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Effects of response readiness on reaction time and force output in people with Parkinson's disease

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Summary

Previous research investigated effects of response readiness in neurologically normal subjects by manipulating the probability of responding. With a high probability of responding, reaction time is fast and the level of response force is low compared with conditions with a low probability of responding. An elaborated view of response readiness assumes that these effects reflect properties associated with the transmission of response activation to the motor output system. The present study employed high- and low-probability trials in a go/no-go task, to investigate whether these processes are impaired in people with mild to moderate Parkinson's disease. It was hypothesized that the patients would demonstrate abnormal patterns of response force with manipulations of response readiness. It was further hypothesized that the patients would display evidence of inability to inhibit responses on no-go trials. Both hypotheses were supported, suggesting that a basic deficit associated with Parkinson's disease is related to the transmission of response activation to the motor system. Response modulation appears to depend on the integrity of basal ganglia structures.

Keywords: response readiness; Parkinson's disease; force

Abbreviations: AM = age-matched (controls); PF = peak force; IS = size of the force impulse; MF = mean force; RT = reaction time

Introduction

The basal ganglia are a subcortical complex of nuclei whose involvement has been linked to both cognitive and motor functions. Parkinson's disease causes neurodegeneration of dopaminergic neurones within the substantia nigra pars compacta, one primary nucleus of the basal ganglia. This degeneration affects not only operations within the basal ganglia circuitry, but also massive projections of dopaminergic neurones to the neostriatum. This, in turn, affects dopamine levels in neocortical regions that receive striatal input (DeLong, 1990).

Parkinson's disease presents a number of observable impairments in movement initiation and execution, including akinesia, bradykinesia, tremor, rigidity and dyskinesia. In addition, cognitive effects that are subtle to casual observation have been demonstrated in experimental work in humans with Parkinson's disease. These include prolonged simple reaction times (RTs), which are often interpreted as deficits in utilizing advanced information during movement selection and initiation (Evarts *et al.*, 1981; Bloxham *et al.*, 1984; Sheridan *et al.*, 1987; Goodrich *et al.*, 1989), problems in procedural learning despite intact declarative knowledge (Knowlton *et al.*, 1996), and a slowing and increased error rate on task switching in both motor and cognitive domains (Cools *et al.*, 1984; Benecke *et al.*, 1987; Hayes *et al.*, 1998).

Existing literature reveals flourishing debate about the precise nature of deficits associated with Parkinson's disease. For example, it has been demonstrated that people with Parkinson's disease show clear advantages with the presentation of valid compared with invalid peripheral cues that precede the occurrence of a target in choice tasks (Rafal *et al.*, 1984). In addition, a study on people afflicted by an asymmetrical degree of Parkinson's symptoms to the two hands demonstrated that mean RT was worse for the more affected hand in both simple and choice RT tasks to a comparable degree (Rafal *et al.*, 1989). These studies call into question the claim that Parkinson's disease produces deficits related to the use of advanced information. These findings also raise the possibility that the observed slowing on simple RT tasks may be due to later rather than earlier stages of motor programming, although such effects are difficult to capture using RT measures alone.

Curiously, the observable symptoms of Parkinson's disease range from what appears to be too little movement activation to what appears to be an extremely high level of movement activation. Examples of the former include the symptom akinesia and the more subtle cognitive problems associated with prolonged simple RT to initiate movement. At the other end of the spectrum, it is possible that too high a level of response activation results in inability to inhibit unwanted movement. One is struck when observing the rather extreme case in which a person with Parkinson's disease is seen to take off at an excessively fast-paced walk following many failed attempts to initiate movement. It is as though recurrent failures to activate the movement accumulate over time until far too high a level of activation is suddenly released in a somewhat uncontrollable manner. These examples suggest that the balance required for an equilibrated response activation system is impaired in Parkinson's disease. What results appears to be either too little or too much force output, depending on the task and the situation.

Experimental manipulations of response readiness may be one way to assess whether the modulator of response activation is impaired in Parkinson's disease. If tested at early stages of the disease progression, when motor impairments are the most prevalent symptoms, one might expect such manipulations to result in abnormal patterns of force output. We sought to investigate this possibility by applying a probability manipulation that is believed to influence response readiness directly. The basis of this manipulation comes from studies in neurologically normal subjects.

In an early study that examined the factors influencing response readiness in neurologically normal subjects, Näätänen (1971) varied the interval between presentations of successive stimuli to create mean intervals in different conditions that ranged from 5 to 40 s. Simple RT was the primary dependent variable. Näätänen reported that the mean simple RT lengthened with the mean interval for all conditions.

Näätänen (1971) interpreted the observed relationship between RT and foreperiod as reflecting a level of response readiness based on the following logic. With expectancy of a short foreperiod, the level of response readiness is high compared with when a longer interval is expected. This high level of response readiness enables the subject to exert only a small additional effort to reach the level of motor activation required for the successful initiation of a response (referred to as a 'motor action limit' by Näätänen). This additional effort would require only a small increase in preparation time (i.e. RT) compared with conditions with a longer foreperiod in which motor readiness was low. Näätänen further elaborated that the neural system must balance between excitatory and inhibitory influences to maintain optimal readiness while preventing the premature motor responses that may occur when levels of response readiness are too high.

Näätänen (1971) was one among a number of studies that demonstrated a relationship between foreperiod and RT (reviewed in Niemi and Näätänen, 1981). Although RT reflects the period of response preparation following stimulus presentation, the question of whether response dynamics were directly influenced by foreperiod remained unanswered. It also remained unclear how temporal uncertainty and stimulus expectancy may influence response dynamics. These issues were examined in more recent studies that incorporated response force measures into their procedures.

Giray (1991; written in German, cited in English in Ja'skowski and Verleger, 1993) appears to have been the first to report that response force as well as RT increases with foreperiod duration. These claims were further investigated by Ja'skowski and Verleger (1993) using manipulations of stimulus expectancy. They designed a task in which a rotary dial pointed to possible stimulus locations while traversing a circular pattern at a constant velocity. This procedure made successive stimulus presentations possible without the need for warning signals. The occurrence of stimuli was highly probable in only one region of the stimulus display. Expectancy was inferred on the basis of the probability of stimulus presentation within this target region, and EEG changes were recorded in order to verify subjective expectancy independently.

Ja'skowski and Verleger (1993) reported a larger peak force (PF) for unexpected compared with expected stimuli. Similar effects were found for RT. The average EEG signal differed little from baseline when the stimulus pointer traversed regions of the stimulus display that were unlikely to contain a stimulus, further indicating that expectancy was low in these regions. The investigators suggested that motor activation may be affected by the level of preparation associated with the expected stimuli. They further concluded that increased force may occur due to subjects' lack of readiness when stimuli are unexpected. Although the study by Ja'skowski and Verleger (1993) did not mention Näätänen (1971), their conclusion appears to be similar to the suggestion by Näätänen to account for effects on RT.

Temporal uncertainty was built into the design of Ja'skowski and Verleger (1993) because each successive stimulus was somewhat unpredictable in time. A more recent study by Mattes and Ulrich (1997) directly tested the relationship between temporal uncertainty and response force. Mattes and Ulrich also pointed out some important considerations concerning what is termed the 'foreperiod' and the predictability of the stimulus. The foreperiod can be used to predict the upcoming stimulus if a constant interval is inserted between a warning signal and the imperative stimulus. If ageing foreperiods are used, the subjective expectancy may change as the foreperiod interval progresses because the probability of stimulus occurrence becomes increasingly higher. In either case, effects of subjective expectancy may be due, at least in part, to response readiness.

Mattes and Ulrich (1997; Experiment 1) sampled response force continuously using either variable or fixed foreperiods following a warning signal. In the variable condition, three possible foreperiod durations were intermixed randomly within a block. In the constant condition, one of the three

possible foreperiods was employed for an entire block. Both RT and response force increased with foreperiod in the constant condition but decreased with foreperiod in the variable condition. The most pronounced effects on both RT and response force occurred with the shortest foreperiods (0.5 s). Notably, according to the motor readiness account, constant foreperiods enable high stimulus predictability, and therefore a high level of motor readiness. In an elaborated version of this model, Mattes and Ulrich (1997) added that only a small increase in force level is needed when high motor readiness brings one sufficiently close to the limit of a motor response.

As pointed out by Mattes *et al.* (1997), strong support for a motor readiness model of the type proposed by Näätänen (1971) would be gained from the demonstration that not only stimulus probability but also response probability affects response force. Mattes *et al.* (1997) examined this issue by varying the probability of a response by displaying a numeric cue that ranged from 10 to 100 to indicate the probability of the upcoming response on that trial. Each number appeared in a unique colour, so that colour would reinforce the meaning of the cue, with the intention of directly manipulating motor readiness. Mattes *et al.* (1997) found that both RT and response force decreased with increasing probability.

In Mattes *et al.* (1997), although the probability manipulation was intended to affect response readiness directly, the investigators pointed out that stimulus probability and response probability were confounded. Mattes and colleagues therefore conducted a second set of studies to examine whether response probability manipulations would alone affect response force (Mattes *et al.*, 2002). Evidence of such a relationship would provide strong support for a motor readiness account. The experiments most relevant to this issue were Experiments 2 and 3 of Mattes *et al.* (2002).

Mattes *et al.* (2002; Experiment 2) presented one stimulus four times as often as another under two different conditions of response readiness. In one response readiness condition, the probability that any stimulus would occur was only 20%. In the other response readiness condition, this probability was 80%. For these two levels of response readiness, a no-go response was associated with presentation of another stimulus letter that occurred with a probability of 80 or 20% for the two response readiness conditions, respectively.

Mattes *et al.* (2002) found that RT was faster with both high stimulus probability and high response probability compared with both low-probability manipulations. Both probability factors also affected response force in that higher PF was produced with low probability. In neither case did stimulus probability interact with response probability. However, as noted by the authors, stimulus probability and response probability remained confounded in this design because different absolute stimulus probabilities were associated with the two different levels of response readiness, even though the relative stimulus probabilities were identical under the two response readiness conditions.

In Experiment 3, Mattes *et al.* (2002) employed four letters as stimuli so that their probability of occurrence could be varied in a manner similar to the previous experiment. However, two of the four letters could occur with equal absolute stimulus probability—in one instance under conditions of high response probability and in the other under conditions of low response probability. This enabled a critical comparison of the effects on RT and response force for the two letters with the same stimulus probability but two different conditions of response readiness. These procedures revealed significant effects of response probability on both RT and response force, indicating that response force was higher with low response probability than with high response probability. It seems safe to conclude that manipulations of both stimulus probability and response probability affect RT and response force. A motor readiness account pointing to properties associated with preparing a response is therefore not only plausible but is likely to account for the effects.

Consideration of the elaborated response readiness model (Mattes *et al.*, 1997, 2002; Näätänen, 1971) leads to an interesting possibility with respect to Parkinson's disease. If an impaired response activation system is one problem associated with the disease, then manipulations of response readiness might be expected to reveal abnormal patterns of response force. An interesting aspect of manipulations of response readiness is that no explicit instructions are given about force. Thus, any effects on force can be viewed as incidental to the primary task demands of speed and accuracy. The present set of experiments measured force output under different levels of manipulated response readiness using a go/no-go task. The procedures were applied to two groups of control participants and a group of participants with mild to moderate Parkinson's disease. We were particularly interested in the possibility that manipulations of response readiness would result in abnormal levels of force output in the Parkinson's disease group. The use of a go/no-go task provided the additional benefit of a means to examine whether inappropriate levels of force output may be registered even when the response is to be withheld. Such evidence may be suggestive of problems in the inhibition of responses.

The general method involved manipulating response readiness using high- or low-probability response cues. Each block of trials consisted of 50% of trials with a cue indicating that a response was highly likely and 50% of trials with a cue indicating that a response was not likely. To be optimally salient, the cues were colours that flooded the entire computer screen. Each colour represented either a high likelihood or a low likelihood that the upcoming stimulus would require a response. Following the high-probability cue, there were four times as many go trials as there were no-go trials. The reverse was the case following low-probability cues.

Force level was sampled continuously on each trial for a period that exceeded the length of the response. RT was computed as the time at which the force level exceeded a criterion. On the basis of previous studies, we predicted that

the control participants would demonstrate faster RT and smaller force output with high response readiness compared with low response readiness. A second prediction was that the Parkinson's disease group would display abnormal patterns of response force with response readiness manipulations compared with controls. However, we made no specific predictions about the direction of this effect, because it is not clear whether impairments would produce too little force or too much. A third prediction was that an abnormally high level of force output might be observed on no-go trials in the patients, perhaps reflecting impairments in inhibiting unwanted movement.

To avoid any confounds in performance that may result from problems associated with symbolic mapping of stimuli to arbitrary responses, we used response-direction-compatible arrows as stimuli. On any block of trials, an arrow would appear to signal a 'go' response, and an equals sign (=) would appear to signal a no-go response. Because Parkinson's disease may affect the two hands differentially, we tested probability effects on each hand in separate blocks of trials. However, we recorded the force output of both hands on each trial to examine any possible effects of bimanual motor coupling that may result in some level of activation in the uninvolved hand.

Because the precise methods of this experiment had not been tested before, we first applied the procedures to a large group of student control participants with the goal of replicating earlier findings (Experiment 1). Having met that goal, we applied the same procedures in a second experiment to 12 people with mild to moderate Parkinson's disease (Parkinson's disease) and 12 age-matched (AM) controls.

Experiment 1: Methods

Participants

The participants were 20 undergraduates from the Otago Psychology Participant Pool. The range of ages was 18–30 years. These and all participants in Experiment 2 gave informed consent to participation in this study, which was approved by the Human Ethics Committee of the University of Otago.

Apparatus

The experiment was carried out in a dimly lit room. A microcomputer controlled stimulus presentation and recorded response force. A set of written instructions was displayed in white on an otherwise black computer screen prior to each block of trials. A foot-operated pedal placed under the table was used to initiate the first trial of each block. The colour cues flooded the entire screen in either green or blue. An arrow (8 × 12 mm) or an equals sign (=) (5 × 7 mm) was displayed at the centre of the computer screen subtending a visual angle of ~1° degree horizontally and 0.75° vertically. Stimulus intensity was ~85 cd/m^2 against a dark background.

Subjects responded with a brief flexion of the left or right index finger (go trials) or by doing nothing (no-go trials), depending on the experimental condition. Responses were measured using force-sensitive keys. A leaf spring (140 × 20 × 2 mm) was supported in a clamp on one end of each response key, and the subject pressed the free side. A force of 15 N bent the free end of the leaf spring ~2 mm. Strain gauges (Type 6/120 LY 41; Hottinger Baldwin Messtechnik, Darmstadt, Germany) were attached near the fixed end of the leaf spring, and the applied force was reflected in an analogue signal with a resolution of ~2.8 mN. The digitized force signal was recorded at 250 Hz. This allowed RT to be measured to the nearest 4 ms. The participant used his or her index finger of the responding hand to press the free end of the force lever, and an armrest supported the rest of the forearm so that it rested comfortably with a slightly bent elbow. The non-responding hand was positioned in the same way as the responding hand, with the index finger on its respective force lever so that force output could also be registered.

Procedure

Each subject was tested in a single session that lasted ~1 h. A session consisted of 10 blocks of 40 trials each. Each block consisted of 20 trials with each cue (high versus low probability), all randomized. In each of these two response readiness conditions, a cue of either green or blue occurred, and the colour-to-probability mapping was counterbalanced across subjects. Subjects were instructed before each block that one colour indicated that a response was likely to occur and the other colour indicated that a response was unlikely to occur. Of the 20 trials cued for high probability, 16 trials (40% of the total) were followed by an arrow stimulus pointing in the direction of the responding hand. The remaining four trials (10% of the total) were followed by an '=' stimulus that indicated the response should be withheld, i.e. no-go. The go and no-go trials were apportioned in the opposite way for the low-probability trials.

Blocks were administered in alternating fashion for the left and right hands, with hand assignment on the initial block counterbalanced across subjects. The initial set of instructions was read aloud to the subject by the experimenter. On subsequent blocks, the same instructions were read alone by the subject. After reading the instructions, a message on the screen indicated that the foot pedal should be pressed to initiate the first trial. Each trial began with a colour cue displayed for 1000 ms. Following cue onset was a baseline period of 200 ms during which force from both response levers was recorded continuously. An arrow stimulus indicating a go trial or an '=' stimulus indicating a no-go trial then appeared until a response was registered, or for 2200 ms, whichever came first. Subjects were instructed to respond with the hand indicated by the direction of the arrow, or to withhold responding if '=' appeared. They were instructed to respond as fast as possible without errors. Force was continuously recorded for a full epoch of 2200 ms, including

the baseline interval. This sampling period was long enough to collect the entire force–time function of each response.

Following a correct response, the word 'correct' appeared at the bottom of the screen for 600 ms. An incorrect response was determined as a response on a no-go trial (force exceeding a 100 cN threshold), or the lack of response on a go trial for the responding hand. Following an incorrect response, the word 'incorrect' appeared at the bottom of the screen together with an auditory tone, each lasting 1200 ms. An intertrial interval of 1200 ms occurred before onset of the colour cue for the following trial.

Data analysis

From here on, the term 'involved' will refer to the hand that was supposed to produce the go response in any block of trials. The term 'uninvolved' will refer to the hand that was not to respond on that block of trials. Trials will be discussed for both go and no-go trials for the involved hand and for the uninvolved hand, given that force was sampled for both hands on all trials.

Trials that were in error because there was no response when a response was required or because there was a response when no response was required were tallied to compute the percentage correct. Four sets of analyses were conducted separately on each of the following trial types: involved hand on go trials; uninvolved hand on go trials; involved hand on no-go trials; and uninvolved hand on no-go trials. Computation of each dependent variable will be explained first. Results of each analysis will then be described in turn.

For the involved hand on go trials, RT was computed as the time at which the force first exceeded 100 cN. Mean RT and its standard deviation were then computed across trials of high probability and trials of low probability. Peak force (PF) and size of the force impulse (IS) were computed as measures of force for the involved hand on go trials. PF was computed as the peak value of force on the impulse for that trial. IS was computed as the total integrated force in excess of the criterion level of 100 cN. Both PF and IS were computed for the following reasons. For go trials of all participants, the force pulse always showed an initial rise that monotonically increased to a peak, followed by a monotonic decrease back to a rest (baseline) level, as would be expected for a normal keypress response (Fig. 1). In developing the appropriate dependent measures for making comparisons across groups, we needed to consider that some Parkinson's disease patients (Experiment 2) demonstrated a slight tremor during responding, and physiological tremor often occurs even in neurologically normal controls. We observed that these tremor signals were cyclical, with a slight positive value followed by a slight negative value. Although this cyclicity produces negligible changes in the size of the overall force impulse, any single measure of PF may be less reliable than total force integral. To be consistent in our analyses of all groups, both the mean and the standard deviation of PF and IS were computed for go trials of the involved hand.

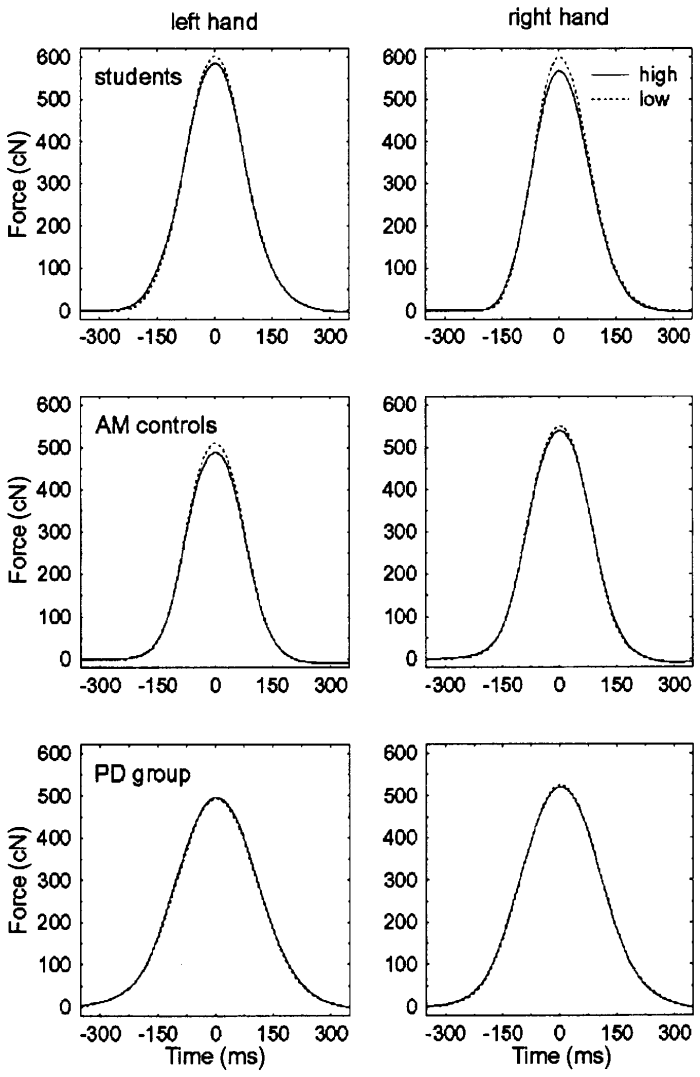

Fig. 1 Average force impulse for high- and low-probability go trials for the involved hand. The impulses are time-locked to PF and averaged separately for the left and right hands. Averages for each hand are shown for student controls (*top panels*), AM controls (*middle panels*) and the Parkinson's disease group (*lower panels*).

For the remaining three trial types (uninvolved hand on go trials, involved hand on no-go trials, and uninvolved hand on no-go trials), the most feasible approximation of impulse size was computed. Note that these trials did not result in regularly shaped force profiles because often only a residual level of force was produced without an actual keypress response (Figs 2–4). We therefore refer to these as 'mean force' (MF), given that the force profile did not usually resemble an impulse. Moreover, these force profiles tended to be quite irregular and variable across the response interval, even within individuals. To preserve any reliable differences that occurred at particular time windows of the response interval, we divided the 1500 ms interval following stimulus presentation into 15 epochs of 100 ms. These epochs will be referred to according to the middle point of each. For example, the label for the 0–100 ms epoch is '50'. MF was calculated for each of the 15 epochs for the three different trial types. Because the force

Table 1 *Mean response measures of student controls: involved hand on go trials with high and low probability*

	Reaction time (ms) Cue condition		Peak force (cN) Cue condition		Impulse size (cN) Cue condition	
	High	Low	High	Low	High	Low
Mean	354	391	618	643	23 207	23 856
SD	102	123	196	211	10 146	9946

level in these trials did not tend to reach our cut-off criterion for RT, only force was analysed. Both MF and its standard deviation were analysed separately for each of the 15 epochs.

Separate ANOVAs (analyses of variance) were conducted on the mean and standard deviation of RT and IS for the involved hand on go trials using the within-subjects factors Hand (left, right) and Cue (high probability, low probability). The same analyses were performed for MF separately for each of the 15 epochs for all remaining trial types. To avoid long lists of statistical results for the 15 separate epochs, where statistically significant effects span more than one contiguous interval the F values are reported in a combined form as being less than or greater than a particular value. Similarly, where null effects apply for more than one epoch or factor in the analysis, we often simply state $F < 1.00$ or $P > 0.05$.

Results

Go trials

Figures 1 and 2 show the averaged force–time patterns on go trials of the involved and uninvolved hands. As can be seen from Fig. 1, the force–time patterns of both hands appeared relatively smooth and bell-shaped for the student controls (upper panels). In contrast, the averaged force–time patterns were quite variable for the uninvolved hands (Fig. 2, upper panels).

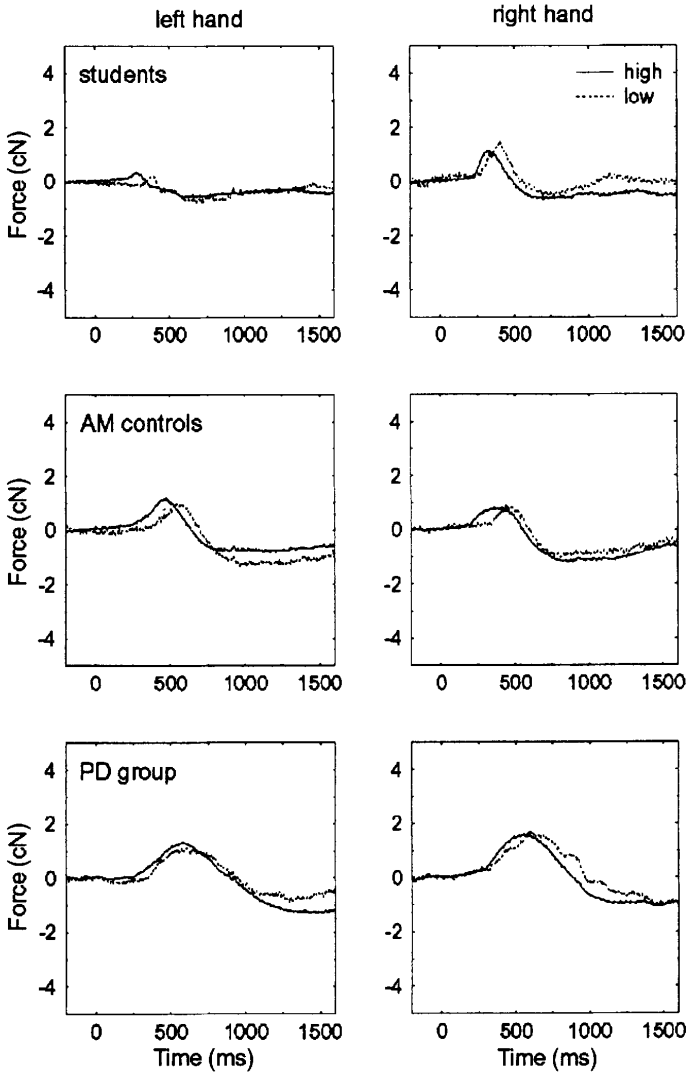

Fig. 2 Mean force computed across the 1500 ms interval following stimulus presentation for the uninvolved hand for high- and low-probability go trials. Averages for the left and right hands are shown for the student controls (*top panels*), AM controls (*middle panels*) and the Parkinson's disease group (*lower panels*).

Response errors

The overall percentage correct was 98.7, indicating that few errors were produced across all participants. Errors did not differ across Cue condition or Hand, nor did these factors interact (all $P > 0.05$).

RT

As expected, there was a highly significant effect of Cue condition on mean RT of the involved hand, with a faster average RT on high-probability compared with low-probability trials [$F(1,19) = 25.17$, $P < 0.001$]. The average values for each dependent variable for the effect of Cue appear in Table 1. Hand produced an unexpected, although only marginally significant, main effect on RT [$F(1,19) = 3.59$, $P = 0.07$], with the mean RT slightly longer for the left hand (mean = 378 ms) compared with the right (mean = 367 ms). The Cue × Hand interaction was not significant [$F(1,19) = 0.71$, $P > 0.05$]. There were no significant main effects or interactions on the standard deviation of mean RT for the involved hand on go trials [Cue, $F(1,19) = 2.76$, $P = 0.11$; Hand and Cue × Hand, both $F(1,19) < 1.00$].

PF and IS: involved hand

As expected from previous studies, the mean PF of the involved hand on go trials was smaller in the high-probability condition than in the low-probability condition [$F(1,19) = 6.89$, $P = 0.017$]. Hand did not produce a main effect on mean PF, nor did Hand and Cue condition interact for the involved hand (both $P > 0.05$). There were no significant main effects

or interactions on the standard deviation of PF for the involved hand (all $P > 0.05$).

There were no statistically reliable main effects or interactions on impulse size for the involved hand. However, as can be seen from the values in Table 1, the effect of Cue condition was in the expected direction [$F(1,19) = 2.20$, $P = 0.15$]. Close examination of Fig. 1 (upper panels) reveals that the difference between the high and low Cue conditions is slightly larger for the right hand (difference = 1272 cN) than for the left hand (difference = 27 cN), but this Cue × Hand interaction was only marginally significant [$F(1,19) = 3.31$, $P = 0.09$]. The main effect of hand did not approach significance [$F(1,19) < 1.00$]. There were no other main effects or interactions on mean IS or its standard deviation (all $P < 0.05$).

MF: uninvolved hand

For later epochs of the trial (epochs 850–1050), the uninvolved hand produced a significant level of force output on go trials [all $F(1,19) > 4.85$, all $P < 0.05$]. These epochs generally followed RT of the involved hand, suggesting that a form of bimanual coupling in residual force may have occurred on the output of the uninvolved hand.

For the first 500 ms (five epochs of 100 ms each), a larger MF was produced by the right hand than by the left, as can be seen in the top panel of Fig. 2. This main effect was statistically significant for four out of five of the epochs of this interval [all $F(1,19) > 5.00$, all $P < 0.05$] and marginally significant for the remaining epoch [epoch 150, $F(1,19)$ 3.63, $P = 0.072$]. Cue condition also interacted with Hand in epochs 50, 150, 650, 1050, 1150 and 1250 [all $F(1,19) > 5.00$, all $P < 0.05$]. The pattern of this interaction generally revealed that the right hand produced a larger MF on low compared with high-probability trials, whereas the left hand produced the opposite pattern. These results indicate that, at some epochs following stimulus presentation, even the uninvolved hand produced a measurable force, and the magnitude of this force was generally larger for the right hand than for the left. With respect to the time epochs of these primary effects, differences between hands tended to occur early in the trial, on average, and the interaction of Cue and Hand tended to occur at the later epochs. There were no other significant main effects or interactions on MF produced by the uninvolved hand on go trials.

No-go trials

Averaged force–time patterns for the involved and uninvolved hands of no-go trials appear in Figs 3 and 4, respectively. As can be seen in Fig. 3 (upper panels), the student control group produced a small peak in force on high-probability trials that was not apparent in the low-probability trials. In addition, as can be seen in Fig. 4 (upper panels), the force–time patterns were quite variable about the 0 force level for the uninvolved hand of the student control group.

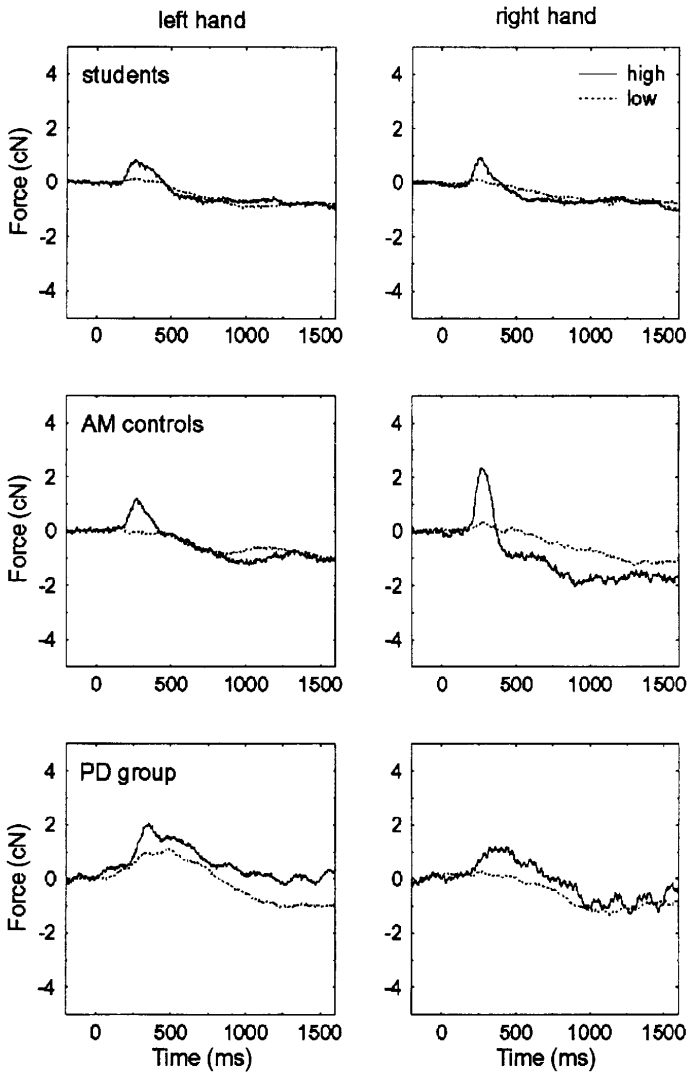

Fig. 3 Mean force computed across the 1500 ms interval following stimulus presentation for the involved hand for high- and low-probability no-go trials. Averages for the left and right hands are shown for student controls (*top panels*), AM controls (*middle panels*) and the Parkinson's disease group (*lower panels*).

Response errors

Fewer errors overall were produced in the low-probability condition (percentage correct = 99.0) compared with the high-probability condition (percentage correct = 94.8) [$F(1,19) = 11.97$, $P = 0.003$]. The average number of errors did not differ for the left and right hands, nor was there a Cue × Hand interaction (both $F < 1$).

MF

As can be seen in Fig. 3 (upper panels), a small level of force was apparent on the no-go trials for both hands. This level of force was significant in epochs 150–650 [all $F(1,19) > 8.26$, all $P < 0.05$]. This finding is novel, given that force output has not been examined previously on no-go trials. At epoch 250, MF was larger on high- compared with low-probability trials [$F(1,19) = 8.63$, $P = 0.008$]. This difference was approxi-

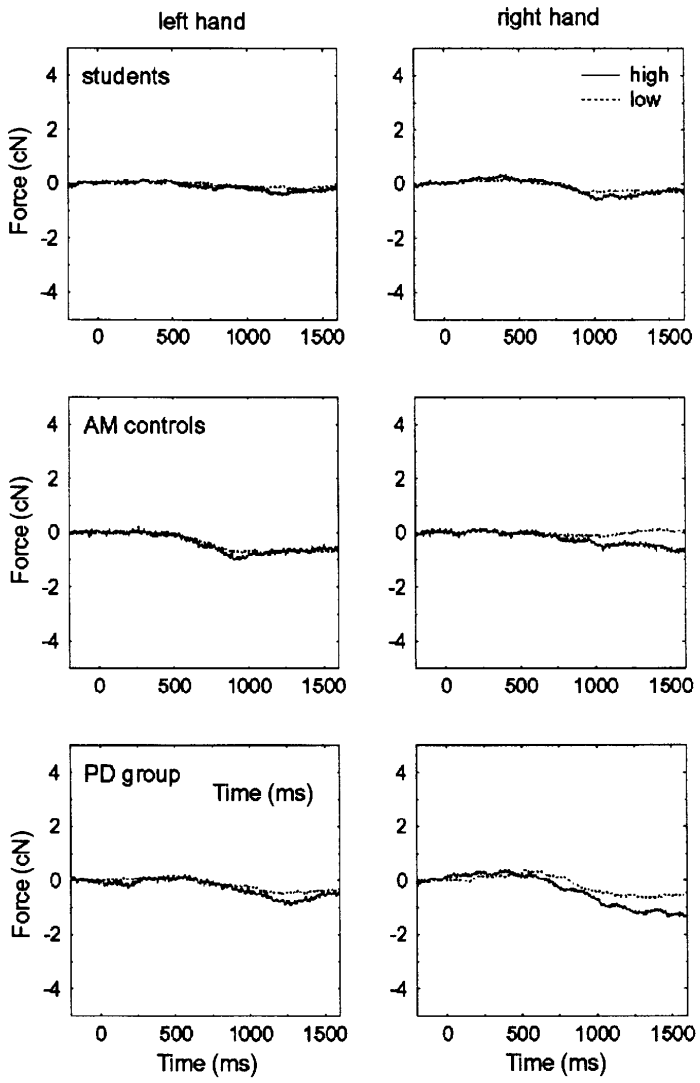

Fig. 4 Mean force computed across the 1500 ms interval following stimulus presentation for the uninvolved hand for high- and low-probability no-go trials. Averages for the left and right hands are shown for student controls (*top panels*), AM controls (*middle panels*) and the Parkinson's disease group (*lower panels*).

mately equivalent for the left and right hands [$F(1,19) < 1.00$]. Although a significant force level occurred in epochs 150–650, MF was not differentiated on the basis of Hand or Cue for any of these epochs. In addition, there were no main effects or interactions on MF of the uninvolved hand on no-go trials (all $P > 0.05$). The average force–time profiles for the uninvolved hand on no-go trials can be seen in Fig. 4 (upper panel).

Discussion

As expected on the basis of previous studies, this experiment showed faster RT and smaller PF for high-probability compared with low-probability responses in a young group of neurologically normal control participants. The main effect of Cue was not significant for IS on go trials, counter to what we may have expected on the basis of the PF measures. However, differences in IS across the two Cue conditions were in the expected direction, with a larger impulse occurring on the low-probability compared with the high-probability trials. These impulses were quite variable, both across trials and across subjects, which may account for the lack of statistical significance of this main effect. Indeed, it is clear from the values presented in Table 1 that the ratio of the standard deviation to the mean was proportionately larger for the IS measures (ratio ~0.43) compared with the PF measures (ratio ~0.32).

Unlike in past studies, we tested the effects of manipulating the probability Cue on the left and right hands separately. There was a marginally significant difference between the hands on both RT and IS for the involved hand on go trials. This result suggests that testing the two hands separately may be reasonable, especially for patient groups in whom one hand may be affected more than the other.

For MF, we attempted to capture effects that may be apparent at specific epochs of time, particularly for residual force effects that may occur on no-go trials, and for the uninvolved hand on both go and no-go trials. The addition of a force measure to the standard RT measure revealed two novel and potentially interesting findings. First, the uninvolved fingers generally produced small but significant force outputs. Thus, responding did not seem to be a totally all-or-none process. Secondly, for the involved hand, MF was significantly larger on high- compared with low-probability no-go trials in the 200–300 ms epoch. This clear peak in the force–time function (Fig. 3, top panel) may be suggestive of an early weak response that is especially large on high-probability no-go trials. We suggest that this response is 'early' because it occurs before RT would normally occur in the case of a go trial. Notably, mean RT for go trials occurred between 350 and 400 ms. We investigated further whether this peak may have been due to excessively large forces on few trials or whether the effect was somewhat stable across trials. A frequency distribution of PF values was computed for each trial type using bin widths of 10 cN. Frequency distributions for three of the four trial types can be seen in Fig. 5 (top panels). The omitted condition in Fig. 5 is the involved hand on go trials, for which PF was generally much larger than 100 cN (see horizontal axis of the graphs). As can be seen from Fig. 5, the student controls produced force pulses predominantly within the range of 10–50 cN, with no obvious outliers. Therefore, some level of PF is usually observed, making it unlikely that a significant peak in force was the result of averaging a few aberrant trials.

To summarize, in addition to the two novel findings, results of the present manipulation of stimulus–response probability replicated those of previous work for RT and PF. Furthermore, the general pattern of effects on IS was in the predicted direction. These findings are consistent with the elaborated motor readiness model (Näätänen, 1971; Mattes and Ulrich, 1997). We therefore felt it was appropriate to apply the same procedures to the testing of Parkinson's disease patients and age-matched controls. The primary

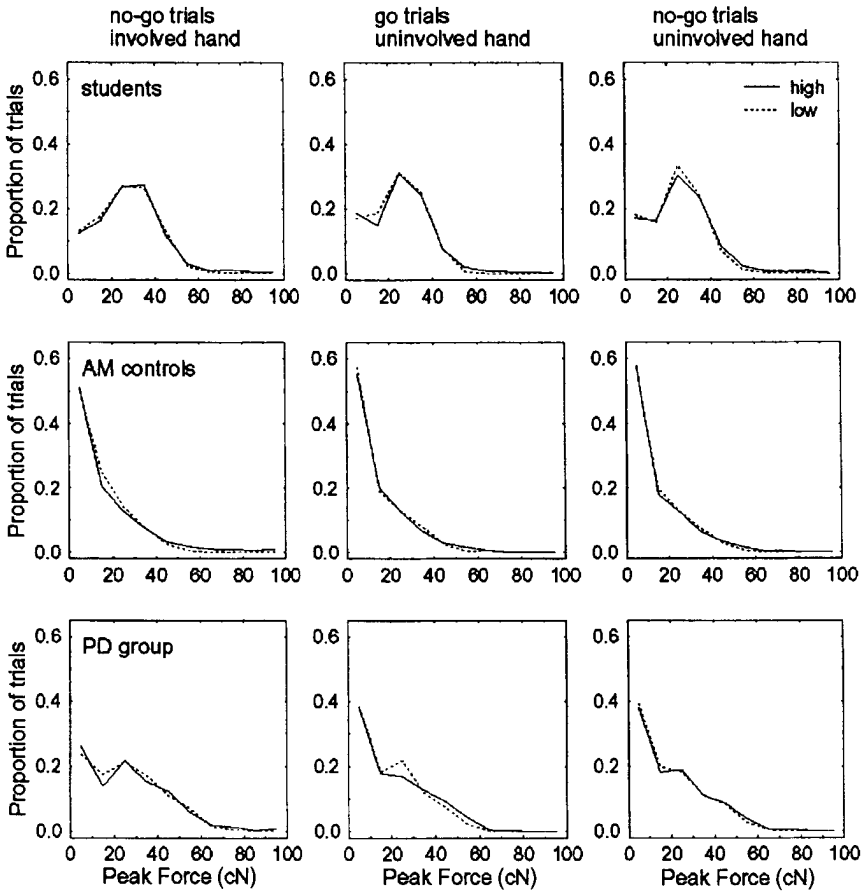

Fig. 5 Frequency distributions of PF values are shown for the involved hand for no-go trials and the uninvolved hand on go and no go trials. The proportion of trials within each bin of of 10 cN width was computed across the range of 0–100 cN. Average data for each trial type are shown for student controls (*top panels*), AM controls (*middle panels*) and the Parkinson's disease group (*lower panels*).

question of interest was whether differential patterns of response activation would be observed in the patients.

Experiment 2: Methods

The experimental group consisted of 12 people with mild to moderate Parkinson's disease, recruited from local Parkinson's disease community organizations. Participants were right-handed and there were equal numbers of males and females. The age range for the Parkinson's disease group was 55–76 years (mean = 66.0, SD = 6.07). All participants underwent a pretest examination that included a number of standard neurological and motor tests and a depression inventory. All participants scored very low on the Beck Depression Inventory (Beck *et al.*, 1961), indicating no marked signs of depression. No participant showed evidence of dyskinesia. Participants followed their normal medication schedules during testing, and they were tested at a time during the day that suited them best. Additional demographic details appear in Appendix 1.

The control group consisted of 12 age- and sex-matched right-handed controls (AM group). The age range was 59–74 years (mean = 65.1 years, SD = 4.25 years). No AM participant had any knowledge of any existing neurological condition, and all appeared to be healthy and normally active. This group underwent the same pretest examination that was administered in the Parkinson's disease group, and all showed normal performance for their age, both cognitively and motorically. The apparatus, procedure and design were identical to those of Experiment 1.

Data analysis

Mixed-design ANOVA was applied separately for each dependent variable for both groups combined using Group (AM and Parkinson's disease) as a between-subjects factor and Cue condition (High versus Low probability) and Hand (Left, Right) as within-subjects factors. These analyses were conducted separately for go trials and no-go trials and for involved and uninvolved hands. Note that for all trial types except the involved hand on go trials, separate ANOVA was applied to each of the 15 time epochs, as in Experiment 1. Otherwise the design of these analyses was identical to that applied to the involved hand of go trials. Those effects that

Table 2 *Mean response measures of AM and Parkinson's disease groups: involved hand on go trials with high and low probability*

		Reaction time (ms) Cue condition		Peak force (cN) Cue condition		Impulse size (cN) Cue condition	
		High	Low	High	Low	High	Low
Parkinson's disease							
Left	Mean	488	532	558	549	27 583	27 191
	SD	120	132	161	152	12 497	11 911
Right	Mean	484	516	575	563	27 985	26 413
	SD	125	128	154	137	12 199	9897
AM							
Left	Mean	455	483	493	512	15 820	16 461
	SD	119	90	137	134	6822	6748
Right	Mean	464	498	531	540	19 367	19 608
	SD	137	108	151	159	8523	8606

reached statistical significance to a level of 0.05 will be reported. Effects that were marginally significant and supported a meaningful pattern of results are also reported for completeness.

Results

Go trials

Figures 1 and 2 show the averaged force–time patterns on go trials of the involved and uninvolved hands, respectively. The force–time patterns of the involved hands appeared relatively smooth and bell-shaped for both the AM group (middle panel) and the Parkinson's disease group (lower panel). In contrast, the averaged force–time patterns were quite variable for the uninvolved hands of both groups, as shown in Fig. 2 (middle and lower panels).

Response errors

The overall percentage correct was 99.3 for the AM group and 97.7 for the Parkinson's disease group. No significant main effects or interactions were found on this variable (all $P > 0.05$).

RT

Analyses on the two groups combined revealed a highly significant main effect of Cue on mean RT [$F(1,22) = 16.75$, $P < 0.001$]. These results confirm that both the AM and the Parkinson's disease participants produced a faster mean RT on high-probability compared with low-probability trials, a finding that is consistent with Experiment 1 and earlier studies on normal controls. This small difference in RT between the groups was not significant [$F(1,22) < 1.00$]. No main effects or interactions on the standard deviation of RT came close to statistical significance [Cue × Group interaction, $F(1,22) = 2.79$, $P = 0.11$; all other main effects and interactions, $F < 1.00$]. These effects were confirmed by within-group analyses. The AM group produced a faster mean RT on high-probability trials compared with low-probability trials of the involved hand [$F(1,11) = 8.65$, $P = 0.013$]. Similarly, the Parkinson's disease group produced a faster mean RT on high-probability trials compared with low-probability trials [$F(1,11) = 8.32$, $P = 0.015$]. The mean and standard deviation of RT, together with corresponding values for both measures of force, are shown in Table 2 for each hand separately.

PF and IS: involved hand

For mean PF on the involved hand, there were no main effects of Cue or Hand, and these two factors did not interact (all $P > 0.05$). There was also no main effect of Group ($F < 1$). However, a marginally significant effect was found in the Cue × Group interaction [$F(1,22) = 3.60$, $P = 0.07$]. The pattern of the means revealed a trend in which a smaller mean PF was produced on high-probability trials (mean = 512 cN) compared with low-probability trials (mean = 526 cN) for the control group. However, a trend towards the opposite pattern was found in the Parkinson's disease group, with a higher PF on high-probability trials (mean = 566 cN) compared with low-probability trials (mean = 556 cN). This trend was potentially interesting, given that the Parkinson's disease group produced the opposite pattern to the AM group, the student controls in Experiment 1 and the earlier studies cited above. The Cue × Group interaction was also marginally significant for the standard deviation of PF, with a pattern similar to that found in the means just reported [$F(1,22) = 2.96$, $P = 0.10$]. The values of PF appear in Table 2 for both hands.

Consistent with effects on PF, the between-group analysis revealed that neither Cue nor Hand resulted in significant main effects on IS for the involved hand [both $F(1,22) < 1.00$]. Of primary importance was a significant Cue × Group interaction on IS of the involved hand [$F(1,22) = 4.88$, $P < 0.038$]. The direction of this interaction was disentangled using within-group analyses. For the AM group, IS was smaller, on average, for high-probability compared with low-

probability trials. However, the data were too variable to detect reliable differences [$F(1,11) = 1.92$, $P = 0.19$]. For the Parkinson's disease group, mean IS for the involved hand was larger for the high-probability trials (mean = 27 784 cN) compared with the low-probability trials (mean = 26 802 cN), but again there was too much noise in the data to yield a statistically significant effect on the within-group analysis [$F(1,11) = 3.074$, $P = 0.11$]. It is notable that, despite the wide range of variance in IS, the increased power of the between-group analysis revealed a clear interaction for the two groups depending on Cue condition. These values appear in Table 2. No other significant main effects or interactions were observed on IS in the between-group analyses (all $P > 0.05$). There were also no significant main effects or interactions on the standard deviation of IS for the involved hand on go trials [Cue × Group, $F(1,22) = 2.79$, $P = 0.11$; all other effects, $F < 1.00$]. Taken together, the data on Group × Cue interaction for both PF and IS suggest that the probability cue produced opposite patterns of results on force output for the two groups.

MF: uninvolved hand

A significant level of force output was produced in epochs 250–550 [all $F(1,22) > 6.49$, all $P < 0.05$], and the later epochs of 1050–1450 [all $F(1,22) > 6.68$, all $P < 0.05$] for the uninvolved hand on go trials for the two groups combined. Within-group analyses indicated that force output of the uninvolved hand was significant for the AM group only in epochs 150, 850 and 950 [all $F(1,11) > 4.97$, all $P < 0.05$], indicating that the effect was somewhat sporadic in the control group. For the Parkinson's disease group, significant levels of force output were found for epochs 350–650 [all $F(1,11) > 8.59$, all $P < 0.05$]. These effects are suggestive of a somewhat consistent force output of the uninvolved hand in the Parkinson's disease group in time epochs surrounding the RT of the involved hand. These effects may be accounted for by a form of bimanual coupling in force output.

With respect to MF, for epochs 650, 750 and 850 there was a main effect of Group [all $F(1,22) > 6.00$, all $P < 0.05$]. The AM group produced an MF of –0.49 cN averaged across the three epochs, indicating slight lifting of the key. Parkinson's disease subjects produced an MF of 0.85 cN, indicating a slight press on the key. A slight lift of the key may be suggestive of a volitional strategy to avoid responding. Although the performance of the AM group is consistent with this type of strategy, the Parkinson's disease group produced a residual force even with the uninvolved hand on time epochs following the time of response onset of the involved hand.

As in Experiment 1, we computed a frequency distribution of PF values using bins of 10 cN width to examine whether the distribution of PF was smooth across the range of PF values. As can be seen from the middle and lower panels of Fig. 5, the average distribution of PFs was relatively smooth across the range of PF values for both the AM and the Parkinson's disease group. However, close comparison between groups for all trial types suggests that the Parkinson's disease group produced comparatively more trials in the 20–40 cN range than the AM group, and comparatively fewer trials at the smallest force levels. Nonetheless, the relative smoothness of PF values across the distributions suggests that differences between groups were not due to a small proportion of trials with excessively large force values.

No-go trials

Averaged force–time patterns for the involved and uninvolved hands of no-go trials appear in Figs 3 and 4, respectively. As can be seen in Fig. 3 (middle panels), the AM group produced a small peak in force on high-probability trials that was not apparent in the low-probability trials, like the student controls. The Parkinson's disease patients (Fig. 3, lower panels) also produced higher force values on high-probability compared with low-probability trials, but the averaged force–time profile appeared much more variable than in the AM group. Interestingly, the Parkinson's disease group appeared to produce force even on the low-probability trials, unlike the other groups. In addition, as can be seen in Fig. 4 (middle and lower panels), the force–time patterns were quite variable about the 0 force level for the uninvolved hand of both the AM and the Parkinson's disease groups.

Response errors

The percentage correct on no-go trials was 98.3 for the control group and 97.5 for the Parkinson's disease group. There were no significant main effects or interactions on percentage correct (all $P > 0.05$).

MF: involved hand

A statistically significant level of force was produced in epochs 150–850 [all $F(1,22) > 4.96$, all $P < 0.05$]. As in Experiment 1, this reveals the novel finding that a significant force output occurs even on no-go trials.

For no-go trials, the primary effects in between-group analyses were observed for the involved hand. A clear main effect of Cue condition can be seen in Fig. 3 in the early epochs of 250 and 350 for the AM group (middle panel) and the Parkinson's disease group (lower panel). This effect was marginally significant for epoch 250 [$F(1,22) = 4.155$, $P = 0.054$] and significant for epoch 350 [$F(1,22) = 6.72$, $P = 0.017$]. For both groups, the force level was higher on high-probability compared with low-probability trials, which is similar to the effect shown by the student controls (upper panel).

MF differed for the two groups in epochs 450, 550, 650 and 750 [all $F(1,22) > 4.00$, all $P < 0.05$]. In all these epochs, the Parkinson's disease group produced a larger MF than the control group. As can be seen by comparing the middle and

lower panels of Fig. 3, this group difference appears to be due primarily to the wider distribution of force output across time for the Parkinson's disease group. Interestingly, on average across these epochs, the AM group produced an MF of –0.503 cN, which indicates a movement in the direction opposite to that required for a keypress movement. As mentioned above, this type of behaviour might be expected if one were to try to inhibit a movement by lifting rather than pressing the key. In contrast, the Parkinson's disease group produced an MF of 0.547 cN, indicating that these participants may have lacked the inhibition necessary to fully prevent a response from being activated.

For epochs including the range indicated for the main effects just described (epochs 450–850), Group significantly interacted with Cue for the involved hand [all $F(1,22) > 5.00$, $P < 0.05$, except for epoch 750, $F(1,22) = 3.61$, $P = 0.07$]. For all epochs within this range, AM control subjects produced a smaller MF on high- compared with low-probability trials. In contrast, the Parkinson's disease group produced larger MFs on high-probability compared with low-probability trials. In all cases, the MF was negative for the control subjects, again indicating that they actually lifted the key slightly, on average. In contrast, the values were predominantly positive for the Parkinson's disease group. This interaction can be clearly seen by comparing the middle and lower panels of Fig. 3. Note also that the direction of this interaction was similar to that observed for the involved hand on go trials. There was also a main effect of Hand in epochs 450, 550, 850 and 950, indicating that the force level was slightly smaller for the left hand compared with the right [all $F(1,22) > 4.0$, all $P < 0.05$]. Because these epochs were quite distributed, these effects of Hand do not seem particularly revealing.

For the uninvolved hand, the only significant effect across all epochs was a main effect of Group observed in epochs 550 and 650 [both $F(1,22) > 6.00$, both $P < 0.05$]. For these epochs, the AM control subjects lifted the key slightly, whereas the Parkinson's disease subjects produced small downward keypress responses. Note that these two intervals were within the range in which group differences were found for the involved hand (although they are too subtle to see in Fig. 4, middle and lower panels). This may be suggestive of a form of bimanual coupling in force, which surprisingly occurred even on no-go trials.

Discussion

This experiment compared the performance of Parkinson's disease patients and AM controls on a task that manipulated response readiness by varying the probability of responding. From the continuous force–time function on go trials, RT and two measures of force were assessed—PF and IS. Our primary interest was in whether Parkinson's disease patients would show evidence of impairments in response activation, which we predicted would be apparent in their atypical patterns of force output. Using a go/no-go task also enabled us to assess whether impairments in response activation are present even when participants are required to withhold the response.

Consistent with the effects on student controls in Experiment 1 and with previous studies, both groups produced faster RTs on high-probability compared with low-probability trials. Thus, the two groups were not differentiated on the basis of RT, a variable believed to reflect response preparation processes. The primary effects of interest were on measures of response force. For both measures of the force amplitude (PF and IS), control participants produced smaller values of force on high-probability go trials compared with low-probability go trials for the involved hand, consistent with previous findings. In contrast, Parkinson's disease patients produced the opposite pattern of results, with larger forces on high- compared with low-probability trials. These differential patterns of force output despite similar patterns of RT with the probability cue point to processing differences between the two groups at the late stages of response activation. The observed pattern of results on response force is consistent with the possibility that Parkinson's disease participants produce a constant increment of force regardless of the level of internal activation. This possibility will be considered in more detail in the General Discussion.

Another primary question of interest in this study was whether Parkinson's disease patients would show evidence of impairments in response activation even on no-go trials. Although it has not been reported previously, both groups did produce small increases in force output on no-go trials. Interestingly, for both the involved and the uninvolved hand, Parkinson's disease patients produced a larger MF compared with control participants on no-go trials for time epochs ranging from 400 to 800 ms following stimulus presentation. This is suggestive of a lack of ability to inhibit responding completely. Note that we were unable to record RT on these trials because the force level did not reach the criterion of 100 cN. Considering the mean RT on go trials as a reasonable estimate, it appears that MF differences between groups began to occur at a point in time that coincided (approximately) with average RT for each of the groups. The elevation in MF for the Parkinson's disease group persisted for an additional 250 ms (or so), suggesting that the apparent problems in inhibition remained even after a response of average latency would have already been produced. These results suggest that, in addition to a problem in inhibiting an unwanted movement, Parkinson's disease patients may experience problems in rapid termination of the transmission of force output to the motor system.

In addition to group differences on no-go trials for epochs ranging from 400 to 800 ms following stimulus presentation, Group also interacted with Cue on these trials. This Group × Cue interaction produced the same general pattern of results as for the involved hand on go trials. Specifically, control participants produced a smaller MF on high-probability compared with low-probability trials, whereas Parkinson's disease participants produced the opposite pattern.

Force output was also measured for the uninvolved hand on both go and no-go trials. For the uninvolved hand on go trials, a larger MF was produced by the Parkinson's disease group compared with the AM group. For the uninvolved hand on no-go trials, similar effects differentiated the two groups on time epochs ranging from 500 to 700 ms only. The same general pattern occurred as in the go trials, revealing a higher force output for the Parkinson's disease group compared with the AM group. Interestingly, these particular time epochs follow the time that mean RT would be predicted to occur on go trials. This leads to the inference that, for no-go trials, the residual force output on the uninvolved hand occurs after rather than before the time when the response would normally occur. The similarity of effects for the involved and uninvolved hands is suggestive of a form of bimanual coupling in force across the hands.

General discussion

Operations of the basal ganglia have been implicated in a wide variety of motor and cognitive functions including response initiation, procedural learning and task switching in humans (see Introduction). It is difficult to discern what properties are common across this multitude of tasks in an attempt to hypothesize what, if any, basic function(s) the basal ganglia actually perform. This study investigated the possibility that one function of the basal ganglia is related to response activation. Parkinson's disease was used as a model of impaired basal ganglia function.

The present data indicate that properties of response force are influenced differently in Parkinson's disease participants by probability manipulations of response readiness. The primary effects on force output revealed a pattern of results that is opposite to the pattern produced by controls. In addition to abnormal patterns of force output with response readiness manipulations, the present results are suggestive of a general problem of inhibiting motor output when responses are to be withheld (no-go trials). Both of these primary effects may lead to implications about the modulation of response activation to the motor system, one operation that may underlie the abnormal patterns of force output. Before considering putative operations of the response modulator, we discuss implications of the lack of group differences on RT and total force output.

A number of earlier studies on the effects of Parkinson's disease have used RT as the primary dependent measure. As described in the Introduction, some of these studies reported significantly longer simple RTs in Parkinson's disease participants compared with controls (e.g. Heilman *et al.*, 1976; Bloxham *et al.*, 1984, 1987), leading to the suggestion that deficits in Parkinson's disease are related to preprogrammed responding. However, some inconsistency has been reported concerning whether or not Parkinson's disease participants are able to use advanced information to plan responses (Bloxham *et al.*, 1984; Rafal *et al*, 1984, 1989; Stelmach *et al.*, 1986). In particular, the finding that Parkinson's disease participants are able to benefit from valid peripheral cues that precede the presentation of targets challenges the strong claim that these participants are unable to process advance information related to movement planning (Rafal *et al.*, 1984).

Flowers (1978) found that Parkinson's disease participants failed to employ the normal strategies of prediction during visual tracking, suggesting the possibility of impairments in the internal mode on which prediction depends. It seems plausible that the impairments associated with the simple RT studies described earlier may also reflect internally generated processes rather than failure to incorporate information related to external cues. The present findings shed new light on this possibility, given that the observed impairments relate to force activation and modulation with levels of response readiness, which are undoubtedly dependent on internally driven processes.

As the above arguments suggest, accumulating evidence indicates that measures of response force reveal information that cannot be determined from measures of RT alone. Most previous experiments that have measured both RT and response force with manipulations on response readiness in neurologically normal subjects have reported increases in both RT and response force with low compared with high levels of response readiness. Of these, recent experiments reported within-subjects correlations between RT and response force as being close to 0 (Mordkoff *et al.*, 1996; Mattes and Ulrich, 1997; Mattes *et al.*, 1997; Ulrich *et al.*, 1998). Moreover, some stimulus manipulations have been found to affect RT and response force differently. For example, Ulrich *et al.* (1998) found that measures of response force were affected by a larger range of stimulus duration than were measures of RT. The present study supports a neural distinction between RT and measures of response force, given the similarity between groups in RT despite differences in the patterns of force.

The present findings on response force are consistent with the elaborated response readiness model described earlier. According to the model, the motor action limit is the threshold of internal response activation that must be exceeded in order for an overt response to occur. According to findings based on neurologically normal participants, a high level of response readiness during response preparation results in a level of internal activation that is close to the motor action limit. In contrast, a low level of response readiness results in a level of internal activation that is further below the motor action limit. A number of studies, including the present one, have demonstrated that neurologically normal individuals produce a higher level of force output in conditions of low compared with high response readiness, as though they overshoot the amount of activation necessary to initiate a response when the level of response readiness is low. These findings indicate that the normal system modulates force output on the basis of the level of internal activation (or response readiness).

On the other hand, the system does not appear to modulate force output on the basis of response readiness in Parkinson's disease patients. The significant Group × Cue interactions on measures of force, and specifically the relative lack of cueing effect on force in this group, suggest a disruption in the interface between the current level of internal activation and the level of activation needed to generate an overt response. As indicated earlier, the present study did not explicitly require subjects to manipulate the forcefulness of their responses. However, force-related deficits have been documented in previous work using explicit force requirements. For example, using isometric force tasks involving elbow flexions, Stelmach and colleagues have reported that Parkinson's disease participants have correct internal representations of force level, as shown by their ability to attain a value of force that matches a visually presented cursor. However, the force profiles produced by Parkinson's disease participants were more irregular, and the rates of force production were slower than those of control participants (Stelmach and Worringham, 1988; Stelmach *et al.*, 1989). Thus, it appears that the ability to programme a desired force level is not affected, but the explicit regulation of force is more variable with Parkinson's disease. In addition, the present results indicate that implicit force-regulatory mechanisms are also disrupted in Parkinson's disease.

Studies on handwriting in people with Parkinson's disease have also revealed problems related to force output. Margolin and Wing (1983) examined handwriting in people with Parkinson's disease to test predictions of a force impulse model developed by Wing (1978). According to the model, changes in letter height when writing may be due to changes in applied force or in the timing of the strokes that make up the trajectory of handwriting. Margolin and Wing concluded that micrographia, or the diminution of handwriting size that occurs with Parkinson's disease, is due to a decrease in force rather than being the result of timing effects. The diminution of writing size continues as one keeps writing, which suggests that force levels decrease further through successive attempts at activation. It may therefore be the case that, with continuous movements, impairments of force modulation are somewhat cumulative. Similarly, our results may be viewed as suggesting that force is lower with more preparation time (low-probability trials) than with less preparation time (high-probability trials). On this interpretation, our results indicate that decreases in force in Parkinson's disease may come about through longer response preparation as well as through longer response execution.

Consistent with the research just described, the level of force was not statistically different between the Parkinson's disease and AM groups in the present study. Thus, it does not seem that Parkinson's disease patients are impaired in recruiting the appropriate level of force output, in this case using brief finger-press responses. Furthermore, given that the patterns of effects on RT were not significantly different for the two groups, we can conclude that both groups are able to recruit the levels of activation necessary to initiate a response elicited by a visual cue. Instead, the abnormality seems to arise during the final generation of an increased activation pulse to initiate the overt response; this pulse seems to be larger than necessary or optimal in Parkinson's disease patients. Importantly, the present study examines force activation with fast, discrete responses, not throughout the course of movement. Thus, while handwriting shows micrographia, or a diminution of force level, the present study demonstrates too high a force pulse under conditions of high response readiness. As suggested in the Introduction, Parkinson's disease presents a curious mix of symptoms that appears to reflect too little movement activation in some circumstances and too much movement activation in others. We propose that a basic deficit in response activation results in these two extremes. With slower ramp-like movements or normal speeds of handwriting, the problems in response activation may occur repeatedly throughout movement generation. One possibility is that a higher than normal force pulse occurs initially with high readiness, and this decays quickly through time. If taken to the extreme, continuous movements such as handwriting may require numerous reactivation cycles. If a diminution of force occurs with each repeated cycle of activation, the end result will be a lower than normal force, i.e. micrographia. Indeed, multiple EMG bursts have been observed in Parkinson's disease participants performing elbow flexion movements of a lever. Interestingly, these multiple bursts occurred at slow movement speeds, but not when participants were instructed to move fast (Teasdale *et al.*, 1990). In a recent model of micrographia in Parkinson's disease, a similar idea is elaborated with respect to specific operations of basal ganglia circuitry (Contreras-Vidal *et al.*, 1995). The remainder of this discussion will focus on the implications of the present findings for our understanding of the underlying neural processes, and possible models to account for specific aspects of these findings.

The neuroanatomical and functional properties of the basal ganglia complex make this circuitry a likely candidate for involvement in response activation. The output nucleus of the basal ganglia, known as the globus pallidus internus (GPi), receives input from direct and indirect circuits within the basal ganglia. Depending on the level of GPi activation, the thalamus becomes disinhibited via its direct input from the GPi. The thalamus, in turn, sends direct projections to the motor cortex, where volitional movement is initiated (DeLong, 1990). Damage to operations performed by this circuitry may therefore influence the modulation of internal levels of activation to the external levels of output registered as response force.

Ulrich and Wing (1991) described a Parallel Force Unit Model (PFUM), which may be useful in understanding the generation of force within the basal ganglia. This model formalizes the intuition that a rapid force pulse can be conceptualized as the summation of a number of independent force units. These units are each activated for a particular duration following a random delay that incurs due to noise in

Table 3 *Mean response measures for pre-peak impulse: Student, AM, and Parkinson's disease groups: involved hand on go trials with high and low probability*

	Cue	Impulse duration (ms)	Pre-IS (cN)	Pre-rate (cN)
Student controls	High	208	11 555	82*
	Low	207	11 636	85
AM controls	High	220	8994	65*
	Low	221	9178	67
Parkinson's disease group	High	357*	13 922†	70
	Low	352	13 368	70

*Significant within-group main effect of cue condition; †marginally significant main effect of cue condition. Pre-IS = prepeak impulse size; Pre-rate = prepeak average rate.

the system (for a clear depiction of this model see Fig. 2 of Ulrich and Wing, 1991). One important aspect of the model is that force pulses do not operate on an all-or-none basis but rather by modulation, at least in the normal system. According to the model, one mode of modulating PF is to vary the number of force units recruited. If this mode is adopted, the force–time function should be scaled to different sizes of the same basic form. Another mode is to increase the duration of activation of each force unit recruited. If this mode is adopted, then force–time functions will differ in shape as well as in PF.

Both PF and duration could be used as simple approximations to assess whether modulation of rate and/or duration were influenced differentially in the AM and Parkinson's disease groups. Because the increasing portion of the force impulse can be viewed as an indicator of response activation, we first computed the total force impulse from the 100 cN criterion level up to the PF (prepeak impulse size). Secondly, we computed an approximation of the average prepeak rate as the ratio of prepeak IS divided by the time from the 100 cN criterion to the time of PF. Thirdly, we computed the standard measure of impulse duration by calculating the length of time during which the force level exceeded the 100 cN criterion. These computations were applied to each go trial for the involved hand, and then averaged over trials for each participant. The values were then analysed using separate ANOVAs for each dependent variable, using the same within-subjects and between-subjects factors as in our primary analyses.

For brevity, we report and discuss only the significant effects for each group (at $P < 0.05$). Note that the effects that are not reported were not even close to reaching levels of statistical significance. The values for each dependent variable are shown in Table 3.

The group comparisons of the AM and Parkinson's disease participants were of primary interest. There was a significant interaction of Cue with Group for the pre-impulse size, indicating the same basic pattern of results as for the Group × Cue interaction for the total IS reported earlier [$F(1,22) = 5.09$, $P = 0.034$].

There was no main effect of Group ($P > 0.05$), but there was a significant Cue × Group interaction for the comparison of the AM and Parkinson's disease groups on the average rate of force output for the prepeak impulse [$F(1,22) = 5.83$, $P = 0.025$]. As can be seen from the values in Table 3, there was a faster average rate of force output on the low-probability compared with high-probability Cue condition in the AM group [$F(1,11) = 7.18$, $P = 0.021$]. These findings are consistent with those obtained for the student controls, although the latter effect was only marginally significant [$F(1,19) = 4.30$, $P = 0.052$]. In contrast, the average rate of force output was approximately identical for the two Cue conditions of the Parkinson's disease group [$F(1,11) = 1.13$, $P = 0.31$].

These results suggest that, for both control groups, the larger impulse size on low compared with high response readiness trials was correlated with a faster rate of force output. In contrast, the rate of force output in the Parkinson's disease group appeared to remain approximately the same across the two levels of response probability, despite this group's smaller IS on the low-probability compared with the high-probability trials. These findings suggest that while control participants altered the rate of force output with different levels of response readiness, the Parkinson's disease group did not.

The analysis of impulse duration was also quite revealing in terms of differentiating the Parkinson's disease and AM groups. In the AM versus Parkinson's disease comparison, there was a main effect of Group, indicating that the Parkinson's disease group produced a longer force duration, on average, than the AM group [$F(1,22) = 13.93$, $P = 0.001$]. This difference can be seen by comparing the middle and lower panels of Fig. 1 and by viewing the mean values in Table 3. Clearly, the Parkinson's disease group's average impulse is wider (and duration is longer) than the average impulse of the AM group. In addition, within the Parkinson's disease group there was a main effect of Cue condition on impulse duration, revealing a longer average duration on high- compared with low-probability trials [$F(1,11) = 5.048$, $P = 0.046$]. These results indicate that the larger impulse produced in the high- compared with low-probability Cue condition occurred with a longer impulse duration in the Parkinson's disease group.

It appears that control participants modulate the rate of force output to result in larger overall impulses in low-probability compared with high-probability conditions, with-

out changes in duration. In contrast, the force profiles of Parkinson's disease participants revealed a longer average duration for larger impulses, despite no differences in rate. Other research has demonstrated a tendency for Parkinson's disease patients to alter duration (movement time) rather than movement speed on certain types of movement tasks. For example, a very early study by Draper and Johns (1964, cited in Teasdale *et al.*, 1990) reported that Parkinson's disease participants produced a nearly constant movement velocity with movements of different amplitude compared with control participants, who demonstrated the normal increase in movement velocity with increasing amplitude. Similar findings were later reported by Flowers (1976). In a task that required displacement of a lever using an elbow flexion movement, Teasdale *et al.* (1990) found that Parkinson's disease patients could vary movement duration when the task demanded different movement speeds. However, the Parkinson's disease patients were slower to achieve PF than the control participants, and the initial impulse to the time of peak was longer in Parkinson's disease participants. Interestingly, these authors also suggested that deficits in Parkinson's disease are related not to calculating the required forces or energizing the muscles but to controlling the muscle activation.

Interestingly, Ulrich and Wing (1991) speculated, on the basis of the very limited data set available at the time, that perhaps damage to basal ganglia structures would produce deficits in force recruitment that are compensated for by increases in impulse duration. While our findings are consistent with the prediction that Parkinson's disease participants compensate for deficits in force modulation by changing impulse duration, an even simpler interpretation arises from the elaborated response readiness model. The model assumes different levels of response readiness depending on probability cue. A high level of readiness prior to stimulus onset characterizes the high-probability condition. A low level of readiness prior to stimulus onset characterizes the low-probability condition. If Parkinson's disease patients produce a constant increment in activation regardless of this prior level of response readiness (as described earlier), then the measurable region of the force impulse would be wider (i.e. of longer duration) on high compared with low response readiness conditions. The apparent differences in duration across cue conditions may therefore be a direct consequence of the differences in level of activation exceeding the motor action limit.

With respect to no-go trials, a novel finding from the present results is the small force pulse that occurs at the early time epochs for all groups (Fig. 3). This pulse is larger, on average, for high-probability compared with low-probability trials. At this time, it is unclear how the elaborated response readiness model can account for this novel finding of an early weak response in force. Because the frequency distributions of peaks revealed a reasonable spread across all values of PF for all groups (Fig. 5), this average peak in force appears to be evidence of an early weak response that occurs on the majority of trials, particularly under conditions of high response readiness on no-go trials.

Model simulations by Ulrich and Wing (1991) revealed that, at small levels of force, holding the number of force units constant while varying duration resulted in a skewed rather than a symmetrical force–time profile. In our data, the small force output produced on no-go trials of Parkinson's disease patients reveals an average force–time function similar to the model's prediction (Fig. 3, lower panel). The force level appears to decay much more slowly with time, on average, than the force level produced by either of the control groups. It is possible that, with a normal response activation system, one operation initiates the process of force modulation to the motor system and another causes it to terminate. Accordingly the latter operation may be impaired in Parkinson's disease. This operation may be akin to a form of active inhibition that would normally halt transmission of force to the motor system. Indeed, the differences between the AM and Parkinson's disease groups in force level even on no-go trials are suggestive of a rather late component of residual force in the patients. It is clear from Fig. 3 (middle and lower panels) that the decay of force level takes more time in Parkinson's disease participants than in controls. Other research has demonstrated, using presses of a strain gauge apparatus, that people with Parkinson's disease demonstrate problems in releasing force in order to resort to a baseline level (Kunesch et al., 1995). These authors suggested that people with Parkinson's disease may be unable to interrupt a motor programme that is already engaged.

A slight variation of the possibility raised above is that, once the process of force modulation begins, this process is unable to switch efficiently back to its inactive state. This may be one instance of a switching problem of the type that Benecke *et al.* (1987) initially observed.

In summary, the present results point to one function of basal ganglia circuitry as being related to response activation and deactivation processes. With manipulations of response readiness, Parkinson's disease participants produced patterns of force output opposite to those of the control groups despite similar patterns of RT. The Parkinson's disease group produced larger average impulses, and impulse duration was measurably longer, following high-probability compared with low-probability cues. In contrast, the controls produced smaller average impulses and a slower rate of force following high- compared with low-probability cues. The elaborated model of response readiness can account for these findings easily, which strongly suggest that the Parkinson's disease participants produced a constant increment in activation in order to initiate a response, regardless of the prior level of response readiness. The normal system, in contrast, modulates the level of output activation depending on the prior level of response readiness. In addition, the Parkinson's disease group demonstrated an increased force output at the later stages of no-go trials and similar effects were found for the uninvolved hand, which is suggestive of a form of bimanual coupling of force. This novel effect also extends the

notion that the motor output system is unreliable and noisy in people with Parkinson's disease. We attribute these effects to impairments at the late stages of response activation and deactivation. These processes appear to depend on the integrity of basal ganglia structures.

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Appendix 1
Details of Parkinson's disease group

Subject	Sex	Age (years)	Education (years)	Years since onset	UPDRS-L	UPDRS-R	MMSE	Digit span	Medication
1	M	61	10	18	12	14	29	6	Sinemet, amantadine
2	F	64	10	4	8	7	27	8	Medopar
3	M	55	11	4	12	8	29	5	Sinemet
4	F	70	7	4	3	3	28	6	Sinemet, Sinemet CR
5	F	64	10	9	12	6	29	8	Sinemet
6	M	71	8	10	7	6	26	6	Sinemet
7	M	69	8	12	17	16	30	6	Eldepryl, Propananol
8	F	76	8	13	7	8	27	6	Sinemet, Sinemet CR
9	F	73	9	3	3	2	28	7	Sinemet
10	M	66	16	5	7	4	29	5	Sinemet
11	F	64	15	5	18	13	27	7	Sinemet
12	M	59	10	5	12	12	29	5	Sinemet

UPDRS = Unified Parkinson's Disease Rating Scale; L = left hand; R = right hand; MMSE = Mini-Mental State Examination.