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Brief report

Executive functions in uncomplicated Tourette syndrome

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ABSTRACT

Previous studies reporting executive deficits in Tourette syndrome (TS) often failed to control for co-morbid conditions. We investigated executive functions in forty patients with TS without co-morbid psychiatric diagnoses (uncomplicated TS). Patients exhibited executive deficits which were unrelated to tic severity, suggesting executive dysfunction may be a core component of TS.

1. Introduction

Tourette syndrome (TS) is a neurodevelopmental disorder characterised by multiple motor and phonic tics. It is thought that the motor symptoms of TS involve striatal dysfunction, and neuroimaging studies in TS populations have reported changes in this region (Peterson et al., 2003; Makki et al., 2008). However, changes in TS are unlikely to be restricted purely to the motor domain. As with other disorders involving dysfunction of the basal ganglia (such as Parkinson's disease and Huntington's disease), alterations in the functioning of frontostriatal circuits which connect the striatum and prefrontal cortex (e.g. Alexander et al., 1986) have the potential to impact upon patients' cognitive abilities.

Over the past few decades, many studies have investigated cognitive functioning in TS. Adults and children with TS have been reported to exhibit difficulties with broader cognitive functions including attention (Silverstein et al., 1995) and memory (Stebbins et al., 1995), and more specific executive functions, such as verbal fluency (Bornstein, 1990; Bornstein 1991) and working memory (Channon et al., 1992). A recent review of the literature (Eddy et al., 2009) highlighted many inconsistencies in reported findings across studies. However, there is reasonably strong evidence that deficits in inhibition, albeit mild, are linked to TS (Channon et al., 2006, 2009; Eddy et al., 2010b).

One of the main problems in drawing conclusions from the available literature is that many studies have failed to control for the presence of the most common co-morbid conditions, such as obsessive-compulsive disorder (OCD) and attention-deficit hyperactivity disorder (ADHD) (Freeman et al., 2000; Cavanna et al., 2009). It is therefore unclear whether executive deficits reported by many studies are specifically linked to TS or could be the result of accompanying disorders.

Another difficulty related to the assessment of executive function in TS is in determining whether any observed deficits are a direct result of experiencing tics. For example, patients with TS may have problems focusing attention not due to a primary difficulty with attention, but rather as a result of experiencing distracting tics. Bornstein et al. (1991) suggest that cognitive deficits in TS may be inversely related to symptom severity, and a few other studies have shown that greater impairment in inhibitory functioning (Ozonoff et al., 1998; Channon et al., 2006) can be seen in association with greater symptom severity. If executive deficits were found that were not associated with tic frequency and severity, this might imply that such difficulties were directly linked to TS rather than occurring as an incidental result of having tics.

In the current study, we aimed to assess three core executive functions in the largest sample of patients with uncomplicated TS (who had no co-morbid psychiatric conditions) tested to date, to help determine whether reported deficits in verbal fluency, working memory and inhibition are likely to be specifically linked to TS. We also investigated the relationship between executive performance and patients' tic severity, to explore whether

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executive deficits may be independent of the experience of tic symptoms.

2. Method

2.1. Participants

Forty patients with TS (29 males) and 20 healthy controls (15 males) took part in this study. The mean age of participants was 32 years (S.D. 14.29, range 16–64) for the TS group, and 27.35 years (S.D. 10.34, range 18–55) for the control group. Patients with TS had mean 13.55 years of education (S.D. 14.29, range 16–61) and controls had 14.35 years (S.D. 10.34, range 18–55). Patients exhibited TS according to Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) criteria, and the mean number of years since tic onset was 9.73 years (S.D. 8.10, range 2–51 years). Medications were as follows: none $n=16$; risperidone $n=7$ (1+pimozide+clonidine); sulpiride $n=3$; haloperidol $n=5$ (1+clonidine); aripiprazole $n=7$ (1+clonidine); clonidine $n=2$. Mean tic severity according to the Yale Global Tic Severity Scale (excluding impairment scores) was 27.3/50 (S.D. 7.84, range 11–47). No co-morbid conditions were diagnosed in this patient sample, following neuropsychiatric assessment and screening with a TS-specific semi-structured clinical interview, the National Hospital Interview Schedule for TS (NHIS-TS) (Robertson and Eapen, 1996). For the diagnosis of various TS-associated behavioural disorders including OCD and ADHD, the NHIS-TS was originally developed by incorporating the relevant questions and items from the Diagnostic Interview Schedule to yield a diagnosis as per DSM-III-R, and was later updated based on DSM-IV-TR criteria.

2.2. Tasks

All participants completed the following tasks in the same order after giving written informed consent.

2.2.1. FAS test

During this verbal fluency test, participants were required to say out loud as many words as they could think of beginning with a given letter of the alphabet. One minute was given for each letter: F, A and S. Total scores represented the number of different words generated over the entire test.

2.2.2. Digit Ordering Test-Adapted (DOT-A: Werheid et al., 2002; Cooper et al., 1991)

Participants listened to individual streams of digits before rearranging the digits and saying them back in ascending order. Streams increased from 3 to 8 digits over testing. A pair of streams was presented of each length. The maximum span was the longest stream to which participants could respond. Participants who only responded correctly to one stream of a single length had 0.5 points deducted from their maximum span.

2.2.3. Stroop test

The Stroop test contained two conditions: baseline and test. Baseline stimuli were a sheet of XXXs printed in different coloured inks (red, yellow, green, blue) arranged in a pseudorandom order. Stimuli in the test condition were the names of colours ('red', 'yellow', 'green', 'blue') printed in different coloured inks (red, yellow, green, blue) which did not match the written word. For each condition the participants went along the rows of stimuli from left to right naming the colour of the ink of each item (i.e. participants were told not to read the words). Errors and times taken for each condition were recorded.

3. Results

Patients with TS and controls did not differ significantly for age (Mann-Whitney U test (MWU)=349.5, $p=0.428$) or years of education (MWU=485, $p=0.176$).

The performance of patients with TS and controls on executive measures is shown in Table 1. Patients with TS generated significantly fewer words on the FAS test than controls (MWU=573, $p=0.007$), and had slightly shorter maximum DOT-A spans than controls (MWU=526, $p=0.043$). Patients with TS also exhibited a significantly greater effect of interference during the Stroop task according to differences in time taken to complete the baseline and test conditions (MWU=200, $p=0.005$), but not in relation to error differences (MWU=288.5, $p=0.160$). To investigate whether medications may have affected task performance, we compared the task performance of medicated patients ($n=24$) and unmedicated patients ($n=16$).

Table 1
Performance of patients with Tourette syndrome and controls on executive measures.

Measure	FAS test (verbal fluency)	Digit Ordering Test-Adapted (working memory)	Stroop test (inhibition)	
			Errors	Time
Patients with TS	41.60 (13.61) 40 (32–48)	6.04 (0.78) 6 (5.5–6.5)	2.00 (2.40) 35.58 (26.92–52.3)	38.83 (15.96) 1 (0–3)
Controls	50.55 (10.81) 50 (44–54)	6.50 (0.92) 6.5 (5.5–7.5)	1.32 (2.00) 26.01 (16.14–34.38)	27.62 (14.79) 0 (0–3)

Key: Above=mean (standard deviation), Below=median (interquartile range).

These groups did not differ significantly for age, education or tic severity. However, the un medicated group performed better on the Stroop in terms of time taken (MWU=265, $p=0.014$), with smaller time differences indicating a smaller interference effect. There were no other task differences.

Spearman's correlations indicated relationships between patients' executive deficits, age of tic onset and tic severity score. Three correlations were significant at the 0.05 level. These indicated a negative relationship between FAS scores and Stroop time differences (Sr=−0.511, $p=0.001$), a positive relationship between FAS scores and DOT-A spans (Sr=0.345, $p=0.029$) and a negative relationship between DOT-A spans and Stroop time differences (Sr=−0.611, $p<0.001$).

4. Discussion

In this study, patients with uncomplicated TS performed more poorly than healthy controls on three executive tasks. The verbal fluency and working memory deficits exhibited by the current patient group are in contrast with some previous studies reporting no evidence of deficits in these aspects of executive functioning (Stebbins et al., 1995; Channon et al., 2003; Crawford et al., 2005; Goudriaan et al., 2006; Eddy et al., 2010a). Indeed, findings from previous studies which did reveal a deficit were often limited by the presence of co-morbidities. The deficit on the Stroop task in relation to time measures suggests that inhibitory functioning was poor in the TS group, as suggested by several previous studies, including uncomplicated samples (e.g. Channon et al., 2009). Importantly, the lack of a significant difference in errors between patients and controls may suggest that the use of response times is critical in revealing more subtle differences in performance in TS.

Inhibition is likely to refer to a collection of abilities (Aron, 2007), with some of these abilities appearing related to processes involved in working memory (McNab et al., 2008). Inhibitory difficulties could have affected patients' performance on the verbal fluency and working memory tasks. For example, problems generating words during the FAS test could be related to problems inhibiting words that have just been said, or other irrelevant words that come to mind. Poor inhibition could also have made a smaller contribution to difficulties during the working memory task, perhaps through poor inhibition of digits remembered in previous trials. Such possibilities could help explain the relationships in performance across these tasks shown by the patient group, emphasising the difficulties associated with determining the specificity of executive deficits. The application of a wider range of executive tasks to larger samples and analysis of performance using data reduction techniques may help shed further light on the exact nature of patients' difficulties.