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The Wisconsin Card Sorting Test and the assessment of frontal function in obsessive-compulsive patients: An event-related potential study

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The most consistent finding across the studies in obsessive-compulsive disorder (OCD) is the deficit in tasks involving shifting in cognitive set. The cognitive operations needed to perform the Wisconsin Card Sorting Test (WCST), searching for a new category and the consolidation of the correct classification category, are closely related to shifting cognitive set. This work aimed to study whether patients with OCD present difficulties in shifting cognitive set and to examine the topographical distribution of brain electrical changes and their temporal dynamics during the performance of the WCST. For this purpose, we selected 18 nondepressed OCD patients. The effects of clomipramine treatment on these variables were also assessed. Both behavioural and neuroelectric data supported the idea that OCD patients have an impaired capacity for shifting cognitive set. This deficit was interpreted as being due to problems in inhibitory control, as a consequence of a dysfunction in an inhibitory pathway in the prefrontal cortex. This would explain the poor performance of OCD patients in the WCST in terms of their inability to inhibit or suppress previous incorrect responses. Nevertheless, it is not clear whether shifting cognitive set is an enduring ''trait'' marker or a finding that fluctuates with changes in the clinical state.

Over the past decade, there has been increasing interest in the characteristics of cognitive functioning in obsessive-compulsive patients (Flor-Henry, Yendall, Koles, & Howarth, 1979; Insel et al., 1983; Rapoport et al., 1991; Rauch & Jenike, 1993). A wide range of tests has been administered and a variety of

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interpretations made about the nature of the observed deficits. Clinical, psychosurgical, biochemical, and neuroanatomical evidence have suggested that the basal ganglia and frontal lobes play a role in the pathogenesis of obsessive-compulsive disorder (OCD). Although much has been learned about OCD in recent years, the nature of the cognitive dysfunction of this disorder is not clear.

Frontal lobe dysfunction has been revealed by topographic evoked potential mapping showing reduced P300 amplitudes in frontal areas in OCD patients (Malloy, Rasmussen, & Bradon, 1989). Studies involving the electroencephalogram, with visual and computerised analysis, and with evoked potential and slow potential studies, tend to associate frontal region dysfunction with OCD (Khanna, 1988). Moreover, analyses of frontal cortical metabolism by PET (positron emission tomography) have reported modifications of glucose metabolism in OCD patients. Most PET studies of OCD have reported increased metabolism or blood flow in orbitofrontal and anterior cingulate cortices, as much as in the head of the caudate nucleus (McGuire, 1995, Rauch et al., 1994). Functional magnetic resonance imaging has also showed abnormal patterns of brain activity in OCD, which consistently suggest frontal lobe dysfunction. (Breiter et al., 1996; Pujol et al., 1999)

However, the neuropsychological data relevant to this model of frontal dysfunction in OCD are still not definitive. In fact, neuropsychological studies have provided conflicting results (Abbruzzese, Bellodi, Ferri, & Scarone, 1995a; Abbruzzese, Ferri, & Scarone, 1995b; Christensen, Won Kim, Dysken, & Hoover, 1992; Insel et al., 1983; Malloy, 1987). There is no general evidence of ''frontal deficits'' in OCD patients. Perhaps the Wisconsin Card Sorting Test (WCST) is the most used test to evaluate frontal function (Milner, 1963). It has been considered to be an abstract reasoning test and involves shifting in cognitive set (Stuss & Benson, 1986). The WCST consists of 64 different cards that can be distinguished by number, colour or shape of the figures. Subjects have to complete many series (10 trials each series) attending different sorting criterion (colour, shape, number). The subject has to sort the cards searching for the correct classification category at the beginning of each series and maintaining the correct sorting classification during the series (10 trials) (Heaton, 1981). Searching for a new category involves shifting cognitive set and to find the correct one is closely related to trial and error learning and the ability to attend to feedback from ongoing chains of behaviour.

Perseverative responses are the most characteristic error in frontal patients and consists of paying attention to a wrong classification criterion even when the subject has detected the criterion is wrong. It seems to be related to the capacity to shift cognitive set. Perseverative responses have been considered as an example of inflexibility, the same as compulsive and repetitive behaviour in OCD patients. The urge to repeat compulsive acts may be related to the difficulty to attend to feedback information from ongoing chains of behaviour,

given the difficulties in confirming the adequacy of the acts. Supporting this theory are several studies reporting more perseverative responses and the completion of fewer categories in OCD patients (Goodwin & Sher, 1992; Harvey, 1987; Head et al., 1989).

Poor performance on the WCST is considered to be due to damage in the left frontal lobe (Drewe, 1974), but it is not clear if there is participation of each hemisphere in its performance (Robinson, Heaton, Lehman, & Stilson, 1980, Taylor, 1979). Most neuroimaging studies have reported activation of several brain areas during WCST performance. Activation of the dorsolateral prefrontal cortex is the most consistent finding in studies using regional cerebral blood flow (rCBF) (Catafau et al., 1994; Marenco, Coppola, Daniel, Zigien, & Weinberger, 1993; Rezai, Andreasen, Alliger, & Cohen, 1993; Weinberger, Berman, & Zee, 1986). However, recent reports provide evidence of possible implications of parietal, medial temporal, and hippocampal cortices in card sorting (Anderson, Damasio, Jones, & Tranel, 1991; Corcoran & Upton, 1993; Hermann, Wyler, & Richey, 1988; Mountain & Snow, 1993; Upton & Corcoran, 1995).

Despite the relatively good spatial resolution provided by rCBF studies, these techniques are ill-suited to disentangling the split-second nature of cognitive operations taking place during WCST performance, and are therefore unlikely to reveal possible alterations in the course of information processing. In particular, rCBF results fail to differentiate between correct and incorrect response periods, or between early and late trials within a WCST series. As few studies have focused on the components of the event-related potential (ERP) in relation to WCST performance, in a previous work we examined the topographical distribution of brain electrical changes and their temporal dynamics during the performance of the WCST in a sample of normal volunteers (Barceló, Sanz, Molina, & Rubia, 1997). Two cognitive operations were tested in different trial periods. First, the process of searching for a new sorting category at the beginning of each new series (novel classification trials; in our validation study these were called WIS23 trials). The sorting category was changed and the subject did not know the new one, and it is discovered by trial and error. When the subject discovers the correct classification category he/she has to sort the cards based on it during the series. At the end of the series we consider that there is an automatisation of the correct classification rule when, after answering correctly during the series, the classification rule is consolidated. We examined a different cognitive process at the end of the series and tested the consolidation of the correct classification in these repetition trials. These were called WIS67 trials in our validation study (Barceló et al., 1997). We found a greater ERP activation in frontal as compared to nonfrontal brain areas during WCST performance in both conditions (WIS23, WIS67). In addition, we also found that prefrontal activation was greater during novel classification trials (WIS23) as compared to repetition trials (WIS67).

The aim of the present study was to study the following. (1) Whether patients with OCD present difficulties in shifting cognitive set, as indicated by impaired performance in a WCST. (2) The topographical distribution of brain electrical activities and their temporal dynamics during the performance of the WCST in OCD patients as compared to normal volunteers. In addition, the effects of drug treatment with clomipramine on these variables were examined.

METHODS

Subjects

A total of 18 obsessive-compulsive disorder (OCD) patients took part in the study. All were between 18 and 50 years old. All had completed at least 17 years of education necessary to go to university, according to the Spanish education system. Patients suffering from other neurological or psychiatric illnesses or with a total score in the Hamilton depression scale more than 10 were excluded. No subject had a history of alcohol or drug abuse, and none were undergoing pharmacological treatment. Patients who had been taking medication underwent a wash-out period of a month. All subjects were right-handed and had normal or corrected-to-normal vision. They received detailed information about the study protocol and gave written consent. OCD patients were selected from the outpatients clinic. Ten of the participants were psychotropic-naive and this was their first acute episode. Previously published data on healthy volunteers (Barceló et al., 1997) were used here to represent a control group for OCD patients.

Basic demographic data and years of education are given in Table 1. We used parametric comparisons (Student's *t*-test for independent samples) to analyse the mean differences between groups (normal controls/OCD) in sociodemographic data. The Shapiro–Wilks test indicated that we could accept the normality distribution of the sample. There were no statistical difference between groups regarding age, sex, and years of education.

TABLE 1
Sociodemographic characteristic of the sample

	Normal controls (n = 24)	*OCD patients* (n = 18)
Age	*M*: 20.5 (18–34)	*M*: 25.8 (18–44)
Gender	Male: 55.6% Female: 44.4%	Male: 45.8% Female: 54.2%
Cultural level	University: 100%	Primary and secondary school: 30% University: 70%

Assessment

Patients were diagnosed using a structured clinical interview for DSM III-R (SCID; Spitzer, Williams, Gibbon, & First, 1987). Psychopathology was assessed with the Yale–Brown Scale (Y-BOCS) (Goodman et al., 1989a,b), the Hamilton Depression Scale (Hamilton, 1960), and the Hamilton Anxiety Scale (HARS). The last of these was administered in order to record anxiety level during the study.

Patients were interviewed and registered twice, drug-free; and under treatment with clorimipramine in 250–300 mg doses. Eight patients were under treatment when they were included in the study but without acute symptoms, and were therefore first registered under treatment. They subsequently stopped taking medication, and after at least one month (wash-out period), and when acute symptomatology appeared again, they took the second interview and the electroencephalogram study was carried out. This permitted us to observe if there is a learning effect in the second study. Five of the eighteen patients dropped out of the study before their second event-related potential (ERP) session, after treatment.

Recording system

Electroencephalogram (EEG) activity was recorded from the scalp through tin electrodes inserted in a preconfigured cap (Electrocap International). Recording systems included FP1, FP2, F7, Fz, F8, T7, Cz, T8, P4, Pz, P3, O1, and O2 of the International 10–20 system (Pivik et al., 1993). Linked mastoids were used as the reference, and Fpz as ground. The electrooculogram (EOG) was recorded bipolarly from electrodes placed above and adjacent to the outer canthi of the right eye. Electrode impedances were kept below 5 kohms. All EEG and EOG channels were amplified with a SYNAMP (NeuroScan Inc.) DC coupled amplifier system. Recordings were made from DC with a low pass filter set at 50 Hz (12 dB/octave roll-off). Single-trials epochs were digitised at 4 ms/sample and stored on a magnetooptical disk for off-line analysis, together with event markers and response latencies. Each epoch was of 1700 ms duration, including a 200 ms prestimulus baseline.

Stimuli

We used the computerised version of the WCST incorporated with the NeuroStim package in the same way as in our previous study (Barceló et al., 1997). As described there, the package was used as a task model, but its administration protocol was modified in order to improve task control and to eliminate ambiguous responses. With this purpose, 64 colour cards were built up from the original material of the standard WCST. The stimulus material was presented on a computer screen facing the subject at a distance of 80 cm, with

each card forming a visual angle 2.8° wide and 3.5° high. The four key-cards were always present on the upper third of the screen and allowed eye movement with a maximum visual angle of 12° horizontally. The experimental design, the stimulus sequence, and the coding of response were programmed and controlled through the NeuroStim package.

Procedure

We used the same procedure as in the previous study (Barceló et al., 1997). Subjects sat in a comfortable seat in an electrically shielded, quiet and dimly lit (2 luxes) cubicle. Each WCST trial began with the display of the four key-cards on the upper third of the computer screen, plus one choice-card occupying the right-hand corner of the lower third of the screen. Subjects were asked to classify the choice-card by pressing one of four buttons on a response panel. The far left button corresponded to the key-card on the far left side of the screen, the far right button corresponded to the key-card on the far right side, and so on. Subjects used their thumbs for pressing buttons while holding the response panel with the palms of the hands. Feedback was provided by means of a computer-generated tone (2000 Hz for correct, and 500 Hz for incorrect, 300 ms in duration), with a 1600 ms gap between button-press and feedback onset. The inter-trial interval varied randomly between 300 and 4000 ms. There was no time limit for emitting a response, but subjects were encouraged to respond quickly and to score as many correct responses as possible.

As in the previous study with normal volunteers, the three possible classification criteria were mentioned beforehand, as these could change during the task in order to restrict the influence of variables such as intelligence. This allowed us to focus the investigation on the process of searching for a new classification criterion, and on the consolidation of the correct classification criterion. The WCST administration protocol consisted of two blocks with 18 series of seven trials each. The length of the series remained constant regardless of performance. Both the order of the categories and the presentation of choice-cards within each series were determined on a semirandom basis in order to comply with the following constraints: (1) colour, shape and number categories appeared the same number of times; and (2) ambiguity was eliminated from the first four trials in the series. Ambiguous trials were defined as those that could be scored as correct under two or more classification rules simultaneously (Nelson, 1976). Elimination of ambiguity from the early trials in the series facilitated correction of the test, and improved the signal-to-noise ratio in the ERPs. The average duration of each block was 15 min, with a 5 min rest period between blocks. There was also a 5 min practice period to ensure that the instructions had been understood.

WCST score

An approach to the standard scoring criteria was made. Accordingly, the following variables were defined:

- Perseverative errors: All consecutive errors starting from the second trial in the series.
- Random errors: Those occurring after at least one correct response.
- WIS67 random errors: Random errors occurring in the last two trials of the series.
- Categories completed: The criteria for achieving a category were: (a) there was no anticipation; (b) there were less than three perseverative errors; and (c) there were no WIS67 random errors.

The correlation between scores and psychopathology was also studied.

Response latencies in controls and patients were recorded before and after treatment. We used a one-way ANOVA to compare each variable between groups (controls/OCD patients; OCD patients with and without treatment). When we repeated the analyses using years of education as a covariable the results did not change.

ERP analysis

Separate ERP waves were computed for two different WCST task conditions:

1. WIS23 trials: The second and third trials in each series were averaged together to yield a WIS23 condition waveform regardless of the subject's performance. As explained earlier, the WIS23 condition was taken to reflect an active search for a new classification rule, after having received negative feedback in the first trial. Even if the new and correct classification category was found in the second trial, the third trial was also included in the WIS23 averaging under the assumption that the new classification rule would not yet be consolidated.
2. WIS67 trials: Correct trials sixth and seventh in a series were averaged together to yield the WIS67 condition, which was taken as an indicator of automatisation of the correct classification rule, as already mentioned in the introduction.

The characteristics of the analysis were exactly the same as in the previous study. Continuous EEG recordings were epoched from 200 ms prior to stimulus onset to 1500 ms after it. Blinks and horizontal eye movements were corrected on a trial-by-trial basis using a standard linear correction procedure (Semlitsch, Anderer, Schusler, & Preslich, 1986). After EOG artefact correction, trials exceeding amplitudes of ± 75 microvolts at any of the active electrodes were

automatically discarded from the averages. Finally, all records were visually edited to double-check the accuracy of the correction and rejection procedures. Any linear trend within the recording epoch was removed prior to averaging, and waveforms were aligned to a 200 ms prestimulus baseline. WIS23 and WIS67 ERP waves were composed of 60 trials on average (55–72 trials).

Averaged ERP waveforms were computed for each event type at each electrode for each subject and across subjects. Mean values of ERP components were observed in eight different latency windows: P50 (30–80 ms); P100 (80–120 ms); N150 (120–180 ms); P200 (180–270 ms); P3a (270–350 ms); P3b (350–450 ms); slow wave 1 (SW1, 450–800 ms) and 2 (SW2, 800–1200 ms). The decision to use these time windows was made on empirical grounds after inspection of overall mean waves. ERPs during feedback were not evaluated due to the possible influence of expectancy and/or motivational factors.

Statistical analyses

1. We used an ANOVA design to analyse within-subjects differences for ERP data, which consisted of Electrode (6 levels: frontopolar, frontotemporal, frontal, temporal, parietal, and occipital), Hemisphere (2 levels: right and left), and Task (2 levels: WIS23 vs. WIS67). Mid-line electrodes were not included in these analyses. In the ANOVA design, WIS23 and WIS67 conditions were compared for OCD patients with treatment and OCD patients without treatment. In our previous, validation study (Barceló et al., 1997) we found that greater prefrontal activation is elicited during novel classification trials (WIS23) as compared to repetition trials (WIS67). We performed the same analyses in the present group of patients in order to study the differences in prefrontal activation comparing the two conditions. This ANOVA design was repeated for ERP mean values for each of the eight time windows considered. ANOVA results are reported with Greenhouse–Geisser adjusted degrees of freedom where appropriate. The Bonferroni procedure was used to determine the significance level using a familywise error rate of 0.05. Statistical analyses were performed using the BMDP package from the Complutense University mainframe.

2. We also analysed the differences between controls and OCD patients without treatment on the WIS23 and WIS67 tasks separately through the same ANOVA model. We now used the group variable (control/patient) as independent variable. Again we repeated the analysis for ERP mean values for each of the eight time windows considered.

3. A third analysis was carried out in order to reveal the effect of treatment on ERP mean values in each task (WIS23/WIS67). We used the same ANOVA design with the group variable (OCD patient with/without treatment) as

independent variable. It was also carried out for ERP mean values in each of the eight time windows for each task separately.

4. As in the first ANOVA analyses, significant differences were found between controls and OCD considering electrode and hemisphere in every interval in WIS23 and WIS67 tasks. A univariant analysis using parametric *post-hoc* comparisons (Student's *t*-test for independent samples) was performed in order to analyse the mean differences between groups (normal controls/OCD) in each electrode. This was performed for both tasks separately (WIS23, WIS67) at every time window. Parametric comparisons were used because the data complied with the constraints for this type of calculations (Shapiro–Wilks test indicated that we could accept the normality distribution of the sample. We also applied Levene's Test for Equality of Variances).

5. We calculated the correlation coefficients between the differences in the ERP mean value in normal control/OCD patients and the level of patients' anxiety at the time of the study for time windows in which significant differences were found.

6. We calculated the correlation coefficients between the severity of psychopathology and WCST performance.

RESULTS

Performance data

Response latencies were significantly longer in both conditions (WIS23/WIS67) ($p < .05$) in OCD patients when compared to normal controls who carried out the validation study. After pharmacological treatment reaction time shortened, but the difference pre-post-treatment was not statistically significant. In all groups, response latencies in WIS23 were significantly longer than in WIS67 ($p < 0.01$) (Table 2).

TABLE 2
Behavioural data controls/OCD in WCST performance

	*Categories***	*Perseverative***	*Total errors***	*Random errors*	*WIS67 errors**
Controls (n = 24)	*M*: 32.6; SD: 7.26	*M*: 18.3; SD: 10.4	*M*: 58.9; SD: 11.2	*M*: 4.6; SD: 3.75	*M*: 1.9; SD: 2.4
OCD (n = 18)	*M*: 27.56; SD: 6.7	*M*: 32.1; SD: 16.4	*M*: 71.7; SD: 19.2	*M*: 5.9; SD: 4.04	*M*: 4.62; SD: 4.9

* $p < .05$;** $p < .01$.

WCST score

Compared with controls, OCD patients free of treatment completed fewer categories ($F = 11, 84$; $p < .01$), and made more total errors ($F = 8, 29$; $p < .01$), more errors in WIS67 ($F = 5, 4$; $p < .05$), and more perseverative responses ($F = 9, 24$; $p < .01$) (Table 3). Only total errors showed a significant correlation with the presence and severity of obsessions and compulsions at the time of the study ($r = .54$; $p < .05$). There was no correlation between HAS score and these performance data, nor between the obsessions subscale score and performance data (Table 4).

After pharmacological treatment, OCD patients improved performance on the WCST. They made fewer total errors and perseverative responses and completed more categories (Table 3). Only number of categories was statistically significant ($p < .03$). In the six patients tested, first under pharmacological treatment the differences were smaller and nonsignificant. This result suggests that learning has an influence on WCST performance. The Yale–Brown score in this group showed a significant correlation with the WCST score.

Event-related Potentials

In OCD patients we observed the same ERP components at each time window as observed in our validation study (Barceló et al., 1997), but with significant differences when compared to normal volunteers. The first one is that we did not

TABLE 3
Behavioural data OCD without/with treatment in WCST performance

	*Categories**	*Perseverative*	*Total errors*	*Random errors*	*WIS67 errors*
OCD without drugs ($n = 13$)	*M*: 27.3; SD: 6.9	*M*: 32.5; SD: 17.8	*M*: 73.9; SD: 19.8	*M*: 6.64; SD: 4.2	*M*: 5; SD: 5.3
OCD with drugs ($n = 13$)	*M*: 31.8; SD: 3.4	*M*: 27.4; SD: 8.5	*M*: 67.6; SD: 10.5	*M*: 4.64; SD: 3.2	*M*: 2.64; SD: 2.1

* $p < .05$.

TABLE 4
Correlation coefficients behavioural data between WCST/Yale–Brown score

Yale–Brown treatment	*Categories*	*WIS67 errors*	*Total errors*	*Perseverative responses*	*Random errors*
Before	−3317	.3797	.5385*	.4060	.4275
After	−6096*	.6450*	.6576*	.6693*	.3049

* $p < .05$.

observe in OCD patients the differences in ERP with within-subjects analysis (WIS23/WIS67 comparison) observed in normal controls in our validation study (Barceló et al., 1997). The first ANOVA analyses yielded significant differences between controls and OCD considering electrode and hemisphere in every time window. Namely, we observed less activity over right hemisphere in OCD patients in P50 during WIS23: $F(1, 38) = 5.32$, $p < 0.03$, and WIS67: $F(1, 38) = 4.2$, $p < .05$, and in P100 time window: $F(1, 38) = 5.4$, $p < .05$ for WIS23 and $F(1, 38)$; 5, $p < .05$ for WIS67. As already mentioned, we performed an univariant analysis using parametric *post-hoc* comparisons (student's *t*-test for independent samples) to analyse the mean differences between groups (Normal controls/ OCD) in each electrode. We compared controls and OCD in both tasks (WIS23 and WIS67). The explanations for the significant results in every time window for each task are as follows:

In the P50 time window differences were observed between controls and OCD patients in WIS23 in the following electrodes: FP1 (T: 3.9, *df* 40, $p < .001$), FP2 (T: 4, *df* 40, $p < .001$), F4 (T:3.5, *df* 40, $p < .01$), F8(T: 2.6, *df* 39, $p < .05$), T8 (T: 3.6, *df* 40, $p < .019$, p4(T:2.7, *df* 40, $p < .01$). For WIS67, we observed differences in: FP1(T:4.2, *df* 40, $p < .001$), FP2(T:4, *df* 40, $p < .001$), F3(T:3.3, *df* 40, $p < .01$), F4(T:4.4, *df* 40, $p < .001$) F8(T: 3.9, *df* 39, $p < .001$), T8(T: 3.3, *df* 40, $p < .01$), P4(T: 2.8, *df* 40, $p < .01$).

Very similar differences were observed in the P100 time window in WIS23: FP1(T:4.36, *df* 40, $p < .001$), FP2(T:4.37, *df* 40, $p < .001$), F4(T:3.1, *df* 40, $p < .01$), F8(T:3.3, *df* 40, $p < .01$), and T8 (T: 3.9, *df* 40 $p < .001$ for T8). In WIS67 the significant differences were: FP1 (T:4.2, *df* 40, $p < .001$), FP2(T: 4.3, *df* 40, $p < .001$), F4(T:3.4, *df* 40, $p < .01$), F8 (T:4, *df* 40, $p < .001$), T8 (T: 3.4, *df* 40, $p < .01$), P4 (T:3, *df* 40, $p < .01$).

In the validation study (Barceló et al., 1997) we found that the earliest reliable difference between WIS23 and WIS67 in normal controls appeared in the 120–180 ms time window at F7. This effect was explained by a unilaterally more negative onset of the P200 wave for WIS23 as compared to WIS67 trials. It is worth pointing out that we did not find WIS23/WIS67 differences in OCD patients (Figures 1 and 2). We observed an overlying negative electrical field starting at 120 ms in OCD patients in the WIS23 condition, as observed previously in normal controls (Figure 1), but there were no modifications during the WIS67 condition (Figure 2).

The P200 component was less prominent in patients for both tasks (WIS23 and WIS67) (Figure 3). Analysis data showed significant differences at frontopolar sites bilaterally in both conditions between groups at the N150 (T: 4,38, *df* 40 $p < .001$ for FP1 and T: 4,39, *df* 40, $p < .001$ for FP2) and P200 time windows (T: 4.12, *df* 40, $p < .001$ for FP1 and T: 4.2, *df* 40, $p < .001$ for FP2) (Figure 3).

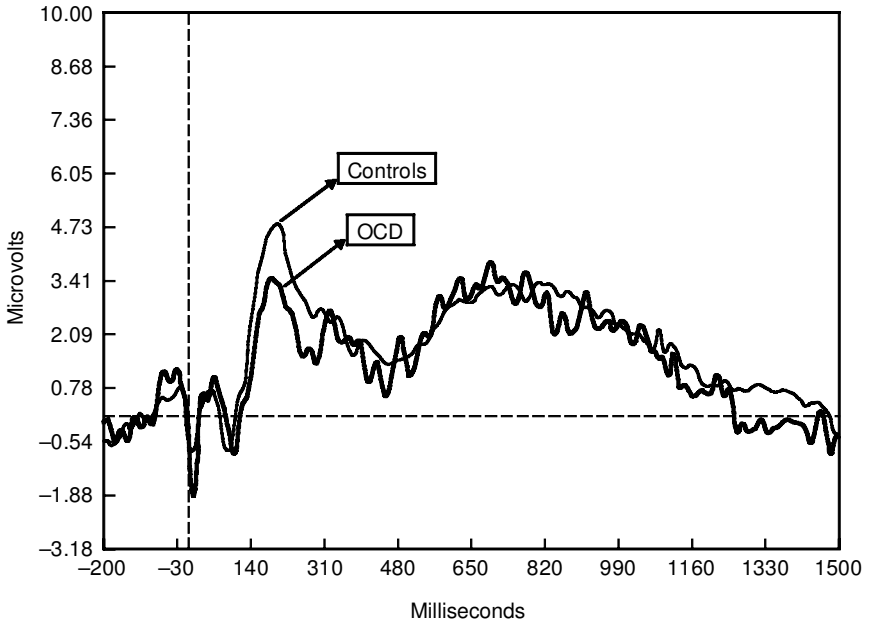

Figure 1. Obsessive-compulsive disorder patients and Controls: The WIS23 trial. F7 electrode.

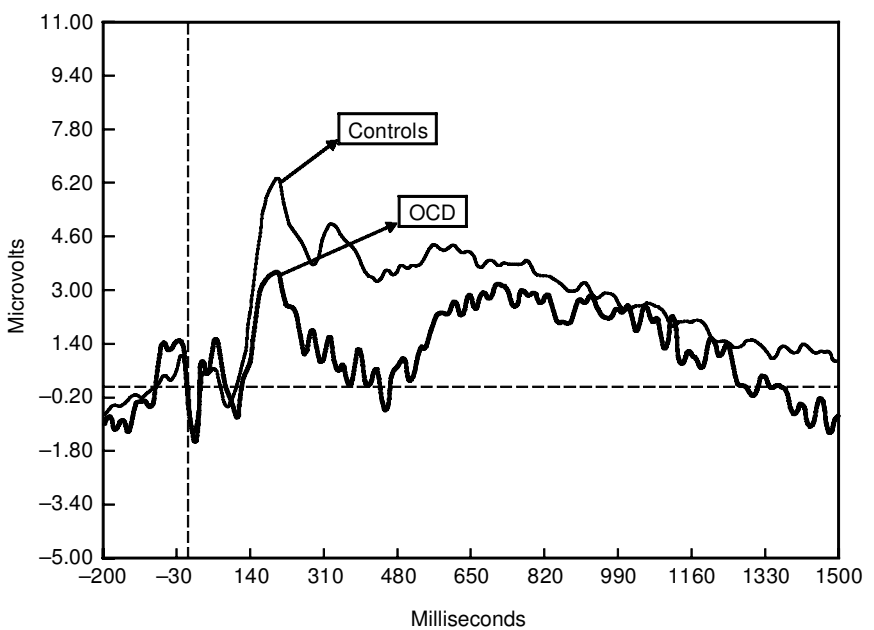

Figure 2. Obsessive-compulsive disorder patients and Controls: The WIS67 trial. F7 electrode.

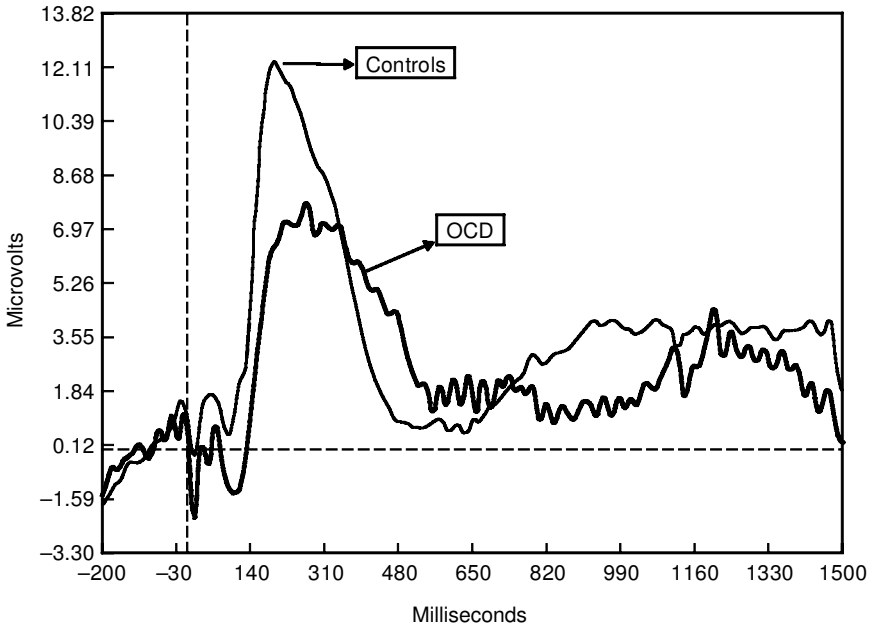

Figure 3. Obsessive-compulsive disorder patients and Controls: The WIS23 trial. FP2 electrode. P200 wave.

The P3b component showed less amplitude in OCD patients when compared to normal controls in both tasks. For WIS23 we obtained the following significant results: T: 2.7, *df* 40, $p < .01$ in for P4; T: 2, *df* 40, $p < .06$ for P3; T: 4, *df* 40, $p < .001$ for O1 and T: 2.8, *df* 40, $p < .01$ for O2. We observed no enhancement of this component in WIS67 condition in OCD patients as had been observed in normal controls (Barceló et al., 1997). Of course, the differences were apparent at posterior leads (Figure 4). Once again there were no WIS23/WIS67 differences in OCD patients related to different cognitive processes on each task.

Thus, we observed differences between groups in both conditions: Less prominent P200 and P3b components. We observed no modification of overlying negative field observed at the 120–180 msec time window and no enhancing of the P3b component in the WIS67 condition in OCD patients. We should emphasise that although we observed differences between tasks in normal controls because of the different cognitive processes, the ERP waveforms were very similar when comparing the WIS23 and WIS67 tasks in OCD patients.

ERP modifications after treatment.

We found a significant difference in the mean ERP amplitudes only when comparing pre- and post-treatment conditions in frontal (Matched T = 2.5, *df* 12, $p < .05$) and frontotemporal (Matched T = 2.3, *df* 12, $p < .05$) left electrodes for

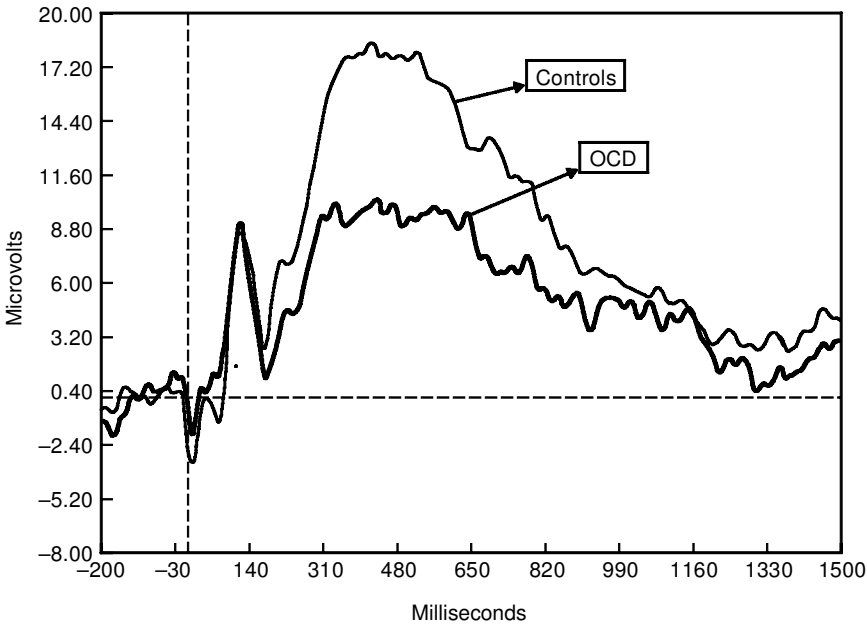

Figure 4. Obsessive-compulsive disorder patients and Controls: The WIS67 trial. PZ electrode. P3b wave.

the N150 time window in the WIS67 condition. Thus, the negative beginning of the P200 wave in WIS67 was less marked in patients with treatment, bringing these findings closer to those of normal controls. Data showed the same values for patients who participated in the study first under pharmacological treatment than for those who did so free of treatment. Thirteen patients were registered twice: Drug-free and under pharmacological treatment.

DISCUSSION

Both behavioural and neuroelectric data support the idea that OCD patients have an impaired capacity to shift cognitive set. OCD patients showed a poorer performance in the WCST and longer response latencies than normal controls. With regard to neuroelectric data, it is very interesting to note that the early differences between WIS23 and WIS67 at the 120–180 ms time window observed in normal controls (Barceló et al., 1997) were not observed in OCD patients. We interpreted a more negative beginning of the P200 wave for WIS23 as compared to WIS67 trials in normal controls because of an activation of the left dorsolateral prefrontal cortex during execution of the WCST. It is reasonable that a greater amount of activation affected the WIS23 trials, because during these trials the subject is assumed to look for the correct criterion and shift

cognitive set. We should underline that there was no difference between WIS23 and WIS67 in OCD patients. As explained below, we interpret this result in terms of the OCD patients' inability to inhibit previous incorrect response and to maintain a cognitive set.

This difficulty for maintaining a cognitive set could make the mental representation of the correct category blurred. This process would be related to the P3b component that we observed as less prominent in OCD when compared to control subjects. Lower ERP amplitudes in the right hemisphere at all the considered time windows and a less prominent P200 component may be in agreement with other authors' findings regarding an impairment in visuospatial ability in OCD patients (Boone et al., 1991; Zielinski, Taylor, & Juzwin, 1991) and a poorer than normal score in voluntary saccadic eye movement measures (Gambini, Abbruzzese, & Scarone, 1993).

We cannot draw any firm conclusions from our results with regard to the positive effect of clomipramine treatment on cognitive functioning.

WCST performance

Obsessive-compulsive disorder patients completed fewer categories and made more total errors and perseverative responses. These measures improved after pharmacological treatment, but only the number of categories was statistically significant. It should be noted that WCST variables did not show any significant correlation with the Yale–Brown global score and that a significant correlation appeared after treatment between psychopathology and WCST performance. Presumably, acute psychopathology interfered with WCST performance. The significant correlation found between psychopathology and WCST performance after treatment suggests that cognitive function may have improved as psychopathology disappeared. However, no clear relationship was found between poor performance on the WCST and clinical characteristics. No conclusion can be drawn because we do not know the learning effect in WCST performance. A larger sample is necessary, together with the study of this learning effect. It is not clear whether shifting of cognitive set is an enduring ''trait'' marker or a finding that fluctuates with changes in clinical state.

Performance on the WCST needs systematic and repetitive changes in sort criteria, therefore being an estimate, among others, of cognitive set shifting. Failure to shift cognitive set causes perseverative responses and the completion of fewer categories. The results of the present study are in agreement with the hypothesis that the OCD patients have difficulties in shifting cognitive set. There are also previous studies reporting more perseverative responses and the completion of fewer categories in OCD patients (Goodwin & Sher, 1992; Harvey, 1987; Head et al., 1989). Harvey (1987) is the only author reporting a significant correlation between severity of psychopathology and perseverative errors on the WCST in OCD. In present study, the Leyton Obsessional Inventory

was used to assess psychopathology. This instrument does not distinguish between symptom and feature (Goodman & Price, 1992; Yaryura-Tobias & Nerizoglu, 1983) and this may be the reason why we did not find any consistent relationship with the severity of the clinical process, especially in acute episodes.

Abbruzzese et al. (1995a,b) did not observe more perseverative responses in OCD when compared to normal controls. They supported that OCD patients have an orbitofrontal dysfunction, not a dorsolateral frontal lobe dysfunction. Inconsistencies in the literature may be due to one or more sources of variability within samples, such as symptom severity, diagnostic heterogeneity, comorbid depression and subtle brain abnormalities which are difficult to locate (neurological soft signs). Many authors have considered IQ as an important variable (Cox, Fedio, & Rapoport, 1989; Head et al., 1989). We did not measure this variable directly, we only included patients who had completed higher education. It is worth noting that the 70 per cent of patients went to university. Accordingly, our sample was quite homogenous in terms of education and very similar to the control group. Nevertheless, we used years of education as a covariable and this did not affect the results.

It is also important to note that we used a computer version of the WCST for the OCD patients with the aim of analysing electrical activity and its topographical distribution during WCST performance. Accordingly, it is not easy to make a direct comparison of the present study with previously reported data.

ERP analysis

Obsessive-compulsive disorder patients showed lower ERP amplitudes in the right hemisphere at all the time windows considered. As mentioned above, this appears to be the physiological correlate of the difficulties that these patients show in a test requiring good visuospatial ability. In the literature it is possible to find studies on deficits in visual memory and in visual construction capacity, all of which also indicate nonverbal deficits in the nondominant hemisphere (Boone et al., 1991; Martinot et al., 1990; McGuire et al., 1994; Zielinski et al., 1991).

In our previous validation study, we suggested that the conspicuous P200 wave, which was apparent at frontotemporal and frontopolar leads, might reflect activation of the frontal eye fields, during the visual scanning of the stimuli display (Barceló et al., 1997), which play a role in the initiation of voluntary eye movements and visual search. In particular, they are said to take part in the processes of selection, comparison, analysis and integration of various stimuli of the visual scene. Their lesion results in a visual search disorder with a deficit in the active component of perception (Stuss & Benson, 1986). As we mentioned above, several studies on visuospatial capacities in OCD patients refer to problems in these processes, such as difficulties with comparison, analysis, and integration in the active component of perception. Gambini et al. (1993)

observed that patients performed more poorly than control subjects in smooth pursuit eye movements and, to a lesser extent, voluntary saccadic eye movements. However, there was no relationship between neuropsychological performance and these findings. It may be useful in future research to study the influence on differential activation of the frontal eye fields during the visual scanning of the stimuli display in OCD patients.

We previously proposed (Barceló et al., 1997) that the hemispheric asymmetry affecting the P200 wave at the frontotemporal region could be interpreted in terms of an overlying negative electrical field centred on the left dorsolateral prefrontal cortex (DLPFC) which reduced the amplitude of an otherwise symmetrical left frontotemporal P200 wave. We suggested that early differences between WIS23 and WIS67 reflect the activation of the DLPFC during execution of the WCST, with a greater amount of DLPFC activation affecting WIS23 trials. As discussed, this interpretation would be in agreement with many functional neuroimaging studies that have consistently reported increases in activation of the DLPFC of the left hemisphere during performance of the WCST (Kawasaki et al., 1993; Nagahama et al., 1995; Rezai et al., 1993). It is not surprising that DLPFC activation was stronger during an active search for a new classification rule (WIS23). This overlying negative electrical field was very similar to that of normal controls in WIS23 in OCD patients. However, OCD patients showed in WIS67 a very similar activation to that found in WIS23. They seemed to require the same cognitive effort for classifying when the correct classification rule is supposed to be consolidated (WIS67) as during active search for a new classification rule (WIS23).

Deficits in attention set shifting ability and perseverative responses may both be linked to problems in inhibitory control, the consequence of a dysfunction in an inhibitory pathway in the prefrontal cortex of OCD patients. This would explain the poor performance of OCD patients in WCST in terms of their inability to inhibit previous incorrect responses. The performance data support this hypothesis. Perseverative responses, WIS67 errors, and number of completed categories measured this difficulty. The hyperactivation of the DLPFC during WIS67 when compared to normal controls may indicate an attempt to compensate the ineffectiveness of the inhibitory processes in OCD patients, so that they require the same DLPFC activation during the two conditions (WIS23 and WIS67). Sensitivity to DLPFC function has been demonstrated in the performance of the set shifting task (Dias, Robbins, & Roberts, 1996). The patients' deficits in this task suggest that DLPFC may be involved in the pathophysiological features of OCD. Most PET studies of OCD have reported increased metabolism or blood flow in the orbitofrontal and anterior cingulate cortex and the head of the caudate nucleus. Although some of these studies have involved symptom provocation (McGuire, 1994; Rauch et al., 1994), they did not use a specific paradigm to study DPLFC function, so that it is impossible to compare them to the present study. Future neuroimaging studies of

OCD patients will benefit from the use of cognitive activation paradigms to examine activation while controlling the mental state of patients (Purcell, Maruff, Kyrios, & Pantelis, 1998).

We also observed another conspicuous feature during the WCST performance, whereby WIS23 and WIS67 trials elicited large P3b waves, though the amplitudes were reliably larger for repetition trials. As we have already discussed, the appearance of larger P3b waves during WIS67 trials is consistent with the context-updating model proposed by Donchin and Coles (1988) for P3b. Our P3b component meets the prediction that P3b amplitude is proportional to the degree of updating of memory representations of the relevant stimulus dimension within each classification series (Donchin & Fabiani, 1991). It is possible that the problems of shifting cognition set in OCD patients are related to difficulties in only paying attention to the relevant stimulus dimensions and ignoring irrelevant ones, which makes mental representation of the correct category blurred. This process may elicit a lower P3b amplitude in OCD patients. Moreover, P3b is related to working memory. Good visuospatial ability and the integrity of the attentional processes of the frontal lobe are necessary for proper functioning of working memory.

Normal spatial working memory performance has been associated with increased activation in mid DLPFC during PET investigations (Owen, Doyon, Petrides, & Evans, 1996a; Owen, Evans, & Petrides, 1996b). We observed that after pharmacological treatment the overlying negative electrical field centred at the left DLPFC has less intensity in WIS67 task, with activity closer to normal controls than in patients without treatment. We can speculate that this is related to problems in inhibitory control, as a consequence of a dysfunction in an inhibitory pathway in prefrontal cortex and central serotonergic neurotransmission. However, despite the fact that this is a very interesting hypothesis, we cannot draw any firm conclusions on this matter from the present study.

CONCLUSIONS

Obsessive-compulsive disorder patients show difficulties in shifting cognitive set. This deficit may be due to problems in inhibitory control, as a consequence of a dysfunction in an inhibitory pathway in the prefrontal cortex. This would explain the poor performance of OCD patients on the WCST in terms of their inability to inhibit or suppress previous incorrect responses. We propose that, in order to balance this inability, there is a hyperactivation in the left DLPF during WCST performance in both conditions (WIS23 and WIS67). Although our results suggest a relationship between efficacy of inhibitory pathways in prefrontal cortex and central serotonergic transmission we cannot arrive at any firm conclusions. Finally, it is not clear whether shifting cognitive set is an enduring ''trait'' marker or a finding that fluctuates with changes in the clinical state.

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