Abnormal visual event-related potentials in obsessive-compulsive disorder without panic disorder or depression comorbidity

F. Di Russo\textsuperscript{a}, G. Zaccara\textsuperscript{b}, A. Ragazzoni\textsuperscript{b}, S. Pallanti\textsuperscript{c,*}

\textsuperscript{a}IRCCS S. Lucia, Rome, Italy
\textsuperscript{b}Clinical Neurophysiology Unit, Florence Health Care Service, Florence, Italy
\textsuperscript{c}Institute of Neurosciences, V.le Ugo Bassi 1, 50137 Florence, Italy

Abstract

Visual event-related potentials and spline map topography during a discriminative response task (DRT) were studied in 8 obsessive-compulsive disorder (OCD) patients without comorbidity for panic disorder or depression and in 12 age-matched controls. In the DRT task (like in a go/no-go task) the subject had to press a button when the target stimuli appeared and had to retain the response when the non-target stimulus appeared (vertical bars were intermixed with an equal probability of horizontals). OC patients had greater N1 latency than controls and their N1 and P3 amplitude was larger for the target stimuli, but not for non-target stimuli. In the normals, non-target stimuli (no-go task) produced a larger activation than target stimuli (go task). In the OCD patients the target stimuli produced the same large activation as the non-target. These findings are consistent with theories that consider OCD to be an attentional disorder deriving from a misallocating of cognitive resources. Moreover, spline map topography confirmed that P3 hyperactivation is localised principally on the frontal lobes.

\textcopyright{} 2000 Elsevier Science Ltd. All rights reserved.

Keywords: OCD; Comorbidity; P3; Cognitive functions; Evoked potentials; DRT

1. Introduction

Cognitive dysfunction has been documented through the study of event-related potentials (ERPs) in some OCD patients, even though there is still disagreement about whether alterations are related to a dysfunction of neural structures underlying the information processing (Purcell et al., 1998), or whether they may be considered as an expression of a metacognitive effect as a result of the anxiety component of the disorder (McGuire et al., 1994).

Previous studies with auditory modality ERP have shown reduced P3 latencies in OCD patients than normal controls with an increasing task difficulty and larger amplitude negativity than normal controls in the N200 region (Towey et al., 1990). N200 amplitude has been generally reported as larger in OCD patients than in normals (De Groot et al., 1997).

Tendency to overfocus in attentional performances has been suggested by Towey et al. (1994) in an interesting experiment where, in comparison to healthy controls, in OCD patients reduced P3 amplitudes were recorded with target stimulus but enlarged ones were recorded with non-target stimulus. This hypothesis is consistent with neuropsychological studies of inhibitory processes in these patients, which have used, for example, the negative priming task. In this task, OCDS failed to exhibit the normal negative priming effect and there was a faster response than in controls (Enright and Beech, 1993). The same psychophysiological significance can be attributed to the shorter N1 and P2 latencies on the AEP (Savage et al., 1994). In OCD patients, peak P1 and P2 latencies were topographically undifferentiated and N2 was delayed. (Oades et al., 1996).
Some researchers have used the ‘oddball’ paradigm and task types that are differentiated by difficulty (Ciesielski et al., 1981; Beech et al., 1983), lending support to the hypothesis of cortical hyperactivity and ultrafocused attention in OCD patients. Apart from the ‘oddball’ paradigm, the go/no-go paradigm has often been used, which because it involves the appearance of the contingent or ‘warning’ stimulus and the maximum uncertainty of the target stimuli, exacerbates the difficulty of inhibiting the response following the appearance of a no-go stimulus (Jodo and Kayiama, 1992; Falkenstein et al., 1995).

Given the hypothesis of frontal dysfunction in OCD, there is need for a more effective electrophysiological paradigm and types of stimulus than other already-existing ones, in order to register frontal functionality/dysfunctionality (Behar et al., 1984; Martinot et al., 1990; Veale et al., 1996; Purcell et al., 1998). The ERPs paradigms usually used in previous studies (P3 ‘oddball’ and go/no-go) have been criticised because of their limited efficacy in measuring frontal functionality (Towey et al., 1994; Morault et al., 1997).

In the classical ‘oddball’ paradigm, the high probability of non-target stimuli probably permits only a small involvement of the frontal inhibition system (Ritter et al., 1983). In the go/no-go paradigm, one could point out that the greater wave amplitude that occurs when the subject doesn’t have to respond to the stimulus (no-go) is caused by the warning stimulus and not only by the inhibitory activity itself. Therefore, in reality it is not certain that only the inhibitory activity (without a warning stimulus) is sufficient to produce a greater wave amplitude (Ritter et al., 1983).

Consequently, to emphasise the aspects of activation and inhibition, a task similar to a go/no-go paradigm was chosen, but without a warning signal. This paradigm could also considered as an equal-frequency variant of the ‘oddball’ paradigm. In the present paper visual ERPs were examined in OCD patients during a discrimination response task (DRT) employing simple visual stimuli. In this paradigm (the auditory version was devised by Ritter) the non-target stimulus requires a high degree of inhibition with considerable frontal involvement (Ritter et al., 1983).

The purpose of present study is to attempt to introduce an original modality variant of Ritter’s paradigm, variant in the quest for better paradigms with which to investigate putative fronto-striatal dysfunction in OCD and to clarify the confounding issue of task difficulty and stimulus complexity. Moreover, because comorbidity is a common condition in OCD (Hollander, 1998) and abnormalities of ERP have also been documented both in major depression (Vandooolaege et al., 1998) and panic disorder (Clark et al., 1996), we consider in the present study OCD patients without Axis I comorbidity, which was evaluated with the SCID-P.

As treatment seems to bring both clinical and neurophysiological improvements (Morault et al., 1997), we only selected drug-naive patients.

2. Material and methods

2.1. Subjects

Eight OCD patients (mean age 29.7 ± 6.3, 4 females) and 12 age-matched normal controls (30.4 ± 5.3 years, 6 females) participated in this study after informed consent; all subjects were right-handed and have normal or corrected vision. Patients were recruited at the Institute of Neurosciences (Florence). Diagnostical and clinical assessment included SCID P (Spitzer et al., 1990) which generated both a principal diagnosis and a comorbid psychiatric diagnosis. The OCD inclusion diagnosis was carried out by SP and three other senior psychiatrists who are not involved in the present paper. Patients with panic disorder, unipolar depression, or bipolar disorder were excluded from the study. Assessment of symptomatology was elicited by means of the Obsessive Compulsive Scale, Y-BOCS (Goodman et al., 1989a, 1989b). The median values of our patients was 30.5 ± 6.40 (normal values 0–40). Individual values are shown in Table 1. The duration of illness ranged between 36 and 48 months (mean 42.7 ± 4.3 months). All the patients were drug-naive at the moment of the ERPs recording.

2.2. Procedure

Subjects were comfortably seated in a dimly lit, sound-dampened room and stimuli came from a VGA computer monitor at a distance of 100 cm, the screen provided a 24° × 18° visual angle. A small circular red spot (0.3° × 0.3°) in the centre of the display was the fixation point. Stimuli were generated by the STIM® system (NeuroScan Inc.) and were composed of vertical and horizontal yellow bars (5° × 0.5°). The stimuli were present in the centre of the screen for 100 ms on a dark grey background, the vertical and horizontal
line sequence was random with a Stimulus Onset Asynchrony (SOA) of 2.5 sec and with an equal probability ($p = 0.5$).

Every subject performed two tasks: (1) a discriminative response task (DRT) for horizontal bars; the subjects had to press a button with their right hand, as quickly as possible, only when a horizontal bar appeared on the screen (the horizontal bar was the target and the vertical bar was the non-target). (2) a DRT for vertical bars (reverse condition).

The two runs for the DRT condition consisted of a sequence of 101 trials each. The first trial of each run was excluded from further analysis to avoid orienting response contamination. A warm-up was included; subjects had to press the button when a bar appeared. The order of presentation was randomised across subjects. The duration of each condition was six minutes with a pause of one or two minutes between the two (total duration about 15 min.).

2.3. Data recordings

The reaction times (RTs) and ERPs were recorded on-line as the subjects performed the tasks. EEG and EOG were sampled continuously at 2 ms/channel using NeuroScan Inc. software (SCAN ver. 3.1) on a Pentium PC. The EEG was recorded from 20 scalp electrodes (Fp1, Fp2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1, Oz, O2) according to the 10–20 system using an electrode cap (Electro-Cap International). Vertical and horizontal EOG was recorded with disk electrodes situated above and below the right eye and on the outer canthi of each eye respectively (both bipolar). The EOG was amplified 25,000 fold (dynamic range 11 mV, sensitivity 0.168 $\mu$V/bit), the EEG was amplified 50,000 fold (dynamic range 5.5 mV, sensitivity 0.084 $\mu$V/bit) using a SYNAMPS DC coupled amplifier, band-pass DC 50 Hz (−12 dB down). Linked mastoids were used as signal reference for all EEG electrodes and FPz was used for the signal earth.

2.4. Data analysis

The reaction-time window was from 100 to 800 ms after stimuli. Epochs of 1200 ms duration including a 200 ms pre-stimulus baseline were extracted from the continually digitised EEG. All epochs in which EOG amplitudes were greater than $\pm 80 \mu$V and EEG amplitudes greater than $\pm 60 \mu$V were excluded from further analysis. Epochs were also excluded if a miss or false alarm was associated with eliciting stimulus.

ERPs from the two DRT runs were combined and sorted into two categories for each subject: ERPs for

![Fig. 1. Grand average ERP in normal and ODC patients for target (right panel) and non-target (left panel) conditions recorder in five selected electrodes.](image-url)
non-target stimuli (non-target condition) and ERPs for target stimuli (target condition).

Peak amplitudes (relative to the pre-stimulus baseline) and peak latencies of major ERPs component were calculated for each subject in the following time window: P1 (70–150 ms), N1 (130–230 ms), P2 (200–300 ms), N2 (250–350 ms) and P3 (300–500 ms).

The data of each time window were evaluated with a separate factorial analysis of variance (ANOVA). Considered the low number of subjects, the electrode sites included in the analysis were reduced in order to be able to perform the ANOVAs and were selected those sites where the respective components are most frequently observed at greatest amplitudes in similar visual paradigms. For early components (P1, N1 and P2) one two-level independent factor was the group (normals and OCD patients), one two-level repeated factor was the task (target, non-target) another eight-level repeated factor was the electrode position (T5, P3, Pz, P4, T6, O1, Oz and O2), $2 \times 2 \times 8$ design. For late components (N2 and P3) one two-level independent factor was the group (normals and OCD patients), one two-level repeated factor was the task (target and non-target) another nine-level repeated factor was the electrode position (F3, Fz, F4, C3, Cz, C4, P3, Pz and P4), $2 \times 2 \times 9$ design.Behavioural data from RT were submitted to one factor ANOVA (group) with two levels. The post-hoc comparisons were conducted with the Tukey Honest Difference test. To avoid the risk of inflated p values, the overall alpha value was fixed at 0.01.

2.5. Mapping

Electric field maps were generated using a spherical spline map interpolation algorithm. For the spline maps FOCUS 1.1 software was used and the algorithm was licensed by INSERM U. 280. The 20 electrodes were considered to be located on the best fitting sphere. The spline interpolation was performed on the sphere and reconstructed on 2D maps by computing the radial projection from the vertex (top-view). The topography was represented by iso-voltage contours.

Fig. 2. Mean latency (upper panels) and amplitudes (lower panels) of early components.
3. Results

3.1. Behavioural data

The motor reaction time did not differ between groups ($F_{(1,18)} = 1.209$ NS), the mean latencies were $286 \pm 16$ ms for normals and $331 \pm 32$ ms for OCD patients. The error rate for normals was 2.7% (omission 2.1%, false alarm 3.3%), for patients was 3.1% (omission 2.4%, false alarm 3.8%).

3.2. ERP data

The grand average ERP waveforms of normal subjects and OCD patients are presented in Fig. 1. Five major peaks were always identified across the three conditions, a small positive peak (P1) at around 100 ms, a large negative peak (N1) at around 150 ms, a positive peak (P2) around 240 ms, a negative peak (N2) at around 320 ms and a large positive peak (P3) at around 370 ms.

3.3. Latencies

For P1 latency (Fig. 2a) no effects or interactions were significant. Mean latency was $95 \pm 4$ ms. N1 latency (Fig. 2b) showed a significant effect of group ($F_{(1,18)} = 4.427$ p $< 0.01$); OCD patients’ N1 latency was slower ($179 \pm 7$ ms) than normals ($147 \pm 5$ ms). Other interactions or effects were not significant. For P2 latency (Fig. 2c) no effects or interactions were significant. Mean latency was $253 \pm 8$ ms. For N2 latency (Fig. 3a) no effects or interactions were significant. Mean latency was $291 \pm 9$ ms. For P3 latency (Fig. 3b) no effects or interactions were significant. Mean latency was $377 \pm 10$ ms.

3.4. Amplitudes

For P1 amplitudes (Fig. 2d) no effects or interactions were significant. Mean amplitude was $2.2 \pm 0.4$ μV. For N1 amplitudes (Fig. 2e) no effects or interactions were significant. Mean amplitude was $-4.7 \pm 0.3$ μV. For P2 amplitudes (Fig. 2f) no effects or interactions were significant. Mean latency was $377 \pm 10$ ms.

Fig. 3. Mean latency (upper panels) and amplitudes (lower panels) of late components.
were significant. Mean amplitude was $3.6 \pm 0.4$ μV. For N2 amplitudes (Fig. 3c) no effects or interactions were significant. Mean amplitude was $-2.1 \pm 0.4$. P3 amplitudes (Figs. 3d and 4) showed a significant group by task by electrode-location interaction ($F_{(8,144)}=8.243$ $p<0.01$); post-hoc analysis showed that in normals P3 amplitude for non-target was larger ($p<0.001$) than target only for the Cz and Fz electrodes (Cz non-target $=6.7 \pm 0.5$ μV, Fz non-target $=7.6 \pm 0.6$ μV, Cz target $=3.5 \pm 0.4$ μV, Fz target $=2.7 \pm 0.6$ μV). In patients non-target (6.4 ± 0.5 μV) and target (6.3 ± 0.5 μV) did not differ ($p=0.1480$), in target condition Fz amplitude (7.1 ± 0.7 μV) was higher ($p<0.01$) than Pz (5.3 ± 0.7 μV). Moreover, target P3 amplitude in patients was higher ($p<0.005$) than normals while in non-target condition normals and patients’ P3 amplitude did not differ. Other comparisons were not significant.

3.5. Spline map topography

For almost all ERPs components, spline map topography did not show a great difference in scalp distribution between subjects. P1 component showed a posterior activation located on the middle occipital areas. N1 component showed a bilateral activation of the parietal areas. N2 showed a spatial distribution centred on the middle central-parietal area. The only component that appears to change between tasks and between groups was that of P3. In normal subjects, target P3 activation (Fig. 5) was centred on the vertex, while non-target P3 was centred on frontal lobe. In patients, target P3 topography showed two activation, one centred on frontal lobes and another on central areas. The scalp distribution of the non-target P3 component was centred on frontal areas.

4. Discussion

The obsessive-compulsive patients showed altered visual ERPs: N1 latency was delayed and Target P3 amplitudes was increased. The main result that we found was that OCD patients do not show any differences in the two different conditions (go/no-go): P3 is as large in both conditions as observed in normals during the no-go condition. In normals, the non-target

Fig. 4. Mean latency (upper panels) and amplitudes (lower panels) of P 3 components recorded in three selected electrodes.
stimuli produced a larger P3 amplitude than target stimuli (as usually is the case in the go/no-go paradigm). Target and non-target P3 had different distributions in normals as well as in OCD patients. The present results show a larger non-target P3 with the maximum activation located on the frontal areas, which are presumably involved in the inhibition system. Our data support the hypothesis that no-go P3 reflects the activity of a response inhibition system in the brain (Jodo and Kayama, 1992; Roberts et al., 1994).

A hypothetical explanation for this data is that for OCD patients the decision to respond or not respond to a stimulus involves the same amount of energy from a cognitive point of view. Thus, in this case it can be supposed that both the P3 in response to go to no-go occur at the frontal level, an area which in normals becomes active only in the no-go condition. These results support the overfocused attention hypothesis with hyperactivation of frontal lobe regions in OCD patients (Towey et al., 1994).

Apart from task difficulties, the other item requiring discussion is stimulus complexity. In the work of Beech et al. (1983) the visual stimulus was complex and the N220 and P3 amplitudes were decreased, while in Towey et al. (1994) the auditory stimulus was simple and the N200 amplitudes were increased. Finally, in Morault et al. (1997) the auditory stimulus was complex and the N2 and P3 amplitudes were decreased. These ERPs abnormalities in OCD have been interpreted in terms of increased arousal to minimal stimulation (Beech et al., 1983); overfocused attention with cerebral hyperactivation of the frontal lobe region and a prevalence of task-directed processes that induces a subsequent loss of information (Towey et al., 1994); OCD subjects are overfocused on the physical features defining the relevant stimuli (Morault et al., 1997). Moreover, while previous studies did not adopt rigorous selection methods for the sample as regards comorbidity between OCD and depression, panic and social phobia, we considered OCD patients without Axis-I comorbidity, evaluated with SCID P (Spitzer et al., 1990). Morault et al. (1997), on the other hand, adopted only generic exclusion criteria, without indicating the instruments used for evaluation. The hyperfrontability that we found is, therefore, particularly reliable characteristic data for OCD, given that the sample did not include anyone with affective or anxiety disorders and all were drug naive.

Vandoolaeghe et al. (1998) have, in fact, observed in a sample of depressed patients electrophysiological patterns that are comparable to those of OCD patients, for example a larger P3 latency.

These findings maintain the hypothesis of an electrophysiological tendency on the part of OCD patients, which has a certain degree of correspondence at a cognitive level: patients with OCD showed specific cognitive deficit on tasks of executive and visual memory function, reflecting dysfunction of the frontal-striatal system (Purcell et al., 1998).

The findings of the present study, when patients either with comorbidity for panic disorder (where enlarged P3 due to stimulus change has been documented) (Clark et al., 1996) or for depression (where documentation of prolonged P300 amplitude and increased P200 amplitude were also interpreted as a possible predictor for subsequent antidepressive therapy) (Vandoolaeghe et al., 1998) were excluded, confirm the presence of a pattern of hyperfrontability in OCD patients without comorbidity. It remains to be established, given the possible predictive value hypothesised in major depression, if there could be any clinical correlation with course (e.g. chronic or episodical) or with prognostic features and treatment response, as suggested by Morault et al. (1997) for the N2 component.

Furthermore given that the equal probability of the occurrence of stimuli envisaged by the DRT paradigm that we used increases the complexity of the task, one might ask whether the ERP modifications that we observed are specific to this kind of task, whether, that...
is, they arise only with this type of task. To clarify this, it would be necessary to conduct different types of task with the same sample of patients.

A further consideration regards the possible correlation between electrophysiological patterns and neurophysiological tests, which were not evaluated in our study, but which would permit the monitoring of activity linked to specific cerebral areas, whose functionality can be revealed electrophysiologically: target and non-target P3 had different scalp distributions, in normal as well as in OCD patients and this could suggest that target and non-target stimuli activate (between 300 and 400 ms) at least two different neural generators, one centrally located (target P3) and another frontally located (non-target P3) (Johnson, 1993).

Further research associating neuropsychological and neurophysiological tests, with a clinical subtyping that is not only symptomatological but which regards also course, would be useful in order to establish the possible clinical usefulness of electrophysiological data.

Acknowledgements

We would like to thank Irina Boscagli and an anonymous reviewer for the help and discussions.

References


