Response choice in Parkinson’s disease

The effects of uncertainty and stimulus—response compatibility

Richard G. Brown,¹ Marjan Jahanshahi¹ and C. David Marsden¹,²

¹Medical Research Council Human Movement and Balance Unit and the ²Department of Clinical Neurology, Institute of Neurology, National Hospital for Neurology and Neurosurgery, London, UK

SUMMARY

Reaction time paradigms provide a set of methods for assessing aspects of the planning and execution of voluntary movements in Parkinson’s disease. Attention has focused mainly on the issue of programming of responses, employing a combination of simple reaction time (SRT) and choice reaction time (CRT) paradigms. The first part of the present study replicated an earlier finding in which patients showed a disproportionate slowing in CRT compared with SRT. The main aim of the study was to investigate the possible role of response choice, a key stage prior to motor programming in this CRT deficit. Two factors were manipulated: (i) response uncertainty and (ii) stimulus—response compatibility. The patients showed a normal increase in reaction time with increasing uncertainty in the compatible conditions, and a normal response to stimulus—response compatibility in the two-choice task. However, the two groups showed qualitatively different patterns of interaction between the two experimental factors, with only the patients showing a disproportionate slowing with incompatible stimulus—response relationships in the four-choice task. The data were interpreted in terms of Hasbroucq et al.’s (1990) list—rule model of stimulus—response compatibility effects, which suggested that the patients and controls were using different strategies for dealing with incompatible stimulus—response relationships. The use of different strategies makes it impossible to determine whether or not the processing of the patients is impaired in Parkinson’s disease, although further research is suggested to clarify the question. However, the present data suggest that any impairment in response choice is unlikely to contribute to the slowing in CRT in Parkinson’s disease under conditions of high stimulus—response compatibility.

INTRODUCTION

A popular approach to the study of motor deficits of Parkinson’s disease has been to employ reaction time paradigms in an attempt to determine which stage or stages of processing are impaired. Particular interest has focused on motor programming, with the suggestion that the basal ganglia may have an important role to play in this process (Marsden, 1982).

Evidence for a deficit in programming in patients with Parkinson’s disease comes from a number of studies which have reported significant slowing in simple reaction time (SRT)
but not in choice reaction time (CRT) paradigms (Evarts et al., 1981; Bloxham et al., 1984; Sheridan et al., 1987; Pullman et al., 1988; Goodrich et al., 1989). In CRT paradigms, the nature of the response is not known until the presentation of the imperative stimulus. Only then can the subject programme and initiate the response. In SRT paradigms, however, the same response is produced on every trial. The subject, therefore, has the opportunity to programme the response in advance of the stimulus to move, i.e. to pre-programme. However, this pre-programming is an optional strategy, which may involve attentional processes (Goodrich et al., 1989). The differential slowing of Parkinson’s disease on SRT tasks relative to CRT tasks has been taken to imply that the patients fail to take advantage of the opportunity to pre-programme their response in advance in the SRT tasks. The result is that programming takes place after the imperative stimulus with a consequent increase in reaction time.

This pattern of normal (or not significantly slowed) CRT in the presence of impaired SRT, however, has been found in only a minority of studies. Most have found impaired CRT, but differ in whether the slowing is less than, equal to or greater than the slowing in SRT (Wiesendanger et al., 1969; Stelmach et al., 1986; Mayeux et al., 1987; Dubois et al., 1988; Lichter et al., 1988; Reid et al., 1989; Pullman et al., 1990; Yanagisawa et al., 1990; Daum and Quinn, 1991; Jahanshahi et al., 1992). Jahanshahi et al. (1992) found a slowing of both SRT and four-choice CRT in 16 patients with Parkinson’s disease, but with a differential slowing in the CRT task. These findings, however, were based on a relatively small number of trials for each condition. One aim of the present study, therefore, was to attempt to replicate our findings with a larger number of trials.

A slowing of CRT may indicate a programming deficit. Rather than a failure to pre-programme, as would be suggested by a selective slowing in SRT, the patients may be slow to programme. If programming occurs after the onset of the stimulus, as in CRT tasks, the result would be an increase in the overall reaction time. Evidence from Jahanshahi et al. (1992) suggests that, when provided with spatial information about a forthcoming movement, patients with Parkinson’s disease are slower than normal controls in using that information to prepare a response.

Discussion so far has concentrated on the differences between SRT and CRT paradigms in terms of programming, either before the imperative stimulus (SRT) or after (CRT). However, the two types of task differ on a number of other, possibly important, dimensions, any one of which may contribute to the pattern of impairment in patients with Parkinson’s disease. In SRT tasks, assuming that the response has been pre-programmed, it is necessary only for the subject to detect the imperative stimulus in order to trigger the response. In CRT tasks, however, the subject must not only detect but also indentify the stimulus. From this the subject must choose a corresponding response specifying the spatial and temporal course of the movement. Critically, the response programming stage is preceded by stages involved in ‘stimulus identification’ and ‘response choice’.

In order to assess the integrity and functioning of the different processing stages in Parkinson’s disease, it is necessary to have some way of manipulating experimental variables which involve one stage but not others. The most popular methodology for stage analysis of reaction processes is Sternberg’s (1969) additive factor model. The logic is that if a pair of experimental manipulations (A and B) have an additive effect on reaction time (i.e. the effect of manipulation A and B combined is the same as the sum of the effects of A and B assessed independently), it is assumed that each manipulation is affecting
a different processing stage. If, however, the two factors interact (i.e. the effect of A and B together is either greater than or less than the effect of A and B assessed independently), it is assumed that they are affecting a common stage. This methodology and its logic is not without its critics (e.g. Sanders, 1980). Even these, however, consider that the additive factor model has a role to play as an heuristic tool for investigating reaction processes, particular in those areas where consistent patterns of additive and interactive factors have been discovered across studies.

Returning to choice reaction processes in Parkinson’s disease, we will take the risk of ignoring the processing stages involved in identifying the stimulus. This is done, not on the basis of empirical evidence that these processes are normal in Parkinson’s disease, but for simplicity. Application of the additive factor model in normal subjects has indicated that factors such as signal contrast, quality and discriminability appear to affect these processing stages (Sanders, 1980). The way is open, therefore, for future studies to investigate stimulus processing in CRT tasks in Parkinson’s disease. For the present, we will concern ourselves with the processing stage which follows stimulus identification, namely response choice.

What processes may be involved in response choice in CRT? The subject starts with a representation of the imperative stimulus which has been identified from the set of stimuli used in that experiment. The subject has also, in memory, abstract representations of the set of responses, one of which will provide the basis for the subsequent stage of motor programming. A key element in response choice is applying the instructions of the experiment to perform a sensory-motor transformation as a result of which the appropriate response representation is retrieved from a set of responses held in memory (Hasbroucq et al., 1990). Any factor which influences this stimulus—response transformation stage would be expected to prolong the time needed to choose the appropriate response and thus lengthen CRT. Two such factors are response uncertainty (the number of stimulus—response alternatives) and the compatibility of the stimulus—response association [see Sanders (1980) for a review]. That these two factors affect a common processing stage has been suggested (applying the additive factor model) by their interaction in CRT tasks (e.g. Broadbent and Gregory, 1965).

The issue of response uncertainty will be considered first. One of the most replicable phenomena in reaction time studies is that reaction time in normal subjects increases with the number of response alternatives. The nature of the relationship is represented by the Hick—Hyman law where \( RT = a + b \log_2 N \), where \( a \) and \( b \) are constants and \( N \) is the number of alternatives (Hick, 1952; Hyman, 1953). Given the number of studies on reaction time in Parkinson’s disease, it is surprising that only one has manipulated the level of uncertainty in a CRT paradigm. Stelmach et al. (1986) used an eight-CRT task in which the stimulus and associated response was classified according to three spatial components: side (left—right), direction (up—down) and extent (near—far). They employed Rosenbaum’s (1980) pre-cueing paradigm, in which the subject receives advance information about some or all of the relevant dimensions of the movement. For example, the subject may be told, in advance, which hand to use but not which direction, nor the extent of the movement. Precuing either none, one, two or all three of these dimensions, Stelmach et al. (1986) thus produced levels of uncertainty equivalent to eight-, four- and two-choice CRT tasks and an SRT task, respectively. The results showed, in both patients and controls, that reaction time followed the predicted linear relationship with level of uncertainty.
Furthermore, the slope of the function was the same in both groups. Stelmach et al. concluded, from this finding, that response choice was normal in Parkinson's disease. Whether or not this conclusion is valid, of course, depends upon the replicability of this finding, and its robustness with manipulation of other factors believed to influence response choice. A second aim, of the present study, therefore, was to assess reaction time under different levels of uncertainty. In contrast to Stelmach et al. (1986), however, 'true' CRT tasks were used instead of varying the amount of advance information provided to the subject. The use of true CRT tasks would seem to be indicated by the results of Jahanshahi et al. (1992) which suggest that the use of advance spatial information may not be normal in Parkinson's disease.

Turning now to the issue of stimulus—response compatibility. Fitts and Seeger (1953) and Fitts and Deininger (1954) employed, in normal subjects, a variety of eight-CRT tasks in which they varied the spatial configuration of the response apparatus, the nature and arrangement of the stimulus set and finally the relationship between the two. While the nature of the stimulus and the nature of the response affected reaction time, a strong determinant of performance was the nature of the stimulus—response relationship. Pairings which 'conform to population stereotypes' produced faster reactions than those where such pairing did not occur. Fitts et al. referred to these findings as 'stimulus—response compatibility effects'. Simon et al. (1981) classified the pairings as either spatial, where there is a correspondence between spatial arrangement of stimuli and responses (e.g. a left stimulus indicating a left response) or symbolic, where there is a correspondence between stimulus and response codes (e.g. the number 12 indicating a response to the upper position of circular, clock-like array of buttons).

Evidence that stimulus—response compatibility is acting at a separate and, presumably, prior stage to programming comes from studies showing that stimulus—response compatibility effects are additive with factors concerned with the specification of the particular movement, including the limbs and muscles to be used, the amplitude and velocity of the response (see Hasbroucq et al., 1989) and length of a response sequence (Inhoff et al., 1984). In line with the argument that both stimulus—response compatibility and uncertainty affect response choice, the two factors have been shown to have an interactive effect on reaction time (e.g. Broadbent and Gregory, 1965). At the extremes of compatible stimulus—response pairings, the normal increase in reaction time with number of alternatives may be absent altogether. For example, where the stimulus is vibration to the tip of the finger to be lifted, reaction time is constant, regardless of the number of fingers (Leonard, 1959). Other situations where this holds true are where the subject must point to a light (Fitts et al., 1963) or name a visually presented numeral (Fitts and Switzer, 1962).

Of the studies of CRT in patients with Parkinson's disease, all but one have used a single stimulus—response relationship, most with a relatively high level of compatibility. The only report, to date, of CRT performance in Parkinson's disease under different conditions of stimulus—response compatibility is that of Brown et al. (1991). A two-choice CRT task was employed, in which the subject responded by lifting the right or left index finger. The stimulus was either spatially compatible (a lateralized visual signal) or an arbitrary symbol indicating hand of response. As expected, both patients and controls were faster in the compatible rather than the arbitrary condition. Unfortunately, the authors
do not report whether the stimulus—response compatibility effect was the same in the two groups.

The aims of the present study were first, to replicate our previous finding comparing SRT and CRT, and secondly, to explore the role of response choice as a possible mechanism for any slowing in CRT observed in Parkinson's disease. Response choice was investigated by both a compatible and an incompatible CRT task. Furthermore, to determine the nature of the relationship between stimulus—response compatibility and uncertainty, both two-choice CRT and four-choice CRT tasks were employed. It was predicted, in line with the additive factor model, that stimulus—response compatibility and uncertainty would interact in normal subjects. A deficit in response choice in patients with Parkinson's disease might manifest itself either in an increased effect of stimulus—response compatibility or uncertainty, and/or an increased interaction between these two factors.

METHODS

Subjects
Eight patients with Parkinson's disease (five male, three female, mean age 64.1 years, SD = 5.2) and eight control subjects (two male, six female, mean age 64.7 years, SD = 5.2) took part in the study. All of the patients and seven of the controls were right-handed. The patients had an approximate mean duration of illness of ~9.9 years (SD = 7.1), with a mean Webster rating (Webster, 1968) of 8.8 (SD = 6.5). One patient was in Hoehn and Yahr (1967) stage I, five in stage II, and two in stage III. All patients were taking dopaminergic medication with peripheral decarboxylase inhibitor. Other medication included selegeline (n = 6), amantadine (n = 2) and benzhexol (n = 1). The control subjects were recruited from a panel of volunteers comprising the relatives of patients, hospital employees and members of the general population. All control subjects were screened for evidence of psychiatric or neurological illness, and for the presence of physical problems which might interfere with performing the experimental tasks. Informed consent was received from all subjects.

Procedure
Subjects completed the Beck Depression Inventory (Beck and Beamesderfer, 1974) and were given the Folstein Mini Mental State Examination (MMSE) (Folstein et al., 1975) to screen for depression and dementia, respectively. The subjects were also assessed on the Purdue Pegboard (PPB) (Purdue Research Foundation, 1948), a task requiring speeded, accurate eye–hand coordination. Subjects performed the task with their left hand, right hand and bimanually. Each test took 30 s. Subjects received a total score for the three conditions. The reaction time tasks were then administered (see below). Total testing took between 2 and 2.5 h including breaks between tests.

Reaction time tasks
The response apparatus was a rectangular box bearing six circular buttons each 2.5 cm in diameter. The two central buttons were 15 cm apart (distance from centre to centre), one on the left and one on the right. These served as the 'home' keys. Twenty centimetres above the home keys were two red buttons, with two green buttons the same distance below. These four buttons were the response keys. Stimuli were presented on a visual display unit, at eye level and ~1 m from the subject. A 1 cm cross was continuously present in the centre of the screen and served as a fixation point and as a reference for the relative spatial location of the target in the CRT tasks. Each trial was initiated by the subject placing his/her index finger(s) on the home key(s). After a random and variable delay of 2–6 s, the imperative stimulus (a 1 cm square) appeared. There was no warning signal.

In the SRT task, one home key and one of the upper response keys were exposed. The imperative stimulus appeared at the fixation point. Reaction time was measured from the appearance of this stimulus to the subject lifting their finger from the home key. Movement time was measured from this point to when the subject
pressed the response key. Returning to the home key initiated the next trial. Each subject received 50 trials with their left hand and 50 trials with their right hand. Order of testing was counterbalanced across subjects.

In the two-choice CRT tasks, both home keys and the upper two response keys were exposed, while in the four-choice CRT tasks all six keys were exposed. In the two-choice CRT tasks the imperative stimulus appeared to the right or left of the fixation point, while in the four-choice CRT tasks the stimulus appeared in one of the four positions above or below, and right or left of the fixation point. In each case, the subject had to respond as quickly as possible by moving their index finger from the home key to the appropriate response key. Each task comprised 100 trials, with an equal number of the possible responses in each case. Median reaction times were calculated for each task. The data represented in the following figures represent the group means (and standard errors) of the individual median reaction times.

To discourage anticipatory responding, subjects were told to respond only after the presentation of the stimulus. Reaction times of < 100 ms (anticipation errors) were rejected, as were trials where reaction time was > 3000 ms (long responses). In the CRT tasks, trials in which the subject responded by pressing the wrong response key (decision errors) were also rejected.

Each of the two CRT tasks was administered twice. In one of the conditions, the nature of the response was spatially compatible with the position of the stimulus. For example, in the two-choice CRT task a stimulus to the left of the fixation point required a response of the left hand to the left response key. In the four-choice CRT task a stimulus below and to the right of the fixation point required the subject to move the right hand to the lower right response key. In the second condition, the response was spatially incompatible with the target position. For example, in the two-choice CRT task a stimulus to the left of the fixation point required a response with the right hand to the right response key. In the four-choice CRT task a stimulus below and to the right of the fixation point required the subject to move their left hand to the upper left response key.

Subjects were tested first on the SRT task, followed by the two-choice CRT tasks. Half were tested first on the compatible condition and half on the incompatible condition. Next, subjects were tested on the four-choice CRT task, again with the two conditions in balanced order. Finally, subjects were re-tested on the SRT task.

Stimulus presentation and experimental control was achieved with an IBM compatible microcomputer. Timing and digital input was handled by a CED 1401 Laboratory Interface (Cambridge Electronic Design, UK).

Statistical analysis

The main statistical procedure was repeated-measures analysis of variance (ANOVA) using the MANOVA procedure from SPSS (Norusis, 1988). Where significant interactions were revealed, further post hoc comparisons were performed to help interpret the pattern of results within and between groups. Because of marked deviations from normality in the error data, non-parametric methods were used in their analysis. Where independent \( t \) tests were employed, the group data were first assessed for homogeneity of variance. Where the \( F \) ratio indicated unequal variance in the two groups, separate variance estimates were employed in calculating the \( t \) statistic, and is reflected in the smaller and fractional degrees of freedom term.

RESULTS

The two groups did not differ in age \((t = 0.24, \text{ d.f.} = 14, P > 0.10)\) or score on the MMSE \((\text{patient mean} = 29.1, \text{SD} = 1.1; \text{control mean} = 29.4, \text{SD} = 0.53 (t = 0.65, \text{d.f.} = 14, P > 0.10)\). No subject in either group scored less than 27 out of 30 on the MMSE. The patients performed worse on the PPB \((\text{patient mean} = 26.5, \text{SD} = 9.2; \text{control mean} = 39.4, \text{SD} = 5.1 (t = 3.3, \text{d.f.} = 14, P < 0.01))\), and had higher Beck Depression Inventory scores \((\text{patient mean} = 11.1 \text{SD} = 5.4; \text{control mean} = 1.3 \text{SD} = 1.2 (t = 4.5, \text{d.f.} = 14, P < 0.01))\). However, no patient scored more than 17, a recommended cut-off for the classification of moderate to severe depression (Beck, 1970).

Taking the difference between the second and first SRT tests the patients showed significantly more slowing across the course of the experiment \((\text{mean} = 56 \text{ms, SD} = 47)\) than the control subjects \((\text{mean} = 9 \text{ms, SD} = 21) (t = 2.54, \text{d.f.} = 9.7, P < 0.05)\).
Because of this disproportionate effect of test occasion in the patients, the difference score between the first and second SRT was used as a covariate in subsequent analyses of the CRT data. In practice, however, this ‘fatigue’ score was not a significant covariate in any analysis.

Comparison of SRT and CRT

Figure 1 shows the data for the compatible four-choice CRT and first SRT tests. The mean reaction time of the patient group was slower overall \([F(1,13) = 10.1, P < 0.01]\) and there was a significant main effect of reaction time condition (SRT/CRT) \([F(1,14) = 144.6, P < 0.001]\). The interaction was also significant \([F(1,14) = 20.1, P < 0.01]\), with the patients showing a disproportionately greater increase in CRT relative to SRT (patients 174 ms, controls 79 ms). The patients were slower than the controls for CRT \([F(1,13) = 12.5, P < 0.01]\), while for SRT the group difference approached, but did not reach significance \([F(1,14) = 3.9, P = 0.07]\).

Effects of compatibility and uncertainty on CRT

Figure 2 shows reaction time data for the two groups under the compatible and incompatible CRT conditions. The results of the ANOVA are given in Table 1.

Overall, the patients were significantly slower than the controls. Across groups and conditions of compatibility, four-choice CRT was slower than two-choice CRT, and across groups and conditions of uncertainty, incompatible CRT was slower than compatible CRT. Contrary to prediction, the Uncertainty \(\times\) Compatibility interaction was not significant, at least when averaged across the two groups. However, all three interactions involving group were significant: Group \(\times\) Uncertainty; Group \(\times\) Compatibility and Group \(\times\) Compatibility \(\times\) Uncertainty. To help interpret these interactions and main effects, a series of post hoc analyses were conducted (see Table 1).
First, the effects of Uncertainty and Compatibility were analysed separately within each group. The patient group showed significant main effects of Uncertainty and Compatibility and an Uncertainty × Compatibility interaction which approached significance. For the control group, the main effect of Compatibility was significant while the effect of Uncertainty only approached significance. The Uncertainty × Compatibility interaction was not significant. Thus both groups showed clear increases in reaction time in the incompatible relative to the compatible conditions. However, as indicated in Fig. 2, the groups appeared to differ in terms of the effect of Uncertainty and its interaction with Compatibility. Further analyses help to clarify this pattern of results. Considering only the compatible conditions, the patients are slower than the controls overall, but show a similar increase in reaction time in the four-choice-CRT task compared with the two-choice CRT task. For the incompatible conditions, however, the Group × Uncertainty interaction was significant. This interaction can be explained by the fact that the patients were significantly slower on the incompatible four-choice CRT task than on the two-choice CRT task (mean difference = 222 ms, SD = 141) \((t = 4.5, \text{d.f.} = 7, P < 0.01)\), while the control group's mean reaction time for the two incompatible conditions did not differ (mean difference = 10 ms, SD = 125) \((t = 0.2, \text{d.f.} = 7, P = 0.83)\).

Secondly, the effects of compatibility were considered for each of the two levels of uncertainty. For the two-choice CRT conditions, the two groups showed an approximately equal increase in reaction time in the incompatible compared with the compatible condition. Contrasting the two four-choice CRT tasks, however, revealed a significant Group × Compatibility interaction, with the patients showing an increase in reaction time with incompatibility of 373 ms \((SD = 193)\), compared with an increase in the control group of only 151 ms \((SD = 53)\) \((t = 3.1, \text{d.f.} = 8.1, P < 0.05)\).
### Table 1. Results of ANOVA of the Influence of Stimulus-Response Compatibility and Uncertainty (Two-CRT and Four-CRT) Median Reaction Time in the Parkinson's Disease and Control Groups

<table>
<thead>
<tr>
<th>Within-subject factors</th>
<th>Effects (d.f.)</th>
<th>F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Two-CRT versus four-CRT (Uncertainty)</td>
<td>Group (1,13)</td>
<td>22.4*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Compatible versus Incompatible (Compatibility)</td>
<td>Uncertainty (1,14)</td>
<td>33.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Compatiblity (1,14)</td>
<td>106.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Uncertainty x Compatibility (1,14)</td>
<td>&lt;1.0</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Group x Uncertainty (1,14)</td>
<td>13.1</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>Group x Compatibility (1,14)</td>
<td>8.3</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>Group x Uncertainty x Compatibility (1,14)</td>
<td>4.8</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Parkinson group</td>
<td>Uncertainty (1,7)</td>
<td>32.2</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>Compatibility (1,7)</td>
<td>51.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Uncertainty x Compatibility (1,7)</td>
<td>3.7</td>
<td>&lt;0.09</td>
</tr>
<tr>
<td>Control group</td>
<td>Uncertainty (1,7)</td>
<td>3.9</td>
<td>&lt;0.09</td>
</tr>
<tr>
<td></td>
<td>Compatibility (1,7)</td>
<td>93.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Uncertainty x Compatibility (1,7)</td>
<td>1.3</td>
<td>NS</td>
</tr>
</tbody>
</table>

**Uncertainty effects**

| Compatible two-CRT versus Compatible four-CRT | Group (1,13) | 15.0* | <0.01 |
| Incompatible two-CRT versus Incompatible four-CRT | Group x Uncertainty (1,14) | 2.3 | NS |
| **Compatible effects** | Group (1,14) | 13.2 | <0.01 |
| Compatible two-CRT versus Incompatible two-CRT | Compatibility (1,14) | 59.8 | <0.001 |
| | Group x Compatibility (1,14) | 1.3 | NS |
| Compatible four-CRT versus Incompatible four-CRT | Group (1,14) | 27.6 | <0.001 |
| | Compatibility (1,14) | 54.8 | <0.001 |
| | Group x Compatibility (1,14) | 9.8 | <0.01 |

Where significant interactions were found, further analyses of within-subject and between group effects were performed.

*Analysis with difference between SRT (2) and SRT (1) as covariate; NS = not significant (P > 0.10).

CRT conditions. For the compatible stimulus-response relationships, however, they showed no differential impairment with increasing uncertainty, while for the two-choice CRT tasks they showed no differential impairment with incompatible stimulus-response relationships. The patients' deficit manifested itself most strongly in the interaction between uncertainty and compatibility, with the group being maximally impaired in the incompatible four-choice CRT task. Finally, while the patients showed a large effect of uncertainty in the incompatible CRT conditions, the control subject showed no such effect.

**Effect of practice on CRT in the incompatible conditions**

Does reaction time get faster as the subject has experience with the incompatible reaction time task? To assess this question, the data for the 100 trials in each of the two incompatible conditions were divided into five blocks of 20 trials each. The data for the two CRT
tasks are shown in Fig. 3. As variability was high, particularly in the patient group on
the four-choice CRT task, non-parametric ANOVA (Friedman) was used. Analysis
confirmed the pattern suggested in Fig. 3. In the patient group, reaction time in the four-
choice CRT condition showed a significant decrease across the five blocks of trials from
~1300 ms to 1020 ms ($\chi^2 = 13.3$, d.f. = 4, $P < 0.01$). The effect for the two-choice
CRT task, however, was not significant ($\chi^2 = 1.4$, d.f. = 4, $P > 0.10$). For the
controls, the reaction times did not differ across blocks for either the two-choice CRT
task ($\chi^2 = 4.3$, d.f. = 4, $P > 0.10$), or the four-choice CRT task ($\chi^2 = 4.4$,
d.f. = 4, $P > 0.10$). There is some evidence, therefore, to suggest that the patients,
but not the controls, reduced their reaction times with practice with the incompatible
stimulus–response mapping rules, at least in the four-choice CRT task.

Effects of compatibility and uncertainty on movement time

The median movement time data are shown in Fig. 4. Although the patients movement
time tended to be longer than that of the controls, the main effect of Group was not
significant [$F(1,14) = 3.0$, $P > 0.10$], due partly to the large inter-subject variability
in these data. There was a main effect of Compatibility (Compatible versus Incompatible)
[$F(1,14) = 10.5$, $P < 0.01$] and Uncertainty (two-choice CRT versus four-choice CRT)
[$F(1,14) = 9.1$, $P < 0.001$]. However, none of the two- or three-way interactions
were significant. Group×Compatibility [$F(1,14) < 1$, $P > 0.10$], Group×Uncertainty
[$F(1,14) < 1$, $P > 0.10$], Uncertainty×Compatibility [$F(1,14) = 1.5$, $P > 0.10$] and
Group×Uncertainty×Compatibility [$F(1,14) = 2.0$, $P > 0.10$].

In summary, the patient group tended to move more slowly than the controls, but this
difference was not significant. Movement times increased with the number of response
choices and with incompatibility. The increases, however, did not differ significantly
between the two groups.
Effect of uncertainty and incompatibility on response errors

Errors rates were generally low in both groups in all conditions. The total group errors of each type (anticipations, long responses and decision errors) for each condition are shown in Table 2. The total number of anticipations, across all conditions, comprised 0.58% of patient responses and 0.17% of control responses. The total number of anticipations did not differ between the two groups ($U = 21.5, z = 1.14, P > 0.10$). In contrast, the patients made more long latency responses (>3000 ms) (0.63%) than controls (0.06%) ($U = 12.5, z = 2.2, P < 0.05$). Considering the individual reaction time conditions, however, the two groups differed only for the incompatible four-choice CRT task ($U = 12, z = 2.6, P < 0.05$). Overall, the patients also made more decision errors (0.84% compared with 0.41% in the controls) ($U = 13.5, z = 1.99, P < 0.05$).

### Table 2. Total Number of Anticipations, Long Responses and Decision Errors Made by the Two Groups in the SRT and CRT Conditions

<table>
<thead>
<tr>
<th></th>
<th>SRT (1)</th>
<th>SRT (2)</th>
<th>Compatible two-CRT</th>
<th>Compatible four-CRT</th>
<th>Incompatible two-CRT</th>
<th>Incompatible four-CRT</th>
<th>Total errors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parkinson group (n = 8)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anticipations</td>
<td>2</td>
<td>2</td>
<td>7</td>
<td>6</td>
<td>7</td>
<td>4</td>
<td>28</td>
</tr>
<tr>
<td>Long responses</td>
<td>6</td>
<td>4</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>11</td>
<td>30</td>
</tr>
<tr>
<td>Decision errors</td>
<td>–</td>
<td>–</td>
<td>3</td>
<td>1</td>
<td>24</td>
<td>9</td>
<td>27</td>
</tr>
<tr>
<td>Control group (n = 8)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anticipations</td>
<td>1</td>
<td>3</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>Long responses</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Decision errors</td>
<td>–</td>
<td>–</td>
<td>0</td>
<td>7</td>
<td>2</td>
<td>4</td>
<td>13</td>
</tr>
</tbody>
</table>
Within the conditions, however, the two groups differed only in the incompatible two-choice CRT task \((U = 7.0, z = 2.8, P < 0.01)\), where 3% of the patient responses were errors, compared with only 0.25% of the control responses.

In summary, error rates were low in both groups, although the patients made more long latency responses in the incompatible four-choice CRT task and more decision errors in the incompatible two-choice CRT task.

**DISCUSSION**

The first aim of this experiment was to replicate a previous finding (Jahanshahi et al., 1992) of differential impairment in CRT relative to SRT in patients with Parkinson's disease. Estimates of SRT and CRT were based on relatively large numbers of trials using uncued and unwarned tasks. Employing such methods, a differential slowing in CRT was shown in the patient group. One difference from our earlier results was that the slowing in SRT was significant in the former study, but only approached significance here. The magnitude of the difference, however, was almost identical in the two cases and the discrepancy in statistical significance may be attributed to differences in sample size. Indeed, a slowing in SRT is almost universally found in Parkinson's disease. Variations in its magnitude may be attributable to variations in procedure and patient sampling, and differences in statistical significance attributable to sample size and variability. Given the overall consistency of this reported SRT slowing in Parkinson's disease, the question of statistical significance becomes somewhat arbitrary. One may accept, with some certainty, that the initiation of a response in an SRT task is slowed in Parkinson's disease. As already noted in the Introduction, this consistency of findings for SRT is in contrast to the literature on CRT. The present study demonstrates that, with a procedurally simple task, CRT can be differentially affected in Parkinson’s disease. Such a finding justifies the second aim of the present study, to investigate the processing stage(s) responsible for any slowing specific to CRT in Parkinson's disease. The main focus of attention in the present study was the role of response choice. The remainder of this discussion will focus on this issue. It will be divided into three sections: (i) the effect of response uncertainty on reaction time; (ii) the effect of stimulus—response compatibility; (iii) the interaction of these two factors.

The majority of published studies on patients with Parkinson's disease have employed CRT tasks with levels of spatial stimulus—response compatibility equivalent to the compatible condition in the present experiment. Under these conditions, the patients with Parkinson's disease showed normal increases in reaction time with increasing uncertainty from a two-choice to a four-choice task. This result is in agreement with the finding of Stelmach et al. (1986), who also found a normal uncertainty effect employing a partial pre-cueing paradigm to manipulate the number of stimulus—response alternatives.

Just as the effect of uncertainty can be most simply seen under the condition of maximum stimulus—response compatibility, so the effect of manipulating the level of compatibility can be seen most clearly in the condition of minimum uncertainty, i.e. the two-choice CRT task. Under this condition, both groups showed an increase in reaction time in the incompatible compared with the compatible condition. Furthermore, the increase in reaction time did not differ in the groups.

Thus, when considered independently, two factors known to affect response choice,
uncertainty and stimulus—response compatibility, both not only lead to increased reaction times in patients with Parkinson's disease, but also to similar degrees to those shown by normal controls. The one remaining factor to consider is the interaction between these two task parameters. This is important for two reasons: (i) to test the assumptions of the additive factor model; (ii) to investigate the performance of the patients in conditions where a double burden of uncertainty and incompatibility is placed on the processes of response choice.

Based on previous evidence it was predicted, in line with the additive factor model, that stimulus—response compatibility and uncertainty would interact in the normal subjects. In fact, no such interaction was observed, and from Fig. 2 it would appear that the effect of uncertainty may even have been reduced in the incompatible conditions. How can we account for this failure to obtain the predicted interaction between uncertainty and stimulus—response compatibility in normal subjects? All subjects were tested on the incompatible two-choice CRT task before the four-choice CRT task. Therefore, it is possible that the control subjects were able to benefit from their experience on the incompatible two-choice CRT task, when it came to performing the more difficult four-choice CRT task, thereby reducing their reaction time and masking any interaction between stimulus—response compatibility and uncertainty. Contrary to this hypothesis, however, is the absence of any decrease in reaction time, with practice, over the 100 trials on the two-choice CRT task (Fig. 3). This insensitivity of stimulus—response compatibility effects to practice-effects in normals has been shown by Fitts and Deininger (1954) with testing over 2 days, although with extended testing, certain aspects of incompatibility may become attenuated (Brebner, 1973).

A second explanation relates to the nature of the task, and the strategies which the subjects might use to deal with the problem of incompatibility. Hasbroucq et al. (1990), in common with others (e.g. Fitts and Deininger, 1954; Simon et al., 1981) have commented that stimulus—response compatibility involves a number of different effects. In one set of procedures there is a conceptual link between the stimulus and response sets. For example, a coloured stimulus indicates a response with a particular coloured button, or a spatial stimulus indicates a response to a particular spatial position. Under these conditions stimulus—response compatibility can be manipulated by changing the nature of the stimulus—response mapping. For example, by asking the subject to press a green button for a red stimulus, or the left button for a right stimulus. In another class of tasks, stimulus—response compatibility is manipulated by asking the subject to base their response on an arbitrary stimulus—response relationship where there is no conceptual link between the stimulus and response sets. For example, pressing a left button for a red stimulus and a right button for a green stimulus. In these cases the subject must match the stimulus with its arbitrarily associated response. Based on this procedural distinction between mapping and matching stimulus—response compatibility effects, Hasbroucq et al. (1990) suggested that subjects may resolve situations of stimulus—response incompatibility by adopting one of two strategies. Where there is no conceptual relationship between stimulus and response, as in the case of pairing colour with position, the subject can perform the task only by searching through a list of stimulus—response pairs, defined by the experiment, and held in memory. This is an example of a what can be termed a list-search strategy. One important implication is that the larger the list the longer it will take, on average, to find the match and the longer the response time, i.e. there will be an effect of
stimulus—response compatibility which will interact with the level of uncertainty (i.e. the list length). In other tasks, where the stimulus and response sets have a common conceptual feature (e.g. both spatial or both colours), the choice of strategy is determined by whether or not the stimulus—response mapping can be achieved by applying an algorithm, in which the response is defined as a function of the stimulus. For example, a subject might be instructed to press the left button for a right stimulus and the right button for a left stimulus. With a rule-based strategy one would not predict any interaction between stimulus—response compatibility and uncertainty as the same mapping rule ‘press the opposite’ button could be applied regardless of the number of stimulus—response alternatives. Instead, one would find an additive effect on uncertainty caused by the extra time needed to apply the incompatible mapping rule.

A third situation arises where there is a conceptual relationship between stimulus and response, but where it cannot be expressed by a single transformation function (e.g. a left-upper stimulus indicates a right-upper response, and a right-upper stimulus indicates a left-lower response, etc.). In such a situation, the subject would have to resort to a list-search strategy, with an associated increase in processing time with increasing uncertainty.

Thus, where there is an arbitrary stimulus—response association, whether or not the stimulus and response sets have a conceptual link, the subject will employ a list-search strategy and stimulus—response compatibility and uncertainty would interact. Only where a mapping rule can be applied would an additive pattern be predicted. Thus the list—rule model suggests that the determination of a symbolic representation of the response code can be achieved by two qualitatively different strategies, presumably employing different sets of processing structures. Response choice, therefore, may not be a unitary stage but a set of alternative stages, where the one adopted may vary from task to task, individual to individual, or possibly even trial to trial.

Returning to the data from the present study. In both the two-choice CRT and four-choice CRT incompatible tasks, the stimulus and response sets were both spatial. Furthermore, the nature of the stimulus—response relationship could be expressed by a simple mapping rule, i.e. ‘press the button opposite the location of the stimulus’. Indeed, this precise instruction was used when explaining the nature of the task to the subjects. The additive nature of the relationship between uncertainty and stimulus—response compatibility in the control subjects was consistent with them applying a rule-based mapping strategy to deal with the problem of the incompatible stimulus—response relationships as predicted by Hascroucq et al.’s (1990) list—rule model.

The relationship between stimulus—response compatibility and uncertainty in the controls was in direct contrast to that of the patients where the two factors had an interactive effect on reaction time (see Fig. 1). In the compatible conditions, four-choice CRT was 116 ms slower than two-choice CRT, while for the incompatible conditions a difference of 218 ms was found between the two levels of uncertainty. According to the list—rule model this pattern of results would imply that the patients were using a list-search strategy and despite the fact that a rule-based solution was available and despite receiving the same instructions. If this interpretation is correct, then it implies that the two groups were tackling the problem of incompatibility in qualitatively different ways. However, there is some suggestion that the patients may have shifted their strategy during the course of the experiment. This may be inferred from the significant decrease in reaction time shown by the patients across
the 100 trials of the incompatible four-choice CRT task, where the 422 ms mean difference between incompatible two-choice CRT and four-choice CRT tasks for the first 20 trials was reduced to 138 ms for the last 20 trials. Such an improvement is likely to have been due to strategy change, given the general insensitivity of stimulus—response compatibility effects to practise (Fitts and Deininger, 1954).

If, indeed, the two groups were employing different strategies, at least initially, this raises the question as to whether slowed performance can be defined as 'impaired'. As noted by other authors, aspects of motor performance in Parkinson's disease, such as the slowness to initiate and execute a ballistic movement, may be a strategic adaptation to cope with a 'noisy' and less accurate motor system (Sheridan et al., 1987). In the same way, the use of a list-search strategy may be more efficient under general constraints imposed on aspects of information processing in Parkinson's disease. Although there is no direct evidence, one might speculate that applying a rule-based strategy requires conscious and sustained effort, while the list-search strategy may be a more automatic process. If such effortful processes are impaired in Parkinson's disease, the patients might fall back on the less effort-demanding strategy. This hypothesis could be easily tested by manipulating the processing resources of normal subjects with a concurrent attention-demanding secondary task. A reduction in processing capacity available for stimulus—response mapping might lead to a shift from the rule-based strategy with its additive relationship between stimulus—response compatibility and uncertainty to a list-search strategy with the corresponding appearance of an interactive relationship between the two factors.

The results from the present study, therefore, are equivocal with regard to the issue of response choice in Parkinson's disease. On the one hand, although slower overall, the patients exhibited a normal response to changes in uncertainty under conditions of high stimulus—response compatibility and to changes in stimulus—response compatibility under conditions of low uncertainty. The possibility that the two groups employed different strategies to deal with incompatible stimulus—response relationships, particularly in conditions of high uncertainty, makes it impossible to comment on the efficiency with which the patients applied the hypothetical list-search strategy. To test this it would be necessary to assess patients and controls under conditions which constrained both groups to using this strategy, by employing a stimulus—response relationship which cannot be directly mapped.

In conclusion, the results from the present experiment suggest that response choice may be slowed in Parkinson's disease, but that this slowing may only be present in conditions of low stimulus—response compatibility. Furthermore, the behavioural slowing may be due to qualitative differences in the ways in which conditions of incompatibility are handled by the patients. Further research is necessary to determine whether response choice is slowed in patients and controls under conditions where both patients and controls were constrained to employ the same strategy. Finally, it is clear that under conditions of high stimulus—response compatibility, response choice appears to be normal in Parkinson's disease. Therefore, it is unlikely to be an important factor in contributing to the slowing of CRT demonstrated in previous studies. The stage analysis of choice reaction processes in Parkinson's disease will continue to attract attention from investigators. The present study, however, suggests that caution is needed to ensure that the same strategies are, indeed, being employed by the patients and any comparison group.
ACKNOWLEDGEMENT

This research was supported by a grant from the Wellcome Trust.

REFERENCES


