Psychological Medicine, 1999, **29**, 1377–1385. Printed in the United Kingdom
© 1999 Cambridge University Press

Abnormalities of internally generated saccades in obsessive–compulsive disorder

P. MARUFF,[1] R. PURCELL, P. TYLER, C. PANTELIS AND J. CURRIE

From the School of Psychology, La Trobe University, Neurophysiology and Neurovisual Research Unit and Cognitive Neuropsychiatry Unit, Mental Health Research Institute of Victoria, Parkville, and Department of Psychiatry and Psychology, University of Melbourne, Victoria; and Brain Research Unit, Drug and Alcohol Services, Westmead Hospital, Sydney, New South Wales, Australia

ABSTRACT

Background. We aimed to utilize tests of saccadic function to investigate whether cognitive abnormalities in obsessive–compulsive disorder (OCD) arise from a dysfunction of inhibitory processes or whether they reflect a more general difficulty in guiding behaviour on the basis of an internal representation of task goal.

Methods. Twelve patients with OCD and 12 matched controls performed a visually-guided saccade task, a volitional prosaccade task and an antisaccade task. The latency and gain of saccades was compared between groups for the three saccade tasks. The number of antisaccade errors was also calculated and compared between groups.

Results. There was no difference for antisaccade error rates between the groups. The latency of visually guided saccades did not differ between groups, however the latency of both volitional prosaccades and antisaccades was significantly slower in the patients with OCD than in controls. The difference in latency between volitional prosacades and antisaccades, however, was equal between groups.

Conclusions. These results suggest that patients with OCD have an abnormality in guiding behaviour on the basis of an internal representation of the task goal, rather than a problem with inhibiting reflexive behaviour.

INTRODUCTION

Obsessive–compulsive disorder (OCD) is an anxiety disorder characterized by marked distress associated with recurrent and intrusive ideas, thoughts or impulses, and ritualized or repetitive behaviours (American Psychiatric Association, 1994). Sufferers of the disorder frequently experience difficulties inhibiting internal, cognitive stimuli (obsessions), as well as behavioural or motor programmes (compulsions), resulting in stereotyped or often rigid behaviour. Recent research has begun to consider the brain–behaviour relationships associated with the disorder. Structural and functional neuroimaging studies have consistently identified abnormalities of frontal and subcortical brain regions in patients with OCD (McGuire *et al*. 1994; Rauch *et al*. 1994; Lucey *et al*. 1995; Perani *et al*. 1995; Robinson *et al*. 1995; Breiter *et al*. 1996). Consistent with these observations, neuropsychological studies report that patients with OCD perform poorly on tests of executive function hypothesized to depend on the integrity of frontal lobe brain areas and their subcortical connections (Malloy, 1987; Galderisi *et al*. 1995; Veale *et al*. 1996; Purcell *et al*. 1998*a*, *b*; Schmidtke *et al*. 1998).

One intuitively appealing brain–behaviour hypothesis of OCD is that abnormalities in executive function manifest as general deficits in the inhibitory control of cognitive processes. Some of the strongest evidence in support of this

[1] Address for correspondence: Dr Paul Maruff, Neurophysiology and Neurovisual Research Unit, Mental Health Research Institute of Victoria, Parkville, VIC 3052, Australia.

https://doi.org/10.1017/S0033291799008843 Published online by Cambridge University Press

hypothesis comes from ocular motor studies that report patients with OCD to have difficulty performing the antisaccade task (Tien *et al.* 1992; Rosenberg *et al.* 1997). Antisaccades are eye movements made deliberately in the direction opposite to that of a sudden onset peripheral target. To perform the antisaccade task, subjects must suppress or inhibit a reflexive saccade towards the target, but attend to and use the target's visual information to move their eyes to a symmetrical but unmarked location in the contralateral visual field (Hallet, 1978; Currie *et al.* 1991; Crawford *et al.* 1995; Pierrot-Deseilligny *et al.* 1995). Abnormal performance on the antisaccade task is indicated by an increased number of reflexive glances towards the target (antisaccade error rate), or when antisaccades are made correctly, the latency of these may be increased significantly. This abnormal performance has been interpreted as a dysfunction of inhibitory processes associated with the prefrontal cortices and their subcortical connections based on the observation that patients with lesions that involve the prefrontal cortex and basal ganglia show abnormally high error rates on the antisaccade task (Guitton *et al.* 1985; Goldman-Rakic, 1987; Pierrot-Deseilligny *et al.* 1995).

In our recent neuropsychological studies of OCD, we found no evidence of disinhibition or perseveration on tests of executive function (Purcell *et al.* 1998*a*, *b*; Barnett *et al.* 1999). Instead, patients with OCD had difficulty only on a task that required them to guide performance on the basis of an internal representation of the task goal. On problem-solving tasks of equivalent or greater difficulty, but where the task goal remained visible throughout testing, the patients with OCD performed normally. On the basis of this finding we proposed that cognitive deficits in OCD may be characterized parsimoniously as a difficulty in guiding behaviour on the basis of an internal representation of the task goal (Purcell *et al.* 1998*b*). This abnormality in cognitive function suggests that hypotheses regarding deficits in inhibitory function in OCD, based on antisaccade task performance, may be incorrect or incomplete. As antisaccades must be made to a target location that is not visible, impaired performance on the antisaccade task may reflect difficulties in using an internal representation of the saccade goal rather than from a difficulty in inhibiting reflexive saccades.

According to this hypothesis, impaired performance should occur on any saccade task that requires saccades to be executed to goal locations represented internally, irrespective of the requirement for inhibition. Therefore, the aim of this study was to compare performance on a visually guided prosaccade, a volitionally guided prosaccade and an antisaccade task between patients with OCD and matched controls. On the visually guided prosaccade task an external representation of the saccade goal is provided. However, both the volitional prosaccade and antisaccade tasks require saccades to be programmed on the basis of an internal representation of the target location. The antisaccade task has the additional requirement that subjects inhibit any reflexive glances towards the target. We hypothesized that patients with OCD would be impaired in making volitional prosaccades and antisaccades, but show no impairment in making visually guided prosaccades.

METHOD

Subjects

The patients with OCD were referrals to the University of Melbourne/Royal Melbourne Hospital Psychology Out-patient Clinic. Patients who met the DSM-IV (American Psychiatric Association, 1994) criteria for OCD were screened for inclusion in the study. Exclusion criteria were: a co-morbid Axis I disorder; a neurological disorder or head injury; a history of alcohol or other substance abuse; or a serious medical illness. The 12 patients who met the study criteria were administered the Anxiety Disorders Interview Schedule for DSM-IV (ADIS-IV, Brown *et al.* 1994) to confirm the diagnosis of OCD and the Hamilton Depression (HAM-D: 24 item) and Anxiety Rating Scales (HARS: 17 item) (Hamilton, 1960) to assess the presence and severity of co-morbid symptoms. The Yale-Brown Obsessive–Compulsive Scale (YBOCS, Goodman *et al.* 1989) was used to assess the severity of OCD symptoms. All patients had normal or corrected vision and no patient had a history of oculomotor damage. Nine patients were medicated at the time of testing (paroxetine, $N = 3$; clomipramine, $N = 1$; tranylcypromine sulfate, $N = 1$; fluoxetine,

https://doi.org/10.1017/S0033291799008843 Published online by Cambridge University Press

$N = 4$), while the remaining three patients had been medication free for at least 6 months. No subject was taking benzodiazepine medication. A summary of the subjects' descriptive and clinical characteristics is provided in Table 1.

A group of healthy, normal controls were recruited from advertisements and were matched to the patient group according to sex, age, handedness and education. Control subjects were screened with the ADIS-IV to exclude a history of mental illness, significant family history of mental illness or a history of alcohol or other substance abuse. Controls were also administered the HAM-D, HARS and YBOCS to assess the presence of any depression, anxiety or OCD symptoms. After complete description of the nature and requirements of the study, each subject provided written informed consent to participate.

Procedure and tasks

Eye movement recording

No subject had participated in oculargraphy studies before and thus were considered task naïve. Eye movements were recorded using high resolution infrared oculography (IRIS, Skalar), with the head stabilized in a chin rest. Subjects were seated 1 metre from a screen onto which a laser target was projected, computer controlled by X–Y mirror galvanometres (General Scanning, MA). Eye and target position signals were recorded at 1 kHz and stored for off-line analysis. Eye position was differentiated using a computer based algorithm to obtain eye velocity. The recording and scoring of eye movements have been described in greater detail elsewhere (Currie *et al.* 1991; Maruff *et al.* 1998).

Visually guided prosaccades were generated by asking patients to fixate on a central green light-emitting diode which was then extinguished simultaneously with the appearance of a peripheral red target positioned either 10° or 15° to the left or right of the central fixation point. The red target remained visible for 2000 ms. Subjects were instructed to make a saccade to the target location and hold their gaze there until returning to central fixation with the reappearance of the green central target (3·5 s). Displacement and timing (2·0–2·5 s after fixation) of the appearance of the peripheral red target was random.

Volitional prosaccades and antisaccades were generated using the same paradigm as for visually guided prosaccades except that the target was extinguished 100 ms after it appeared at one of the peripheral locations. For the volitional prosaccade task, subjects were instructed to make a saccade to the location occupied previously by the target as soon as it appeared and to hold their gaze there until returning to central fixation with the reappearance of the green central target (3·5 s). A correct volitional prosaccade was an initial saccade to the location occupied previously by the peripheral red target. For the antisaccade task, subjects were instructed not to look at the target but to make a saccade to a location of equal amplitude in the opposite visual field. When this was completed they were to hold their gaze at that location until the central green target reappeared.

Subjects performed the visually guided prosaccades, volitional prosaccades and antisaccades in blocks of 36 trials each. The order in which each task was presented was varied across subjects. In total, subjects performed 106 trials on each saccade task. For each task, measurements were made of the latency and accuracy of initial saccades to a target step. For the antisaccade task, any initial reflexive eye movement towards the target was recorded as incorrect, even if a subsequent correction to the correct location was made. Trials that involved blink, head movement or anticipatory artefact were rejected. This was low in both groups ($< 2\%$ across each task). Each subject performed 10 practice trials before the first block of trials for each saccade task. These trials were excluded from any analysis. For each subject, the mean latency and gain of correct visually guided prosaccades, volitional prosaccades and antisaccades was calculated. For the antisaccade task, the number of incorrect reflexive glances towards the target was calculated for each subject and expressed as a percentage of valid trials (antisaccade error rate %).

Statistical analysis

Antisaccade error rates for each of the saccade tasks were compared first using a *t* test and then using the Mann–Whitney U (MW*U*) test. Each subject's mean latency and mean gain for each saccade task was submitted to separate 2 (group) × 3 (saccade task) ANOVAs with repeated measures on the saccade task factor. In

https://doi.org/10.1017/S0033291799008843 Published online by Cambridge University Press

order to protect against violation of the assumption of compound symmetry, repeated effects with degrees of freedom greater than one were tested using the multivariate analogue to the repeated measures. Significant interactions were investigated using *post hoc* interaction contrasts and *post hoc t* tests with error rate adjusted according to the Bonferroni procedure. Relationships between significant effects and demographic measures and symptom levels were investigated using Pearson's and Spearman's *r* correlations.

RESULTS

For saccade gain, there was a significant main effect for task ($F(2,21) = 131$; $P < 0{\cdot}001$), but no effect for group ($F < 1$), and no group by task interaction ($F(2,21) = 1{\cdot}3$; $P = 0{\cdot}32$, Table 2). Investigation of the task effect indicated that the gain of visually guided saccades was greater than that for volitional prosaccades ($F(1,21) = 43$; $P < 0{\cdot}001$). The gain of volitional prosaccades was in turn greater than that for antisaccades ($F(1,21) = 18{\cdot}1$; $P < 0{\cdot}001$, Table 2). The median antisaccade error rate was not significantly different between the patients with OCD (median = 10%, range 2–53%) and controls (median = 10%, range 0–25%, MW$U = 56{\cdot}5$; $P = 0{\cdot}37$, Fig. 1). Inspection of the data indicated that error rates in two of the OCD subjects were outside the normal range of performance established in our laboratory (e.g. 0–25%, Currie *et al.* 1991; Maruff *et al.* 1996, 1998). However, due to the large number of saccade trials, a sufficient number of saccades remained following exclusion of error trials to allow reliable estimates of antisaccade latency for these two subjects.

Table 1. *Comparison of demographic and symptom characteristics of control and OCD groups* (*all values mean* (S.D.) *unless indicated otherwise*)

Measure	OCD	Control	*P*
Sex (*N* female/male)	7/5	7/5	NS
Age	47·0 (8·5)	46·0 (9·9)	NS
Handedness (*N* right/left)	10/2	9/3	NS
Education (years)	13·1 (3·2)	14·2 (2·9)	NS
Age onset of illness	20·7 (13·4)	N/A	—
Length of illness (years)	24·4 (15·9)	N/A	—
YBOCS			
Total score	24·2 (10·3)	0·0	—
Obsessions	11·7 (6·5)	0·0	—
Compulsions	11·6 (6·9)	0·0	—
HAM-D	9·0 (4·4)	1·96 (1·76)	< 0·001
HARS	12·9 (8·7)	1·34 (1·56)	< 0·001

Table 2. *Mean* (+S.D.) *gain for saccade tasks in control and OCD groups*

	Control Mean (S.D.)	OCD Mean (S.D.)
Visually-guided prosaccade	0·95 (0·05)	0·94 (0·08)
Volitional prosaccade	1·05 (0·06)	1·09 (0·09)
Antisaccade	1·05 (0·08)	1·10 (0·05)

For saccade latency, there was no significant main effect for group ($F(2,21) = 1{\cdot}64$; $P = 0{\cdot}21$), but a significant effect for task ($F(2,21) = 175{\cdot}04$; $P < 0{\cdot}0001$) and a significant task by group interaction ($F(2,21) = 7{\cdot}4$; $P = 0{\cdot}004$, Fig. 2). This interaction was decomposed with two group × saccade task interaction contrasts. The first group and saccade task contrast (visually guided prosaccade, volitional prosaccade) showed a significant interaction ($F(1, 22) = 14{\cdot}1$; $P = 0{\cdot}001$). The latency of visually guided prosaccades was equivalent between groups ($t < 1$), but the latency of volitional prosaccades was significantly slower in the patients with OCD than in controls ($t(22) = 5{\cdot}6$; $P = 0{\cdot}01$). The second group and saccade task contrast (volitional prosaccade, antisaccade) found no interaction ($F < 1$), although there was a main effect of group ($F(1,22) = 4{\cdot}53$; $P = 0{\cdot}02$). The mean latency of both volitional prosaccades and antisaccades was slower in the patients with OCD than in controls.

As there was considerable variability in antisaccade error rate in the OCD group, the variability in the general deficit in making volitional saccades was investigated. To achieve this, a visual–volitional difference score was calculated for each subject by subtracting the mean latency of visually guided saccades from the mean latency of volitional prosaccades (Fig. 3). Levine's test for homogeneity of variance was non-significant ($F(1,21) = 2{\cdot}0$; $P = 1$), indicating that there was no significant difference between groups for the variability in the visual–volitional differences scores. Finally, for the patients with OCD, there was no correlation between the visual–volitional difference score

https://doi.org/10.1017/S0033291799008843 Published online by Cambridge University Press

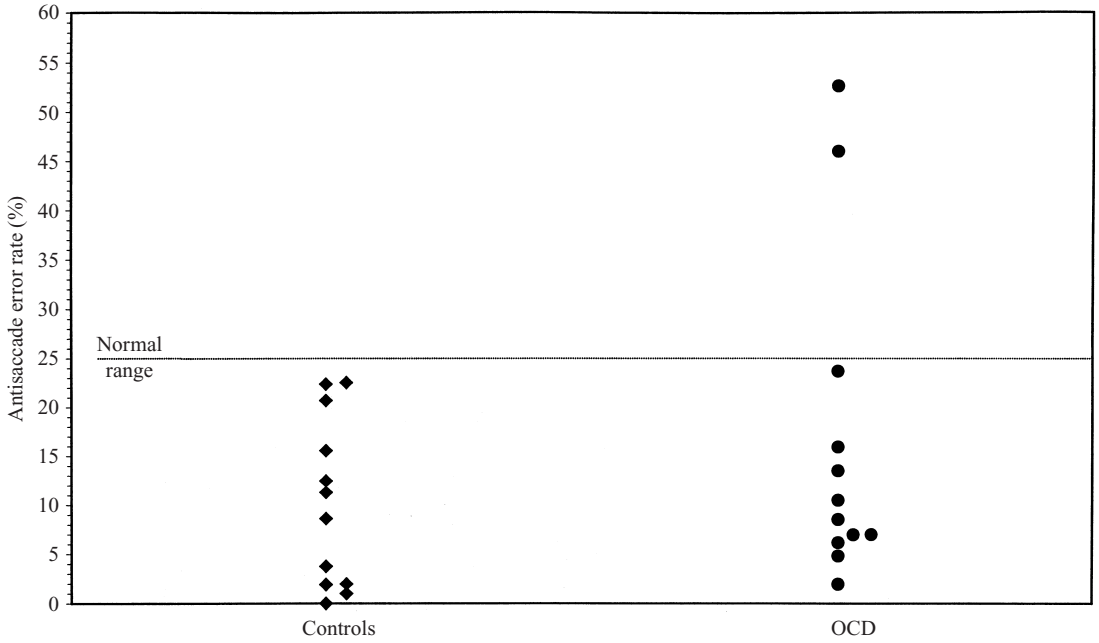


FIG. 1. Scatterplot of antisaccade error rates in control (◆) and OCD (●) groups. Normal range for antisaccade performance derived from references 17, 26 and 27.

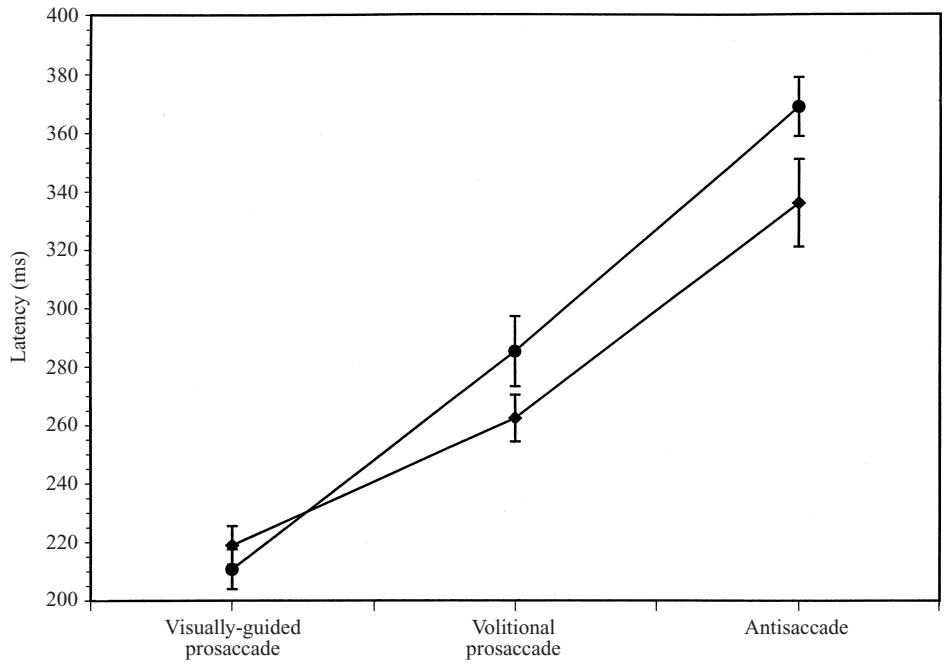


FIG. 2. Mean (+S.D.) latency for visually-guided prosaccade, volitional prosaccade and antisaccade tasks in control (◆) and OCD (●) groups.

https://doi.org/10.1017/S0033291799008843 Published online by Cambridge University Press

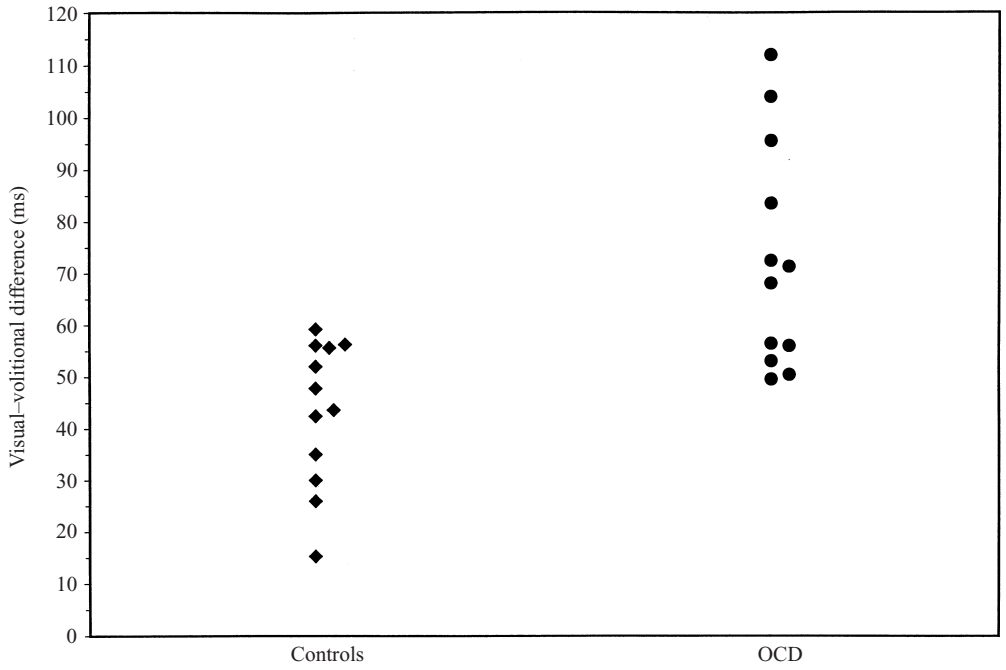


FIG. 3. Scatterplot of visual–volitional difference scores in control (◆) and OCD (●) groups.

and any demographic, medication or symptom variables.

DISCUSSION

The results of this study suggest that patients with OCD require more time to prepare saccades that are based on an internal representation of the saccade goal, in comparison with the situation when external validation of the task goal is presented. This occurs irrespective of whether saccades must to be made to, or away from, the initial target. The slower preparation time was demonstrated by the increased latency of volitional prosaccades and antisaccades when compared with visually guided saccades (Fig. 2). When the difference between the latencies of visually-guided prosaccades and volitional prosaccades was calculated for each subject and compared (visual–volitional difference score, Fig. 3), very little overlap between the distributions of scores from the patient and control groups was observed. More importantly, the variability in these difference scores was equivalent between the control and OCD groups. This suggests that, unlike the increased antisaccade error rate (Fig. 1), abnormal slowing in planning volitional saccades occurred in all of the patients with OCD. These results support the hypothesis that patients with OCD have difficulty in guiding behaviour on the basis of internal representations of the task goal. As in our previous studies, there was no relationship between cognitive performance and symptom severity, suggesting that these two manifestations of OCD are independent (Purcell *et al.* 1998*a*, *b*; Barnett *et al.* 1999).

The percentage of errors on the antisaccade task was generally within normal limits (Currie *et al.* 1991; Maruff *et al.* 1996, 1998). Interestingly, the magnitude of the difference in latency between volitional prosaccades and antisaccades was equivalent between patients and controls. This additional slowing in the latency of antisaccades has been inferred to represent the additional processing time necessary to inhibit reflexive saccades towards the target and invert the saccade programme so that the eyes are driven away from the target (Hallet, 1978; Guitton *et al.* 1985; Goldman-Rakic, 1987; Currie *et al.* 1991; Crawford *et al.* 1995; Pierrot-Deseilligny *et al.* 1995). Thus, when compared with the slow volitional prosaccades, there is no evidence of any specific slowing of

https://doi.org/10.1017/S0033291799008843 Published online by Cambridge University Press

inhibitory processes in OCD. However, had the antisaccade latency been compared directly to the latency of visually-guided prosaccades, as is generally the case (Guitton *et al*. 1985; Currie *et al*. 1991; Pierrot-Deseilligny *et al*. 1995; Maruff *et al*. 1996, 1998) then the current results would have been interpreted as showing impairments in ocular motor inhibitory processes. Performance on the volitional prosaccade task is, therefore, a more suitable control condition for the antisaccade task than is performance on the visually guided prosaccade task.

The normal latency of visually guided prosaccades observed in the patients with OCD is consistent with all previous studies of ocular motor function in adults with this disorder (Nickoloff *et al*. 1991; Tien *et al*. 1992; Gambeni *et al*. 1993; Rosenberg *et al*. 1997). To date, two studies have investigated antisaccade performance in OCD. Tien *et al*. (1992) found that mean antisaccade error rates were higher in patients with OCD than controls. However, inspection of their data shows that antisaccade error rates were within the normal limits for 11/16 of their patients. Tien *et al*. noted this heterogeneity and suggested that it was gender-related, with error rates in male patients higher than in females. However, this *post hoc* hypothesis was not supported statistically. Unfortunately, Tien *et al*. did not report the latency of antisaccades in their group. Rosenberg *et al*. (1997) also reported that mean antisaccade error rates were significantly higher in patients with OCD than in matched controls. However, this abnormality occurred only when targets appeared at 8° from fixation. While Rosenberg *et al*. did not present their raw data, inspection of the standard deviations at the 8° location indicates that there was no overlap in the distributions of antisaccade error rates between groups. Rosenberg *et al*. also reported that mean antisaccade latency did not differ between control and OCD groups, although the group means for this variable were not presented. Both the Tien and Rosenberg studies interpreted the increased antisaccade error rates in OCD as reflecting dysfunction of inhibitory ocular motor processes that were associated with function in the prefrontal cortex.

It is likely that points of methodology and statistical analysis in these two studies limit the extent to which performance on the antisaccade test can be inferred to represent inhibitory deficits in OCD. First, in the Tien *et al*. (1992) study subjects made only 10–16 antisaccades. Therefore, for any one patient the reliability of the measure of antisaccade error rate is questionable. Any difficulties related to understanding test instructions, test anxiety or delay in learning how to make antisaccades would have increased antisaccade errors, particularly at the beginning of the task. Due to the small number of trials, any initial errors would have had a considerable influence in increasing the patient's antisaccade error rate. As the number of trials increase the effects of these factors decreases. Previous research by our group and by others suggest that at least 40 antisaccade trials are required to obtain reliable estimates of error rate (Currie *et al*. 1991; Crawford *et al*. 1995; Maruff *et al*. 1996, 1998). While Rosenberg *et al*. (1997) had their subjects perform 36 trials of the antisaccade task, they found higher error rates at only one target amplitude. Patients with OCD made, on average, 35% errors when targets appeared at the 8° amplitude. As three different target amplitudes were used, this error rate reflects only four errors out of 12 trials, which raises doubt about the validity of this result. The finding of increased antisaccade latency in the current study is also inconsistent with the Rosenberg *et al*. (1997) study, which found no such difference between groups. However, in the Rosenberg *et al*. study, patients with OCD showed an antisaccade error of 60% when averaged across the different target amplitudes. Appropriately, these trials were excluded from further analysis. Consequently, for each subject, the mean antisaccade latency would have been calculated from approximately 15 trials (40% of 36 trials = 15). This raises the possibility that the failure to find any differences in antisaccade latency occurred because the measure of antisaccade latency was also unreliable in each subject, thereby increasing the estimate of variance in antisaccade latency for each group. The criticisms made of the estimates of antisaccade latency and antisaccade error rate in both the Tien *et al*. and Rosenberg *et al*. studies can be countered if studies use a sufficient number of trials in their saccade tasks to provide reliable measures for the variables of interest. On the basis of limitations identified in these studies we measured saccade performance using more than 100 trials for each task. The failure to

https://doi.org/10.1017/S0033291799008843 Published online by Cambridge University Press

replicate the increased antisaccade error rate in OCD supports our criticisms of these methodologies.

The clinical characteristics of OCD, with the difficulties suppressing inappropriate thoughts or behaviour, make it intuitively appealing to argue that cognitive deficits observed in this disorder may also be characterized by difficulties of inhibition. However, the results of the current study suggest that OCD cannot be characterized cognitively as a general disorder of inhibition. While a small proportion of patients with OCD may have difficulty inhibiting prepotent responses, the clinical significance of this subgroup remains to be determined using a larger sample. We believe a more parsimonious explanation for the results of studies of saccadic function in OCD is that patients have difficulty in guiding purposive behaviour on the basis of internal representations of the goal of the behaviour. This abnormality is consistent with our recent neuropsychological investigations, which concluded that a major abnormality in patients with OCD was in guiding behaviour on the basis of an internal representation of the task goal (Purcell *et al*. 1998*b*). This impairment may have relevance to the clinical presentation of OCD. For example, checking compulsions may reflect impaired internal representations of behaviour (e.g. switching off the stove), that necessitate external verification (e.g. checking the stove). While this link between neuropsychological and clinical manifestations of OCD is speculative, it does have support in those studies that find decreased confidence in memories, and increased deficits in memory for actions in patients with OCD (McNally & Kohlbeck, 1993; Ecker & Englekamp, 1995). This hypothesis is supported by the present results and provides an interesting direction for further research.

We wish to thank Kellie Mahoney and Justin Curtin for their help with eye movement recordings.

REFERENCES

American Psychiatric Association (1974). *Diagnostic and Statistical Manual of Mental Disorders, 4th edn*). American Psychiatric Association: Washington, DC.

Barnett, R., Maruff, P., Purcell, R., Wainwright, K., Brewer, W., Kyrios, M. & Pantelis, C. (1999). Impairment of olfactory identification in obsessive–compulsive disorder. *Psychological Medicine* **29**, 1227–1233.

Breiter, H. C., Rauch, S. L., Kwong, K. K. & Baker, J. R. (1996). Functional magnetic resonance imaging of symptom provocation in obsessive–compulsive disorder. *Archives of General Psychiatry* **53**, 595–606.

Brown, T. A., DiNardo, P. A. & Barlow, D. H. (1994). *Anxiety Disorders Interview Schedule for DSM-IV*. Graywind Publications Incorporated: New York.

Crawford, T. J., Haeger, B., Kennard, C., Reverly, M. A. & Henderson, L. (1995). Saccadic abnormalities in psychotic patients. I. Neuroleptic-free psychotic patients. *Psychological Medicine* **25**, 461–471.

Currie, J. N., Ramsden, B., McArthur, C. & Maruff, P. (1991). Validation of a clinical antisaccadic eye movement test in the assessment of dementia. *Archives of Neurology* **48**, 644–648.

Ecker, W. & Engelkamp, J. (1995). Memory for actions in obsessive–compulsive disorder. *Behaviour and Cognitive Psychotherapy* **23**, 349–371.

Galderisi, S., Mucci, A., Catapano, F., Damato, A. C. & Maj, M. (1995). Neuropsychological slowness in obsessive–compulsive patients – is it confined to tests involving the fronto-subcortical systems? *British Journal of Psychiatry* **167**, 394–398.

Gambeni, O., Abbruzzese, M. & Scarone, S. (1993). Smooth pursuit and saccadic eye movements and Wisconsin Card Sorting Test performance in obsessive–compulsive disorder. *Psychiatry Research* **48**, 191–200.

Goldman-Rakic, P. S. (1987). Circuitry of primate prefrontal cortex and regulation of behaviour by representational memory. In *Higher Cortical Function. American Physiological Society Handbook of Physiology*, *5* (ed. F. Plum and V. Mountcastle), pp. 373–417. American Psychological Society: Bethesda.

Goodman, W. K., Price, L. H., Rasmussen, S. A. & Mazure, C. (1989). The Yale-Brown Obsessive–Compulsive Scale: I. Development, use, and reliability. *Archive General Psychiatry* **46**, 1006–1011.

Guitton, D., Buchtel, H. A. & Douglas, R. M. (1985). Frontal lesions in man cause difficulties in suppressing reflexive glances and in generating goal directed saccades. *Experimental Brain Research* **58**, 455–472.

Hallet, P. E. (1978). Primary and secondary saccades to goals defined by instructions. *Vision Research* **18**, 1279–1296.

Hamilton, M. (1960). A rating scale for depression. *Journal of Neurology, Neurosurgery and Psychiatry* **23**, 56–62.

Lucey, J. V., Costa, D. C., Blanes, T., Busatto, G. F., Pilowsky, L. S., Takey, N., Marks, I. M., Ell, P. J. & Kerwin, R. W. (1995). Regional cerebral blood flow in obsessive–compulsive disordered patients at rest. Differential correlates with obsessive–compulsive and anxious–avoidant dimensions. *British Journal of Psychiatry* **167**, 629–634.

McGuire, P. K., Bench, C. J., Frith, C. D. & Marks, I. M. (1994). Functional anatomy of obsessive–compulsive phenomena. *British Journal of Psychiatry* **164**, 459–468.

McNally, R. J. & Kohlbeck, P. A. (1993). Reality monitoring in obsessive–compulsive disorder. *Behaviour Research and Therapy* **31**, 249–253.

Malloy, P. (1987). Frontal lobe dysfunction in obsessive–compulsive disorder. In *The Frontal Lobes Revisited* (ed. E. Perecman), pp. 207–223. IRBN Press: New York.

Maruff, P., Pantelis, C., Danckert, J., Smith, D. & Currie, J. (1996). Deficits in the endogenous control of covert attention in chronic schizophrenia. *Neuropsychologia* **34**, 1079–1084.

Maruff, P., Danckert, J., Pantelis, C. & Currie, J. (1988). Saccadic and attentional abnormalities in schizophrenia. *Psychological Medicine* **28**, 1091–1100.

Nickoloff, S. E., Radant, A. D., Reichler, R. & Hommer, D. W. (1991). Smooth pursuit and saccadic eye movements and neurological soft signs in obsessive–compulsive disorder. *Psychiatry Research* **38**, 173–185.

Perani, D., Colombo, C., Bressi, S., Bonfanti, A., Grassi, F., Scarone, S., Bellodi, L., Smeraldi, E. & Fazio, F. (1995). [F-18] FDG PET study in obsessive–compulsive disorder – a clinical

https://doi.org/10.1017/S0033291799008843 Published online by Cambridge University Press

metabolic correlation study after treatment. *British Journal of Psychiatry* **166**, 244–250.

Pierrot-Deseilligny, C., Rivaud, S., Gaymard, B., Muri, R. & Vermersch, A. I. (1995). A cortical control of saccades. *Annals of Neurology* **37**, 557–567.

Purcell, R., Maruff, P., Kyrios, M. & Pantelis, C. (1998*a*). Cognitive deficits in obsessive–compulsive disorder on tests of frontal-striatal function. *Biological Psychiatry* **43**, 348–357.

Purcell, R., Maruff, P., Kyrios, M. & Pantelis, C. (1998*b*). Neuropsychological deficits in obsessive–compulsive disorder: a comparison with unipolar depression, panic disorder and normal controls. *Archives General of Psychiatry* **55**, 415–423.

Rauch, S. L., Jenike, M. A., Alpert, N. M., Baer, L., Breiter, H. C., Savage, C. R. & Fischman, A. J. (1994). Regional cerebral blood flow measured during symptom provocation in obsessive–compulsive disorder using oxygen 15-labelled carbon dioxide and positron emission tomography. *Archives of General Psychiatry* **51**, 62–70.

Rauch, S. L., Savage, C. R., Alpert, N. M., Dougherty, D., Kendrick, A., Curran, T., Brown, H. D., Manzo, P., Fischman, A. J. & Jenike, M. A. (1996). Probing striatal function in obsessive–compulsive disorder using PET and a sequence learning task. *Neuroimage* **3**, (suppl.), s507.

Robinson, D., Wu, H., Munne, R. A. & Ashtari, M. (1995). Reduced caudate nucleus volume in obsessive–compulsive disorder. *Archives of General Psychiatry* **52**, 393–398.

Rosenberg, D. R., Dick, E. L., O'Hearn, K. M. & Sweeney, J. A. (1997). Response-inhibition deficits in obsessive–compulsive disorder: an indicator of dysfunction in fronto-striatal circuits. *Journal of Psychiatry*, *Neuroscience* **22**, 29–38.

Schmidtke, K., Schorb, A., Winkelmann, G. & Hohagen, F. (1998). Cognitive frontal lobe dysfunction in obsessive–compulsive disorder. *Biological Psychiatry* **43**, 666–673.

Tien, A. Y., Pearlson, G. D., Machlin, S. R. & Bylsma, F. W. (1992). Oculomotor performance in obsessive–compulsive disorder. *American Journal of Psychiatry* **149**, 641–646.

Veale, D. M., Sahakian, B. J., Owen, A. M. & Marks, I. M. (1996). Specific cognitive deficits in tests sensitive to frontal lobe dysfunction in obsessive–compulsive disorder. *Psychological Medicine* **26**, 1261–1269.

https://doi.org/10.1017/S0033291799008843 Published online by Cambridge University Press