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Neuropsychological Slowness in Obsessive–Compulsive Patients
Is It Confined to Tests Involving the Fronto-Subcortical Systems?

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Background. Although it is acknowledged that obsessive–compulsive (OC) patients may be slower than healthy controls in performing neuropsychological tests, speed has usually been treated as a confounding variable. It is possible, however, that the slower performance of OC patients is itself the result of a dysfunction of specific neural circuits (in particular of fronto-subcortical systems).

Method. A neuropsychological battery including tests sensitive to fronto- and temporo-subcortical dysfunction was administered to a group of OC patients and a group of healthy controls. Each test provided independent indices of accuracy and speed.

Results. OC patients were significantly slower than controls only when performing tasks involving the fronto-subcortical systems, whereas they did not differ from controls with respect to accuracy indices.

Conclusion. It may be that neuropsychological slowness of OC patients is not merely an epiphenomenon of meticulous concern for correct test execution or intrusion of obsessive thoughts, but reflects the dysfunction of fronto-subcortical systems.

Although it is acknowledged that obsessive–compulsive (OC) patients may be slower than healthy controls in performing neuropsychological tests (Insel *et al*, 1983; Zielinsky *et al*, 1991; Christensen *et al*, 1992), speed has usually been regarded as a confounding variable, i.e., it has implicitly or explicitly been maintained that the slower performance of OC patients reflects factors such as meticulous concern for the correct execution of the test, or intrusion of obsessive thoughts disturbing the subject during the task. These interpretations, however, disregard the possibility that the slower performance of OC patients on neuropsychological tests may itself be the result of the dysfunction of specific neural circuits; in particular, slowness has been reported in patients suffering from disorders of the fronto-subcortical systems (Cummings, 1986), and the involvement of these systems in the pathogenesis of the OC syndrome has been suggested by various authors using brain imaging (Baxter *et al*, 1988, 1992; Martinot *et al*, 1990).

In this investigation, a neuropsychological battery, including tests sensitive to fronto- and temporo-subcortical system dysfunction, and allowing speed and accuracy to be evaluated independently, was administered to a group of OC patients and a group of healthy controls. The objective was to check whether neuropsychological slowness in OC patients is confined to, or more marked on, tests involving the fronto-subcortical systems.

Methods

Subjects

Twenty-two patients (13 men and nine women), fulfilling the DSM–III–R criteria (APA, 1987) for the diagnosis of obsessive–compulsive disorder (OCD), were consecutively recruited from the out-patient and in-patient facilities of the University of Naples Psychiatric Department. They had a mean age of 26.6 years (s.d. 7.3; range 17–46), a mean of 9.9 years education (s.d. 3.9; range 3–19), a negative neurological examination, and no history of substance abuse or of neurological or other medical illnesses. The presence of a major depressive episode, as defined in the DSM–III–R, was a criterion for exclusion, even when OCD was the primary diagnosis, but depressive symptoms *per se* were not cause for exclusion. All patients completed a drug-free period of at least 15 days before testing.

Twenty-one healthy volunteers (14 men and seven women) comparable with patients for age (±3 years), handedness and education (±2 years), recruited among the Department personnel and medical students, served as controls. They had a negative neurological examination, and no history of substance abuse or of psychiatric, neurological or other medical illnesses.

All subjects were right-handed, as assessed by the Edinburgh Inventory (Oldfield, 1971).

Neuropsychological tests

The neuropsychological test battery included: (a) the Spatial and Non-Spatial Conditional Associative Learning Tasks (Petrides, 1985); (b) the Self-Ordered Pointing Tasks (drawings and words) (Petrides & Milner, 1982); (c) Corsi's Block Tapping Task and Hebb's Digit Recurring Sequences (Milner, 1978).

To each subject, neuropsychological tests were administered by the same examiner in one session and in the same order (a, b, c).

Here we provide a brief description of the test characteristics and procedures (further details can be found in Milner, 1978; Petrides & Milner, 1982; Petrides, 1985; Gruzelier *et al*, 1988).

(a) Spatial and non-spatial conditional associative learning tasks

The spatial task uses six lamps and six cards, and the position of each lamp is associated with a card; in the non-spatial task, each of six coloured lights is associated with one of six hand postures. In these tests, the subject has to learn, by trial and error, the correct association between pairs of stimuli. Both tests were designed by Petrides (1985) as analogous to the delayed response tasks used in animal experiments, and they test the ability to select the appropriate response to a given stimulus. The spatial test has proven sensitive to right frontal lesions and to extensive right temporo-hippocampal damage; the non-spatial one is sensitive to both right and left frontal lesions, as well as to extensive left hippocampal lesions (Petrides, 1985). In both these tests, the learning procedure by trial and error (procedural knowledge) requires, according to Mishkin & Petri (1984), an intact functioning of the basal ganglia.

(b) Self-ordered pointing tasks (drawings and words)

In these tests, the subject is presented with sets of cards. Each card contains several drawings or words, and the subject has to touch a different item on each card, in any sequence he/she wishes, but without touching any item more than once. Both test the ability of the subject to initiate and organise sequences of responses, and to carry them out while constantly monitoring their execution. The tests are sensitive to left frontal lobe lesions, due to the crucial role played by this area in the programming of responses, whereas right frontal lobe lesions and extensive damage to the ipsilateral hippocampus have been related to an impaired performance only on the test using drawings (Petrides & Milner, 1982).

(c) Corsi's block tapping task and Hebb's digit recurring sequences

These tests use 24 sequences of blocks and digits. All sequences are one item in excess of the subject's immediate memory span, which is assessed beforehand. In Corsi's test, the examiner taps sequences of blocks and the subject has to repeat each sequence immediately; in Hebb's test, the patient listens to the examiner presenting sequences of digits and has to repeat each sequence immediately; unknown to the subject, the same sequence recurs every third trial. Both test the ability to learn a recurring sequence, whose memory trace is expected to be reinforced more than those of the nonrecurring sequences. Hebb's test is impaired by left temporo-hippocampal dysfunction, while Corsi's test is sensitive to right temporo-hippocampal dysfunction (Milner, 1978).

Psychopathological assessment

Psychopathological evaluation was carried out on the same day as neuropsychological testing. The following instruments were used: the Yale–Brown Obsessive–Compulsive Scale (Goodman *et al*, 1989), providing a separate score for obsessions and compulsions, and a total score; the Maudsley Obsessive–Compulsive Inventory (Hodgson & Rachman, 1977), exploring checking, cleaning, slowness and doubt, providing a separate score for each symptom area and a total score; and the 17-item Hamilton Rating Scale for Depression.

Statistical data analysis

Accuracy and speed indices were first submitted to a preliminary statistical analysis to assess normality and homoscedasticity. Since none of the indices met these requirements, data were transformed. For both accuracy and speed indices, all values were log-transformed, except for ratios that were submitted to the arctangent transform. Transformed data met the above specified requirements and were used for further analyses. Outliers (subjects showing values exceeding the 75th or the 25th percentile by 1½ times the interquartile range) on each of the considered indices were excluded from the analyses.

Separate overall MANOVAs were run for accuracy and speed indices. When the overall MANOVA (Hotelling's T^2) yielded a significant effect of diagnosis or a significant hemisphere × diagnosis interaction, further MANOVAs were performed for each test. Follow-up univariate tests were performed only when MANOVA showed significant effects.

Pearson's test was used to investigate correlations between neuropsychological indices and demographic or psychopathological variables.

Results

The mean total score for all patients on the Yale–Brown scale was 26 (s.d. 5.5); the mean scores on compulsions and obsessions were 13.6 (s.d. 3.8) and 12.4 (s.d. 3.9), respectively. The mean total score on the Maudsley inventory was 16.6 (s.d. 6); the mean scores on the subscales Checking, Cleaning, Slowness and Doubt were 5.7 (s.d. 2.3), 5.3 (s.d. 2.7), 2.9 (s.d. 1.1) and 4.6 (s.d. 1.6), respectively. The mean total score on the Hamilton scale was 11.9 (s.d. 4.1); three patients had a total score greater than 16; all the statistical analyses were run with and without these subjects.

The overall MANOVA for accuracy indices of neuropsychological tests did not yield any effect of diagnosis; a significant hemisphere effect was found ($F_{12,19}=7.8$, $P<0.0001$), due to a greater accuracy on all the tests exploring left hemisphere functions. No interaction between diagnosis and hemisphere was found.

The overall MANOVA on speed indices yielded a significant effect of diagnosis ($F_{3,30}=3.87$, $P<0.02$) and of hemisphere ($F_{3,30}=9.52$, $P<0.0001$); the diagnosis/hemisphere interaction did not reach the significance level. No change was observed after the exclusion of the three patients with a total Hamilton score >16. Differences on speed indices between obsessives and healthy subjects for each test were then investigated using separate MANOVAs.

On the conditional associative learning tasks, significant effects of diagnosis and hemisphere ($F_{1,37}=9.61$, $P<0.004$; $F_{1,37}=9.15$, $P<0.004$, respectively) and a significant hemisphere/diagnosis interaction ($F_{1,37}=4.8$, $P<0.03$) were found, since obsessives were slower than healthy subjects on the spatial test only ($F_{1,37}=14.7$, $P<0.0005$) (Fig. 1). The diagnosis/hemisphere interaction only approached the statistical significance level when the three patients with a total Hamilton score >16 were excluded ($F_{1,34}=2.77$, $P=0.1$).

As to the speed indices of the self-ordered pointing tasks, a significant effect of hemisphere was observed ($F_{1,35}=21.6$, $P<0.0001$); diagnosis only approached significance when considering the whole group ($F_{1,35}=3.5$, $P<0.07$), but the effect was significant when excluding patients with a total Hamilton score >16 ($F_{1,32}=4.8$, $P<0.03$). No significant interaction diagnosis/hemisphere was found, as OC patients were significantly slower than controls on both the verbal and the non-verbal task (Fig. 2).

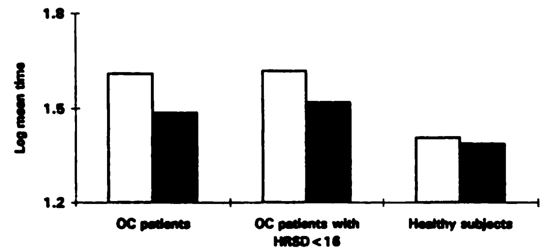

Fig. 1 Log mean time on the spatial (□) and non-spatial (▨) conditional associative learning tasks (SCAL and NSCAL, respectively), in obsessive–compulsive (OC) patients and healthy subjects. OC patients as a whole were significantly slower than healthy subjects only on the SCAL ($P<0.005$). OC patients with a total score on the Hamilton Rating Scale for Depression (HRSD) <16 were significantly slower than healthy subjects on both SCAL and NSCAL ($P<0.001$).

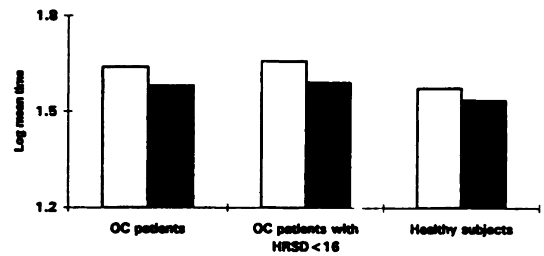

Fig. 2 Log mean time on the self-ordered pointing tasks (SOPT-drawings (□) and SOPT words (▨)), in obsessive-compulsive (OC) patients and healthy subjects. OC patients with a total score on the Hamilton Rating Scale for Depression (HRSD) <16 were significantly slower than healthy subjects on both SOPT-drawings and SOPT-words ($P<0.03$).

For Corsi's and Hebb's tests, MANOVA did not yield either a significant main effect of diagnosis or a significant diagnosis/hemisphere interaction (Fig. 3).

The speed indices of all the tests showed a large overlap between individual values for both patients and controls. However, in 12/22 patients, the mean time on the spatial conditional associative learning task was outside the range of the healthy subjects.

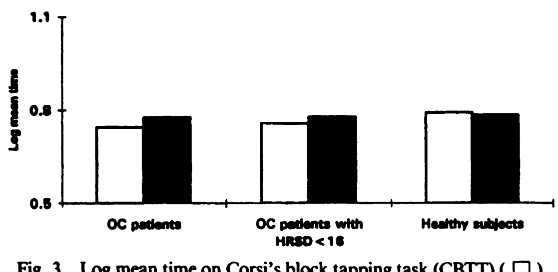

Fig. 3 Log mean time on Corsi's block tapping task (CBTT) (□) and Hebb's digit recurring sequences (HDRS) (▨) in obsessive-compulsive (OC) patients and healthy subjects. (HRSD = Hamilton Rating Scale for Depression).

The mean time spent on each self-ordered pointing task was positively correlated with the score for obsessions on the Yale–Brown scale ($r=0.56$, $P<0.01$ for the non-verbal task; $r=0.48$, $P<0.05$ for the verbal task). No significant correlation was observed between the mean time on any neuropsychological test and the global score on the Hamilton scale.

Discussion

In our experimental setting, OC patients were significantly slower than controls only when performing tasks which involve the fronto-subcortical systems, i.e. the conditional associative learning tasks and the self-ordered pointing tasks. They were found to be slower on both the verbal and the non-verbal subtests, suggesting a bilateral dysfunction. Since several neuropsychological and electrophysiological investigations have found that abnormalities in OC patients mainly involve the right hemisphere (Insel *et al*, 1983; Khanna, 1988; Boone *et al*, 1991; Zielinski *et al*, 1991; Christensen *et al*, 1992; Kuskowski *et al*, 1993), it might be worth noting that: (a) the difference between patients and controls was larger on the spatial version of the conditional associative learning task (tapping the functioning of the right fronto-subcortical system) than on the non-spatial one; moreover, on the former test, but not on the latter, 12/22 subjects had values outside the healthy controls' range; (b) the r value of the correlation between the mean time on the self-ordered pointing tasks and the score for obsessions on the Yale–Brown scale was higher for the non-verbal task (right fronto-subcortical systems) than for the verbal one.

No significant correlation was found between the mean time on any neuropsychological test and the global score on the Hamilton scale. Moreover, the exclusion of patients with a global score on the Hamilton scale greater than 16 did not affect the results of some tests (Corsi's block tapping task, Hebb's digit recurring sequences, and the spatial conditional associative learning task) and even produced a greater mean time difference between OC patients and healthy controls on the others (the self-ordered pointing tasks and the non-spatial conditional associative learning task). This argues against the influence of depressive symptoms on the slowness observed in our OC patients; this aspect, however, should be verified in a larger sample.

No difference between OC patients and healthy controls was found for the speed indices of Corsi's and Hebb's tests. Patients were even slightly faster than controls on Corsi's task.

This pattern of results argues against the hypothesis that slowness in OC patients is due to either meticulous concern for the correct execution of the test or the intrusion of obsessive thoughts disturbing the subject during the task. If it were so, slowness would have been observed on all the tasks.

The lack of differences between OC patients and healthy controls in the accuracy indices of all the tests administered was an unexpected finding, as in other studies OC patients were found to be less accurate than healthy controls in the performance of several neuropsychological tests (Head *et al*, 1989; Boone *et al*, 1991; Zielinsky *et al*, 1991; Christensen *et al*, 1992). However, findings from the literature have not been consistent, and several methodological issues have been invoked to explain this (Christensen *et al*, 1992). The most important are: the selection of patients based on the identification of isolated symptoms, instead of international diagnostic criteria; the inclusion of patients with clinically relevant depression; an inadequate matching of patients and controls; statistical data analysis based on multiple tests, without correction for α inflation and without adequate data treatment for achieving normality and homoscedasticity; failure to use appropriate tests for assessing functions under investigation; failure to provide independent evaluation of speed and accuracy; and differences in testing methodology.

In conclusion, in tasks involving fronto-subcortical systems, OC patients are as able as healthy controls to provide the correct response, but require a longer time. It is tempting to speculate that, just like obsessions, slowness in these patients is the result of a difficulty in suppressing intrusive and perseverative responses: before acting, patients have to choose from many competing responses, that in other subjects are automatically rejected. This interpretation appears in line with findings from several brain imaging studies, showing in OC patients a hyperactivity of the circuit including the orbitofrontal, the prefrontal and the cingulate cortex, as well as the caudate nucleus (Baxter *et al*, 1992). The frontal and the cingulate cortex are crucial for the activity of generating internal cues for initiating, planning and monitoring behavioural responses; the basal ganglia, in turn, are partly responsible for the gating mechanisms of both inner and external sensory input. As a consequence of the hyperactivity of this circuit, OC patients might be overwhelmed by internal cues, and might take longer to choose those relevant to the ongoing task and to exclude the irrelevant ones.

The positive correlation between the mean time on both self-ordered pointing tasks and the score on the Yale–Brown obsession subscale supports the hypothesis that an inadequate early inhibition of competing internal cues may be the mechanism underlying both slowness and obsessions.

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