The Simon effect and attention deficits in Gilles de la Tourette’s syndrome and Huntington’s disease

Nellie Georgiou,1 John L. Bradshaw,1 Jim G. Phillips,1 Judy A. Bradshaw1 and Edmond Chiu2

1Department of Psychology, Monash University, Clayton and the 2Huntington’s Disease Clinic, Department of Psychiatry, University of Melbourne, Victoria, Australia

Correspondence to: Nellie Georgiou, Department of Psychology, Monash University, Clayton 3168, Victoria, Australia

Summary

Tourette’s syndrome and Huntington’s disease have long been clinically associated with attentional deficits. In this study, we aimed to determine the nature and quantify the extent of such deficits. A technique was devised to ascertain the efficiency with which Tourette’s syndrome and Huntington’s disease patients could shift and direct attention away from naturally expected stimulus-response (S-R) linkages. This was done by varying the relationships formed between stimulus and response location. Attentional efficiency was indicated by relative speed of responding to relevant (congruent) and irrelevant (incongruent) stimuli, in a paradigm developed from the Simon effect. There were five conditions progressively increasing in complexity. The stimuli consisted of left and right pointing arrows and, in some cases, various conditionality manipulations were also employed, such that in the presence of a certain symbol (i.e. ‘x’) the nature of the response had to be reversed, whereas in the presence of an alternative symbol (i.e. ‘=’), the response was compatible with the direction of the arrow. As predicted, Tourette’s syndrome and Huntington’s disease patients, regardless of medication or depression status and unlike controls, were particularly disadvantaged in responding to various conflicting S-R configurations. Tourette’s syndrome and Huntington’s disease patients may experience difficulties in making attentional shifts, or in inhibiting inappropriate responses; they may also be more susceptible (than controls) to the conflict that can arise when the spatial code formed for the stimulus is irrelevant for selecting the appropriate response. We conclude that our findings support the notion that cognitive deficits in Tourette’s syndrome and Huntington’s disease may stem from abnormalities of the major pathways interconnecting the basal ganglia and the frontal lobes.

Keywords: Tourette’s syndrome; Huntington’s disease; Simon effect; attention

Abbreviations: CRT = choice reaction time; RT = reaction time; S-R = stimulus-response; SRT = simple reaction time

Introduction

Basal ganglia dysfunction is typically associated with disturbances of movement. Affected patients may have additional associated behavioural and cognitive changes, including alterations in intellectual function, personality and mood (Rothlind et al., 1993). Attention deficits in basal ganglia disorders, however, have received limited experimental investigation, and, as a consequence, there is little understanding about their underlying mechanisms.

The behavioural and cognitive changes accompanying putative subcortical damage may be profitably viewed in terms of a series of parallel frontal-subcortical circuits that have been proposed as linking various regions of the frontal lobes with corresponding subcortical structures (Alexander et al., 1986, 1990; Alexander and Crutcher, 1990). The prototypic structure of all such circuits (i.e. motor, oculomotor, dorsolateral prefrontal, lateral orbitofrontal and mesial frontal/anterior cingulate) has its origin within the frontal lobes. Individually, they project to various striatal structures (caudate, putamen and ventral striatum) and onwards to the globus pallidus and the substantia nigra. They then project from these structures to specific thalamic nuclei, and finally back to the frontal lobes. All circuits share common structures (i.e. frontal lobes, striatum, globus pallidus, substantia nigra and thalamus) and are contiguous, but remain anatomically segregated throughout (Cummings, 1993). Damage to subcortical structures can, therefore, disrupt motor, cognitive and limbic function.

Gilles de la Tourette’s syndrome and Huntington’s disease
are two hyperkinetic movement disorders; Huntington's disease is inherited by autosomal dominant transmission, whereas recent evidence suggests that Tourette's syndrome may be inherited as a single gene disorder (Eapen et al., 1993). Both disorders may be the result of dopaminergic dysfunction arising from subcortical disturbances. In addition, both disorders may be associated with disturbances of other neurotransmitter systems which are also involved in the frontal-subcortical circuits; these include serotonin, norepinephrine, gamma-aminobutyric acid and acetylcholine (Devor, 1990; Shoulson, 1990; Devinsky and Geller, 1992).

Tourette's syndrome is associated with simple and complex motor and vocal tics, which are characterized by sudden muscle jerks occurring at irregular intervals. In support of basal ganglia involvement in the aetiology of Tourette's syndrome, brain imaging has revealed abnormalities in the frontal cingulate cortex and the inferior corpus striatum (Chase et al., 1984, 1986). Other researchers (Peterson et al., 1993; Singer et al., 1993) have reported that the putamen and globus pallidus (i.e. lenticular nuclei) in the left hemisphere of Tourette's syndrome sufferers is reduced in volume as compared with the situation in the control group. Moreover, there may be a chemical imbalance associated with increased levels of dopamine within these structures.

Unlike Tourette's syndrome, Huntington's disease is a progressive neurodegenerative disorder, most often characterized by the onset of uncontrollable choreiform movements (Brandt, 1991). Huntington's disease is a consequence of progressive and selective neuronal degeneration within the basal ganglia. Brain imaging techniques typically reveal bilateral atrophy of the caudate and putamen (i.e. striatum), with more global cortical atrophy (beginning in the frontal lobes) in the later stages of the illness (Simmons et al., 1986; Savoiardo et al., 1991; Starkstein et al., 1992; Oliva et al., 1993). Indeed, behavioural and cognitive abnormalities in Huntington's disease (i.e. problems in planning, set, sequencing, organizing and scheduling, loss of flexibility and fluency, etc.) correlate with severity of metabolic changes in the caudate which receives major inputs from the dorsolateral orbitofrontal cortices (Mazziotta, 1990). Moreover, the behavioural and cognitive similarities between patients with basal ganglia disorder and patients with frontal lobe injury may be attributable to the dysfunction of the multiple frontal-subcortical circuits described above (Cummings, 1993).

More specifically, it has been reported that 60% of Tourette's syndrome patients may suffer from attention deficit hyperactive disorder (Comings, 1990; Channon et al., 1992). Huntington's disease has also been associated with attentional dysfunctions which manifest in problems in attention span, concentration and impulsivity (Butters et al., 1978; Brandt et al., 1988). Channon et al. (1992) administered a wide range of clinical and experimental measures of attention to a group of Tourette's syndrome patients and their controls. Attention deficits were clearly noted in the Tourette's syndrome group, as compared with the controls, on several of the more complex tasks, such as Serial Addition, Block Sequence Span (forwards), the Trail-Making test, joining ascending sequences, and a Letter Cancellation task. Given that both groups did not differ significantly in their IQ scores, the authors argue that the attention deficits observed in Tourette's syndrome may represent a selective deficit rather than an overall global impairment. Various other clinical paper-and-pencil neuropsychological tests (e.g. Wisconsin Card Sort Test, Porteus Maze Test, Stroop Interference Test, etc.), which are known to be highly sensitive to prefrontal pathology, have extended the clinical picture (Girotti et al., 1988; Jason et al., 1988; Bamford et al., 1989); however, there has been very little, if any, systematic experimental research to reveal the underlying nature of the attention deficit. Given that symptoms of attention deficit hyperactive disorder tend to be less pronounced in Tourette's syndrome adults, we attempted to elucidate the subtle neurocognitive deficits relating to attention which may tend to persist in these patients.

In the present study we attempted to elucidate the nature of the attention deficit and to further understand the neural mechanisms underlying Tourette's syndrome and Huntington's disease. Since these diseases may disturb similar structures, we may expect similar underlying functional disturbances as far as switching is concerned. It is of interest to determine the extent to which attentional processes can overcome automatically coded spatial relationships. This was done by progressively increasing the complexity of S-R relationships. A technique was devised to determine the efficiency with which Tourette's syndrome and Huntington's disease patients can shift and direct attention, by employing the Simon effect and conditionality manipulations, such that, in the presence of a certain symbol, the nature of the response must be reversed.

The Simon effect
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. One of the most important and conspicuous features that determines the speed of a response in a choice reaction time (CRT) task is S-R compatibility. Various early experiments addressing this phenomenon (Simon, 1969; Wallace, 1971; Umlită and Nicoletti, 1985, 1990; Umlită and Liotti, 1987) presented subjects with two nonspatial patterns or colours (presented either to the right or left of a computer screen), and subjects were required to press with their left hand in response to one pattern or colour, and with their right hand in response to the other pattern or colour. The nonspatial code of the stimulus therefore had to be translated into the (directional) spatial response code (i.e. either left or right) in order to select the correct response. Even though stimulus position was task irrelevant, reaction times (RTs) were typically faster when the spatial location of both stimulus and response were congruently related (i.e. right–right or left–left), than when they were incongruently related (i.e. left–right or right–left).
Two explanations have been put forward to account for the Simon effect; the attentional and the coding hypotheses. The attentional hypothesis maintains that spatial attention is automatically directed to the side of space wherein the stimulus is presented. Therefore the correspondence, in this explanation, is not between the stimulus and the response code, but rather between the side of space where attention is directed and the side of the response (Simon, 1969, 1990; Verfaellie et al., 1988, 1990). The coding hypotheses, on the other hand, maintain that the irrelevant spatial code of the stimulus produces a Stroop-like interference either at the response-selection stage (Wallace, 1971, 1972; Umiti and Nicolletti, 1985, 1990), i.e. where a translation is made between the nonspatial stimulus code (e.g. the shape or colour) and the spatial response code (i.e. either left or right), or at the response encoding stage (Hasbroucq and Guiard, 1991), i.e. where the relevant dimension of the stimulus acquires a spatial connotation because it signals a spatially defined response.

Jahanshahi et al. (1993), although not incorporating the Simon effect into their experimental design, employed a simple reaction time (SRT) and a CRT paradigm with patients with Parkinson’s disease, Huntington’s disease and cerebellar disease. They found that Parkinson’s disease patients were able to respond faster in the SRT as compared with the CRT procedure, while, for Huntington’s disease patients, this SRT/CRT difference was nonsignificant. The authors suggest that Huntington’s disease patients were failing to engage in preprogramming strategies (i.e. automatic internally generated operations) which are deemed necessary for conferring a speed advantage to SRT compared with CRT tasks. In Tourette’s syndrome, to our knowledge, this SRT/CRT contrast has not been investigated.

We know of no experiments using the paradigm of the Simon effect to assess the attention deficits reported to be associated with both Tourette’s syndrome and Huntington’s disease. Attention in the tactile modality has, however, previously been studied with Parkinson’s disease patients, who may be less adept than controls in maintaining attention in space (Bradshaw et al., 1993).

The purpose of this study was, therefore, to determine whether Tourette’s syndrome and Huntington’s disease patients differ from controls in their responses to spatially congruent and incongruent visual stimuli that require different levels of cognitive processing. We adapted a previous visuospatial RT technique (Teng, 1990) by incorporating the Simon effect. The entire experiment consisted of five conditions that progressively incremented the processing load and complexity. The stimuli consisted of left and right pointing arrows which were presented one at a time, either to the far left or far right of a computer screen. The first condition involved SRT; in blocks of trials using only the left, or the right, hand, subjects responded to the appearance of an outwardly pointing and laterally located arrow, irrespective of its orientation or location. The second condition involved CRT; subjects were instructed to respond with the hand indicated by the direction in which the arrow head was pointing. Again, arrows were laterally located and always pointed outwards. The third condition involved CRT plus the Simon effect, and employed congruent and incongruent arrow stimuli. Subjects were instructed to respond with the hand corresponding to the direction indicated by the arrow head, irrespective of the side on which the latter was positioned on the screen. The concept of the Simon effect was now introduced, in that with incongruent stimuli, for example, a leftward pointing arrow located on the right, or a rightward pointing arrow located on the left, there was S-R incompatibility. The fourth condition was termed a conditional CRT task; however, this time only congruent arrow stimuli were presented which were now paired with either an ‘=’ (equal) or an ‘x’ (wrong) sign which lay directly above the shaft of the arrow. Subjects were instructed to respond with the hand indicated by the arrow head when it was paired with the ‘=’ sign (i.e. maintain cognitive set), and to respond in the opposite direction to which the arrow head was pointing (i.e. with the opposite hand) when it was paired with the ‘x’ sign (i.e. change cognitive set). The final and most difficult task incorporated concepts from both Conditions 3 and 4, and was termed Conditionality plus Simon effect. As well as the (congruent arrow) stimuli presented in Condition 4, incongruent arrow stimuli were now also included, and were again paired with either an ‘=’ or an ‘x’ sign. Subjects were required to maintain cognitive set by making a congruent response to incongruent arrow stimuli that were paired with an ‘=’, and to change cognitive set by making a congruent response to incongruent arrow stimuli that were paired with an ‘x’ sign. It was predicted that Tourette’s syndrome and, especially perhaps, Huntington’s disease patients (due to the more pervasive basal ganglia damage), would be considerably disadvantaged, and thus take longer to respond in the following two cases: (i) when there were incongruent stimuli involving S-R incompatibility (as compared with congruent stimuli involving S-R compatibility); and (ii) when there was conflict stemming from negation (i.e. response incongruency) of an otherwise compatible S-R configuration, as in Condition 5.

We predicted that controls would respond in a more consistent fashion across such manipulations.

**Method**

**Subjects**

Two groups of patients (Tourette’s syndrome and Huntington’s disease) participated, together with their age-matched controls with no history of neurological disorder. Control subjects for both groups were recruited from a healthy population, and were matched individually to patients by sex, age (within 2 years), IQ and Short Test of Mental Status score. There were 10 male patients with Tourette’s syndrome and their matched controls, all of whom were right-handed with a mean age of exactly 31 years for each
Disease patients were significantly more depressed than their matched controls. One-way ANOVAs showed that there were no significant differences between Tourette's syndrome and control subjects for either Digits Forward or Backward $F(1, 9) = 1.78$, $P > 0.20$ and $F(1, 9) = 3.13$, $P > 0.09$, respectively. On the other hand, there were significant differences between Huntington's disease and control subjects for both Digits Forward and Backward $F(1, 9) = 5.83$, $P < 0.05$ and $F(1, 9) = 5.36$, $P < 0.05$, respectively. Control subjects were individually chosen to match Tourette's syndrome and Huntington's disease patients on predicted full scale IQ using the National Adult Reading Test (Nelson and O'Connell, 1978). One-way ANOVAs for both Tourette's syndrome and Huntington's disease patients and their matched controls showed no significant differences $F(1, 9) = 0.56$, $P > 0.46$ and $F(1, 9) = 1.24$, $P > 0.28$, respectively.

All patients and control subjects gave their informed consent to participate in this study.

**Apparatus**

Each subject sat directly in front of a Toshiba 486 portable computer, 70 cm from the screen. Both arms were 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 button boxes sat inside a rectangular board positioned so as to support the arms. Each button was elevated -4 mm up from the box and was 17 mm in diameter. The responses were achieved by pressing one of the two buttons with the index finger of either hand as quickly and as accurately as possible.

**Procedure**

The entire experiment consisted of five conditions that progressively added to the processing load by increasing the complexity of S-R relationships. Conditions were always presented in the same order (1–5) to permit a gradual increase in processing demands. All five conditions involved RT responses to the presentation of visuospatial stimuli on a computer screen. The experimenter initiated each trial via a button press. A fixation point appeared in the screen centre for 1.2 s, which subjects were required to fixate until the stimulus appeared. A blank screen followed the fixation point for 1 s, after which the stimulus item appeared for 10 s.

The stimuli consisted of left (←) and right (→) pointing arrows, which were presented one at a time, either to the far left or far right of the screen. Each arrow was 56 mm in length, and the fins of the arrow heads were 20 mm long. Responses were made with either the left or right hand. Reaction time (in milliseconds) was measured from stimulus presentation to subjects' button-press response. Errors were also automatically recorded. A pilot study determined that an initially set maximum 'time-out' period of 3.5 s was not,

<table>
<thead>
<tr>
<th>Tourette's syndrome</th>
<th>Huntington's disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>10</td>
</tr>
<tr>
<td>Female</td>
<td>0</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>31</td>
</tr>
<tr>
<td>Mean duration of illness (years)</td>
<td>6.6</td>
</tr>
<tr>
<td>Mean MAS score</td>
<td>9.8</td>
</tr>
<tr>
<td>Mean STMS score</td>
<td>34</td>
</tr>
<tr>
<td>Mean NART score</td>
<td>118.8</td>
</tr>
<tr>
<td>Mean Digits Forward</td>
<td>7.1</td>
</tr>
<tr>
<td>Mean Digits Backward</td>
<td>5.6</td>
</tr>
</tbody>
</table>

MAS = Mood Assessment Scale; STMS = Short Test of Mental Status; NART = National Adult Reading Test (predicted full scale IQ).
in fact, adequate, as many genuine response times were being disregarded. A 'time-out' period of 10 s was therefore set in order to accommodate a majority of responses; the stimulus would therefore remain displayed on the screen for 10 s, or until the subject had made a response. In any case, each subject was instructed to respond as soon as the arrow appeared on the screen. If a response anticipation was made before the presentation of the arrow, the trial was repeated.

Halfway through each of the five conditions, the button boxes were interchanged, in order to counterbalance for any mechanical differences between the buttons. At the beginning of each condition subjects were given verbal instructions, and were made familiar with the stimuli via stimulus cards, which also showed the appropriate responses required. Each condition employed a particular pseudorandom order which was reversed for half the subjects. There were 12 practice trials at the beginning of each condition, except for the fifth condition which consisted of 16 practice trials. See Fig. 1 for a visual representation of the stimuli for each of the five conditions.

1. Simple RT task
Two congruent visuospatial stimuli were presented: a left pointing arrow, positioned to the far left, and a right pointing arrow, positioned to the far right of the screen. There were 48 trials, 24 left and 24 right pointing arrows presented in a pseudorandom order, with six left and six right pointing arrows in each block of 12 trials. For this task, subjects were required to respond with one hand (in blocks) to each arrow presentation irrespective of the direction it was pointing. Halfway through, subjects were instructed to respond in the same way with the opposite hand.

2. Choice RT task
The two arrow stimuli that were presented above were also used in this condition. There were 48 trials, 24 left and 24 right pointing arrows presented in a pseudorandom order, with six left and six right pointing arrows in each block of 12 trials. As in the above condition, each subject was instructed that the position of the arrow would be unpredictable; however, this time, subjects were required to respond with the hand indicated by the direction in which the arrow head was pointing.

3. Choice RT plus Simon effect
Forty-eight trials were presented, again involving 24 left and 24 right pointing arrows. This time, in addition to the two (congruent) stimuli that were presented above, two incongruent stimuli were also included: a right pointing arrow, positioned to the far left (i.e. requiring a right incongruent response), and a left pointing arrow, positioned to the far right of the screen (i.e. requiring a left incongruent response). There were four stimulus items in each block of 12 trials, requiring six left and six right hand responses. Each subject was instructed to respond with the hand indicated by the arrow head, irrespective of the side on which the latter was positioned on the screen. This task introduced the concept of the Simon effect, in that, with incongruent stimuli, there was S-R incompatibility.

4. Conditional choice RT task
Again 48 trials were presented, 24 left and 24 right pointing arrows. There were four stimulus items in each block of 12 trials, requiring six right and six left hand responses. The two arrow stimuli that were adopted in Conditions 1 and 2 were again presented in this condition; however, this time,
they were paired with either an ‘=’ (equal) or an ‘X’ (wrong) sign which lay directly above the shaft of the arrow. These four figures can be designated as L (=), L (x), R (=) and R (x), where L and R indicate left or right side of the screen, and ‘=’ and ‘X’ indicate maintained and changed responses, see Fig. 1. For example, the subject was instructed to respond with the hand indicated by the arrow head when it was paired with the ‘=’ sign (i.e. maintain cognitive set), and to respond in the opposite direction to which the arrow head was pointing (i.e. with the opposite hand) when it was paired with the ‘X’ sign (i.e. change cognitive set). This task was called conditional, because each response was conditional upon the ‘=’ or the ‘X’ sign.

5. Conditionality plus Simon effect
This task incorporated concepts from both Conditions 3 and 4. This time, 96 trials were presented, 48 left- and 48 right-sided items pseudorandomly ordered. As well as the four stimuli presented in the condition above, four additional stimuli were presented. There were therefore eight different stimulus items, two of each type, in each block of 16 trials. The additional four stimuli were as follows: a left pointing arrow, positioned to the far right of the screen, paired with either an ‘=’ or an ‘X’ sign, requiring a left (i.e. incongruent) and a right (i.e. congruent) response, respectively; and a right pointing arrow, positioned to the far left of the screen, paired with either an ‘=’ or an ‘X’ sign, requiring a right (i.e. incongruent) and a left (i.e. congruent) response, respectively (see Fig. 1). Subjects were, therefore, required to maintain cognitive set when congruent or incongruent arrow stimuli were paired with an ‘=’, and to change cognitive set when these stimuli were paired with an ‘X’ sign. Coding conflicts tended to emerge in the following two cases: (i) in the presence of S-R incompatibility (Simon effect); and (ii) when there was conflict stemming from negation of an otherwise compatible S-R configuration.

Results
Due to the observed variability between patient and control groups (illustrated only for Condition 5, see Fig. 2), the data were tested for homogeneity of variance using the Bartlett–Box (1937) test, one of the most widely used. Results from this test indicated that there was a violation of the ANOVA assumption of homogeneity of variance for the Tourette’s syndrome patients and their controls, as well as for the Huntington’s disease patients and their controls [F(1,972) = 0.87, P < 0.01 and F(1,972) = 6.87, P < 0.01, respectively]. Violation of the ANOVA assumption of homogeneity of variance was also shown by the Cochran test. Since a logarithmic or other transform would in turn have violated assumptions of additivity in RT data, the data were analysed separately for each of the four groups.

Overall analyses
The overall means for each of the five conditions were calculated in order to provide a comparison across group and condition. Given that the Bartlett–Box (1937) test had showed a violation of the ANOVA assumption of homogeneity of variance between the two patient groups and their matched controls, overall group analyses were again deemed inappropriate. It can be clearly seen (see Fig. 3), however,
compared with congruent (531 ms and 1029 ms, respectively) slower to incongruent (556 ms and 1355 ms, respectively) as patients, there was a significant main effect of Congruency respectively; both patient groups responded significantly for both the Tourette’s syndrome and Huntington’s disease means and standard errors). Two-way ANOVAs (Congruency, Table 2 for (congruent, incongruent) for each group (see Figure 4 shows RT plotted as a function of Congruency Hand) were conducted for each of the four groups separately. For both the Tourette’s syndrome and Huntington’s disease patients, there was a significant main effect of Congruency (Hand) [F(1,9) = 14.36, P < 0.001, and F(1,9) = 4.18, P < 0.056, respectively] performance differences (26 and 24 ms, respectively) between the SRT and CRT conditions. For both the Tourette’s syndrome and Huntington’s disease control groups, however, there were significant or near significant [F(1,9) = 16.01, P < 0.01], there was no significant main effect or interaction involving Conditionality. The Tourette’s syndrome controls, however, there were no significant main effects or interactions. For this condition, all four groups produced errors. The error data for each group were separately submitted to a one-way ANOVA. For the Tourette’s syndrome controls, there was a significant main effect of Congruency [F(1,9) = 5.76, P < 0.05]; more errors were made when they responded to incongruent (1.7) as compared with congruent (0.6) stimuli. There was no significant main effect for the other three groups.

<table>
<thead>
<tr>
<th>Condition 1</th>
<th>Huntington’s disease (HD) patients</th>
<th>Controls (HD)</th>
<th>Tourette’s syndrome (TS) patients</th>
<th>Controls (TS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left hand</td>
<td>594 (63)</td>
<td>264 (15)</td>
<td>344 (38)</td>
<td>232 (9)</td>
</tr>
<tr>
<td>Right hand</td>
<td>576 (75)</td>
<td>253 (16)</td>
<td>332 (30)</td>
<td>228 (8)</td>
</tr>
<tr>
<td>Condition 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left hand</td>
<td>637 (67)</td>
<td>264 (15)</td>
<td>369 (33)</td>
<td>289 (13)</td>
</tr>
<tr>
<td>Right hand</td>
<td>581 (58)</td>
<td>253 (16)</td>
<td>360 (29)</td>
<td>293 (15)</td>
</tr>
<tr>
<td>Condition 3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congruent</td>
<td>1029 (57)</td>
<td>446 (25)</td>
<td>514 (31)</td>
<td>376 (14)</td>
</tr>
<tr>
<td>Incongruent</td>
<td>1355 (113)</td>
<td>479 (34)</td>
<td>555 (36)</td>
<td>397 (23)</td>
</tr>
<tr>
<td>Condition 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congruent  =’</td>
<td>1537 (178)</td>
<td>569 (34)</td>
<td>753 (45)</td>
<td>454 (21)</td>
</tr>
<tr>
<td>Incongruent ‘X’</td>
<td>1974 (225)</td>
<td>619 (51)</td>
<td>818 (52)</td>
<td>467 (37)</td>
</tr>
<tr>
<td>Condition 5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congruent  =’</td>
<td>1417 (154)</td>
<td>623 (37)</td>
<td>763 (50)</td>
<td>507 (19)</td>
</tr>
<tr>
<td>Congruent  ‘X’</td>
<td>2187 (283)</td>
<td>732 (53)</td>
<td>958 (75)</td>
<td>614 (68)</td>
</tr>
<tr>
<td>Incongruent  =’</td>
<td>1579 (135)</td>
<td>672 (56)</td>
<td>826 (60)</td>
<td>528 (28)</td>
</tr>
<tr>
<td>Incongruent  ‘X’</td>
<td>1864 (229)</td>
<td>675 (46)</td>
<td>824 (57)</td>
<td>552 (45)</td>
</tr>
</tbody>
</table>

Conditions 3, 4 and 5 have been collapsed across hands.

that although for all groups there was an elevation in RTs as the processing load increased, Tourette’s syndrome and especially Huntington’s disease patients were much more affected by increased processing demands as compared with the control groups. In order to examine the SRT/CRT differences (which are often reported in the basal ganglia literature; for example, see Bloxham et al., 1984; Pullman et al., 1988; Jahanshahi et al., 1993), separate one-way ANOVAs were conducted for each of the groups. For both the Tourette’s syndrome and Huntington’s disease patients separately there were no significant [F(1,9) = 0.33, P > 0.57, and F(1,9) = 0.07, P > 0.80, respectively] performance differences (26 and 24 ms, respectively) between the SRT and CRT conditions. For both the Tourette’s syndrome and Huntington’s disease control groups, however, there were significant or near significant [F(1,9) = 14.36, P < 0.001, and F(1,9) = 4.18, P < 0.056, respectively] performance differences (61 and 42 ms, respectively) between the SRT and CRT conditions (see Table 2). However, it should be noted that the CRT condition always followed SRT in the hierarchy of ascending levels of difficulty. No errors were made in either task.

**Choice RT plus Simon effect condition**

Figure 4 shows RT plotted as a function of Congruency (congruent, incongruent) for each group (see Table 2 for means and standard errors). Two-way ANOVAs (Congruency, Hand) were conducted for each of the four groups separately. For both the Tourette’s syndrome and Huntington’s disease patients, there was a significant main effect of Congruency [F(1,9) = 5.77, P < 0.05 and F(1,9) = 6.45, P < 0.05, respectively]; both patient groups responded significantly slower to incongruent (556 ms and 1355 ms, respectively) as compared with congruent (531 ms and 1029 ms, respectively) stimuli. There was no significant main effect or interaction involving Hand. For the two control groups, however, there were no significant main effects or interactions.

For this condition, all four groups produced errors. The error data for each group were separately submitted to a one-way ANOVA. For the Tourette’s syndrome controls, there was a significant main effect of Congruency [F(1,9) = 5.76, P < 0.05]; more errors were made when they responded to incongruent (1.7) as compared with congruent (0.6) stimuli. There was no significant main effect for the other three groups.

**Conditional choice RT condition**

Figure 5 shows RT plotted as a function of Conditionality (maintain ‘=’, change ‘X’) for each group (see Table 2 for means and SEMs). Once again, two-way ANOVAs (Conditionality, Hand) were conducted for each of the four groups separately. For both the Tourette’s syndrome and Huntington’s disease patients, there was a significant main effect of Conditionality [F(1,9) = 5.75, P < 0.05, and F(1,9) = 5.36, P < 0.05, respectively]; there was no main effect or interaction involving Hand. Overall, the Tourette’s syndrome and Huntington’s disease patients were significantly slower when making a change (818 ms and 1975 ms, respectively) in response (i.e. when the arrow was paired with an ‘X’) as compared with maintaining (753 and 1537 ms, respectively) a response (i.e. when the arrow was paired with an ‘=’). For the Tourette’s syndrome control group, despite there being a significant main effect of Hand [F(1,9) = 16.01, P < 0.01], there was no significant main effect or interaction involving Conditionality. The Tourette’s syndrome controls were significantly slower in responding with their left (476 ms) as compared with their right (446 ms)
hand. For the Huntington's disease control group, there were no significant main effects or interactions.

The error data for each group were separately submitted to a one-way ANOVA. The Tourette's syndrome controls made significantly more errors when required to make a change (x) in response (2.6) as compared with when required to maintain (=) a response (0.4) \(F(1,9) = 7.56, P < 0.05\). There was no significant main effect for the other groups.

**Conditionality plus Simon effect condition**

Figures 6 (Tourette’s syndrome) and 7 (Huntington’s disease) show RT plotted as a function of Congruency (congruent, incongruent stimuli) for each group (see Table 2 for means and SEMs). Separate three-way ANOVAs (Congruency, Conditionality, Hand) were conducted for each group. For the Tourette’s syndrome patients (see Fig. 6), there was a significant main effect of Congruency \(F(1,9) = 8.74, P < 0.05\) and of Conditionality \(F(1,9) = 10.00, P < 0.05\). Moreover, there was a significant Congruency \(\times\) Conditionality interaction \(F(1,9) = 19.66, P < 0.01\); however, no main effect or interaction involving Hand achieved significance. For the Tourette’s syndrome controls (see Fig. 6), no main effects or interactions approached significance.

**Post hoc** one-way ANOVAs for the congruent responses indicate that Tourette’s syndrome patients were significantly slower when making a change (x) in response (958 ms) as compared with when they had to maintain (=) their response (763 ms); for incongruent responses, however, these differences were non-significant.

Three-way ANOVAs (Congruency, Conditionality, Hand) for the Huntington’s disease patients and separately for their matched control group showed that there was, in both cases, a significant main effect of Conditionality \(F(1,9) = 7.83, P < 0.05\) and \(F(1,9) = 6.05, P < 0.05\), respectively and a Congruency \(\times\) Conditionality interaction \(F(1,9) = 9.60, P < 0.05\) and \(F(1,9) = 6.74, P < 0.05\), respectively.

**Post hoc** one-way ANOVAs, for the Huntington’s disease and the control subjects separately, showed that, for congruent
responses, both groups were significantly ($P < 0.05$ and $P < 0.001$, respectively) slower when making a change ('X') in response (2187 ms and 732 ms, respectively) as compared with when they had to maintain ('=' ) their response (1417 ms and 623 ms, respectively); for incongruent responses, however, these differences were non-significant (see Fig. 7).

The error data for each group were separately submitted to a two-way ANOVA (Congruency, Conditionality). For the Huntington's disease patients, there was a significant main effect of Conditionality [$F(1,9) = 5.50$, $P < 0.05$]; more errors were made when they were required to make a change ('X') in response (1.00) as compared with when required to maintain ('=' ) a response (0.35). For the Tourette's syndrome controls, there was a significant main effect of Congruency [$F(1,9) = 11.94$, $P < 0.01$]; more errors were made for incongruent responses (2.1) as compared with congruent responses (0.45).

**Duration and degree of illness in Huntington's disease**

In order to determine any possible confounding influence of duration of illness, and/or Shoulson and Fahn (1979) rating score on Huntington's disease patient's performance, Pearson's product moment correlations were conducted for Condition 5, the most complex condition. No correlations approached significance, however.
Medication status
The question whether medication may have differentially affected Tourette's syndrome and Huntington's disease performance needs to be addressed. Since five Tourette's syndrome patients were on medication and five were unmedicated, mixed ANOVAs were conducted for each of the five conditions. No main effects or interactions involving Group (i.e. medicated versus unmedicated) even approached significance for any of the five conditions. Since three Huntington's disease patients were medicated and seven were unmedicated, statistical analyses were not conducted. In any case, overall means were calculated for each group across each of the five conditions. The medicated group \((n = 3)\) were overall only a little slower \((1238 \text{ ms})\) as compared with the unmedicated \((n = 7)\) Huntington's disease group \((1156 \text{ ms})\). Since the majority of patients were unmedicated, the pattern of results is unlikely to be largely due to medication.

Depression status
Since both Tourette's syndrome and Huntington's disease patients were significantly more depressed than their matched controls, mixed ANOVAs were conducted for each of the five conditions in order to determine whether or not performance was differentially affected by depression. Yesavage et al. (1983) recommend that the 'cut-off' for depression be 10 (out of a maximum of 30). Four Tourette's syndrome patients were depressed and six were not depressed according to this criterion. However, because one patient scored 9, for the purposes of statistical analyses he was regarded as depressed in order to equate the number of subjects in each of the two groups \((n = 5)\). No main effects or interactions involving Group (i.e. depressed versus non-depressed) even approached significance for any of the five conditions.

Since five Huntington's disease patients were depressed and five were not depressed, mixed ANOVAs were again conducted. With one exception, there were no significant main effects or interactions involving Group for any of the five conditions. For Condition 5, however, there was a significant Group by Conditionality interaction \([F(1,8) = 6.45, P < 0.05]\). One-way ANOVAs showed that for both the depressed and non-depressed Huntington's disease patients there were significant \((P < 0.05, \text{ for both groups})\) performance differences between when they had to make a change \((x')\) of response \((2675 \text{ ms and 1276 ms}, \text{ respectively})\) as compared with when they had to maintain \(('=')\) their response \((1769 \text{ ms and 1226 ms}, \text{ respectively})\). Thus the magnitude of the conditionality effect, though significant in both cases, was somewhat larger in the depressed Huntington's disease group.

Discussion
The efficiency with which Tourette's syndrome and Huntington's disease patients can shift and direct attention was examined using the Simon effect and conditionality manipulations. The results can be summarized as follows: overall, both Tourette's syndrome and Huntington's disease patients were considerably more disadvantaged than their matched controls by Simon effect and conditionality manipulations, as can be observed from Fig. 3. While the magnitude of the slope appears to be far greater for the Huntington's disease patients than the Tourette's syndrome, there are qualitative similarities in performance between these two patient groups, suggesting that there may be similar underlying functional disturbances as far as switching set is concerned. For both Tourette's syndrome and Huntington's disease patients, differences between SRT (first condition) and CRT (second condition) were non-significant, whereas both control groups responded significantly faster in the SRT as compared with the CRT condition. Although Jahanshahi et al. (1993) did not use control subjects in their experiment, it has been argued that patients with basal ganglia disorder (in particular Parkinson's disease; for example, see Bloxham et al., 1984; Pullman et al., 1988) may not be as effective as controls in pre-programming, a strategy which has been suggested (Jahanshahi et al., 1993) as conferring a speed advantage in SRT over CRT. With the third condition (i.e. CRT plus Simon effect), Tourette's syndrome and Huntington's disease patients were considerably more disadvantaged by spatially incongruent (incompatible) configurations, as compared with spatially congruent (compatible) configurations; the control groups, however, were not differentially affected under these circumstances. With the fourth condition (i.e. conditional CRT), Tourette's syndrome and Huntington's disease patients' RTs increased significantly in response to the \((x')\) as compared with the \(('=')\) conditionality manipulation; neither control group, however, was differentially affected by these circumstances. With the fifth condition (i.e. conditional CRT plus Simon effect), Tourette's syndrome and especially Huntington's disease patients were once again affected by the manipulations involving the Simon effect and conditionality; Huntington's disease controls were also disadvantaged by these manipulations, although to a much lesser extent. Neither medication nor depression greatly affected the observed pattern of results in any of the conditions. Moreover, neither duration of Huntington's disease illness nor Shoulson and Fahn (1979) score affected the pattern of results in Huntington's disease patients. However, the significant differences between the Huntington's disease patients and the controls on both the Digits Forward and Backward further indicate that Huntington's disease patients experienced considerable difficulty (compared with controls) on tasks that involve some attentional load.

Umiltà and Liotti (1987) and Stofffer (1991) suggest that by directing attention to a certain position in space, the spatial code of the position is formed. This notion is based on the premotor model of spatial attention (Rizzolatti et al., 1987), which maintains that to move attention to a given location, an (implicit) saccadic movement to that location must be programmed, irrespective of whether the attentional
movement is actually accompanied by a shift of gaze. Sheliga et al. (1994) in investigating the validity of the premotor theory asked subjects to make (antisaccadic) eye movements to an arbitrary point in space and not to the location of the imperative stimulus. The stimulus had therefore to be attended to and detected without any eye movements towards it. The results showed that oculomotor saccades were modified (i.e. there was a deviation of the saccadic trajectory opposite to where the imperative stimulus was presented) by attention allocation to different predetermined spatial positions. The results support the notion that spatial attention involves an activation of oculomotor circuits which are driven by overt oculomotor responses (Rizzolatti et al., 1987; Umiltà et al., 1991; Sheliga et al., 1994).

Although no eye movement recordings were made in the present study, oculomotor abnormalities in Huntington's disease have long been identified; slow saccades and difficulties in initiating saccades towards a visual target are the most common findings (Lasker et al., 1987, 1988). Consequently, for Huntington's disease patients, one explanation for the increased response times, especially with S-R incompatibility, may invoke slowed activation of covert oculomotor programmes to redirect attention from the central fixation point to the laterally located target. Indeed, generally, increases in RTs, especially with S-R incompatibility, may stem from a combination of a difficulty in initiating the saccadic programme towards an intended location in space, together with conflict that may arise when the spatial code formed of the stimulus is irrelevant for selecting the appropriate response. The irrelevant spatial code produces a Stroop-like interference which presents itself in the form of the Simon effect (Kornblum et al., 1990; Kornblum, 1994).

This explanation becomes particularly apposite in Conditions 4 and 5. When a congruent arrow is paired with an 'X' sign (i.e. change cognitive set), the natural response tendency (to respond in the direction in which the arrow head is pointing) must be inhibited, and a corresponding incongruent response selected and executed. In Condition 5, the simultaneous occurrence of both Simon-type and conditionality manipulations should place a particularly heavy load upon compromised saccadic and/or attentional-control mechanisms in Huntington's disease, in the presence of potential conflict at the levels of both stimulus coding and response-selection. As indicated in the Introduction, it is known that attention may be compromised in both Tourette's syndrome and Huntington's disease (Butters et al., 1978; Brandt et al., 1988; Channon et al., 1992). Whether or not a mediating role of implicit saccades is invoked in shifting attention, the present findings, that Tourette's syndrome and Huntington's disease patients may be unduly susceptible to irrelevant stimulus information (the Simon effect), and may experience undue difficulty at the response-selection stage in inhibiting no longer appropriate responses (the conditionality effect), are compatible with a general deficit in attentional processes in the disorders.

At a more general level, the present findings can also be interpreted in the context of a deficit in the ability to inhibit inappropriate responses either explicitly, via conditionality manipulations, or implicitly, via the Simon effect. There are other reports in the literature both with respect to Huntington's disease (Brandt, 1991) and Tourette's syndrome (Baron-Cohen et al., 1994) of problems of response inhibition. Baron-Cohen et al. (1994) describe the 'Intention Editor' as being triggered when there are several competing intentions which parallel one another. They suggest that the intention editor interrupts one of many simultaneously activated intentions, thus preventing it from executing its action, whether it be utterance or thought. Although only children served as participants in their experiment, they reported that Tourette's syndrome subjects performed far worse than normal controls when required to inhibit a particular response when it coincided with another.

Peterson et al. (1993) and Singer et al. (1993), in two recent studies, reported that the lenticular nuclei in the left hemisphere of Tourette's syndrome patients are reduced in volume as compared with the situation in the control group. The possibility that anomalous brain lateralization is a factor in Tourette's syndrome was not supported in the present study; there was no evidence of abnormal hand asymmetry in any of the five conditions, though it might be noted that in the conditionality manipulation (Condition 4) the right hand superiority shown by controls was absent in the Tourette's syndrome data. Although no impairment of general intellectual functioning has been previously reported, Tourette's syndrome patients may have impaired visual-perceptual and reduced visual-motor skills (Shapiro et al., 1978; Erenberg et al., 1987). This may account for the fact that, overall, Tourette's syndrome patients were more disadvantaged by Simon and conditionality manipulations than their control group. Tourette's syndrome patients were considerably disadvantaged in making cognitive shifts in attention between congruent and incongruent stimuli/responses; controls, on the other hand, showed no performance differences between these configurations. In both the Tourette's syndrome and Huntington's disease data, the main effects of Congruency and Conditionality (Conditions 3 and 4), and the significant Congruency×Conditionality interaction (Condition 5) indicates that for stimuli in which there was S-R incompatibility, the irrelevant spatial code which was formed produced a Stroop-like interference, causing conflict at the response-selection stage and/or the stimulus encoding stage for both patient groups.

Somewhat surprisingly, the Tourette's syndrome and Huntington's disease controls, in many cases, showed no effect of congruency and conditionality, effects which have been previously reported by other researchers (Simon, 1969; Umiltà and Nicoletti, 1985, 1990; Umiltà and Liotti, 1987).

In summary, both patient groups, Tourette's syndrome and Huntington's disease, showed elevations in RT which progressively increased concomitantly with increasing processing demands, demands which involved explicit (the conditionality manipulation) or implicit (the Simon effect)
inhibition of inappropriate responses. Both patient groups, unlike the controls, were particularly disadvantaged by incongruent (S-R incompatible) spatial relationships, and by the imposed need to reverse the direction of their responses; qualitative similarities suggest similar functional disturbances. Indeed, the nature of the attention deficit seems to reside in an inability to effectively shift and/or change cognitive set. These effects were unlikely to stem from differences in depression or medication status. We conclude that basal ganglia-frontal disturbances, known to be responsible for the motor symptoms of Tourette's syndrome and Huntington's disease, may also possibly cause cognitive problems at the level of attentional control and response inhibition, especially for Huntington's disease patients.

It is noteworthy that Jankovic and Ashizawa (1995) have recently published a case study of a male patient initially presenting with symptoms of Huntington's disease, with subsequent development of motor and vocal tics as well as other features associated with Tourette's syndrome. Although tourettism has not been previously described as a manifestation of Huntington's disease, obsessive compulsive disorder, on the other hand, is a feature well recognized in both Tourette's syndrome and Huntington's disease. Moreover, similar neurochemical imbalances have been proposed for both Tourette's syndrome and Huntington's disease (Storey and Beal, 1993; Kurlan, 1994), again underlining the probability of common cognitive deficits in these two basal ganglia disorders.

Acknowledgements
We wish to thank the Victorian Tourette Syndrome Association, the Huntington's Disease Clinic, and all of its members who participated, for their help and cooperation. We also wish to thank Bob Wood, Frank Devlin, Truong Nguyen and Mike Durham for designing and maintaining the apparatus and software. This work was supported by grants from the Australian Brain Foundation and Australian Research Council.

References


Kurlan R. Hypothesis II: Tourette’s syndrome is part of a clinical spectrum that includes normal brain development. [Review]. Arch Neurol 1994; 51: 1145–50.


Received March 10, 1995. Revised May 9, 1995. Accepted May 30, 1995