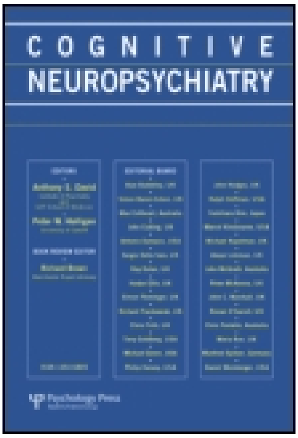

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Social reasoning in Tourette syndrome

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Social reasoning in Tourette syndrome

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Introduction. Tourette syndrome (TS) is thought to be associated with striatal dysfunction. Changes within frontostriatal pathways in TS could lead to changes in abilities reliant on the frontal cortex. Such abilities include executive functions and aspects of social reasoning.
Methods. This study aimed to investigate executive functioning and Theory of Mind (ToM; the ability to reason about mental states, e.g., beliefs and emotions), in 18 patients with TS and 20 controls. A range of tasks involving ToM were used. These required participants to make judgements about mental states based on pictures of whole faces or the eyes alone, reason about humour in cartoons that featured sarcasm, irony or "slapstick" style humour, and make economic decisions. The executive measures assessed inhibition and verbal fluency.
Results. Patients with TS exhibited significantly poorer performance than controls on all four tasks involving ToM, even when patients with comorbid obsessive-compulsive disorder were excluded. These difficulties were despite no inhibitory deficits. Patients with TS exhibited impairment on the verbal fluency task but their performance on executive and ToM tasks was not related.
Conclusions. We propose that TS is associated with changes in ToM. The observed deficits could reflect dysfunction in frontostriatal pathways involving ventromedial prefrontal cortex.

Keywords: Humour; Social reasoning; Striatum; Theory of Mind; Tourette syndrome; Ultimatum Game.

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INTRODUCTION

Tourette syndrome (TS) is a neurodevelopmental disorder involving motor and phonic tics: repetitive, involuntary movements and vocalisations. Previous studies have implicated a role for striatal dysfunction in TS (Albin & Mink, 2006; Singer et al., 1993). Striatal dysfunction may impact on the functioning of the frontal cortex, through changes within frontostriatal circuitry (Alexander, Delong & Strick, 1986). The frontal cortex is critical for a range of abilities. These include executive functions (e.g., inhibition, fluency, working memory) and aspects of social reasoning, such as Theory of Mind (ToM; the ability to reason about mental states, e.g., beliefs and emotions). In TS, striatal dysfunction could lead to changes in these abilities through alterations in neural pathways involving the frontal cortex. The present study investigated this possibility using two executive measures and a range of tasks involving ToM.

A number of studies have provided evidence for cognitive changes in TS. Reviews of the literature (Eddy, Rizzo, & Cavanna, 2009; Pennington & Ozonoff, 1996) highlight equivocal evidence for deficits in executive abilities linked to dorsolateral prefrontal cortex such as fluency (Gallard et al., 2000), planning (Rassner et al., 2005), working memory (Levy & Goldman-Rakic, 2000), and cognitive flexibility (Milner, 1963). Many studies of executive function in TS have failed to control for the presence of comorbidities, so it is often unclear whether reported deficits are specifically attributable to TS. However, studies of patients with uncomplicated TS have revealed deficits on inhibitory tasks (Channon, Crawford, Vakili, & Robertson, 2003; Channon, Gunning, Frankl, & Robertson, 2006; Crawford, Channon, & Robertson, 2005; Eddy, Mitchell, Beck, Cavanna, & Rickards, 2010a, 2010b; Verte, Geurts, Roeyers, Oosterlaan, & Sergeant, 2005), which are often linked to activation in the anterior cingulate (e.g., Nathaniel-James, Fletcher, & Frith, 1997; Pardo, Pardo, Janer, & Raichle, 1990).

Patients with TS have also demonstrated impairment on two tasks involving ToM (Eddy et al., 2010a, 2010b), although another study reported no difficulties on other ToM tasks (Channon, Sinclair, Waller, Healey, & Robertson, 2004). The ToM tasks that elicited impairment in the former studies were a faux pas task which required recognition of socially inappropriate remarks, and a nonliteral language task featuring sarcasm. ToM deficits can be related to (e.g., Samson, Apperly, Kathirgamanathan, & Humphreys, 2005) or independent of (e.g., Lough, Gregory, & Hodges, 2001) poor performance on executive tasks. The ToM deficits exhibited by patients with TS were not easily explained by executive difficulties and, overall, studies have found limited evidence of significant executive dysfunction in TS (Eddy et al., 2009). However, poor performance on tasks involving faux pas or nonliteral language has been linked to dysfunction of ventromedial prefrontal cortex (VMPFC; Lough et al., 2001; Shamay-Tsoory, Tomer, & Aharon-Peretz, 2005; Shamay, Tomer, Berger, & Aharon-Peretz, 2003), and a few imaging studies have reported neural changes involving similar regions, including orbitofrontal cortex, in individuals with TS (Braun et al., 1995; Jeffries et al., 2002; Muller-Vahl et al., 2009). It is therefore possible that the deficits exhibited by patients with TS on these tasks resulted from frontostriatal dysfunction involving VMPFC. This possibility was investigated in the current study by using ToM tasks shown to rely on the integrity of the VMPFC.

Shamay-Tsoory and colleagues have shown that VMPFC dysfunction can impair ToM processes involved in the understanding of "socially competitive emotions", such as envy and gloating (Shamay-Tsoory, Tibi-Elhanany, & Aharon-Peretz, 2007). When a subject gloats, they experience happiness in light of another's unhappiness, whereas envy involves feeling unhappy in light of someone else's happiness. Understanding socially competitive emotions therefore involves reasoning about two people's conflicting mental states. Shamay-Tsoory et al. (2007) devised a "socially competitive emotions" task (SCET) featuring emotional facial expressions. These authors showed that patients with VMPFC damage were poor at identifying the character who was the subject of another character's envy or gloating. The current study tested the performance of patients with TS on a short version of this task.

Torralva et al. (2007) found that patients with frontal-variant frontotemporal dementia (which involves degeneration of VMPFC) performed poorly on a version of the "Reading the Mind in the Eyes" test (RMET; Baron-Cohen, Joliffe, Mortimore, & Robertson, 1997), which involves making judgements about mental states based on pictures of pairs of eyes. Parts of VMPFC are heavily interconnected with the amygdala. This structure may be particularly important for the recognition of basic emotional and more complex mental states based on the eyes (Adolphs, Baron-Cohen, & Tranel, 2002), as well as the understanding of faux pas (Stone, Baron-Cohen, Calder, Keane, & Young, 2003). One study assessed the performance of 10 patients with TS on a version of the RMET and failed to reveal a deficit (Baron-Cohen et al., 1997). However, this early version of the test may not have been sensitive enough to detect a deficit in a small sample of patients. The present study tested patients' performance on a more recent version of the RMET (Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001) containing more items, more response options, and complex mental state terms.

The VMPFC and amygdala are also activated by humorous stimuli (Goel & Dolan, 2001; Samson, Zysset, & Huber, 2008). Understanding humour often relies on the detection and then resolution of incongruity, such as that between an expectation and reality (Bartolo, Benuzzi, Nocetti, Baraldi, & Nicelli, 2006). ToM is one mechanism that may be used to resolve a detected incongruity in order to understand a joke (Brunet, Sarfati, Hardy-Bayle, & Decety, 2000). For example, in order to understand jokes based on sarcasm, one must infer that the speaker does not really think or feel exactly what they say. ToM deficits may therefore lead to poor resolution of the incongruity present in a joke involving sarcasm, because the humour derives from an incongruity between the speaker's remark and their mental state. The understanding of other kinds of humour, however, may not rely on ToM. For example, humour involving irony may simply require an appreciation of an incongruity between what may generally be expected and what has occurred. Jokes that rely on simple visual "slapstick" style humour (e.g., violence) may also depend less on ToM, and require simply the detection of, rather than the resolution of, an incongruity (Samson et al., 2008). The present study investigated the comprehension of humour in patients with TS, using cartoons involving sarcasm, irony, and slapstick-style comedy. Previous studies have shown that humorous cartoons activate brain regions thought to be involved in ToM, such as orbitofrontal cortex (e.g., Bartolo et al., 2006).

ToM may also influence decision making, affecting performance on tasks such as the Ultimatum Game (UG). During this task, a sum of money must be split between two players, who act as proposer and responder. The proposer offers a proportion of the money to the responder and will keep the remainder. If the responder accepts this single offer, the money is split as suggested. If the responder rejects the offer, both players receive nothing. Although logical reasoning dictates that any personal gain should be preferable to no gain, if the proposer's offer is low, the responder may reject it. Some estimates suggest neurologically intact individuals acting as responders may reject about half of offers below 20% of the total (Nowak, Page, & Sigmund, 2000) and patients with VMPFC dysfunction may reject even more (Koenigs & Tranel, 2007). Some explanations for why individuals choose to reject offers involve social reasoning (e.g., Polezzi et al., 2008). For example, rejections may be motivated by attributions of negative intent to the proposer, or feelings of envy which contrast with an awareness of the proposer's satisfaction. The influence of ToM on decision making during the UG could help explain why an increased acceptance rate of unfair UG offers has been reported in patients with autism (Sally & Hill, 2006). That is, because people with autism have deficits in ToM, their UG decisions are less likely to be influenced by reasoning about negative intentions of the proposer.

Participants in the current study completed a version of the UG, in addition to versions of the SCET (Shamay-Tsoory et al., 2007), the RMET (Baron-Cohen et al., 2001), and a humorous cartoons task. These tasks were selected because they had been used successfully with other clinical populations, including those with autism and frontotemporal dementia (e.g., Baron-Cohen et al., 2001; Lough et al., 2006). Another advantage of the tasks used in the current study is that they allowed the assessment of a range of different aspects of social reasoning, including making inferences about beliefs and emotions from images and prose, reasoning about two people's conflicting mental states, and understanding ToM involved in nonliteral language and humour. Some of these tasks have also been linked to specific neural substrates such as the ventromedial prefrontal cortex (e.g., the SCET; Shamay-Tsoory et al., 2007). The use of these tasks can therefore allow the generation of hypotheses relating to specifying a neurological basis for any observed deficits. An advantage of using ToM tasks involving images (i.e., the eyes task, SCET, and humorous cartoons task) is that these tasks could make fewer linguistic and working memory demands than story tasks, increasing the likelihood that any difficulties would reflect problems with ToM.

Executive functioning was assessed using two tasks. The first executive task was a black and white Stroop, which was selected to provide an easily administered test of inhibition, the executive function which may be most likely to be impaired in TS (Channon, Crawford, et al., 2003; Channon et al., 2006; Crawford et al., 2005) and which could make a particularly important contribution to performance on ToM tasks (Samson et al., 2005). Developmental research has shown that the black and white Stroop is a useful measure of inhibition (e.g., Beck, Riggs, & Gorniak, 2009), and a previous study revealed a deficit on this task in TS (Eddy et al., 2010b). The black and white Stroop test assesses inhibitory skills in a very similar way to a traditional Stroop task by requiring the participant to suppress a prepotent response and replace it with a rule-based response (i.e., to suppress the name of a colour and instead say the name of a different colour). It may be preferable to a traditional Stroop test when testing patients with movement disorders, as motor symptoms may be more likely to interfere with performance on a traditional Stroop due to the size and arrangement of stimuli. The other executive task was the FAS verbal fluency test, which was included to assess a different aspect of executive functioning which is less consistently impaired in TS (Channon, Pratt, & Robertson, 2003; Schuerholz, 1998; Schuerholz, Baumgardner, Singer, Reiss, & Denckla, 1996; Stebbins et al., 1995) and which may rely more on dorsolateral prefrontal cortex than the Stroop test (Gallard et al., 2000). It was hypothesised that patients with TS would exhibit differences in performance on all four tasks involving ToM, based on previous findings (Eddy et al., 2010a, 2010b). In relation to the humorous cartoons task, it was expected that patients would experience difficulties understanding humour based on sarcasm (see Eddy et al., 2010b), but that their understanding of irony and slapstick-style humour may be similar to that of controls. Any observed executive deficits were expected to be inhibitory in nature, as a review of the literature indicates that tasks assessing this executive function may be more sensitive to TS (Eddy et al., 2009).

METHOD

Participants

Eighteen patients with TS (five females) were recruited from the TS clinic at the Queen Elizabeth Psychiatric Hospital, Birmingham. The mean age of the sample was 26.8 years ($SD = 9.56$, median = 23.5, range = 16–47), with an average of 13.33 years of education ($SD = 2.17$, median = 13, range = 11–18). All individuals in the TS group underwent a comprehensive clinical interview using the National Hospital Interview Schedule (NHIS) for TS, a detailed semistructured interview schedule, which includes personal and family histories and demographic details and which allows a diagnosis of disorders common in TS, such as OCD or ADHD. For the diagnosis of these behavioural disorders, the NHIS was developed by incorporating the relevant questions and items from the Diagnostic Interview Schedule to yield a diagnosis as per DSM-III-R, and was then updated based on the DSM-IV-TR criteria (Robertson & Eapen, 1996). We excluded individuals with comorbid ADHD. Time since onset of TS was mean 16.94 years ($SD = 9.46$, median = 13, range = 7–37). The mean Yale Global Tic Severity Scale (YGTSS; Leckman et al., 1989) score for the whole TS group was 52.5 ($SD = 17.98$), but scores ranged from 28 to 85/100. Five patients had comorbid OCD. Four patients were taking medication for tics (2 Clonidine, 1 Risperidone, 1 Aripriprazole), three were taking Fluoxetine, and two Sertraline. Twenty healthy controls (11 females), of mean age 21.5 years ($SD = 4.43$, median = 20, range = 18–37), with mean 13.8 years ($SD = 1.20$, median = 14, range = 11–17) of education also participated. No patients had been diagnosed with autism, Asperger syndrome, or learning disability.

Procedure

The study was approved by South Birmingham Ethics Committee. Patients were tested in a consultation room at the Queen Elizabeth Psychiatric Hospital, and controls were tested at either this location or the University of Birmingham. All participants gave written informed consent and were debriefed after testing. They undertook two executive tasks, versions of the UG and SCET, the humorous cartoons task, and the RMET. Half of the patient and control groups received the tasks in the following order: black and white Stroop, humorous cartoons, SCET, UG, RMET, and FAS test. The rest of the participants received the tasks in reverse order.

Socially competitive emotions task (SCET)

The stimuli used in this task were taken from Shamay-Tsoory et al. (2007). There were 16 trials. Each trial featured a cartoon face (that we renamed "Harry") surrounded by four other faces, above and below, on the left and right. For half of the trials these other faces were cartoons; for the other half they were photographs of male and female faces taken from Ekman and Friesen (1976). Both Harry and the other four faces exhibited emotional expressions. Harry had either a happy or sad face; the other faces had either happy, sad, surprised, fearful, angry, disgusted, or neutral expressions. For half of the trials Harry's gaze was directed towards the correct answer; for other trials, Harry gazed forwards out of the page.

There were four trials in each of four conditions. Participants had to select the face that Harry either (1) felt the same as, (2) identified with, (3) was gloating over, or (4) was envious of. Condition 1 required a simple match from the expression on Harry's cartoon face to another character. For Condition 2, participants were told that "when you identify with someone you have things in common with them". The correct answer for this condition was again the character with the same expression as Harry. For Conditions 3 and 4 (involving socially competitive emotions), gloating was defined as a "positive experience in the face of another's misfortune" and envy was described as a "negative experience in the face of another's fortune" (as Shamay-Tsoory et al., 2007). For Condition 3, Harry had a happy expression, and the correct response was to pick the character with a conflicting sad expression. For Condition 4, Harry had a sad expression, and the correct response was to select the character with a conflicting happy expression.

Ultimatum Game

For UG trials, participants were told to imagine a hypothetical situation, but to respond as if the money really was available to them. Participants were always responders, and a story character "Sam" was the proposer. They were told to imagine that "the banker" had given Sam 10 pounds, on condition that Sam shared this money with them. Sam would make a single offer of how much money they could have. If they accepted Sam's offer, the money would be split between them as Sam proposed. If they did not accept the offer, neither they nor Sam would get any money. Three individual trials were presented in the same order. The first trial featured an offer to the participant of four pounds, the second offer was one pound, and for the last trial Sam proposed to keep seven pounds and fifty pence and offered the participant two pounds and fifty pence. For each trial, participants were asked whether they would accept or reject the offer. In terms of an individual trial, the logical response is to accept any offer, because even a very small gain should be better than nothing.

Humorous cartoons

The humorous cartoons task involved 12 black and white humorous cartoons, featured on an online database (www.cartoonstock.com). There were three conditions each containing four cartoons: sarcastic humour, ironic humour, and slapstick/physical humour (comparison cartoons). The joke in cartoons from the sarcastic condition was always based on an understanding of sarcasm. For example, one cartoon featured a man sitting at an office desk making paper aeroplanes being asked by a man in a suit if he could "have a moment of his precious time". The ironic cartoons depended on the detection of irony for the joke to be understood. For example, in one cartoon, the first picture featured a man saying he would like to come back (to earth) as a bird, and be free as a bird. The second picture is of a caged bird. The comparison cartoons did not involve sarcasm or irony, and included slapstick-style comedy. For example, one cartoon featured a lady whose knickers had fallen down.

Participants completed a multiple choice test. They were shown each cartoon and asked to select the main reason why they thought the cartoon was meant to be funny, or how it was designed to be funny, from four options. For each cartoon, one option involved appreciation of the sarcasm, irony, or slapstick element of humour, and was considered to be the correct answer. Another option provided a literal or superficial interpretation of the cartoon, which could be selected if a participant could not infer beyond the material presented. A further option described a contradiction to the cartoon picture or statement, which could be a plausible answer if participants understood the incongruity or surprise element of humour, but incorrectly inferred the cartoonist's intentions. The last option (miscellaneous) was based on an inference that could be made from the cartoon that was not related to the joke. These options were were presented in a fixed pseudorandom order.

The "Reading the Mind in the Eyes" test

This task was taken from Baron-Cohen et al. (2001) and obtained from the Autism Research Centre Online (www.autismresearchcentre.com). It contained 36 photographs of pairs of eyes. The expression of each pair of eyes reflected a particular complex mental state. Each photograph was surrounded by four complex mental state terms. Participants were provided with a glossary of these words and were given standardised instructions as laid out by Baron-Cohen et al. They were told to look carefully at each picture and select the word they felt best matched what the person in the picture was thinking or feeling. They were encouraged to refer to the glossary to seek clarification if needed. Responses were scored according to the set of answers provided by Baron-Cohen et al.

Black and white Stroop test

The stimuli for this Stroop task consisted of an A4 page of 40 equally sized squares, which were coloured black or white and arranged in rows in a pseudorandom order. For the baseline condition, participants were instructed to say the colour of each square, going across each row from left to right. The stimuli sheet was obscured by a blank sheet of paper and each row of stimuli was revealed on completion of the row above. The time taken for participants to name the colour of all squares on the sheet was noted along with any errors. For the test condition, the same stimuli sheet was rotated by 180°, and participants were told to say black if they saw a white square, and say white for a black square. The rest of the procedure was identical. The number of errors made and time to complete each condition was recorded for each participant.

FAS word fluency test

For the verbal fluency test, participants were told to say out loud as many words as they could think of beginning with a given letter of the alphabet, until told to stop. One minute was given for each letter: F, A, and S. Total scores represented the number of words generated over the entire test. Repetitions were not counted. If patients stopped responding and said they could not think of any more words they were prompted to continue trying until the time for that letter had elapsed.

RESULTS

Analysis of task performance employed nonparametric Mann Whitney-U (*MWU*) tests and Spearman's Rho (*Sr*) correlation coefficients, as data were not normally distributed.

Patients and controls did not differ significantly for age, $MWU = 124.5$, $p = .103$, or education, $MWU = 134$, $p = .169$.

Socially competitive emotions task

One patient did not complete this task. Controls performed almost at ceiling (mean = 0.1, $SD = 0.31$), while patients made a total of 19 (mean = 1.12, $SD = 1$). This difference was highly significant, $MWU = 60.5$, $p < .001$. Nine patients made at least one error on this task, and the majority of errors were made on the condition where participants had to pick the face that Harry was gloating over. The two errors made by controls were also during this condition. However, patients also made a few errors over the other three conditions (same/identify/envy). Errors were made when Harry was looking straight ahead and when his gaze was directed towards the correct answer.

Ultimatum Game

As can be seen from Table 1, more UG offers were rejected by patients (mean = 1.44, $SD = 1.20$, median = 2, range = 0–3) than controls (mean = 0.5, $SD = 0.61$), and this difference was significant, $MWU = 100$, $p = .013$. Patients made more rejections than controls on each of the three trials. Four patients even rejected the highest offer of 4 from 10, which was unanimously accepted across control group.

Humorous cartoons task

One of the cartoons from the comparison condition (involving slapstick-style comedy) was removed from analysis because half of the control group failed to give the conventional (correct) answer. This left three cartoons in the comparison condition.

Error totals for patients with TS and controls for each condition are shown in Table 2. When asked to select the main reason why the cartoons were meant to be funny, patients with TS made more errors (mean = 2.17, $SD = 2.07$) than controls (mean = 0.4, $SD = 0.68$), and this difference was highly significant, $MWU = 29$, $p < .001$.

The three test conditions were then analysed separately. As can be seen from Table 2, patients made more errors for sarcastic cartoons (mean = 0.89,

TABLE 1
Rejections made by patients with Tourette syndrome and controls for each Ultimatum Game trial

Group	*Measure*	*£1 from £10*	*£2.50 from £10*	*£4 from £10*
Patients with TS ($n = 18$)	Total number of rejections	12	10	4
	% of group rejecting	67	56	22
Controls ($n = 20$)	Total number of rejections	9	1	0
	% of group rejecting	45	5	0

TABLE 2
Errors made by patients with Tourette syndrome and controls during the humorous cartoons task

	Patients (n = 18)	*Controls (n = 20)*
Condition		
Sarcasm	16	4
Irony	12	2
Comparison (e.g., "slapstick")	11	2
Error type		
Literal	26	6
Contradiction	7	1
Miscellaneous	6	1

$SD = 0.83$) than controls (mean $= 0.2$, $SD = 0.41$), and this difference was significant, $MWU = 90$, $p = .003$. Patients also performed significantly more poorly than controls when responding to ironic cartoons, $MWU = 115$, $p = .014$. Patients made mean $= 0.67$ ($SD = 0.91$) errors in comparison to controls, who made mean $= 0.1$ ($SD = 0.31$) errors. Patients (mean $= 0.61$, $SD = 0.92$) even made more errors than controls (mean $= 0.1$, $SD = 0.31$) when asked to select the main reason why cartoons in the comparison condition were meant to be funny, $MWU = 125$, $p = .030$.

Participants' performance was also analysed according to error type. The majority of errors made by patients with TS in each condition involved literal interpretations (sarcastic cartoons: two random, four contradiction, and ten literal errors; ironic cartoons: two random and twelve literal errors; comparison cartoons: three random, three contradiction, and six literal errors). Overall, patients with TS selected more erroneous literal interpretations (mean $= 1.44$, $SD = 1.34$) than controls (mean $= 0.3$, $SD = 0.47$), and this difference was highly significant, $MWU = 68.5$, $p < .001$. Patients were also more likely to select incorrect explanations (mean $= 0.39$, $SD = 0.61$) based on a contradiction, $MWU = 128.5$, $p = .025$ than controls (mean $= 0.05$, $SD = 0.22$), which led to the opposite interpretation to that which should be inferred. However, patients (mean $= 0.33$, $SD = 0.77$) were no more likely than controls (mean $= 0.05$, $SD = 0.22$) to select incorrect answers from the miscellaneous category, $MWU = 148.5$, $p = .116$, which contained explanations based on simple observations or inferences that were not directly prompted by the information provided in the cartoon.

The "Reading the Mind in the Eyes" test

The patient group ($n = 18$) made a total of 180 errors on this task (mean $= 10$, $SD = 4.61$), while controls ($n = 20$) made 117 (mean $= 5.85$, $SD = 2.96$).

Patients performed significantly more poorly, $MWU = 81.5$, $p = .004$. There was no pattern in the spread of errors across trials.

FAS test

Patients with TS (mean = 41.61, $SD = 14.15$) generated fewer words than controls (mean = 49.95, $SD = 11.4$) during the FAS test, and this difference was significant, $MWU = 105.5$, $p = .029$.

Black and white Stroop test

There was no evidence that the patient group had inhibitory difficulties during this task. Patients ($n = 18$) made 16 errors (mean = 0.89, $SD = 1.41$) on the inhibitory condition, while the control group ($n = 20$) made a total of 20 (mean = 1, $SD = 1.08$, median = 0.5, range = 0–3), a difference that was not significant, $MWU = 161.5$, $p = .555$. Each patient took an additional mean 6.62 ($SD = 3.52$) seconds to complete the inhibition condition in comparison to baseline, which was similar to the mean extra 6.05 ($SD =$ 2.44) seconds taken by controls, $MWU = 175$, $p = .884$.

Comorbid OCD. Comorbid conditions such as OCD could impair task performance. Therefore, the five patients with OCD were removed from the patient group and the performance of the remaining patients with TS ($n =$ 13) was compared to the control group. Analysis was reconducted for overall error totals on tasks that elicited evidence of impairment in the patient group as a whole. Patients with TS and no OCD performed significantly more poorly than controls on the FAS test, $MWU = 116.5$, $p = .003$; the SCET, $MWU = 37$, $p < .001$; the RMET, $MWU = 45.5$, $p = .002$; and the humorous cartoons task, $MWU = 16$, $p < .001$; and rejected significantly more UG offers, $MWU = 79$, $p = .043$.

Gender. The patient and control groups were not equally matched for gender, which could contribute to differences in task performance. Sixty-six per cent of the patient group were male, whereas 45% of control subjects were male. We therefore examined whether there was any evidence that females performed better on the ToM tasks than males (as the majority of patients were males). Female controls were found to make slightly more errors than male controls on both the eyes test (mean = 6.4 vs. 5.2 errors) and humorous cartoons task (mean = 1.1–0.7 errors) and there was almost no difference for performance on the SCET (mean = 0.09 vs. 0.11 errors) or UG (mean = 0.55 vs. 0.45 rejections). Given that the ToM tasks used in the current study failed to elicit gender differences in the control group, it is unlikely that gender differences could explain the highly statistically significant group differences.

Correlations. Nonparametric correlations were calculated to investigate possible relationships between patients' performance on executive and ToM measures (Table 3). YGTSS scores were also used in correlational analysis to identify whether individuals with more severe tics performed more poorly on the tasks administered. The variables used were FAS scores, black and white Stroop time differences and errors, number of UG rejections, and total errors made on the SCET, the RMET, and the humorous cartoons task. Significant correlations were found for number of errors made on the RMET and SCET, and number of errors on the humorous cartoons task and SCET. Corrections for multiple comparisons would mean that only the latter correlation would remain significant. However, as nonparametric tests were used (which are associated with lower power and so an increased chance of making a Type II error) a corrected level of significance may not be appropriate.

DISCUSSION

Individuals with TS exhibited significant deficits on all four tasks involving aspects of ToM, which have been linked to VMPFC functioning. Five of the patients with TS tested in the current study had comorbid OCD. However, when these individuals were removed from analysis all deficits for the group as a whole remained significant, providing evidence that TS, rather than OCD, was linked to poor performance on the ToM tasks. As so many individuals with TS have comorbid disorders, only studying those without comorbid disorders may not be representative of the TS population. However, it will be useful for further research to assess ToM in larger groups of individuals with TS and no comorbidities.

Patients' poor performance on ToM tasks was despite limited evidence of executive dysfunction. A relatively mild deficit in verbal fluency was exhibited by the patient group, but there was no evidence that this was linked to the poor performance exhibited on the social reasoning tasks. Studies have shown that deficits in inhibition can be associated with poor performance on ToM tasks (e.g., Samson et al., 2005). However, the patients with TS tested in the present study exhibited no significant inhibitory difficulties. This could have been due to lack of sensitivity of the inhibitory measure used. Other studies (Channon et al., 2006; Crawford et al., 2005; Eddy et al., 2010a) have reported inhibitory impairments in TS on the Hayling test (Burgess & Shallice, 1996), so it is possible this may be a more sensitive measure than the black and white Stroop task. Though the current

TABLE 3
Correlations for patients' tic severity (YGTSS) scores and performance on executive measures, the SCET, the UG, the RMET, and the humorous cartoons comprehension task

	1. Tic severity (YGTSS) scores	*2. FAS scores*	*3. Stroop time difference*	*4. Stroop errors*	*5. RMET errors*	*6. "Socially competitive emotions" task errors*	*7. UG rejections*	*8. Humorous cartoons comprehension test errors*
1.	X	−.257 .303	.181 .473	.417 .085	.078 .759	.391 .121	.248 .321	.393 .107
2.		—	.116 .647	−.441 .067	−.043 .203	−.113 .657	−.163 .518	−.096 .703
3.			—	−.373 .127	−.305 .219	−.226 .368	.235 .348	−.202 .421
4.				—	.338 .170	.338 .170	.054 .832	.331 .180
5.					—	.533 .023*	.123 .625	.674 .002
6.						—	.412 .090	.935 <.001***
7.							—	.356 .148

YGTSS: Yale Global Tic Severity Scale. Top value: Spearman's Rho correlation coefficient; bottom value: *p*-value. * = significant at the .05 level, *** = significant at the .001 level.

study found no evidence that patients' ToM deficits were linked to executive dysfunction, more research is needed to establish whether changes in ToM in TS are independent of executive difficulties. For example, a working memory measure was not included in the current study. However, previous studies have shown little evidence that this executive ability is compromised in TS (Channon et al., 2006; Crawford et al., 2005; Eddy et al., 2010a).

Patients performed significantly more poorly than controls on the SCET, which required matching emotional facial expressions (for same as and identify trials) or selecting a face showing the opposite emotion to Harry (for envy and gloating trials). It is possible that difficulty interpreting eye gaze could influence responses on the SCET. Half of the trials in each condition involved eye gaze and the others did not. However, as patients with TS made errors on both types of trial, difficulties with the interpretation of eye gaze do not provide a parsimonious explanation for patients' deficits. Patients made most errors when asked to pick the face that Harry was gloating over. As the instructions and terms used in the task were well described to all participants, many errors may indicate that patients found it difficult to reason about the contrasting emotions held by two characters (i.e., when one character was happy, and the other sad). Difficulties understanding conflicting mental states could also be linked to the deficits exhibited by TS in previous studies involving a faux pas task (Eddy et al., 2010a, 2010b). The faux pas task also involves two characters with conflicting mental states: a victim who will be offended by a protagonist's remark, and the protagonist, who is unaware of this effect.

The conflicting interests of two people are also present during the UG. Patients with TS rejected significantly more offers overall in comparison to controls during this task and, unlike controls, some patients rejected even the highest (fairest) offer. One possible explanation for the increased number of rejections made by patients with TS involves ToM. It may be that the patients with TS tested in the present study sometimes exhibited elevated rejection rates in comparison to controls because they were more likely to make negative inferences about the mental state of the proposer.

Pillutla and Murnighan (1996) showed that participants in their study who knew that an offer was low and that the proposer knew it was low were far angrier, and rejected more offers than those participants who understood the proposer was unaware of the fairness of their offer. These authors suggest that a responder might reject a low offer because they imagine that the proposer believes they are unworthy or gullible.

It is interesting that the behaviour of patients with TS tested on the UG in this study appears quite different to that of children with autism. These children are more likely to accept low offers than neurologically intact controls, perhaps because their difficulties with ToM mean they are less likely to make negative inferences about the proposer's intentions (Sally &

Hill, 2006). Although the patients with TS tested in the current study exhibited deficits on ToM tasks, it is important to note that not all of their difficulties are consistent with a simple lack of ability to draw inferences about mental states. Rather, patients with TS may exhibit differences in the way that they reason about mental states in comparison to controls.

Some patients with TS exhibit behavioural problems which could be related to VMPFC dysfunction, such as aggression (Cavanna, Servo, Monaco, & Robertson, 2009) and explosive disorder (Budman, Rockmore, Stokes, & Sossin, 2003). Koenigs and Tranel (2007) suggest that the emotional dysregulation and poor impulse control exhibited by patients with VMPFC damage could explain their increased rejection rates during the UG. Another possible explanation for the increased number of rejections made by patients with TS is therefore poor emotional regulation. That is, perhaps the patients tested in the current study were less able than controls to suppress the frustration they felt in response to unfair UG offers, in order to reason in an economically advantageous manner. It could be useful to use reaction time data in further research in order to help rule out the possibility that impulsivity influenced patients' performance on the ToM tasks. However, neither reaction time data nor error counts revealed evidence of impairment or impulsivity on the black and white Stroop task, and if the TS patients (of whom none had ADHD) were making errors on the tasks administered because they were generally impulsive, then this would have been reflected across all tasks. Perhaps patients with TS experience greater difficulty inhibiting behaviour that is associated with an affective component. This could also explain why many standard inhibitory tasks fail to elicit evidence of impairment (see Eddy et al., 2009).

UG rejections may also be motivated by a specific desire to spite the proposer for their unfairness, which may sometimes be as a matter of principle. Such "altruistic punishment" encourages the maintenance of social norms, and though it does not benefit the individual at the time, it does benefit a social group or society in the long term (Fehr & Fischbacher, 2003). This study is limited by the fact that we don't know the reasoning behind TS patients' responses during the ToM tasks. Future studies should include qualitative analysis in order to determine whether individuals with TS are more likely to reject UG offers due to focusing on the consequences of unfair offers on themselves or society.

The version of the UG used in the current study differed in comparison to the version used by other studies which involved offers made by many different proposers rather than a single proposer. When a single proposer makes the offers, this is perhaps most likely to alter decision making if an individual feels they are playing an ongoing bargaining game with an individual. However, in the current study the way that the task was described to participants highlighted that each offer was to be treated as a completely separate situation. By using a consistent identity as the proposer, this may have increased participants' focus on the amounts of money offered, which could be considered a strength of the current study. Although using a different version of the UG could limit comparisons with other studies, the control data for the UG used in the current study was in line with previous research (i.e., neurologically intact individuals rejected around half of offers below 20% of the total amount, e.g., Nowak et al., 2000).

Performance on the RMET provided further evidence for changes in ToM in TS. This task included making judgements about epistemic mental states (e.g., interested), cognitive mental states (e.g., thoughtful), and emotional mental states (e.g., worried) based on a photograph of a person's eyes. Although one study found intact performance on an earlier, less complex version of the task (Baron-Cohen et al., 1997), this study may be the first to test patients with TS using the more recent and perhaps more sensitive version. Studies have indicated that the VMPFC (including OFC) and amygdala are important for this task (Adolphs, 2002; Stone et al., 2003). There is some evidence for orbitofrontal and amygdala involvement in TS (Braun et al., 1995; Jeffries et al., 2002; Ludolph et al., 2008; Muller-Vahl et al., 2009; Peterson et al., 2007). However, further research is crucial to determine whether changes in these brain regions are indeed connected to deficits in performance on the ToM tasks as shown by patients with TS.

Errors on the RMET and SCET were strongly related to poor performance on the humorous cartoons task. This may reflect the fact that the humorous cartoons task required ToM related inferences about the mental state or intention of the cartoonist, and/or the characters featured in cartoons in the sarcastic and comparison conditions. Performance on the UG was also related to performance on the humorous cartoons comprehension task, although less strongly. This is likely to reflect the involvement of different processes during economic decision making, and activity in other neural substrates in addition to the VMPFC during the UG. However, caution is needed in interpreting these findings, due to both the small sample size and the difficulties associated with conducting multiple comparisons.

The difficulties exhibited by patients with TS in understanding humorous cartoons involving sarcasm was expected, as previous research has highlighted evidence of poor sarcasm comprehension in TS (Eddy et al., 2010b). Poor understanding of the sarcastic cartoons could have been due to deficits in ToM that impaired the appreciation of mental state of the speaker of the sarcastic remark. Patients' deficits understanding the humour in the ironic and comparison cartoons were not expected. Irony involves a kind of exaggerated appropriateness, or may require inferences to be drawn about what is commonly expected, in comparison to what is depicted in the cartoon (see Gibbs & Colston, 2007, for a discussion of the mechanisms underlying irony). While poor understanding of the humour in ironic cartoons could indicate that patients with TS have difficulties with indirect forms of communication, the errors made by patients in response to the comparison cartoons are perhaps more surprising. These comparison cartoons relied less on inferential reasoning, and children who do not yet have a fully mature frontal cortex may understand this more superficial level of humour (Schultz, 1972). Perhaps the most parsimonious explanation for patients' difficulties relies on interpreting the overall focus of the cartoons task as a test assessing understanding of the cartoonist's mental state. If the correct explanation for why the cartoon was meant to be funny was reached through inferring the cartoonist's intentions, then difficulties with ToM could have affected patients' performance on all three conditions.

It may be considered that one limitation of the humorous cartoons task was that a control condition was not included. However, it is highly unlikely that difficulties would be elicited by such a simple control task in a patient group with limited evidence of comorbidity and no learning disabilities. It is also the case that all cartoons had both captions and pictures but were not matched for numbers of words per caption across condition. However, patients with TS performed significantly more poorly than controls for all three conditions (sarcasm, irony, and comparison) and this factor would be of greater importance if patients' performance had varied more across conditions.

Patients' tendency towards misinterpretations of the cartoons led them to select many incorrect literal interpretations, and "contradiction" explanations that described the opposite to what should have been inferred. Whereas literal interpretations probably represent a surface level of reasoning, contradiction errors may suggest that patients understand the contradiction element of humour, so indicate more subtle deficits. Some studies (e.g., Gallagher et al., 2000) have shown that cartoons involving ToM activate the VMPFC more than cartoons not involving ToM. However, Moran, Wig, Adams, Janata, and Kelley (2004) suggest that detecting incongruity in humour activates left inferior frontal and posterior middle temporal regions, while solving the incongruity involves activity in bilateral insula and amygdala. It could be that the deficits exhibited by patients with TS across all conditions on the cartoons task were linked to dysfunction in these latter brain regions.

Studies indicate that impairments on social reasoning tasks are shown by individuals who exhibit social difficulties (Lough et al., 2006; Shamay-Tsoory et al., 2003). Because the current study showed that patients with TS can reason about mental states, albeit differently to controls, any resulting difficulties in social interaction may be more subtle than the social difficulties exhibited by patients with autism. A limitation of the current study is that information about everyday social difficulties was not collected. However, there is evidence that TS can be associated with social problems.

For example, Channon, Crawford, et al. (2003) found evidence of social difficulties whereby patients with TS made poor social decisions during a real-life type decision-making task. Moreover, some patients with TS exhibit nonobscene socially inappropriate behaviours, which include making inappropriate or insulting remarks (Kurlan et al., 1996). Further research is needed to determine whether such symptoms could be linked to changes in social reasoning, or whether individuals with TS could exhibit difficulties with inferential reasoning in general.

In summary, patients with TS exhibited significant difficulties on tasks featuring aspects of ToM, some of which involved understanding humour, or economic decision making. These findings indicate that TS could be associated with changes in social reasoning. These changes could also implicate dysfunction within frontostriatal pathways involving VMPFC and the amygdala in the pathophysiology of TS. Future neuroimaging research should investigate this possibility.

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