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Abnormal line bisection judgements in children with Tourette's syndrome

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Abstract

Tourette's syndrome (TS) has been associated with loss of normal basal ganglia asymmetry, as well as loss of normal functional asymmetry, including the leftward bias on traditional visuospatial tasks such as line bisection and turning bias tests. The aim of the present study was to examine the lateralisation of visuospatial attention in TS. We examined the effect of an irrelevant moving-dot background on line bisection judgements. Nine children with a DSM IV diagnosis of TS participated, in addition to 9 healthy controls, individually matched for age, sex and IQ. Horizontal lines of varying length were presented on a computer screen with either a blank background, or a moving, random-dot field. The dots moved either leftward or rightward across the screen at 40 or 80 mm/s, and participants were instructed to ignore these distracting stimuli when judging the lines. TS children were found to be abnormally *right-biased* in line bisection in a similar fashion to unmedicated ADHD children who, in a previous study, showed a similar small, yet significant, right-bias in line bisection. Matched controls showed a small, nonsignificant *left bias*, consistent with past research. Unlike previous findings with hemineglect patients, the irrelevant moving background had no effect on bisection performance for TS children or healthy controls. The present findings suggest a deficit in visuospatial attention consistent with the emerging picture of a lateralised dysfunction of frontostriatal circuitry in TS.

Keywords: Cormorbidity; Laterality; Line bisection; Tourette's syndrome; Visuospatial attention

1. Introduction

Tourette's syndrome (TS), a neurodevelopmental disorder, results in the emergence of motor and vocal tics usually prior to about 10 years of age [26]. Other than the tics that typically change in severity and content as the disorder progresses, TS is often also accompanied by behavioural, emotional and cognitive problems [26]. The frontostriatal neuropathology of TS (i.e. reduced volumes and abnormal asymmetries of the basal ganglia (BG), and abnormal metabolic functioning of frontal and cingulate/limbic cortical regions) predict both motor and cognitive disturbances [8,12,13,20,27,37].

Although the continuous performance test (CPT) seems to readily discriminate ADHD from normal children, suggesting sustained attention problems [18], TS children appear to be relatively unimpaired on this task [35]. Other studies employing neuropsychological batteries have provided some evidence for attentional impairments in TS adults [11,36]. It has been suggested, however, that these neuropsychological deficits are attributable to the influence of comorbid obsessive-compulsive (OC) and ADHD behaviours [36,40]. Although an attention deficit could conceivably result from frontostriatal dysfunction (as is thought to be the case in TS), further research employing tasks *specifically* designed to investigate aspects of attention is required to support such a claim.

The present experiment involved the use of a horizontal line bisection task to examine the lateralisation of visuospatial attention in TS. Line bisection tasks

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may be particularly sensitive to lateral biases in visuospatial attention, such as those that arise in left neglect patients with right-hemisphere damage [9,22,33]. In a previous study of right-hemisphere patients with clinical left neglect using an identical line bisection paradigm, patients were shown to be significantly right-biased in their attempts to bisect the line [23]. An irrelevant, moving patterned background was also found to systematically bias patients' bisection judgements, such that their judgements were significantly shifted toward the neglected or *left* side by the *leftward* moving background [23], but not to the right by the rightward moving background. A further study using the same task demonstrated abnormal (reversed) functional asymmetry in ADHD children *off* stimulant medication [34]. This result perhaps reflects abnormal BG asymmetry in ADHD, as has been shown by neuroimaging studies [10,14,21].

TS has been associated with loss of the normal neuroanatomical BG asymmetries [27,37], as well as loss of the normal functional asymmetries (leftward biases for such traditional neuropsychological tasks as paper-and-pencil line bisection and turning bias tests) [39]. We therefore predicted that TS children would show abnormal visuospatial attention on line bisection in our computerised task. TS adults have been found to be unusually reliant on external visual cues during performance on a sequential button-pressing task [17]. Thus, we also predicted that line bisection performance in TS children might be abnormally affected by an irrelevant moving background. Despite the fact that the moving background array is not essential to perform the task unlike the visual cues in the button-pressing study [17], as noted above, the previous study with neglect patients showed that the leftward moving dots effectively shifted attention leftward and reduced the bisection error [23].

2. Method

2.1. Participants

Fourteen children were recruited through various paediatric outpatient units and the Tourette's Syndrome Association of Victoria. Of a total sample of 14 children with TS, only 9 (all male, 8 dextral and 1 sinistral) had TS without comorbid diagnoses. Of the 5 children with comorbid symptoms, 4 had comorbid ADHD and OCD, and 1 had comorbid ADHD only. Table 1 shows demographic information for the final sample of 9 'pure' TS children. Each child met the DSM-IV criteria for TS (according to a qualified consultant), and scored significantly on the Tourette's Syndrome Global Scale (TSGS, [19]). The mean score on the TSGS for the TS group ($M = 23.7$) indicated a mild level of TS severity [19]. As the severity and complexity of tics in TS increase with age, it is only natural that the severity of TS symptoms was only 'mild' on average in our sample of TS children as these children were generally tested before the disorder had reached its most severe presentation. The severity of comorbid OC and ADHD symptoms was also measured using the Obsessive-Compulsive Disorder Inventory [15] and the ADHD Rating Scale (ADHD RS, [1]) respectively. Any TS child recruited who scored above the cut-off for the ADHD RS ([1] see Table 1 for scale criteria) or the OCD Inventory ([15] see Table 1 for scale criteria) was not included in the final sample. Of note here is one child with TS who scored 25 points thus meeting the first, but not the second requirement of the ADHD RS (see Table 1 for scale criteria). Of the sample of 9 children with TS, 3 were unmedicated and 6 were on typical neuroleptic medications (2 of whom were also taking a stimulant). Typical medications used for the treatment of TS (i.e. neuroleptics) have been shown to have no impact on neuropsychological test perfor-

Table 1
Demographic details of the Tourette's Syndrome (TS) and matched control groups (S.D. in brackets, Ranges bottom line of each cell), and 1-way Group ANOVA statistics

	TS group ($n = 9$)	Controls ($n = 9$)	Significant group difference (1-way ANOVA)
Mean age (years:mths)	12:3 (3:0)	12:1 (2:6)	No ($P = 0.92$)
Age Range	7:0–15:8	7:7–14:10	
Mean IQ score[d]	104.4 (14.4)	110.4 (14.7)	No ($P = 0.76$)
IQ Range	74–125	92–142	
Mean ADHD RS score[b]	12.4 (10.0)	6.2 (4.2)	No ($P = 0.10$)
Range	0–25	0–14	
Mean TSGS[a] score[e]	23.7 (6.7)	–	–
Mean OCD Inv.[c] Score[e]	28.0 (5.5)	–	–

[a] TSGS—Tourette's syndrome Global Scale ('mild' = 0-24, 'moderate' = 25-39, 'severe' = 40-59, 'extreme' = 60–100).
[b] ADHD RS—ADHD Rating Scale (clinically signficant score must always exceed 16, i.e. at least 2 or more for 8 of 14 items and must be over 1.5 S.D.s above norms which vary with age and gender).
[c] OCD Inv.—OCD Inventory (cut-off score for definitely elevated OCD symptoms = 70).
[d] KBIT IQ estimate.
[e] measure only taken for the TS Group.

mance, at least at the doses prescribed for children with TS [2,3,11,35].

Controls were *individually* matched on relevant demographic variables, including age (± 9 months), sex, handedness and IQ estimates (± 10 points) as measured by the Kaufman Brief Intelligence Test [24] (see Table 1). We did not measure nor match for socioeconomic status. Although no quantitative measure of handedness was used for either sample, participants were asked a series of questions to determine which hand they used for several different tasks (e.g. writing, catching a ball, brushing their teeth, opening a door). Only participants who consistently reported using either their left or right hand were included in the study. Every effort was made to exclude children with possible developmental and/or neurological problems, however, it was literally impossible to screen the child and all other family members for all neurological and developmental disorders. Exclusion criteria for control children included a family history of TS, OCD or ADHD (the ADHD Rating Scale was filled out by the parents of each participant), pervasive developmental disorders (e.g. autism), epilepsy, or any specified learning disability. The exclusion criteria were explicitly stated on the parental consent form so that any child with a diagnosed neurological or developmental problem should not have taken part.

2.2. Apparatus

A Toshiba 3100SX portable computer with a VGA monochrome screen (active area = 148 mm (19°) × 198 mm (25°)) was used for the line bisection task. Stimuli (lines, cursor and dots) appeared in amber on a black background.

2.3. Procedure

The task required participants to bisect horizontal lines with or without a moving background array. The viewing distance was held constant at approximately 450 mm. Solid horizontal lines, 2 mm (0.25°) thick and of two different lengths (180 mm or 23° and 140 mm or 18°), were displayed in random order. The different line lengths were used to minimise the likelihood that participants would develop a single response set and perform the task automatically. They were instructed to move a vertical cursor (1mm or 0.13° width; × 8 mm, or 1° height), located at either the left or right end of the line at the beginning of each trial, to the judged centre of the line. They were told to ignore any moving background array if possible. They pressed one of two microswitches to move the cursor leftward (left button) or rightward (right button). The velocity of the cursor was set at 60 mm/s. The task was self-paced, and when satisfied, participants pressed another button (located in the centre of the front panel of the response box) to record the response and move to the next trial. No feedback on accuracy was given. The computer recorded the distance of the cursor from the actual centre of the line to an accuracy better than 1 mm.

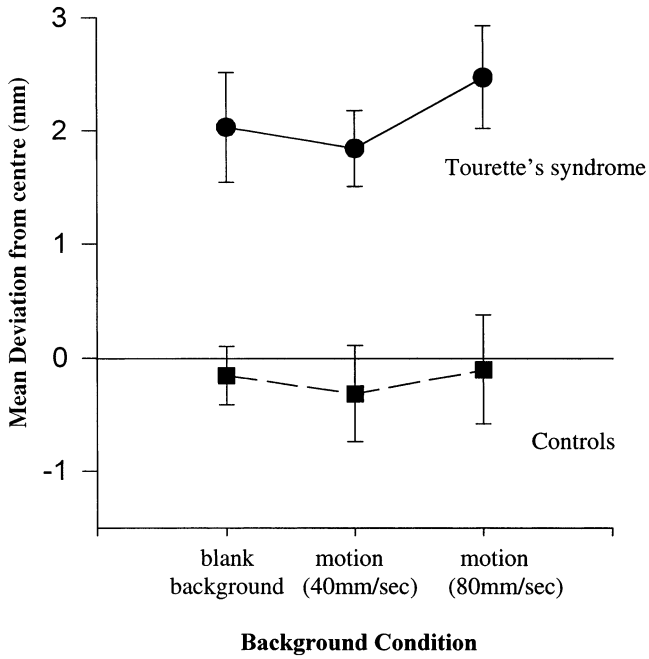

Fig. 1. Mean deviation from centre (mm) for each Background Condition (collapsed across direction) for Tourette's and control children. Positive values indicate rightward error, negative values leftward error. Standard Error bars are shown.

There were 5 different backgrounds that were pseudorandomly allocated to each of 60 trials. The baseline condition was a blank background. There were also 4 different moving background conditions (see below). An array of solid circular dots was displayed in random formation on the screen at a fixed density of 40 dots (20 above and 20 below the line). The diameter of each dot was approximately 4 mm or 0.51°. The dots did not appear within the narrow band that contained the stimulus line and cursor (8 mm or 1°). Two of the four moving background conditions involved leftward motion of either 40 mm/s or 80 mm/s. In the remaining two conditions the background motion was rightward, again at either 40 or 80 mm/s.

Each participant completed 3 blocks of 20 trials (i.e. 60 trials in total). The order of the blocks was counterbalanced across participants.

3. Results

Fig. 1 shows the mean deviation from the centre of the line in the bisection task for each group and for each background condition (blank screen, 40 mm/s,

and 80 mm/s background motion). Note that the effect of Direction of Background Movement is reported below. On average the TS group transected the line 2.1 mm to the right of centre (95% confidence interval range = 1.27 mm to 2.99 mm to the right). By contrast, healthy controls transected the line slightly (mean = 0.20 mm) to the *left* of centre (95% confidence interval range = 1.11 mm to 0.70 mm to the left).

Single-sample *t*-tests (comparing mean bisection errors *across all screen conditions* with zero, i.e. perfect bisection) indicated that the TS group transected the line significantly to the right of centre, $t(8) = 5.73$, $P < .001$; whereas controls did not significantly deviate from the centre, $t(8) = -0.51$, $P > .60$. To examine whether the extent of the bisection error correlated with any participant characteristics (e.g. age, ADHD Rating Scale Scores, etc), Pearson correlational analyses were carried out. None of the correlation coefficients approached significance.

A three-way ANOVA with a between-subjects factor of Group (TS, controls) and within-subjects factors of Background Condition (blank screen, 40 mm/s, and 80 mm/s moving dots) and Cursor Start (left, right) showed a significant main effect of Group, $F(1,16) = 19.10$, $P < .001$, thus confirming the impression of a group difference (see Fig. 1). No significant main effects of Background Condition, $F(2,32) = 1.98$, $P = .16$, or Cursor Start, $F(1,16) = 3.06$, $P = .10$, were found and there were no significant interactions. As the data were not all normally distributed according to the Kolmogorov-Smirnov Goodness of Fit Test, non-parametric tests were conducted to confirm the statistics reported above. All of the parametric results were confirmed. Most importantly, the one-sample sign tests confirmed that the TS group transected the line significantly to the right of centre, $P < 0.04$, and also that the bisection error for the controls did not deviate from centre, $P = 0.94$.

In a subsequent analysis no significant effect of Direction of the irrelevant moving background was found, $F(1,16) = 1.15$, $P = 0.30$; nor was there a significant interaction of Group by Direction, $F(1,16) = 0.21$, $P = 0.65$.

In view of the absence of significant effects involving a number of the factors of interest, post-hoc analyses were carried out to determine statistical power with a sample size of 9 individuals. These revealed that 17% (power = 0.17) of medium-sized effects (alpha level 0.05) would be detected with this sample size. Although this gives even more credence to our significant Group effects, this means that we are limited in the conclusions we can draw from the *lack of* significant effects. It should be recognised, however, that although low power is clearly a factor, it is unavoidable for many neuropsychological studies where the aim is to test 'pure' cases [for example see [8,16,17,23,32,34,39]]. The consequences of these power analyses are elaborated in the Discussion section.

4. Discussion

The present experiment involved the use of a horizontal line bisection task to examine the lateralisation of visuospatial attention in TS. Functional asymmetries in tasks such as line bisection are generally indicative of a metabolic asymmetry in regions of the brain that are important in attentional orienting. For example, unilateral right (predominantly parietal) hemisphere damage underlying left neglect has been shown to result in a large, consistent rightward bias in line bisection suggestive of a deficit in directing attention leftward [9,22,33].

A previous study showed that ADHD children are significantly *right-biased* in judging the midpoint of horizontal extents, but only when *off* stimulant medication [34]. Analogous right-biased line bisection performance was shown by our TS children, who transected lines significantly, and consistently, to the right of centre (see Fig. 1). This right bias can be contrasted with the matched controls' slight (but non-significant) *left* bias in bisection performance — a pattern previously reported with healthy controls [4–6]. Just like the ADHD children, the TS children showed consistent transections to the right of centre, suggesting that the left portion of the line was perceived as slightly shorter, or less salient, than the right portion. This apparent perceptual asymmetry may be due to a reduced ability to direct attention leftward [31].

TS adults have shown abnormal functional asymmetries (e.g. a lack of normal leftward biases in line bisection and turning bias tests) [39]. However, no research to date has shown a significant rightward functional bias for a group of TS patients (adults or children). Indeed, few studies have focused on the neuropsychological or attentional aspects of TS, and even fewer have looked for any lateral biases in performance [2,3,11,36,39,40].

In comparison to the significant right-bias of the TS group, controls showed a slight, nonsignificant left-bias. This result is consistent with previous research involving both visual and kinaesthetic line bisection tasks, where normal right-handers (including children above the age of 6–7 years, [7]) judge the centre of the line to be slightly (and sometimes significantly) to the left of the true centre [4–7].

Neuroimaging and cognitive studies of normal individuals, as well as animal studies, suggest the involvement of right-hemisphere cortical regions (in particular the right prefrontal and parietal cortex) in selective attention and arousal/vigilance [25,30]. Thus, upon structural damage of or functional changes in right hemisphere regions, one might expect altered be-

havioural asymmetries in tasks sensitive to such biases. Indeed, left-neglecting right-hemisphere-damaged patients commonly demonstrate right-biased transections [9,22,31,33], and have been shown to do so in an identical paradigm to the one used here [23]. The neglect patients' performance, however, was also affected by the *direction* of background motion, such that patients' judgements were significantly shifted toward the neglected (left) side by leftward motion of an irrelevant background array [23], but not to the right by rightward motion. The authors of that study concluded that intact motion processing in left-neglect patients can help them overcome a chronic deficit in disengaging their attention from the right.

Just as right-hemisphere damage leads to a rightward attentional bias in neglect, metabolic asymmetries of BG nuclei may have the potential to do the same. The BG have extensive connections with diverse regions of the prefrontal cortex; thus asymmetries of the BG may in turn affect the balance of activity in such frontal regions. Indeed, reversed structural asymmetries of BG nuclei, as well as hypometabolism of right hemisphere frontal regions, have been found in children with ADHD [10,14,21]. Functionally, these neuroanatomical asymmetries in TS and ADHD have the potential to result in attentional biases such as those shown in a line bisection task. An alternative, yet speculative, interpretation of the results of the present study was prompted by a fairly recent neuroimaging study that reported increased metabolic activity in the caudate nucleus as a result of tic suppression in children with TS [28]. It is marginally possible, therefore, that tic suppression resulted in increased competition for the right hemisphere attentional system, thereby disrupting the frontostriatal circuitry necessary for accurate line bisection performance.

The TS children in the present study (as well as the ADHD group we studied previously [34]) showed the expected right-side bias in line bisection. However, the moving background array had no detectable effect on their performance (perhaps due to low power). Thus while TS and ADHD children may perform similarly to patients with unilateral left neglect on some standard clinical tasks (e.g. letter cancellation and line bisection) [38], there are seemingly both *quantitative* and *qualitative* differences in the task performances of these groups. First, the magnitude of the error in tasks such as line bisection is comparatively small for both the ADHD and TS groups. The average bisection error for the TS children in this task was approximately 2 mm to the right of centre, and 1 mm for the unmedicated ADHD group [34], compared with the typically variable, but substantially larger, bisection error for left neglect patients [9,22,23,31,33]. Second, neither TS nor ADHD [34] individuals appear to have the same directional 'stickiness' of attention as the neglect patients [30], as their lateralised performance was independent of background motion. This potential difference, however, must be interpreted with caution due to the limited statistical power arising from the conservative selection criteria adopted for recruiting TS participants in our study. The exclusion criteria adopted ensured that our sample of TS children were homogeneous in their lack of comorbid diagnoses (thereby increasing the generalisability of results); however, this factor also necessarily resulted in a reduction of statistical power.

An observation from the neglect literature is that patients' pathological attentional bias can be significantly reduced, and even normalised, by the occurrence of a spatially uninformative alerting cue [32]. The authors argued that the alerting cue activated a right hemisphere network specialised for maintaining arousal, and that this activation spread to right hemisphere circuits responsible for directing selective attention to the contralateral (left) side. These findings support current neuroanatomical models of attention that suggest that spatial orienting has the potential to be modified by the arousal system [29]. Because TS (and ADHD [34]) children have shown a similar (albeit reduced) visuospatial attentional bias to patients with neglect it would be of interest in future studies to test whether this bias is also susceptible to alerting cues. Although the pathophysiology of TS (and ADHD [34]) differs considerably to that of neglect, the frontostriatal dysfunction of TS could conceivably result in an alerting deficit. Should the small rightward bias in TS children be reduced/normalised by alerting cues in a similar fashion to the bias in neglect, this would support the contention that the attentional biases in these disorders have a similar (probably right hemisphere) neuroanatomical locus. Of course, such findings could not rule out the possibility of an alerting deficit in TS of thalamic or brainstem origin.

In conclusion, this study found TS children to be abnormally right-biased in a line bisection task. Unmedicated ADHD children show a similar significant right-bias in line bisection [34]. The present findings suggest a lateralised frontostriatal deficit of visuospatial attention in children with TS, consistent with recent neuroimaging studies in this group. More research is required to further investigate the extent of lateral biases in TS, particularly to address the question of whether spatially uninformative alerting cues can be used to modulate visuospatial biases of the kind documented in the present paradigm.

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