ten bipolar channels as listed above, EEG power was calculated for delta (1–3.5 Hz), theta (3.5–8 Hz), alpha1 (8–10 Hz), alpha2 (10–13 Hz), beta1 (13–18 Hz), beta2 (18–24 Hz), beta3 (24–32 Hz), and total (averaged) frequency band (1–32 Hz). The results per bipolar derivations are given as absolute power [μV^2]. The mean frequency of EEG activity was computed and averaged globally for all electrode positions, for frontal (F3-C3/F4-C4, F7-T3/F8-T4) and for posterior (P3-O1/P4-O1) channels.

2.3. Statistical analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS version 9.0.1 for Microsoft Windows, SPSS Inc., Chicago, IL, USA). Data were tested for normal distribution (one-sample Kolmogorov–Smirnov test) and equality of variance (Levene test). Means and standard deviations were calculated as descriptive analyses of clinical and electrophysiological variables. Group differences were compared using the unpaired *t*-test for independent samples. Within the patient group, correlations between electrophysiological status and clinical data (i.e. obsessive–compulsive sub-scores) were analysed using Spearman's correlation coefficients (r_s). For this procedure the patients' obsessive (Y-BOCS items 1 through 5) and compulsive (items

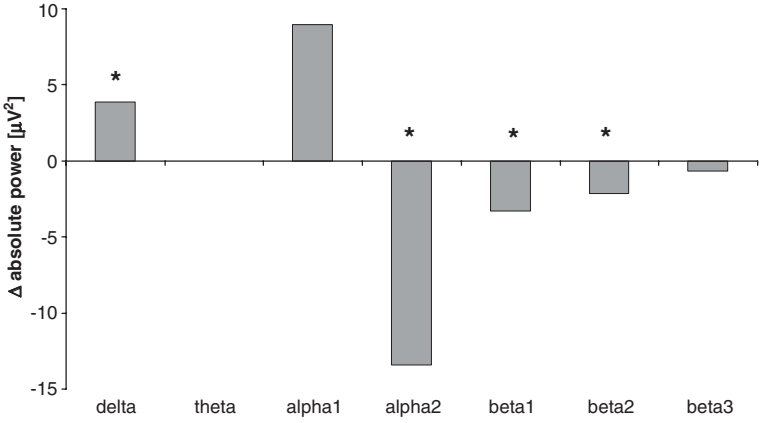

Fig. 2. Differences in mean absolute power [μV^2] per frequency bands (delta, theta, alpha1, 2, beta1, 2 and 3) of patients with OCD versus matched healthy controls; $^*p<0.05$.

Table 3
Mean (±S.D.) frequency [/s] of EEG activity of OCD patients and controls averaged for all bipolar electrode channels (global), for frontal (F3-C3/F4-C4/F7-T3/F8-T4) and posterior/occipital (P3-O1/P4-O2) channels; mean differences between groups and *p*-values (two-tailed, unpaired *t*-test)

	Patients	Controls	Mean difference	*p*-value
Global	7.44±1.28	8.88±1.52	−1.44	$p<0.01$
Frontal	4.35±2.83	6.79±3.36	−2.44	$p<0.05$
Occipital	9.88±1.38	10.07±1.44	−0.19	n.s.

6 through 10) sub-scores were separately correlated with the electrophysiological data (EEG power). p values <0.05 were considered statistically significant. Due to the exploratory character of the study, no alpha correction of the data was performed.

3. Results

3.1. Clinical data

The demographic and clinical data of the study population are given in Table 1. The comparison of demographic data of patients and controls revealed a normal distribution without statistically significant differences.

Disease severity, estimated by the Clinical Global Impression Scores (mean 4.9±2.0), was moderate to marked. The mean obsessive–compulsive score as assessed by the Y-BOCS was 15.3±7.9, with mean obsessive (items 1 through 5) and compulsive (items 6 through 10) sub-scores of 8.4±6.2 (range 0–20), and 6.8±4.9 (range 0–13), respectively. Three patients each scored zero in one of the sub-scores and exclusively suffered from either obsessions or compulsions. However, the number of these more homogeneous subjects was too small for further clinical stratifications, e.g. according to OCD subtypes.

The scales for depression (BDI, HAM-D) revealed only mild comorbid depressive symptoms and were not indicative of significant depressive comorbidity: mean BDI scores were 12.6±8.2 (range 0–28), mean HAM-D scores 7.2±4.9 (range 0–17), with 50% of the patients scoring 7 or less and none of the subjects scoring above 17 (HAM-D).

Table 4
Statistically significant correlations of EEG power spectra in OCD patients and core symptomatology according to Y-BOCS sub-scores "obsessions" and "compulsions"

r_s	Delta	Theta	Alpha2	Beta
Obsessions:				
F7-T3		+0.48†	+0.61‡	
F8-T4			+0.48†	
T3-T5				+0.63‡
C4-P4				+0.54†
P3-O1			+0.69‡	+0.67‡
P4-O2	+0.54†	+0.54†	+0.70‡	+0.62‡
Compulsions:				
T4-T6	−0.60‡		−0.48†	−0.47†
C3-P3	−0.55†			
P3-O1	−0.51†			
P4-O2		−0.54†		

Spearman's correlation coefficients (r_s), †$p<0.05$, ‡$p<0.01$.

3.2. Electrophysiological data

A mean of 71.4±42.3 and 82.9±39.4 (patients and controls, respectively, $p=0.41$, difference not statistically significant) artifact free EEG-segments of 2 s each were eligible for quantitative EEG analysis. The quality of the EEG recordings was comparable in both groups. The number of EEG epochs rejected due to artifacts was not statistically significantly different between patients and controls (78.6±42.3 vs. 67.1±39.4, respectively, $p=0.41$).

Mean absolute power spectra revealed a diffuse and wide spread increase in delta-power in patients versus controls, and a corresponding decrease in alpha2, beta1 and beta2 power (Table 2; Figs. 1 and 2). These differences were statistically significant ($p<0.05$, *t*-test).

EEG background activity, averaged for all electrodes, was significantly slower in the group of patients as compared to controls with a mean frequency of 7.44/s vs. 8.88/s (difference −1.44/s, $p<0.01$, *t*-test).

A separate analysis for the anterior (F3-C3, F4-C4, F7-T3, F8-T4) and posterior (P3-O1, P4-O2) EEG channels revealed, that the significant differences between patients and controls occurred in frontal (−2.44/s, $p<0.05$), but not in posterior regions (−0.19/s, $p=0.68$) (Table 3 and Fig. 3).

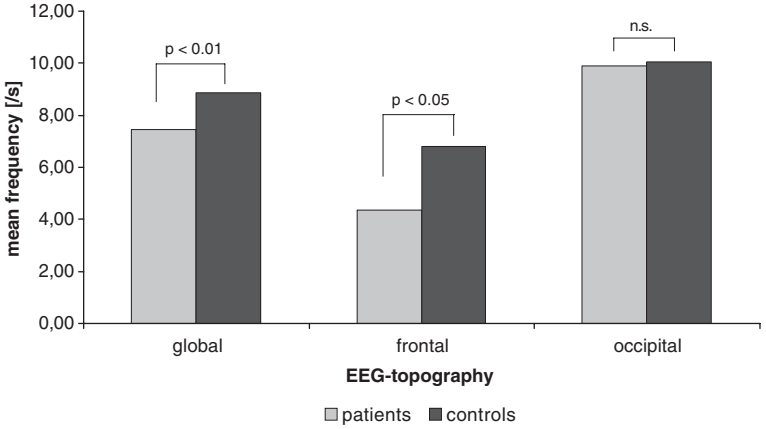

Fig. 3. Mean frequency of EEG activity in patients with OCD and healthy controls; average of all (global), frontal, and occipital electrodes.

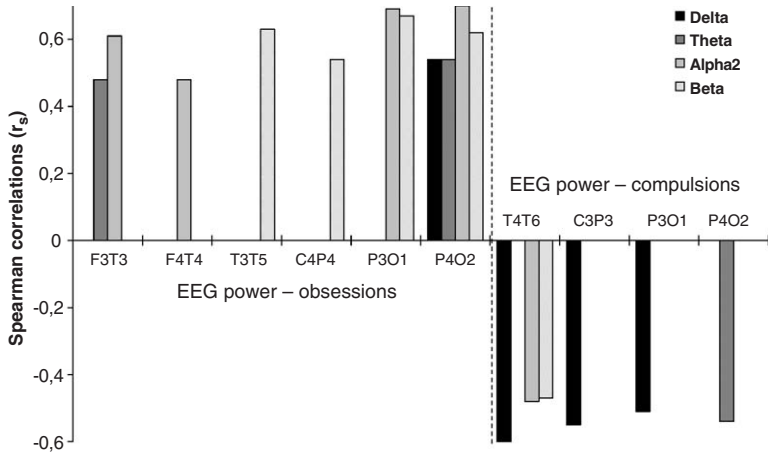

Fig. 4. Significant Spearman correlations (r_s, $p<0.05$) per electrode position between absolute power spectra (delta, theta, alpha2 and beta frequency bands) and clinical data (Y-BOCS sub-scores). Left: "obsessions", right: "compulsions".

3.3. Correlation analyses

Spearman's rank correlation coefficients (r_s) were calculated for the patient group to investigate associations between electrophysiological data and the obsessive and compulsive features of OCD, i.e. sum scores of items 1 through 5 ("obsessions"), and 6 through 10 ("compulsions") of the Y-BOCS.

Spearman correlations showed statistically significant positive correlations of delta, theta, alpha2 and beta1/beta2 power spectra of posterior and temporal electrode pairs with the sub-scores of "obsessions" (r_s between +0.48 and +0.70), whereas "compulsions" correlated negatively (r_s between −0.47 and −0.6), as depicted in Table 4 and Fig. 4.

4. Discussion

According to our data, there are significant neurophysiological alterations in patients with OCD as compared to healthy controls. Basically these results are in line with previous reports by other groups (Jenike and Brotman, 1984; Prichep et al., 1993; Locatelli et al., 1996). Unmedicated patients with OCD showed a significant slowing of EEG background activity in wakeful resting state. Correspondingly, there was an increase in low frequency EEG power (delta), while higher frequency activities (alpha, beta) were reduced. As estimated by a separate analysis per electrode topography, the slowing of EEG activity was pronounced in frontal and frontotemporal regions and, thus, might reflect a different activation pattern in OCD patients within anterior cortical regions.

Frontal changes in OCD have been detected by various functional imaging techniques (Saxena and Rauch, 2000) and might be the substrate of accelerated attentional and cognitive processes in these patients. Electrophysiologically, the frontal hyperactivity in OCD is not characterized by excess frontal alpha and/or beta activity, as might have been expected. However, the topographic distribution of scalp-recorded EEG activity does not allow for an exact localization and spatial allocation of underlying brain functions. In our study, we have rather seen an increase in slow activity, which is quite common in patients with psychiatric disorders and usually is an unspecific finding, interpreted as an indicator of increased central nervous system vulnerability (Herrmann and Winterer, 1996; Hughes and John, 1999). On the other hand, frontal slowing of EEG activity could be explained by the activation of frontal generators for slow (delta) frequencies as postulated by Michel et al. (1992), and as already discussed for OCD patients by Kuskowski et al. (1993). However, differences in frontal slow (delta) activity have to be interpreted with caution, since the frontal EEG activity might have been contaminated by artifacts, especially eye movements or blinks. In our study, we have visually controlled the data for artifacts by two independent investigators, and there were no significant differences between the groups of patients and controls regarding included or rejected EEG epochs. Thus the significant differences in delta power seem to be reliable findings in our investigation.

The clinical correlations between electrophysiological data and the Y-BOCS sub-scores "obsessions" and "compulsions" are less clear throughout the literature, but nevertheless of clinical interest. In our cohort of 18 unmedicated subjects, there were statistically significant correlations between mean EEG power and the respective clinical variables. It is remarkable that these associations were in the opposite direction for the "obsessive" and "compulsive" sub-scores.

Thus our results provide evidence that different neurophysiological mechanisms might be involved in the generation of the two core features of OCD. Patients presenting with high levels of obsessions had higher absolute EEG power measures, especially for the faster (alpha2-, beta1-) frequencies, whereas patients with high compulsion scores were likely to have lower absolute EEG power, especially of slower frequencies. As compared with compulsions, highly expressed obsessions might favor faster (alpha and beta) EEG activity, conceivably as a consequence of increased mental activity.

Whereas Prichep et al. (1993) and Hansen et al. (2003) have been able to identify pathophysiological subgroups within the OCD population, sharing a common clinical expression, but exhibiting differences with regard to their response to serotonergic medication (responders vs. non-responders), we have found evidence for symptom-related electrophysiological

alterations in unmedicated patients with OCD. The data add to the findings of other groups, who as well revealed influences of demographic or clinical characteristics, such as sex, character and severity of the symptoms, or confounding effects of depression, on neurophysiological variables (Tot et al., 2002; Karadag et al., 2003). QEEG, although of limited diagnostic use in psychiatry, should be considered as a tool to investigate the pathophysiological background of psychiatric disorders. Our findings might contribute to the understanding of the neurobiological basis of OCD and further point at the importance of OCD subtypes. Clinical symptoms are often heterogeneous and might interfere with the consistency of neurobiological data reported earlier. In consideration of a substantial number of OCD patients, who are refractory to treatment (Goodman et al., 1989a, 1990), the detection and characterization of pathophysiologically distinct subgroups could be of clinical relevance and might help to improve current therapeutic strategies. There is some empirical evidence, that the pattern of clinical presentation, i.e. the proportion of obsessive and compulsive symptoms contributes to the degree of treatment efficacy (Black et al., 1998; Goodman, 1999). The presented data of our study are preliminary and explorative and, due to the limited number of subjects, it was not possible to further stratify the patients according to defined subgroups neither under clinical nor under treatment aspects. These limitations have to be addressed in further studies with the prospective investigation of more homogeneous OCD subtypes including the course of the symptoms under treatment. Nevertheless, our results are suggestive of neurophysiological differences in clinical subgroups, which consequently might be important for differences with respect to the subjects' responses to medication.

References

Baxter Jr., L.R., Schwartz, J.M., Mazziotta, J.C., Phelps, M.E., Pahl, J.J., Guze, B.H., Fairbanks, L., 1988. Cerebral glucose metabolic rates in nondepressed patients with obsessive–compulsive disorder. Am. J. Psychiatry 145, 1560–1563.

Beck, A.T., Ward, C.H., Mendelson, J., Mock, J., Erbaugh, J., 1961. An inventory for measuring depression. Arch. Gen. Psychiatry 4, 564–571.

Black, D.W., Monahan, P., Gable, J., Blum, N., Clancy, G., Baker, P., 1998. Hoarding and treatment response in 38 nondepressed subjects with obsessive–compulsive disorder. J. Clin. Psychiatry 59, 420–425.

Breiter, H.C., Rauch, S.L., Kwong, K.K., Baker, J.R., Weisskoff, R.M., Kennedy, D.N., Kendrick, A.D., Davis, T.L., Jiang, A., Cohen, M.S., Stern, C.E., Belliveau, J.W., Baer, L., O'Sullivan, R.L., Savage, C.R., Jenike, M.A., Rosen, B.R., 1996. Functional magnetic resonance imaging of symptom provocation in obsessive–compulsive disorder. Arch. Gen. Psychiatry 53, 595–606.

Goodman, W.K., 1999. Obsessive–compulsive disorder: diagnosis and treatment. J. Clin. Psychiatry 60 (S18), 27–32.

Goodman, W.K., Price, L.H., Rasmussen, S.A., Delgado, P.L., Heninger, G.R., Charney, D.S., 1989a. Efficacy of fluvoxamine in obsessive–compulsive disorder. A double-blind comparison with placebo. Arch. Gen. Psychiatry 46, 36–44.

Goodman, W.K., Price, L.H., Rasmussen, S.A., Mazure, C., Delgado, P., Heninger, G.R., Charney, D.S., 1989b. The Yale–Brown Obsessive Compulsive Scale: II. Validity. Arch. Gen. Psychiatry 46, 1012–1016.

Goodman, W.K., Price, L.H., Rasmussen, S.A., Mazure, C., Fleischmann, R.L., Hill, C.L., Heninger, G.R., Charney, D.S., 1989c. The Yale–Brown Obsessive Compulsive Scale: I. Development, use, and reliability. Arch. Gen. Psychiatry 46, 1006–1011.

Goodman, W.K., Price, L.H., Delgado, P.L., Palumbo, J., Krystal, J.H., Nagy, L. M., Rasmussen, S.A., Heninger, G.R., Charney, D.S., 1990. Specificity of serotonin reuptake inhibitors in the treatment of obsessive–compulsive disorder. Comparison of fluvoxamine and desipramine. Arch. Gen. Psychiatry 47, 577–585.

Hamilton, M., 1960. A psychiatric rating scale for depression. J. Neurol. Neurosurg. Psychiatry 23, 56–62.

Hansen, E.S., Prichep, L.S., Bolwig, T.G., John, E.R., 2003. Quantitative electroencephalography in OCD patients treated with paroxetine. Clin. Electroencephalogr. 34, 70–74.

Herrmann, W.M., Winterer, G., 1996. Electroencephalography in psychiatry–current status and outlook. Nervenarzt 67, 348–359.

Hollander, E., Prohovnik, I., Stein, D.J., 1995. Increased cerebral blood flow during *m*-CPP exacerbation of obsessive–compulsive disorder. J. Neuropsychiatry Clin. Neurosci. 7, 485–490.

Hughes, J.R., John, E.R., 1999. Conventional and quantitative electroencephalography in psychiatry. J. Neuropsychiatry Clin. Neurosci. 11, 190–208.

Insel, T.R., 1992. Neurobiology of obsessive compulsive disorder: a review. Int. Clin. Psychopharmacol. 7 (S1), 31–33.

Insel, T.R., Donnelly, E.F., Lalakea, M.L., Alterman, I.S., Murphy, D.L., 1983. Neurological and neuropsychological studies of patients with obsessive–compulsive disorder. Biol. Psychiatry 18, 741–751.

Jenike, M.A., Brotman, A.W., 1984. The EEG in obsessive–compulsive disorder. J. Clin. Psychiatry 45, 122–124.

Karadag, F., Oguzhanoglu, N.K., Kurt, T., Oguzhanoglu, A., Atesci, F., Ozdel, O., 2003. Quantitative EEG analysis in obsessive compulsive disorder. Int. J. Neurosci. 113, 833–847.

Kuskowski, M.A., Malone, S.M., Kim, S.W., Dysken, M.W., Okaya, A.J., Christensen, K.J., 1993. Quantitative EEG in obsessive–compulsive disorder. Biol. Psychiatry 33, 423–430.

Locatelli, M., Bellodi, L., Grassi, B., Scarone, S., 1996. EEG power modifications in obsessive–compulsive disorder during olfactory stimulation. Biol. Psychiatry 39, 326–331.

Machlin, S.R., Harris, G.J., Pearlson, G.D., Hoehn-Saric, R., Jeffery, P., Camargo, E.E., 1991. Elevated medial–frontal cerebral blood flow in obsessive–compulsive patients: a SPECT study. Am. J. Psychiatry 148, 1240–1242.

Michel, C.M., Lehmann, D., Henggeler, B., Brandeis, D., 1992. Localization of the sources of EEG delta, theta, alpha and beta frequency bands using the FFT dipole approximation. Electroencephalogr. Clin. Neurophysiol. 82, 38–44.

Oldfield, R.C., 1971. The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia 9, 97–113.

Pacella, B., Polation, P., Nagle, S., 1944. Clinical and EEG studies in obsessive compulsive states. Am. J. Psychiatry 100, 830–838.

Prichep, L.S., Mas, F., Hollander, E., Liebowitz, M., John, E.R., Almas, M., DeCaria, C.M., Levine, R.H., 1993. Quantitative electroencephalographic subtyping of obsessive–compulsive disorder. Psychiatry Res. 50, 25–32.

Saxena, S., Rauch, S.L., 2000. Functional neuroimaging and the neuroanatomy of obsessive–compulsive disorder. Psychiatr. Clin. North Am. 23, 563–586.

Saxena, S., Brody, A.L., Schwartz, J.M., Baxter, L.R., 1998. Neuroimaging and frontal–subcortical circuitry in obsessive–compulsive disorder. Br. J. Psychiatry 173 (S35), 26–37.

Stein, D.J., 2000. Neurobiology of the obsessive–compulsive spectrum disorders. Biol. Psychiatry 47, 296–304.

Stein, D.J., 2002. Obsessive–compulsive disorder. Lancet 360, 397–405.

Tot, S., Ozge, A., Comelekoglu, U., Yazici, K., Bal, N., 2002. Association of QEEG findings with clinical characteristics of OCD: evidence of left frontotemporal dysfunction. Can. J. Psychiatry 47, 538–545.