Executive function in Tourette's syndrome and obsessive–compulsive disorder

LAURA H. WATKINS[1], BARBARA J. SAHAKIAN[2]*, MARY M. ROBERTSON[4],
DAVID M. VEALE[4], ROBERT D. ROGERS[3,5], KATHRYN M. PICKARD[1],
MICHAEL R. F. AITKEN[3] AND TREVOR W. ROBBINS[3]

[1] *MRC Cambridge Centre for Brain Repair, Departments of* [2] *Psychiatry and* [3] *Experimental Psychology,
University of Cambridge, Cambridge, UK*; [4] *Department of Psychiatry and Behavioural Sciences, Royal Free
and University College School of Medicine, University of London*; *UK*; [5] *Department of Psychiatry,
University of Oxford, Oxford, UK*

ABSTRACT

Background. Cognitive performance was compared in the genetically and neurobiologically related disorders of Tourette's syndrome (TS) and obsessive–compulsive disorder (OCD), in three domains of executive function: planning, decision-making and inhibitory response control.

Method. Twenty TS patients, twenty OCD patients and a group of age- and IQ-matched normal controls completed psychometric and computerized cognitive tests and psychiatric rating scales. The cognitive tests were well-characterized in terms of their sensitivity to other fronto-striatal disorders, and included pattern and spatial recognition memory, attentional set-shifting, and a Go/ No-go set-shifting task, planning, and decision-making.

Results. Compared to controls, OCD patients showed selective deficits in pattern recognition memory and slower responding in both pattern and spatial recognition, impaired extra-dimensional shifting on the set-shifting test and impaired reversal of response set on the Go/No-go test. In contrast, TS patients were impaired in spatial recognition memory, extra-dimensional set-shifting, and decision-making. Neither group was impaired in planning. Direct comparisons between the TS and OCD groups revealed significantly different greater deficits for recognition memory latency and Go/No-go reversal for the OCD group, and quality of decision-making for the TS group.

Conclusions. TS and OCD show both differences (recognition memory, decision-making) and similarities (set-shifting) in selective profiles of cognitive function. Specific set-shifting deficits in the OCD group contrasted with their intact performance on other tests of executive function, such as planning and decision-making, and suggested only limited involvement of frontal lobe dysfunction, possibly consistent with OCD symptomatology.

INTRODUCTION

Tourette's syndrome (TS) is a neurodevelopmental condition characterized by motor and vocal tics that typically develop at 5–7 years of age (APA, 1994; Robertson, 1994, 2000). Obsessive–compulsive disorder (OCD) sufferers have obsessions and/or compulsions which

* Address for correspondence: Professor Barbara Sahakian, Department of Psychiatry (Box 189), University of Cambridge, Addenbrooke's Hospital, Cambridge CB2 2QQ, UK.
  (Email: jenny.hall@cambsmh.nhs.uk)

usually develop in adolescence (Freeman, 1992). Despite the quite different clinical profiles of these two disorders, there is good evidence for genetic linkage between them (State *et al.* 2003). TS and half of OCD cases are thought to be inherited in autosomal dominant fashion, with a single (as yet unidentified) locus for transmission, but with incomplete penetrance and variable phenotype (Pauls & Leckman, 1986; Eapen *et al.* 1993; Pauls *et al.* 1995; Leckman *et al.* 1997).

Both disorders are thought to have a neurobiological basis in the frontal cortex and basal ganglia. Changes in regional cerebral blood flow (rCBF) and metabolism have been observed in TS patients, particularly in the ventral striatum, lateral orbito-frontal cortex (OFC) and the anterior cingulate gyrus (ACG) (Braun *et al.* 1993; for review see Weeks *et al.* 1996; Leckman *et al.* 1997). Dopaminergic abnormalities observed in TS (Devinsky, 1983; Leckman *et al.* 1997) suggest an imbalance in the interactions of the striatum. Similarly, many studies have found abnormal rCBF or metabolism in OCD: with the OFC, ACG and caudate nucleus typically showing overactivity (for review, see Saxena *et al.* 1998; Schwartz, 1998).

Disruption to fronto-striatal circuitry leads to impairment in tasks requiring executive functions such as planning, attention or decision-making, i.e. tasks requiring higher level cognition and optimization of complex cognitive performance (Tranel *et al.* 1994; Robbins, 1996). Thus, whilst spatial working memory and planning tasks strongly involve dorsolateral prefrontal cortex (DLPFC) circuitry (Alexander *et al.* 1986; see Robbins, 1996, for review; Baker *et al.* 1996; Owen *et al.* 1996; Bechara *et al.* 1998), decision-making between options with variable degrees of rewarding and punishing feedback relies on circuitry of the OFC (Bechara *et al.* 1998; Rahman *et al.* 1999; Rogers *et al.* 1999, 2000). Go/No-go and reversal paradigms have also long been known to be sensitive to frontal dysfunction, particularly in the OFC region (Iversen & Mishkin, 1970; Butters *et al.* 1973; Drewe, 1975; Petrides, 1986; Rolls *et al.* 1994; Godefroy *et al.* 1996; Dias *et al.* 1996) and provide measures of inhibitory control mechanisms that may well be disturbed in such disorders as OCD and TS.

Despite its proposed fronto-striatal neuropathology, studies of complex task performance in TS are sparse and findings in OCD have proved inconsistent. This study, therefore, compared performance in the domains of attentional control, planning and decision-making in patients with TS and OCD using neuropsychological tools that have been well-characterized in terms of their sensitivity to other fronto-striatal disorders. This is, thus, perhaps the first detailed neuropsychological comparison of these groups. The study addresses two main

Table 1. *Group characteristics and background test results [values are mean (standard deviation)]*

Group characteristic	TS patients	OCD patients	Controls
Male:female	16:4	8:12	9:11
Age (years)	31·5 (11·6)	38·2 (13·4)	36·6 (12·8)
PVIQ	108·5 (8·1)	111·9 (8·4)	111·0 (6·2)
MMSE	29·4 (0·9)	29·0 (1·2)	29·3 (1·1)
BDI	7·9 (8·9)	19·8 (9·7)	3·7 (2·3)
Duration of disorder (years)	24·5 (12·5)	19·3 (14·3)	
Background tests			
Letter fluency	35·3 (11·0)	40·1 (11·7)	43·1 (10·6)
Animal fluency	21·4 (7·4)	20·5 (4·7)	21·5 (4·4)
Arithmetic % correct	62·1 (31·7)	64·7 (18·1)	64·5 (19·1)
Motor screen (ms)	944 (217)	1083 (238)	920 (210)
Pattern % correct	84·8 (11·2)	82·9 (10·3)	93·5 (6·0)
Spatial % correct	77·3 (11·4)	82·8 (8·0)	86·0 (9·4)
Pattern RT (/ms)	1941 (513)	2295 (616)	1836 (309)
Spatial RT (/ms)	1894 (703)	2548 (919)	1881 (363)

Upper panel: PVIQ, predicted pre-morbid verbal IQ; MMSE, Mini Mental-State Examination; BDI, Beck Depression Inventory. *Lower panel*: Arithmetic, arithmetic subtest of Wechsler Adult Intelligence Scale; Pattern, pattern recognition memory test; Spatial, spatial recognition memory test; RT, correct response latency; N.S., not significant; Statistic, statistical difference.

issues. First, it provides a direct comparison between the two disorders, to test the hypothesis that a common genetic basis and similar neurobiological background would lead to similar cognitive deficits. Second, we tested the hypothesis that the cognitive deficits seen in these two disorders would be more similar to those seen in other disorders that disrupt the OFC circuitry to a greater extent than the DLPFC circuitry (e.g. mild frontal-variant fronto-temporal dementia) than to conditions that preferentially disrupt the DLPFC rather than OFC circuitry (e.g. mild Huntington's disease, see Lawrence & Sahakian, 1996).

METHOD

Subjects

Permission for this study was obtained from the Local Research Ethics Committee and all subjects gave written informed consent. The patient groups comprised 20 TS patients, 20 OCD patients and 20 age- and IQ-matched control subjects (Table 1). TS patients were diagnosed and recruited by MMR from the out-patient clinic at the National Hospital for Neurology and Neurosurgery, London. Diagnosis was made on the basis of interview and completion of the National Hospital Interview Schedule

(Robertson & Eapen, 1996). OCD patients were recruited by D. M. Veale from Grovelands Priory Hospital or an OCD support group. Subjects who scored below 24 on the Mini-Mental State Examination (MMSE) were excluded (Folstein *et al.* 1975), as were those with a history of neurological or psychiatric conditions other than those under study [except depression and attention deficit hyperactivity disorder (ADHD)]. Twenty control subjects were recruited by advertisement in Cambridge and chosen to match the patient groups according to age, pre-morbid IQ and gender ratio. Severity of depression was assessed using the Beck Depression Inventory (BDI; Beck *et al.* 1961) and severity of ADHD in TS patients was assessed using the Attention Deficit Scale for Adults (ADSA; Triolo & Murphy, 1996).

Tourette's syndrome patients

Six patients were unmedicated, 10 were taking a single medication and the remaining four were taking more than one medication. Antipsychotic medications were the most frequent: four patients were taking sulpiride, six were taking haloperidol, three were taking pimozide, two were taking risperidone and one was taking clonidine. One patient was taking an anti-muscarinic drug (benzoptropine), three were taking a selective serotonergic reuptake inhibitor (SSRI) (fluoxetine) and one was taking a benzodiazepine (lormetazepam). The mean Yale Global Tic Severity Scale (YGTSS; Leckman *et al.* 1989) was 43·5 [standard deviation (s.d.) = 19·3] out of 100; this scale assesses motor and vocal tics and their impact on daily activities. After exclusion of patients with distinct co-morbid OCD by the clinician, all remaining candidates were pre-screened with the Leyton Obsessional Inventory (LOI; Cooper, 1970; Snowdon, 1980); those who scored outside the normal range were not tested. The mean LOI score of the 20 TS patients included in the study was 11·1 (s.d. = 6·1), which is comparable to the means obtained by Cooper (1970) of 8·7 (s.d. = 5·6) for male controls (*n* = 40) and 11·4 (s.d. = 6·7) for female controls (*n* = 60). TS patients scored a mean of 153·6 (s.d. = 24·8) on the ADSA, which is within 1 s.d. of the normative mean of 141. Three patients scored greater than 2 s.d. from the normative mean, indicating moderate to severe ADHD.

Obsessive–compulsive disorder patients

Ten patients were unmedicated, eight were taking SSRIs (five taking paroxetine, two taking fluoxetine and one taking sertraline), one was taking a tricyclic antidepressant (clomipramine) and one was taking both a monoamine oxidase inhibitor (moclobemide) and an antipsychotic (trifluoperazine). The mean score on the Yale–Brown Obsessive–Compulsive Scale (YBOCS; Goodman *et al.* 1989) was 19·3 (s.d. = 14·3).

Materials and procedures

The background psychometric tests were as follows: MMSE, National Adult Reading Test [NART; Nelson, 1982, to provide an estimate of pre-morbid verbal IQ (PVIQ)], letter fluency (Benton, 1968), semantic fluency and finally the arithmetic subtest from the Wechsler Adult Intelligence Scale (WAIS; Wechsler, 1981). The fluency and arithmetic tests were included as examples of 'standard' tests of executive function, the arithmetic test assessing working-memory function.

Computerized tests were run on a Carry I portable microcomputer fitted with a Datalux touch-sensitive screen, which was positioned approximately 0·5 m from the subject. Three background computerized tests of motor screening, pattern recognition and spatial recognition (Sahakian *et al.* 1988) from CANTAB (Cambridge Cognition, 2004) were given.

The test battery took approximately 1 h 45 min. The order of the remaining computerized tests was counterbalanced.

Attentional set-shifting test

This test of discrimination learning assesses the ability to selectively attend to and set-shift between shape, colour or number stimulus dimensions (Downes *et al.* 1989). Measures were number of subjects passing each stage, errors and latency at the intra-dimensional (ID) and extra-dimensional (ED) shift stage.

One-touch Tower of London (one-touch TOL)

This is a spatial planning test, involving planning a sequence of moves to achieve a goal arrangement of coloured balls without moving the balls (Owen *et al.* 1995). Measures were the

proportion of perfect solutions and latency to first response.

Decision-making test

This test of decision-making and risk-taking has previously been described by Rogers *et al.* (1999). Main measures were the latency to make a decision, the proportion of decisions with the most likely outcome and the mean percentage points risked at each ratio.

Go/No-go test

This test examines the ability to attend and respond to relevant targets while inhibiting responses to distractors (McLean *et al.* 2004). Measures were response, latencies, correct target presses or 'hits', misses and false-positive errors. Switch blocks (blocks on which the response contingencies are reversed from the previous block) can be compared to non-switch blocks.

Statistical analysis

Data were analysed using SPSS version 11.0.1 (SPSS Inc., 2001). Comparisons of the means of the three groups were via analysis of variance (ANOVA). Standard transformations of each subject's mean score (Howell, 1997) were used to increase homogeneity of variance when this assumption was untenable ($p < 0.10$, Levene's test).

Significant main effects were investigated by Fisher's LSD test (protected *t* procedure for three means), to give a strict control of maximum family-wise error rate, and a significance level of 0·05 is used throughout. Where parametric analyses were unsuitable, data were analysed using the likelihood ratio method (Kullback, 1968; Robbins, 1977) or Mann–Whitney *U* tests.

RESULTS

For five subjects, one of the tests was not completed successfully, and these data are missing from the analyses: BDI (two patients in the OCD group); Go/No-go (one OCD); decision-making task (one TS); TOL (one TS).

Subject characteristics

One-way ANOVAs revealed no significant differences between the three groups in terms of

age, MMSE score or predicted PVIQ [largest $F(2, 57) = 1.54$, $p = 0.22$], although the groups differed in mean (square-root-transformed) BDI scores $F(2, 55) = 24.75$] TS patients had higher BDI scores than did the OCD or control groups [smaller $t(55) = 5.03$], who did not differ significantly [$t(55) = 1.84$, $p = 0.07$].

As the patient groups were not completely matched for age and sex ratio, care was taken to ensure this did not confound interpretation. All subsequent ANOVAs were conducted both with gender and age as predictors (fixed factor, and covariate respectively). If these factors had no significant effects ($F \leqslant 1.0$), they were discarded from the model; thus, hypotheses on the group factor are tested on the observed means only. Otherwise, both full and restricted models were analysed (observed and estimated marginal means), and the more conservative of the two *p* values obtained was used for each hypothesis test on the group factor.

Background neuropsychological tests

Results of the background neuropsychological tests are shown in the lower rows of Table 1. The three groups did not differ on WAIS arithmetic, category fluency or letter fluency ($F < 1$), nor on response latency in the motor screening task [$F(2, 53) = 2.40$, $p = 0.10$]. Significant main effects of group were observed on both (arcsine-transformed) accuracy and (logarithmic-transformed) latencies for the spatial and pattern recognition memory tasks [smallest $F(2, 53) = 3.43$]. The OCD patients were slower than the other groups to respond in both tasks [smaller $t(53) = 2.12$]; response latencies were similar for TS and controls ($t < 1$). The two patient groups did not differ in accuracy of performance on either task [larger $t(53) = 1.33$, $p = 0.19$]; OCD patients were less accurate than controls at the pattern recognition task, and TS patients were less accurate than controls on both tasks [smaller $t(53) = 2.60$].

Attentional set-shifting test
Pass/fail

For purposes of analysis, subjects were scored as to whether they successfully completed all phases, or whether they failed before or after starting the ED shift phase. Likelihood-ratio analyses confirmed that a higher proportion of
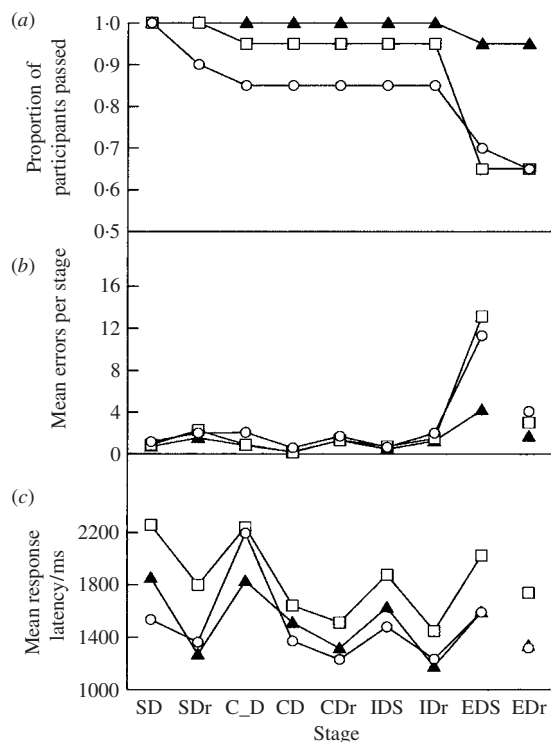
FIG. 1. Attentional set-shifting test. $-\bigcirc-$, TS; $-\square-$, OCD; $-\blacktriangle-$, control. (*a*) Percentage of subjects passing each stage, shown as a cumulative attrition curve. OCD patients and controls performed similarly up to the intra-dimensional reversal (IDR) stage, but significantly more OCD patients failed at the extra-dimensional shift (EDS) stage than controls. (*b*) Mean errors at intra-dimensional shift (IDS) and EDS stages of the attentional set-shifting test. Data are included for all subjects who attempted both stages, regardless of outcome on the EDS stage. Both TS patients and OCD patients made disproportionately more errors at the EDS stage compared with the matched control group. Error bar = 1 standard error of the mean (S.E.M.). (*c*) Mean correct response latencies. There were no significant differences, although the OCD patients tended to be slow. SDr, simple discrimination/reversal; C_D, separated compound reversal; CDr, superimposed compound discrimination/reversal; IDSr, intra-dimensional shift/reversal; EDSr, extra-dimensional shift/reversal. Note that for (*b*) and (*c*) performance at the EDr is disconnected from the EDS stage, as a number of patients failed at the EDS, and therefore did not attempt the EDr.

patients than controls failed to complete all stages [$\chi^2(2) = 7\cdot51$], as shown in Fig. 1*a*. The tendency of TS patients to be more likely than OCD patients to fail prior to the EDS phase was non-significant [$\chi^2(1) = 1\cdot99$, $p = 0\cdot27$].

Error rates and response latencies for those subjects who attempted the ED shift stage of the task are shown in Fig. 1(*b*, *c*). Because all subjects who undertook the ID shift stage also undertook the ED shift stage (20 controls, 19 OCD, 17 TS), comparison of group errors and

response latencies on these two key dimensional shift stages is possible by contrasting performance at these stages in the ANOVA model as a repeated-measures factor. However, estimates of mean population differences in performance will be slightly conservative, as the worst performing subjects in the patient groups did not contribute to these stages.

The groups differed in overall error rates [$F(2, 53) = 5\cdot05$], more errors were made during the ED shift phase [$F(1, 53) = 45\cdot95$], and there was a significant interaction between these two factors [$F(2, 53) = 4\cdot21$]. Separate analysis of the two stages confirmed the pattern seen in pass/fail data. Whilst there were no group differences in errors at the ID shift stage [$F < 1$], there was a significant effect of group upon error rates at the ED shift stage [$F(2, 55) = 4\cdot73$], with both patient groups making more errors than controls [smaller $t(53) = 2\cdot24$]. The two patient groups did not differ in ED shift error rates ($t < 1$).

Response latencies (logarithm-transformed) were similar for all groups, and stages, with no interaction [largest $F(1, 49) = 1\cdot68$, $p = 0\cdot20$].

One-touch Tower of London

The results of this test are shown in Table 2. Separate ANOVAs were performed, contrasting (arcsine-transformed) proportion of trials correct first attempt, and (logarithmic-transformed) mean latency to first response for the three groups, with trial difficulty as a within-subject factor. There was a main effect of difficulty on both measures [smaller $F(4, 208) = 31\cdot66$], but they did not interact with group [largest $F(2, 224) = 1\cdot03$]; the trends for patient groups to take longer and make fewer correct first responses were non-significant [larger $F(2, 56) = 2\cdot01$, $p = 0\cdot14$].

Decision-making test

The proportion of trials on which subjects chose the most likely outcome were 95·9, 98·1 and 98·6 % for the TS, OCD and control groups respectively. With half or more of the subjects in each group scoring 100 %, these data cannot be made suitable for parametric analyses. Kruskal–Wallis analysis revealed that the groups differed [$\chi^2(2) = 6\cdot65$], Mann–Whitney tests confirming that OCD patients and controls chose similarly well ($Z_U = 0\cdot53$) and that TS patients chose the more likely outcome less

Table 2.   *Performance on psychological tests* (*values are untransformed cell means*)

Test	TS patients		OCD patients		Controls	
Decision-making	Latency (ms)	% Bet	Latency (ms)	% Bet	Latency (ms)	% Bet
6 : 4 Ratio	2931	39·4	2692	41·6	2368	40·3
7 : 3 Ratio	2666	54·0	2434	53·6	2069	53·0
8 : 2 Ratio	2325	67·3	2451	68·4	2005	67·3
9 : 1 Ratio	2577	76·2	2215	76·9	1958	74·7
Tower of London	Latency (ms)	% First	Latency (ms)	% First	Latency (ms)	% First
1-move problems	4723	89·5	4500	92·1	4062	92·1
2-move problems	7443	89·5	6260	92·1	5648	89·5
3-move problems	11 857	73·7	11 662	71·1	8313	71·1
4-move problems	19 340	53·9	21 090	52·6	17 377	51·3
5-move problems	25 794	60·5	28 073	64·5	21 856	61·8

% Bet, mean percentage of points staked on trials on which the more likely outcome was chosen. % First, mean percentage of problems on which the correct response was chosen first. Analysis revealed no significant differences between groups on these measures.

frequently than did the other groups (smaller $Z_U = 2 \cdot 11$). However, these non-parametric methods do not allow estimation of the contribution of age and sex to these differences.

The mean choice latency and bet sizes for this task are shown in Table 2. Analysis of the (logarithm-transformed) choice latency and the mean percentage bet size was performed by separate ANOVA models with ratio condition included as a within-subject factor. Ratio significantly influenced bet size [$F(3, 156) = 31 \cdot 10$], but not choice latency ($F < 1$). Crucially, neither measure was influenced by group, nor were there any group × ratio interactions (all F's < 1).

Go/No-go reversal task

Very few targets were missed: 0·7, 0·9 and 1·0% of targets for TS, OCD and control groups respectively. These data are unsuitable for parametric analysis; Kruskal–Wallis analysis revealed no effect of group upon omission errors [$\chi^2(2) = 1 \cdot 16$, $p > 0 \cdot 5$]. Somewhat higher proportions of non-targets were responded to (false-positive errors): 11·8, 8·3 and 7·4 of targets for TS, OCD and control groups respectively. Analysis of these (arcsine-transformed) data was conducted with block type (switch or non-switch) as a repeated-measures factor. This revealed the expected effect of switch, in that subjects made significantly more false-positives on switch blocks [$F(1, 56) = 36 \cdot 78$]; any tendency for the groups to differ in overall false-positive rate was not significant [$F(2, 56) = 2 \cdot 32$, $p > 0 \cdot 1$].

Critically, the detrimental effect of switch on error rates was significantly influenced by subject group [$F(2, 56) = 3 \cdot 30$]; these data are shown
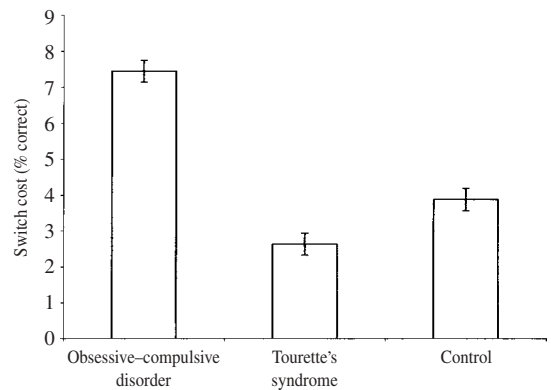

FIG. 2.   Mean change in percentage false alarm rate between switch and non-switch trials for the three groups in the Go/No-go task. Error bars represent 2 S.E.D., estimated from the error term of for the group × switch interaction in an ANOVA, using harmonic mean n. Means and error bars calculated from untransformed values.

in Fig. 2. OCD patients had a significantly greater switch cost (increase in false-positive errors following switch blocks) than did TS patients [$t(56) = 2 \cdot 43$], which was also marginally greater than controls [$t(56) = 1 \cdot 95$, $p = 0 \cdot 055$]. TS patients were no more or less influenced by block type than controls ($t < 1$).

Effects of medication

The results from the patient groups were further analysed to investigate the effects of medication on patient performance. Antipsychotic-medicated TS patients were significantly more accurate on the spatial recognition memory test [$U = 13 \cdot 5$, $p < 0 \cdot 05$] than TS patients who were not taking antipsychotic medication but none of the other core test measures differed between

these two groups. There were no significant differences between the OCD patient group taking SSRIs and the unmedicated OCD patients on any of the core test measures.

DISCUSSION

This study is the first systematically to compare a broad range of 'frontal' executive functions in TS and OCD. Overall, the results clearly show qualitative similarities in cognitive performance between TS and OCD with some differences in the exact form and degree of deficits. This profile was particularly evident for the tests of inhibitory control where both groups were significantly impaired on the shifting component of the Go/No-go reversal task (the OCD group more significantly so) and at the extra-dimensional shifting stage of the CANTAB attentional-set formation and shifting task. TS patients showed a non-significant tendency to have more difficulties with the stages earlier than the extra-dimensional shift. Thus the OCD group, in particular, showed impressive evidence of selectivity of deficits at the shifting stages of both the Go/No-go reversal and CANTAB attentional set-shifting tests. For the tests of recognition memory, again both groups were impaired, however, with some differences, for example the OCD patients had significantly slowed response latencies. Both groups had spared executive function, in terms of performance on conventional tests of verbal fluency and working memory (WAIS arithmetic), the TOL test of planning and decision-making tests. However, the TS group did show a small deficit in quality of decision-making. These profiles of cognitive impairment are striking, given the close genetic relationship between the two conditions and additional similarities of underlying neuropathology (for review, see Leckman *et al.* 1997; Saxena *et al.* 1998). This discussion focuses on the cognitive profiles of the two patient groups, particularly with respect to their relationship to clinical symptoms, and implications for the neuroanatomical bases of these two disorders.

Cognitive performance in OCD

The data for the OCD group help to resolve inconsistencies in the literature and also provide new information on previously unstudied aspects of cognitive functioning in OCD.

By contrast to their intact verbal fluency, arithmetic performance, planning and decision-making, OCD patients were *selectively* impaired at the ED shift stage of the attentional set-shifting test. Three previous studies of OCD (Veale *et al.* 1996; Purcell *et al.* 1997a, 1998) have analysed the data for this test differently by using *trials* to criterion (rather than *errors* to criterion) to index rule learning and Purcell *et al.* (1997a, 1998) did not compare the ID and ED shift stages directly. Veale *et al.* (1996) found gradual attrition throughout the test stages, but their OCD group were mostly in-patients and so may well have been more clinically disabled or had a higher degree of co-morbidity than the current group, probably resulting in fewer patients attempting the ED shift stage, thus reducing the power of detecting differences in attentional set-shifting *per se*. From Veale *et al.* (1996) and the current study it appears that ED shift performance in OCD depends on severity; less clinically impaired OCD patients (present group) are impaired selectively at the ED shift stage, whereas severely affected in-patients show attrition at earlier stages. It is relevant to compare the performance of depressed unipolar patients of similar age, where there has been little consistent evidence to support an ED shifting deficit (Purcell *et al.* 1997b; Elliott *et al.* 1998; Sweeney *et al.* 2000), although this may depend on factors such as the severity of depressive symptoms.

The clear-cut nature of the deficits of the OCD group at the ED shift, compared with other stages, thus suggests a selective deficit in cognitive flexibility in this group, probably not due to depressed mood, but consistent with the hypothesis that some of the tendency towards compulsive modes of behaviour and ruminative tendencies arises from a generalized impairment in inhibitory function at the cognitive level that normally allows adaptive shifting between different actions and thoughts. Further support for this view can be found in the significant deficits by the OCD group in the switching of the Go/No-go reversal task. Whilst the OCD group neither made significantly more false-positive errors overall than controls, nor had a particular difficulty in the

challenging situation of withholding responding to a non-target subsequent to a response to the previous target (which is impaired in Huntington's disease patients; Watkins, L., unpublished observations), the OCD group did respond excessively to the previously rewarded stimulus category (i.e. they perseverated) when required to reverse response categories on switch blocks. This reversal is somewhat akin to tests of simple alternation, in which subjects must reverse reward contingencies on each trial, and which are very sensitive to OCD (Abbruzzese *et al.* 1995; Gross-Isseroff *et al.* 1996; Cavedini *et al.* 1998). Behavioural processes governing performance in Go/No-go paradigms have been particularly associated with the ventro-lateral prefrontal region, from studies with non-humans (e.g. Iversen & Mishkin, 1970; Butters *et al.* 1973), patients with frontal lobe damage (Aron *et al.* 2003) and using functional imaging in healthy humans (Kawashima *et al.* 1996; Casey *et al.* 1997; Konishi *et al.* 1998). The OCD patients in this study were impaired only when *reversing* Go/No-go contingencies, suggesting that, as well as implicating the ventro-lateral region (see Cools *et al.* 2002), such a deficit could be more closely related to the reversal deficits seen after ventral frontal damage (Daum *et al.* 1991; Rolls *et al.* 1994; Dias *et al.* 1996). Indeed, Rolls *et al.* (1994) study employed a Go/No-go reversal paradigm and found that ventral frontal lesion patients although unimpaired on the initial Go/No-go discrimination stage, then perseverated to the previously correct stimulus in subsequent reversal stages; a similar pattern to that seen in the OCD patients here. The selectivity of this impairment is particularly important as the intact Go/No-go performance overall by OCD patients shows that they were not impaired in global aspects of response inhibition, leading for example, to excessively disinhibited or impulsive responding.

The deficient performance of OCD patients on tests of response inhibition contrasted markedly with their intact performance on other 'frontal' executive tests less dependent on inhibitory processes. The preservation of 'look-ahead' planning accuracy in these patients is consistent with previous findings of intact accuracy on TOL planning tasks and the related Tower of Hanoi task (Veale *et al.* 1996; Purcell

et al. 1997*a*, 1998; Schmidtke *et al.* 1998). Use of the one-touch TOL in this study has avoided the potential confounds of online monitoring of (and possibly ruminating over) performance (Goel & Grafman, 1995), allowing confirmation of intact planning ability in OCD, which contrasts markedly with the impairments seen in depressed patients of similar age (Elliott *et al.* 1998; Sweeney *et al.* 2000).

The OCD patients were also unimpaired on a test of decision-making in which they had to select from and 'bet' on outcomes with differing probabilities. Although they exhibited some slowing in deliberation time, this was not significant, and contrasts with the slowing observed in depression. OCD patients are also unimpaired in accuracy on probabilistic reasoning tasks (Volans, 1976; Fear & Healy, 1997).

Although the robust impairment we observed in visual recognition memory on this test may well reflect impaired temporal lobe function (Owen *et al.* 1995), it is also possible that it reflects prefrontal cortex (PFC) dysfunction, there being good evidence that the more posterior OFC regions and the anterior cingulate are important in visual recognition memory (Bachevalier & Mishkin, 1986; Elliott & Dolan, 1999; Frey & Petrides, 2000). The OCD patients were not significantly impaired on the spatial recognition memory task, which, in contrast to visual pattern recognition resembles those tests of spatial working memory that activate the DLPFC (Owen *et al.* 1996), as well as being more sensitive to frontal as opposed to temporal lobe lesions in humans (Owen *et al.* 1995). However, the OCD patients were significantly slower on both tasks, which may reflect a speed-error trade-off strategy that compensates effectively for spatial working-memory deficits. The lengthened latencies of the OCD patients on the memory recognition tasks were not matched by significant overall slowing on the other tasks. However, it should be pointed out that depressed patients are also impaired in recognition memory tests (Elliott *et al.* 1996).

Cognitive performance in TS

By comparison with OCD, the TS group generally showed qualitatively similar, although smaller, deficits, except for the decision-making test. Such impairment was unlikely to have

been due to co-morbid ADHD or OCD in the TS group since neither the mean ADSA score (Triolo & Murphy, 1996) nor the mean LOI (Cooper, 1970; Snowdon, 1980) score were significantly different from normative data and neither score correlated with cognitive performance.

Overall, the cognitive changes in TS were much less clear-cut than for OCD. Over one-third of TS patients failed to complete all stages of the attentional set-shifting test but the pattern was one of gradual attrition, suggesting difficulties in set-formation and set-maintenance, as well as set-shifting. The only previous study comparing performance of TS patients with matched control subjects on the Wisconsin Card Sorting Test found no evidence for impairment (Sutherland *et al.* 1982). However, the results of the current study show that some TS patients have difficulties with set-shifting, and possibly set-maintenance.

Possibly the most surprising finding in the TS group was that of relatively intact Go/No-go performance. This test was designed to detect inhibitory problems at three distinct levels of behavioural regulation: general inability to withhold responding to non-targets; inability to withhold responding to non-targets in the particularly taxing situation of when non-targets directly follow targets; and inability to switch between response categories on different blocks. Only for the last measure was there a statistically marginal tendency for TS patients to be impaired. Ozonoff *et al.* (1994) also found intact Go/No-go and Go/No-go reversal in children with TS. Thus TS patients appear able to inhibit the well-integrated responses required in the Go/No-go paradigm. This indicates that tics are not a result of fronto-executive inhibitory dysfunction operating at a cognitive level of response control, but instead are caused by impairments at a lower level of response control, possibly striatal in origin.

The TS patients were unimpaired on the one-touch TOL, but had a minor deficit in selecting the most likely outcome on the decision-making tests. In summary, the TS patients had some significant deficits in decision-making, attentional set-shifting and in visual pattern and spatial recognition memory accuracy, including a test of spatial working memory, but showed

preservation also of several aspects of fronto-executive function.

Conclusions and implications for the neural substrates of cognitive deficits in OCD and TS

This study has identified a distinct profile of deficits, especially in terms of response inhibition, in the genetically related disorders of OCD and TS. Finding selective impairment of cognitive shifting in OCD, despite intact planning and decision-making helps to resolve several previous discrepancies in the literature. These deficits reflect a general difficulty in shifting of set in OCD patients, which is also seen in their obsessive and compulsive symptoms, perhaps resulting from impaired functioning of fronto-striatal circuitry. The set-shifting impairments are consistent with dorsolateral and ventrolateral prefrontal dysfunction. However, such dysfunction is unlikely to be global, as performance on the TOL test, which is sensitive to dorsolateral prefrontal dysfunction (see Manes *et al.* 2002), was strikingly unimpaired. Similarly, the sparing of decision-making abilities in a test also sensitive to orbito-frontal damage (Rogers *et al.* 1999), also suggests that OCD patients do not suffer from global OFC deficits either. Overall, the pattern of fronto-executive impairment in OCD is consistent with the nature of their clinical symptoms, but does not indicate generalized executive malfunction. In comparison, TS patients showed a similar, but less clear-cut pattern of impairment on tests of pattern and spatial recognition memory, attentional set-formation and shifting and quality of decision-making, consistent with the genetic relationship with OCD. Their limited profile of cognitive impairments, was not, however, simply restricted to fronto-executive function, including, for example a visual recognition memory deficit. The most interesting area of relative preservation of function in TS was for those Go/No-go test measures of impulsive, as distinct from compulsive (switching set), modes of responding. Thus, the TS patients were able to inhibit highly pre-potent voluntary responses, although their syndrome is characterized by a difficulty in suppressing involuntary behaviour. Consistent with the known pathology of TS, but untested here, it is possible that this difference results from impairments in response control

mechanisms at the striatal, rather than the cortical, level.

ADHD (as well as depression) is a common co-morbid feature of OCD and TS, possibly again reflecting fronto-striatal dysfunction. However, a recent study by McLean *et al.* (2004) of adult ADHD, using a similar cognitive battery, showed a distinctly different profile on the Go/No-go test, ADHD patients being slower to respond but not impaired at shifting, and also being worse at planning, than their age-matched controls. Overall, these data are consistent with a cognitive pattern of deficits in OCD that mainly appears to contribute to or promote the perseverative or compulsive tendency, rather than reflecting what Hollander & Rosen (2000) describe as the impulsivity pole of the compulsive–impulsive spectrum.

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