

# Directed attention in Gilles de la Tourette syndrome

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Gilles de la Tourette syndrome (TS) is a basal ganglia (BG) disorder, associated not only with hyperkinetic movements but also with attentional impairments. This experiment sought to ascertain whether overt direct visual attention would influence tactile attentional performance in TS, via the use of a vibrotactile choice reaction time procedure involving biased probabilities of event occurrence. Participants were required to look (i.e., direct gaze) either at the hand receiving the most (expected) vibrations, or the hand less often stimulated (the unexpected), for both crossed and uncrossed arm postures. Contrary to our predictions, *gaze did not* influence attentional performance in TS patients. Furthermore, patients were found *not to be sensitive* to distributions of event probability; that is, they did not demonstrate normal expectancy effects like controls. Attentional deficits in TS (as in Parkinson's disease, another BG disorder) may pertain more to difficulties in *holding rather than in shifting* the focus of attention. Moreover, directing attention towards the unexpected locus in the crossed arm posture improved overall performance in both patients and controls, suggesting that increased task demands (e.g., crossed arm posture), and/or unexpected stimulus location, may be alleviated by directed attention. These impairments may stem from dysfunction in the circuits linking the frontal lobes with the BG.

Keywords: Tourette's syndrome, attention, holding, shifting, gaze, basal ganglia

## 1. Introduction

Gilles de la Tourette syndrome (TS) is a neurological disease characterised by multiple motor tics and vocalisations [25]. Associated comorbid conditions include attention deficit hyperactive disorder (ADHD), obsessive compulsive disorder (OCD), and behavioural abnormalities [6]. TS may be inherited by autosomal dominant transmission [8] and may be the result of dopaminergic dysfunction arising from

disturbances in the basal ganglia (BG) and limbic system [20].

Attentional disturbances in TS have been well documented *clinically*. Recently [26], an attempt was made to determine the extent to which ADHD and OCD symptoms were related to attentional dysfunctions in adults with TS. The authors found that attentional impairments, although evident in pure TS patients, were most pronounced in patients with TS and comorbid ADHD. Both groups, however, were most disadvantaged on tasks involving visual scanning and set shifting, thus suggesting impairments in the focus of attention. Channon et al. [4] have postulated that the attention dysfunctions observed in TS may represent a selective deficit rather than an overall global impairment.

In an attempt to understand the nature of the attentional disturbance in TS adults, which has to date received very little experimental attention, we [13] sought to assess the efficiency with which TS patients could shift and direct attention between various congruent and incongruent visual stimuli by employing a paradigm developed from the Simon effect [27]. One of the most important features that determines the speed of a response in a choice reaction time task is stimulus-response compatibility. The effect upon response speed of the otherwise irrelevant spatial relationship between stimulus and response location is what is conventionally known as the Simon effect [27]. We found that TS patients, as compared to controls, were particularly disadvantaged in making attentional shifts to various conflicting stimulus-response configurations.

In a vibrotactile choice reaction time (CRT) experiment, we [14] further aimed to ascertain whether TS patients were impaired in their ability to *hold* attention at an expected location (i.e., hand, where stimuli and responses have a high probability of occurring), or to *shift* their attention to an unexpected location (i.e., the opposite hand, where stimuli and responses have a low probability of occurring), for both crossed and uncrossed arm postures. We adapted Posner's [22] visual paradigm which manipulated stimulus probability

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at different spatial locations. We found that TS patients, although slower overall, were *not* significantly different from controls in making attentional shifts or in holding attention. Attention deficits using this technique, however, have been reported in other BG disorders, such as Parkinson's disease (PD) [3] and Huntington's disease (HD) [14].

In yet another vibrotactile (CRT) experiment, we introduced overt gaze (i.e., *directed attention*) as a factor which might influence attentional performance while we again manipulated both expectancy and configuration. We previously found that both PD [3] and HD [15] patients' performance significantly improved when they were permitted to gaze (i.e., *direct attention*) at one hand or the other; PD and HD patients therefore were less effective in maintaining their attention when required to operate purely via internally generated cues, a finding previously shown in movement related tasks [10, 11]. Moreover, whereas PD patients experienced difficulties only in *holding* attention [3], HD patients were found to be sensitive with respect to both *holding* and *shifting* the focus of attention.

Since TS, like PD and HD, patients may rely more upon external rather than internal cues to direct attention [12], as in our companion paper with HD [15], we sought to repeat the above experiment with a group of TS patients. While again manipulating both expectancy (i.e., expected/unexpected events) and configuration (i.e., uncrossed/crossed arm postures), participants were required to respond to vibrations, produced by a vibrotactile transducer, with either their left or right hand. (Note, the crossed arm posture may be regarded as a version of the Simon effect, since there may be a coding conflict between the anatomical identity of the operating limb and its spatial location [3].) For a fixed number of trials, participants were required to look (i.e., direct gaze) either at the hand receiving the most (expected) vibrations, or the hand less often stimulated (the unexpected). We predicted that if TS patients are particularly reliant on external cues to direct attention (as we found with PD and HD patients), they should benefit from looking at (i.e., directing attention towards) the operating hand. Note that TS patients' performance was significantly slower than controls' in a motor task where external visual cues were in limitation [12]; external visual cues may assist in directing attention not only in motor, but perhaps also in tactile tasks.

## 2. Methods

### 2.1. Participants

Twelve patients with TS, all volunteers from the Victorian Tourette Syndrome Association, and 12 age matched controls with no history of neurological illness participated. Control participants were recruited from a healthy population and were matched individually to patients by sex, age (within two years), IQ, and Short Test of Mental Status score [16]. Patients with TS met DSM-III-R (Diagnostic and Statistical Manual of Mental Disorders, [1]) diagnostic criteria, with chronic motor and vocal tics, onset before the age of 21 years, and duration of tics of more than one year. Four TS patients were diagnosed with comorbid OCD, two with attention deficit disorder (ADD), and the remaining six with pure TS only. There were eleven males and one female in each group, one left handed and 11 right handed participants. There was no significant difference in age between the TS patients (32.83 years) and the controls (32.75 years). Duration of TS ranged from 2 months to 44 years with a mean duration of 8.7 years ( $SD = 11.7$ ). All participants were screened for dementia using the Short Test of Mental Status [16] which has a maximum score of 38 (scores below 29 are indicative of dementia). A one-way ANOVA showed that the average scores obtained for both the TS patients (33.8) and controls (34) did not differ significantly,  $F(1, 22) = 3.72, p > 0.07$ . To assess depression, the Mood Assessment Scale was administered [30] which has a maximum score of 30. The following cut off points are recommended: 0–9 normal; 10–19 mild depressives; 20–30 severe depressives. One-way ANOVAs showed that the TS patients (9.8) had significantly higher scores than the controls (1),  $F(1, 22) = 7.45, p < 0.05$ . It is difficult, however, from the suggested cut offs, to draw any firm conclusion regarding possible differences in depression between the TS and control group. To predict full scale IQ, both TS patients and controls were administered the National Adult Reading Test [19]. A one-way ANOVA showed that the scores for both TS patients (119,  $SD = 3.9$ ) and controls (121,  $SD = 3.1$ ) did not significantly differ,  $F(1, 22) = 1.10, p > 0.31$ . Finally, four TS patients were unmedicated, and the remaining eight were on haloperidol, thioridazine, pimozide, prozac, and ritalin. Our previous studies have examined the effect of neuroleptic medication on TS performance and have found it to be the same irrespective of medication status [12, 13, 14].

## 2.2. Apparatus

Two Oticon-A ( $47\ \Omega$  impedance) bone conductors were used as transducers, with vibrating surfaces of 1.7 cm in diameter. They were driven by oscillators under the control of a Toshiba 486 portable computer. The vibrotactile stimuli were set at a frequency (250 Hz), intensity (6 V peak-to-peak), duration (80 msec) and rise and fall times (20 msec) that produced a clearly discernible signal. Participants pressed one of two response buttons to the vibrotactile stimulus. Each button was elevated 4 mm up from the box and was 17 mm in diameter. Earphones were worn to eliminate any possible auditory cues.

## 2.3. Procedure

Each subject sat at a table with both arms extended 30 cm from the midline out to the side of the body, with the index finger of each hand resting over one of the two buttons. The buttons sat inside a rectangular wooden board so as to support the arms. Each vibrotactile transducer was attached with Velcro to the topside of each index finger leaving the pad free to respond to the vibration. Participants responded as quickly as possible by depressing the button on which the stimulated finger rested. For each subject, half way through the experiment, the button boxes and vibrotactile transducers were interchanged between hand and side.

Participants sat with their arms either crossed or uncrossed for a block of 12 trials, and within each block, eight, nine, or ten (expected) trials went to one hand (i.e., either left or right), and four, three, or two (unexpected) trials went to the other. Unlike our previous study [14], whereby participants fixated directly ahead, participants now *directed gaze* at the tip of their left or right index finger. Thus participants had to look *at* the expected or unexpected side, or to look *away* from the expected or unexpected side, as a function of arm posture (i.e., uncrossed, crossed). In all cases participants directly fixated on their index finger. Fixation was monitored to ensure that all participants were adhering to these instructions.

There were 384 trials overall, 75% of which were expected and 25% were unexpected, thus generating 288 expected and 96 unexpected trials. The positioning of all trials was systematically organised so that across the experiment the expected and unexpected trials were equally and pseudorandomly distributed. For statistical purposes, 96 expected trials were systemat-

ically *preselected* in order to match the 96 unexpected trials. This was done to ensure intra-subject homogeneity of variance and in accordance with standard practice [3, 14].

There were sixteen conditions corresponding to all possible combinations of Configuration (uncrossed, crossed), Expectancy (expected, unexpected), and Gaze (at, away). Each hand and side received an equal number of trials; however, these factors were not separately analysed. The presentation of the above conditions was alternated so that hand or location changed every block of trials, while direction of gaze changed after every four blocks. Prior to the commencement of each block of trials, participants were informed of their new arm posture (i.e., uncrossed/crossed), of the new expected location (i.e., left/right) and of the direction of gaze (i.e., at/away). There were four different sequences all counterbalanced across participants to avoid any order effect. The instructions given to each subject were as follows: 'I would like you now to uncross (or cross) your arms. This time, *most* of the vibrations will be going to your left (or right) hand (the experimenter lightly tapped the subject's hand). Occasionally, however, some vibrations will be going to the opposite hand. I would also like you to gaze at the left (or right) index finger (the experimenter lightly tapped the tip of the left/right index finger); try to keep your eyes fixed to that location until I tell you otherwise. Respond as quickly and as accurately as possible upon feeling the vibration.'

In order to stabilise RT, there were 48 practice trials at the beginning of each session taking configuration, expectancy, and gaze into consideration. The computer also recorded the errors (i.e., incorrect responses for each conditions; these were of course excluded from the analyses). In order to eliminate any possible RT anticipations, RTs below 150 msec were disregarded; values exceeding 1000 msec were also disregarded as omissions. In any case, RTs which were more than three standard deviations from the subject's overall mean were replaced by this value, in accordance with standard procedures [2]. Very few RTs were involved in these replacements or discards, with the majority of RTs falling within the cut-off values.

## 3. Results

The data were submitted to a four-way ANOVA with the factors of Group (TS, controls), Configuration (uncrossed, crossed), Expectancy (expected, unexpected),

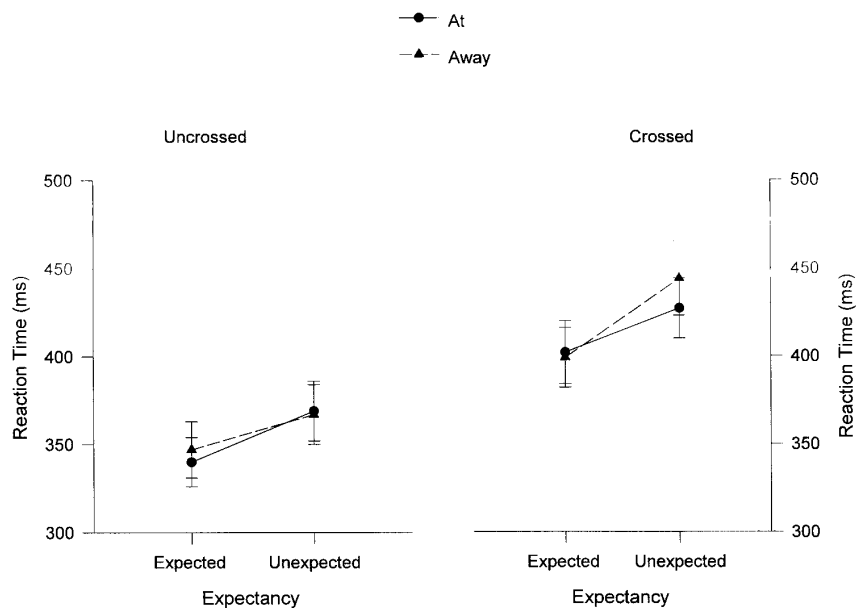


Fig. 1. Mean reaction time (ms) as a function of Expectancy (expected/unexpected events) for both uncrossed and crossed configurations, with gaze at or away from the responding hand. SE bars included.

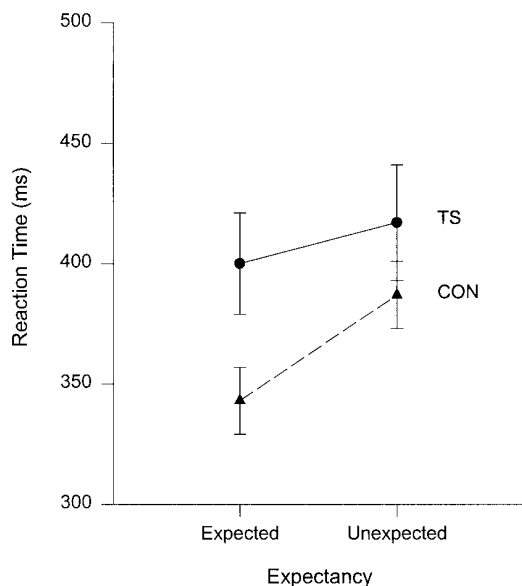


Fig. 2. Mean reaction time (ms) as a function of Expectancy (expected/unexpected events) for both Tourette's syndrome (TS) patients and controls (CON). SE bars included.

and Gaze (at, away), with repeated measures of the last three factors.

There was a significant three-way interaction involving Configuration, Expectancy, and Gaze,  $F(1, 22) = 4.71$ ,  $p < 0.05$ , see Fig. 1. Post-hoc two-way ANOVAs (Expectancy, Gaze), for each of the crossed and uncrossed responses separately, showed that there

was in both cases a significant main effect of Expectancy,  $F(1, 11) = 18.05$ ,  $p < 0.001$ , and  $F(1, 11) = 39.07$ ,  $p < 0.001$ , respectively. Irrespective of arm posture, the expected trials were significantly faster than the unexpected. In addition, wherein lay the locus of the three-way interaction, there was a slight advantage in looking at the unexpected location in the crossed arm posture.

Moreover, there was a significant Group by Expectancy interaction,  $F(1, 22) = 6.04$ ,  $p < 0.05$ , see Fig. 2. Post-hoc one-way ANOVAs showed no significant difference between expected and unexpected responses for the TS patients,  $F(1, 11) = 3.96$ ,  $p > 0.07$ , whereas controls responded faster to expected compared to unexpected events,  $F(1, 11) = 41.55$ ,  $p < 0.001$ . TS patients were unable to effectively make use of expectancies like controls; the difference between the expected and unexpected responses was 17 msec for TS patients and 44 msec for the controls. *TS patients may thus experience problems in holding attention towards an expected locus.*

Overall, despite the absence of significant main effects of Group or Gaze, there were, however, significant main effects of Configuration,  $F(1, 22) = 91.31$ ,  $p < 0.001$ , and Expectancy,  $F(1, 22) = 31.04$ ,  $p < 0.001$ ; crossed arm responses (418 msec) were slower than uncrossed responses (356 msec), and unexpected trials (402 msec) were slower than expected trials (372 msec).

The error data demonstrate that the present results are unlikely to be due to any speed-accuracy trade-offs. The overall error rate for the TS patients and controls was 0.8% and 0.7%, respectively, with many participants making no errors at all. More errors, for both TS patients and controls, were made with the arms crossed (1.3% and 1.2%, respectively) than uncrossed (0.6% and 0.5%, respectively), with unexpected trials (0.9% and 0.9%, respectively) than expected trials (0.7% and 0.4%, respectively), and when looking away (0.8% and 0.8%, respectively) than when looking at (0.7% and 0.6%, respectively).

Given that TS patients were significantly more depressed than controls, a Pearson's product moment correlation was conducted on participants' average CRT data and depression scores, but failed even to approach significance.

#### 4. Discussion

This study sought to ascertain whether overt gaze (i.e., directed attention) would influence performance, particularly for TS patients who may rely more on externally generated information [12]. Contrary to our predictions, however, gaze did *not* influence attentional performance differentially in TS patients. Thus, gaze did not interact with group. Indeed, looking at (i.e., directing attention towards) the unexpected locus in the crossed arm posture improved overall performance for both patients and controls. For the expected events, and irrespective of arm posture, gaze had no effect on the response pattern. However, TS patients were *not sensitive to distributions of event probability*; that is, they did not demonstrate normal expectancies like controls.

The present results demonstrate that gaze direction does not influence performance in TS patients. Though TS patients may rely more upon external information to direct attention in movement-related visual tasks [12], this effect may not extend to the tactile modality. With PD [3] and HD [15] patients, we previously found that performance did improve when gaze was directed at one hand or the other. Whereas TS patients may rely more on covert rather than on overt attentional processes, the reverse may apply with PD and HD patients.

We [14] have previously shown that TS patients, although slower than controls, were not disadvantaged in making attentional shifts or in holding attention. Patients in this experiment, however, failed to show

normal expectancies like controls, that is they were not effective in holding their attention to an expected locus. Thus attentional impairments in TS may pertain *more to difficulties in holding rather than in shifting* the focus of attention. Indeed, these findings have been previously reported clinically [4, 26, 29]. PD [3] and HD [15] patients may also show impairments at holding attention in the presence of competing alternatives [3]. In addition, HD patients also demonstrate problems in shifting attention from expected to unexpected spatial locations [15].

Indeed, the attentional problems in TS, although more subtle in manifestation compared to those observed in our previous studies with both PD [3] and HD [15], suggest frontal-BG disturbances. Recently, Posner and Dehaene [23], and Posner and Petersen [24] proposed a network model of attention following a subdivision of 'anterior' and 'posterior' attentional systems. The 'posterior' system, associated with the parietal lobes, is thought to be responsible for attention *shifting*, whereas the 'anterior' system, involving the frontal-BG circuits, is thought to be responsible for 'executive' functions, such as attention allocation, response flexibility and attention holding. In HD, cortical atrophy in both parietal and frontal regions [17] suggests that both attentional systems may be compromised. This also supports our previous findings; HD patients show deficits in both holding and shifting attention. In PD and possibly TS, there is evidence to suggest that the 'anterior' attention system may be dysfunctional (see also [5, 9]), thus relating to the deficit observed with respect to holding attention.

According to Mesulam's [18] conceptualisation of attention, the distribution of directed attention is mediated by a neural network that contains three independent, although interacting, representations of the extrapersonal world: posterior parietal cortex, frontal lobes, and cingulate cortex. Flexible interaction between these regions allows for effective distribution of attention; however, damage may lead to unilateral neglect or problems in directing attention. In TS, it is less likely that these areas are compromised since patients, like controls, do not benefit in situations where directed attention is manipulated.

Generally, performance was slower in the crossed arm posture for both patients and controls, probably reflecting the coding conflict between the anatomical identity of the operating limb and its spatial location [3]. The coding conflict between the responding hand and the response location may be reduced if attention can be allocated to where the response is to be

made. Indeed, performance in the crossed arm posture tends to be faster when normal participants look *at* the responding hand rather than *away* [21]. In this study, looking *at the unexpected* hand, and only in the crossed arm posture, improved performance for both patients and controls; increased task demands (e.g., crossed arm posture) may be alleviated by directed attention, even though in this vibrotactile task vision can play no direct role.

The present findings suggest that TS patients are impaired in *holding attention* towards an expected locus where stimuli and responses have a high probability of occurring. Dopaminergic fibres project from the substantia nigra to the striatum and from the ventral tegmental area to the frontal lobes [28]. The impairment observed in TS may involve the 'anterior' attentional system, and thus stem from abnormalities of the BG and its associated subcortical-cortical circuitry. TS patients may not benefit by the provision of directed attention in tactile tasks, compared to motor tasks.

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