



Symptom provocation alters behavioral ratings and brain electrical activity in obsessive–compulsive disorder: a preliminary study

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Abstract

Regional brain activity was measured using quantitative electroencephalography (EEG) in six patients with obsessive–compulsive disorder (OCD) during live and imaginal exposure to feared contaminants. OCD symptoms increased significantly from baseline levels during live and imaginal exposures. However, live exposure provoked significantly more OCD symptoms than imaginal exposure. There was a significant change in the anterior-to-posterior scalp distribution of alpha power during live exposure. These preliminary results suggest that: (1) live exposure is more effective than imaginal exposure in altering behavioral and electrophysiological measures; and (2) live exposure is associated with regional EEG changes in OCD. © 2000 Elsevier Science Ireland Ltd. All rights reserved.

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1. Introduction

People with obsessive–compulsive disorder (OCD) have been reported to have increased blood flow in frontal brain regions, as compared to other brain regions, when their symptoms are triggered by feared stimuli. These changes during symptom provocation have been detected with both positron emission tomography (PET: McGuire et al., 1994; Rauch et al., 1994) and functional magnetic resonance imaging (fMRI: Breiter et al., 1996). Because increases in blood flow may reflect increases in neural activity, electrophysiological changes would also be expected in frontal brain regions relative to other brain regions. Using quantitative electroencephalography (EEG), researchers have found regional EEG abnormalities in patients with other anxiety disorders (Bruder et al., 1997; Wiedemann et al., 1999; Davidson et al., 2000) and in subjects selected for trait anxiety (Heller et al., 1997). In OCD, resting EEG findings have been variable and conflicting (e.g. Kuskowski et al., 1993; Prichep et al., 1993; Molina et al., 1995). However, no one has published EEG findings of OCD patients during symptom provocation.

This brief report provides the first characterization of regional brain electrical activity in OCD during symptom provocation. Symptoms were provoked by exposing OCD patients with con-

tamination fears to real feared contaminants (i.e. live exposure), as has been done in prior brain imaging studies (e.g. Rauch et al., 1994; Breiter et al., 1996). The EEG analysis focused primarily on alpha power because decreases in alpha power have been used as an index of increased brain activation (Shagass, 1972; Bruder et al., 1997; Heller et al., 1997; Wiedemann et al., 1999; Davidson et al., 2000). Based on the brain imaging literature, it was hypothesized that OCD patients would show increased brain activation (i.e. decreased alpha power) in frontal brain regions, relative to other brain regions, during live exposure. Obsessive–compulsive symptoms and brain electrical activity were also measured during exposure to imagined contaminants (imaginal exposure) to explore the comparability of the behavioral and/or EEG changes produced by live and imaginal exposure.

2. Materials and methods

Six patients who met DSM-IV criteria for OCD as their primary diagnosis participated in this study. Demographic and clinical features of each patient are shown in Table 1. Three were male, and three were female. The mean age was 34.5 years (S.D. = 2.2). At the time of the EEG recordings, three patients were unmedicated, and three

Table 1
Demographic and clinical features of six OCD patients^a

Patient No.	Age (years)	Sex	Age of onset	Y-BOCS score	CGI-severity	HAM-D score	Medication
1	35	M	6	21	5	10	–
2	37	M	17	24	5	7	Fluoxetine 70 mg/day
3	33	F	23	29	5	10	–
4	36	F	16	22	6	0	Fluoxetine 80 mg/day
5	31	F	10	29	6	9	–
6	35	M	9	22	4	12	Fluoxetine 60 mg/day

^aAbbreviations: M, male; F, female; Y-BOCS, Yale–Brown Obsessive Compulsive Scale; CGI-severity, Clinical Global Impression scale-severity; HAM-D, Hamilton Depression Scale, 17 item.

were maintained on a stable dose of fluoxetine (all for >2 months), but remained clinically symptomatic (see Table 1). None of the patients had a current medical or neurological disorder, a lifetime history of a psychotic disorder, current major depressive or dysthymic disorder, or alcohol/substance abuse or dependence in the past 6 months. The three patients on fluoxetine had a history of major depressive disorder. Eligibility was determined by one of us (H.B.S.) during a comprehensive psychiatric assessment. The psychiatric history was confirmed by the Structured Clinical Interview for DSM-IV (First et al., 1996). Written informed consent was obtained after a full description of the study procedures.

On the day of the EEG recordings, clinical symptoms were assessed by one of us (H.B.S.) using the Yale–Brown Obsessive Compulsive Scale (Y–BOCS; Goodman et al., 1989a,b), the Hamilton Depression Scale (HAM-D, 17-item version; Hamilton, 1960), and the Clinical Global Impression (CGI) scale for severity (Guy, 1976). Clinical symptoms of each patient are shown in Table 1. At the time of the EEG recordings, the mean Y–BOCS score was 24.5 (range 21–29; S.D. = 3.6), and the mean HAM-D score was 8 (range 0–12; S.D. = 4.2).

All six patients had contamination fears and washing rituals, although what they specifically feared differed (e.g. dirt, ‘germs’, bodily secretions). That all had contamination fears permitted standardization of the provocation paradigm as follows: first, all patients held between both palms a sterile gauze pad (clean control condition); next, all patients held a sterile gauze pad while imagining it was contaminated with a feared substance (imaginal exposure condition); finally, all patients held a gauze pad that had touched a feared substance (live exposure condition). This paradigm is similar to that used in OCD brain imaging studies (e.g. Zohar et al., 1989; Rauch et al., 1994; Breiter et al., 1996). Less than 10 min elapsed between the end of one test condition and the start of the next. The presentation of the test conditions was not counterbalanced because preliminary studies by us and others (e.g. Rauch et al., 1994) suggested that live exposure can cause a sustained provocation of OCD symptoms. Behav-

ioral data were collected during each test condition, as described below.

In addition to these three test conditions, behavioral data were also recorded during two resting periods (1,2) when the patients held nothing. Resting 1 occurred just prior to the test conditions; Resting 2 occurred following the live exposure condition after the patients had been allowed to ritualize (i.e. wash). The aim of Resting no. 1 was to permit habituation to the recording booth and procedures; the aim of Resting no. 2 was to explore whether the patients’ OCD symptoms would return to baseline levels within 30 min if permitted to ritualize.

Scalp EEG activity was recorded during the three test conditions while patients sat quietly in a sound-attenuated booth. Patients were instructed to move as little as possible. Each test condition had four 2-min intervals of EEG recordings, for a total of 8 min of EEG recording per condition. During each 2-min interval, the patients’ eyes were either open or closed, in a counterbalanced order (i.e. OCCO or COOC). For each test condition, the appropriate provocation (as described above) was repeated exactly for each 2-min interval. Immediately after each 2-min EEG interval, patients used a 100-point visual analogue scale (VAS) to rate the severity of their OCD symptoms (e.g. obsessive fears and/or urges to ritualize) during that interval (no OCD symptoms = 0; the worst OCD symptoms ever = 100). This scale was adapted from similar scales used in prior brain imaging studies in OCD (e.g. Zohar et al., 1989; Rauch et al., 1994; Breiter et al., 1996). Both resting periods were also divided into four 2-min intervals, and behavioral data were collected for these intervals as described above.

Scalp EEG was recorded from four midline electrodes (Fz, Cz, Pz, Oz) and 13 lateral electrode pairs, using a standard electrode cap (Electro Cap International, Inc.) with a nose reference. Standard Beckman Ag/AgCl electrodes at supra- and infra-orbital sites surrounding the right eye were used to monitor eyeblinks and vertical eye movements (bipolar), and electrodes at right and left outer canthi monitored horizontal eye movements (bipolar). All electrode impedances were below 5 k Ω . EEG was recorded through a Grass

neurodata acquisition system at a gain of 10 k (5 k for eye channels), with a bandpass of 0.01–30 Hz.

EEG data were processed as described elsewhere (Bruder et al., 1997). Briefly, a PC-based EEG acquisition system (NeuroScan) acquired and digitized the data at a sample rate of 100/s. Data were then segmented into consecutive 1.28-s epochs every 0.64 s (50% overlap). Epochs contaminated by blinks, eye movements, and movement-related artifacts were manually excluded. The direct current offset of each epoch was then removed, and the EEG was tapered over the entire 1.28 s using a Hanning window to suppress spectral side lobes (Bendat and Piersol, 1971).

EEG data underwent a power spectrum analysis using a Fast Fourier Transform. The analysis focused primarily on alpha power because it has been used routinely as an index of cortical activation (Shagass, 1972; Bruder et al., 1997; Heller et al., 1997; Wiedemann et al., 1999; Davidson et al., 2000). Alpha power was averaged for artifact-free epochs spanning the recording periods for each subject, and subsequently integrated over 7.8–11.7 Hz. Common logarithms of alpha power were computed to normalize the data. Power in the beta (12.5–18 Hz) and theta (4.7–7 Hz) bands was also computed to determine the specificity of the regional effects to the alpha band.

In contrast to resting EEG studies, EEG recordings were contaminated by a greater amount of movement-related (e.g. eye blinks) and tonic muscle-related (i.e. electromyographic) artifact because of the use of an effective anxiety provocation paradigm. To minimize these sources of noise, data were analyzed only for the eyes closed condition and only from the midline electrodes (Fz, Cz, Pz, Oz). EEG recordings when eyes were open were contaminated by sufficient artifact to preclude a valid analysis of those data; likewise, EEG recordings from lateral electrodes had variable amounts of tonic, muscle-related artifact in some subjects that was not seen at midline electrodes. For each patient, EEG data from the midline electrodes during the two 2-min eyes closed periods were averaged for each test condition. Behavioral ratings for the three test conditions reflect the same intervals as the EEG data.

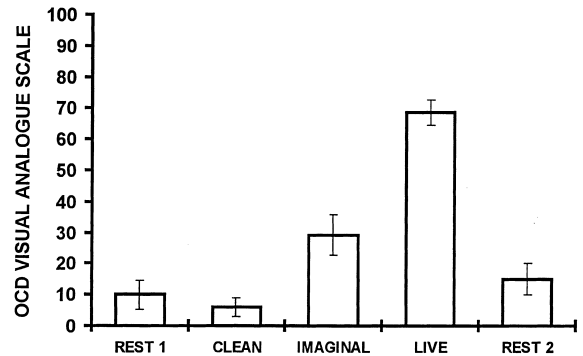


Fig. 1. The mean severity (and S.E.) of OCD symptoms (as measured by the OCD visual analogue scale) in six patients during the three test conditions (CLEAN, clean control; IMAGINAL, imaginal exposure; and LIVE, live exposure) and the two resting periods (Rest 1, Rest 2).

Paired *t*-tests were used to compare OCD symptoms between the three test conditions and between the two resting periods. To examine the hypothesized relative decreases in frontal alpha power during live exposure, a repeated measures analysis of variance (ANOVA) was conducted, using electrode position (Fz, Cz, Pz, Oz) and condition (clean control, live exposure) as within-subject factors. An exploratory ANOVA also evaluated regional differences in alpha power between the imaginal exposure and clean control conditions, using electrode position (Fz, Cz, Pz, Oz) and condition (clean control, imaginal exposure) as factors. *F* ratios were evaluated using degrees of freedom computed using the Greenhouse–Geisser epsilon correction (Jennings and Wood, 1976), where appropriate, to counteract heterogeneity of variance–covariance matrices associated with repeated measures. In all cases, two-tailed tests were used. A *P* value < 0.05 was considered significant.

3. Results

The mean ratings of OCD symptoms for the six patients during the three test conditions and the two resting periods are displayed in Fig. 1. All patients reported a marked increase in OCD symptoms when their symptoms were provoked by

Table 2

Mean log alpha power at midline electrode sites during live exposure and clean control conditions

Electrode site	Live exposure (S.D.)	Clean control (S.D.)	Paired <i>t</i> -tests
Fz	0.136 (0.344)	0.138 (0.390)	$t = 0.048$, d.f. = 5, $P = 0.96$
Cz	0.428 (0.502)	0.407 (0.539)	$t = 0.553$, d.f. = 5, $P = 0.604$
Pz	0.799 (0.734)	0.757 (0.773)	$t = 1.21$, d.f. = 5, $P = 0.281$
Oz	0.800 (0.720)	0.731 (0.767)	$t = 2.56$, d.f. = 5, $P = 0.051$

feared contaminants. While OCD symptoms during live exposure ($t = 9.81$, d.f. = 5, $P = 0.000$) and imaginal exposure ($t = 2.59$, d.f. = 5, $P = 0.049$) were both significantly increased compared to the clean control condition, symptoms during live exposure were significantly greater than those during imaginal exposure ($t = 11.71$, d.f. = 5, $P = 0.000$). Patients were allowed to ritualize (i.e. wash) after the live exposure. OCD ratings after washing approached baseline levels in all patients within 30 min (Resting 1 vs. Resting 2: $t = 0.69$; d.f. = 4; $P = 0.528$).

Alpha activity showed a typical topography with a posterior maximum. In the ANOVA comparing the live exposure and clean control conditions, this was supported by a robust electrode effect ($F = 10.14$; d.f. = 1.48, 7.39; $P = 0.010$). The overall condition effect was not significant ($F = 0.93$; d.f. = 1, 5; $P = 0.378$). However, as shown in Table 2, there was a small decrease in mean log alpha power at the anterior brain site (Fz) and a relatively large increase at the posterior brain sites (Pz, Oz) in the live exposure as compared to the clean control. This shift in the scalp distribution of alpha was supported by a significant condition \times electrode interaction ($F = 5.13$; d.f. = 1.50, 7.51; $P = 0.046$). This shift was not present in either the theta or beta bands (for theta and beta bands, all P values > 0.120 for the condition and condition \times electrode interactions). Post-hoc paired *t*-tests comparing the live exposure and clean control conditions at each midline electrode site were not significant, although there was a trend at the Oz site (Table 2).

When alpha activity during imaginal exposure was compared to the clean control condition, there was a significant electrode effect ($F = 15.37$,

d.f. = 1.61, 8.03, $P = 0.002$), but no significant condition ($F = 1.075$, d.f. = 1, 5, $P = 0.347$) or condition \times electrode interactions ($F = 1.082$, d.f. = 1.020, 5.102, $P = 0.347$). Likewise, when all three test conditions were incorporated into a single ANOVA, there was a significant electrode effect ($F = 14.74$, d.f. = 1.62, 8.09, $P = 0.003$), but no significant condition ($F = 1.05$, d.f. = 1.03, 5.14, $P = 0.355$) or condition \times electrode ($F = 0.802$, d.f. = 1.05, 5.27, $P = 0.416$) interactions.

4. Discussion

To our knowledge, this is the first study to describe changes in brain electrical activity during symptom provocation in OCD patients. Although the findings are preliminary, two results are worth highlighting. First, as demonstrated by others (Zohar et al., 1989; McGuire et al., 1994; Rauch et al., 1994; Breiter et al., 1996; Cottraux et al., 1996; Kim et al., 1997), OCD symptoms can be reliably provoked in a laboratory setting when OCD patients are exposed to naturally feared stimuli. The present study found that live exposure was significantly more effective at provoking OCD symptoms than imaginal exposure in patients with contamination fears, and that only live exposure resulted in significant changes in alpha activity. This is an important observation, given that several brain imaging studies in OCD have used imaginal exposure in all or some of their patients (Rauch et al., 1994; Breiter et al., 1996; Cottraux et al., 1996). Our results suggest that live exposure and imaginal exposure should not be presumed to be interchangeable (also see Zohar et al., 1989).

Second, despite the small sample size, there was a significant shift in the anterior-to-posterior scalp topography of alpha power during live exposure as compared to the clean control condition. Specifically, the increase in OCD symptoms during live exposure was associated with an increase in posterior relative to anterior alpha, although the small sample size precludes a confident identification of the contribution specific electrode sites make to this effect. No significant shifts were found in the beta or theta bands, indicating that the topographical shift was specific to alpha. Decreases in alpha power have been used as an index of increased brain activation (Shagass, 1972; Bruder et al., 1997; Heller et al., 1997; Wiedemann et al., 1999; Davidson et al., 2000). Consequently, the observed changes in alpha topography are interpreted to reflect a relative shift in brain activation from posterior to anterior regions, and are thereby consistent with brain imaging studies describing increased frontal activation during symptom provocation in OCD (McGuire et al., 1994; Rauch et al., 1994; Breiter et al., 1996).

These preliminary findings should be replicated with a larger sample of unmedicated patients who exhibit a wider range of OCD symptoms. Likewise, appropriate patient and normal control groups are needed to establish the specificity of these findings to OCD symptoms, since live and imaginal exposures also trigger non-specific symptoms of anxiety (Zohar et al., 1989; Rauch et al., 1994; Kim et al., 1997). Finally, the possibility that the results were affected by the sequence of stimulus presentation (i.e. imagined stimuli were always presented prior to live stimuli) cannot be excluded. Nonetheless, these preliminary findings suggest the following: (1) live exposure is more effective than imaginal exposure at provoking OCD symptoms; and (2) symptom provocation triggered by live exposure is associated with regional EEG changes in OCD.

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