SHORT REPORT

Reduction in external cues and movement sequencing in Parkinson's disease

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Abstract

To identify the focus of impairment in the performance of sequential movements of patients with Parkinson's disease, the extent of their reliance on external cues was examined. Eighteen patients with idiopathic Parkinson's disease and their matched controls performed a series of button presses at sequential choice points along a response board. The illuminated pathway to be followed successively extinguished ahead of each move according to three levels of reduction of external cues. Patients with Parkinson's disease were particularly disadvantaged with high levels of reduction of external cueing in terms both of movement preparation time (button down time) and movement execution time (movement time between buttons). Moreover, with high levels of reduction of external cueing, patients with Parkinson's disease were particularly subject to progressive slowing (movement time, not down time) further down the sequence. The basal ganglia may help generate internal cues for releasing successive stages of a predefined movement sequence.

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Hypokinesia in Parkinson's disease is clinically characterised by slowing of individual movements¹ and especially of movement sequences.^{2,3} Such slowness may be more pronounced when sequences are performed automatically, without attentional resources,⁴ and when patients must rely on internal rather than external cues.⁵ Thus clinical observation suggests that the provision of external cues improves patients' performance; whereas they may not be able to throw a ball, they can often quickly catch it when this movement is externally triggered by someone throwing it to them. Although there have been previous studies of sequential movements in Parkinson's disease,^{4,6,7} this study is perhaps the first to consider the question of the effect of external cues on the performance of movement sequences. In particular, our serial choice button pressing procedure can independently assess two indices of response

time—button down time and movement time. The first, which measures how long each button is held down before initiating a move to the next one in the sequence, is thought to reflect preparation time, the time needed to assemble the motor programme for the actual move (the movement time) to the next appropriate button.⁸

Subjects depressed the illuminated member of a pair of buttons at each of a series of choice points along a response board, effectively completing a sequential pathway. The entire pathway was initially illuminated, and with each successive button press the visual information was successively reduced, to various extents, in advance of each response. This task, which involved sequential forced-choice responding, also permitted measurement of any progressive slowing as the sequence was traversed, as a function of how external cueing was reduced. Amplitude and velocity of each component in a series may further diminish as the sequence progresses.⁴

Method

SUBJECTS

Eighteen subjects with idiopathic Parkinson's disease and 18 controls with no history of neurological disorder participated. There were 11 men and seven women in each group, all of whom were right handed, with a mean age of 65.8 years for each group. Duration of Parkinson's disease ranged from 1-20 years with a mean duration of 8.9 years. The severity of symptoms of Parkinson's disease were rated by a neurologist at the beginning and end of each session, on the Webster scale⁹ (mean = 11.8, range 4-19). All patients were at either stage II or III¹⁰ of the disease, and were screened for dementia by the short test of mental status¹¹ (patients with Parkinson's disease mean = 31.6; controls mean = 34.4, values well within the suggested range).

APPARATUS

The apparatus has been described in detail elsewhere.¹² Two parallel rows of 10 target buttons were set into a response board. Adjacent buttons were 30 mm apart. In addition two single buttons (S1, S2) at one end were sequentially depressed to initiate the task, and a further single button (F) at the

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other end was pressed to complete the task. Each button could be illuminated by a light emitting diode set into its base. A computer determined the button sequence (the illuminated path) to be followed, and also recorded the time each button was depressed (down time) and the time between release of one button and depression of the next (movement time).

PROCEDURE

The board was positioned across the subjects' midline. A pathway across the board was illuminated, in which there were two-way choice points at each of the 10 sequential pairs of buttons. Subjects followed the illuminated pathway with the index finger of the right hand. External cues were systematically reduced (the illuminated buttons were extinguished in advance of the next movement) in one of three ways during progress along the board: with no reduction in external cues, the next illuminated button was extinguished as the current button was released (no button extinguished in advance); with moderate reduction, the next button was extinguished as the current button was depressed (one button extinguished in advance); with high reduction in external cues, in addition to the next button remaining extinguished, the next-but-one button also extinguished as the current button was released. There were eight different equidistant pathways in which numbers of linear and diagonal movements between successive button pairs were balanced so that, overall, the total distance in each movement sequence was invariant. The different conditions were counterbalanced across subjects, with 16 experimental and six practice trials for each of the three external cue conditions.

Results

DOWN TIME

Figure 1 shows down time plotted as a function of external cue condition for each group. The data were submitted to a mixed two way ANOVA (group, cue condition).

The two highly significant main effects were interpreted via the significant interaction, $F(2,68) = 7.34$, $p < 0.01$. Post hoc one way ANOVAs and Tukey tests showed that whereas controls showed no differences between any of the three external cue conditions, for patients with Parkinson's disease there were significant ($p < 0.01$) differences between high (144 ms) and both no (127 ms) and moderate (129 ms) levels of reduction, whereas the last two did not differ.

MOVEMENT TIME

Fig 1 also gives movement time data. The two main effects were highly significant, as was the interaction, $F(2,68) = 5.35$, $p < 0.01$. One way ANOVAs and Tukey tests showed that for controls there was a significant ($p < 0.05$) difference between high (180 ms) and no (162 ms) levels of reduction. For patients with Parkinson's disease there were significant ($p < 0.01$) differences between high (346 ms) and both no (268 ms) and moderate (281 ms) levels of reduction, whereas the last two did not differ significantly.

ERRORS

The error rate increased between the first and the third cue conditions, and this effect was particularly pronounced in the data from patients with Parkinson's disease. The median errors for the three conditions (no, moderate, and high reduction in external cues) for patients with Parkinson's disease were 1, 1, and 12, respectively, and for controls 1, 1, and 4, respectively. Mann-Whitney U tests conducted on the error data showed that there was a significant difference between the two groups only with high reduction in external cues ($p < 0.05$). Wilcoxon matched pair tests showed that for both patients with Parkinson's disease and control subjects there were significant increases in errors when there was a high reduction in external cues ($p < 0.05$).

SEQUENCE EFFECTS

To determine whether patients with Parkinson's disease became progressively slower across the 10 sequential response locations, trend analyses were conducted for both down time and movement time. For down time there was no evidence of progressive sequential slowing in either group or for any condition, whereas for movement time (see fig 2) there was a significant main effect of sequence, $F(9,306) = 7.82$, $p < 0.001$, and a significant group by sequence interaction, $F(9,612) = 1.98$, $p < 0.05$, which had a significant linear component. The significant three way interaction, group by sequence by cue condition, $F(18,612) = 1.62$, $p < 0.05$, indicates that whereas controls exhibited uniform movement times across the board, with only a slight progressive slowing with high reduction in external cues, these effects were dramatically more pronounced for patients with Parkinson's disease who slowed considerably during the high reduction condition

Figure 1 Down time (DT) and movement time (MT) for patients with Parkinson's disease (PD) and controls (Con) as a function of levels (no, moderate, high) of reduction in external cues.

Figure 2 Mean movement time against each of the 10 sequential buttons for patients with Parkinson's Disease and control subjects, as a function of reduction in external cues.

and noticeably with the moderate reduction condition.

Discussion

Patients with Parkinson's disease displayed considerable difficulty in initiating (down time) and especially in executing (movement time) responses in a sequential task with reduced visual information, when each button position had to be stored and accessed automatically. In particular they may have had problems not so much in assembling as in maintaining and triggering each next phase of a sequence. Error rates also dramatically increased with a high level of reduction in external cues, especially in patients with Parkinson's disease, when in addition to the next button remaining extinguished, the second but one in the sequence also extinguished as the current button was released. Thus a completely new response had also to be stored in motor memory before the current response could be initiated. Execution time has previously been reported to be a more sensitive indicator of Parkinson's disease impairment than initiation time,¹³ again perhaps reflecting the finding that the automatic execution of movements through internal generation may be most affected in patients with Parkinson's disease.

Movement execution (rather than initiation) times in the data from patients with Parkinson's disease also progressively slowed with each successive element in the response sequence, especially at the higher levels of reduction in advance information. Inaccuracy with regard to a single movement causes additional burdens on subsequent movements in a sequence. Parkinson's disease is known to cause particular difficulty in triggering later elements in a movement sequence.^{4,14}

One explanation for the differential slowing of movement with reduced external cues may be that patients with Parkinson's disease require external cues to control their attention¹⁵ and guide their movement. Furthermore, our animal studies¹⁶ indicate that the basal ganglia provide an internal cue to trigger the next submovement in a

sequence. This cue is represented neurally by phasic activity, which turns off sustained premovement activity in the supplementary motor area. The subsequent decline in the activity of the supplementary motor area triggers movement execution. In Parkinson's disease we believe that the cue is abnormal or absent, leading to faulty execution of prepared activity for the next submovement, a difficulty that was exacerbated in the present study by the extent to which we reduced external cues. Thus the more the sequence had to depend on internally generated cues, the slower the resultant movements.

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