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Precision grip and Parkinson's disease

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Summary

In order to investigate sensorimotor processing and force development in Parkinson's disease, 16 patients, four patients with hemiparkinsonism and 12 age-matched normal subjects were assessed during lifting and holding of an object in a precision grip between thumb and forefinger, or holding the object in this grip at a fixed height above a table. In the former case, object loading could be changed between lifts without warning. In the latter case, unexpected step load changes to the object were applied to the object with a torque motor. All procedures could be applied with or without visual control of the hand and the object. Normal subjects lifted an unpredictable load employing the grip force parameters used in the preceding lift. If a load change was encountered, the parameters became adapted to the new conditions during the lift, modulating grip forces to match the loading. Parkinsonian patients retained this strategy and the ability to regulate grip forces according to load. Under all conditions, however, parkinsonian subjects developed abnormally high grip forces in both the lift and the hold phase, although the ratio of these forces remained normal. Lifting height was normal in parkinsonian subjects, but the duration of the lifting task was significantly prolonged, due to a marked slowing in the rate of grip force development in the lead-up to object lift-off and to prolongation of the movement phase. Forewarning of object loading, with or without visual control, did not reduce timing deficits or improve the rate of grip force development. However, it did allow parkinsonian subjects to reduce the safety margin significantly. Responses to step load changes imposed during holding without visual control showed minor abnormalities in the parkinsonian patients: onset latencies and EMG activity in the first dorsal interosseus and thenar muscles were normal up to 140 ms after displacement. Subsequent EMG activity in the first dorsal interosseus remained largely normal, but activity later in the slip response (140–210 ms), subject to voluntary influence, was reduced in the thenar muscle. Differences were less marked under visual conditions, but remained significant. We concluded that the internal parameter set for lifting an object in a precision grip and the automatic processes adapting precision grip to actual conditions are intact in Parkinson's disease. However, parkinsonian subjects generate abnormally high grip forces and require longer than normal subjects to complete a lift, particularly with lighter loads. This deterioration in performance reflects both reduced effectiveness of sensorimotor processing and impairment in the rate of force development in Parkinson's disease.

Keywords: Parkinson's disease; sensorimotor; precision grip

Abbreviations: FDI = first dorsal interosseus; PMA = premotor cortex; SEM = standard error of the mean; SMA = supplementary motor area

Introduction

Any study of the motor deficits arising from neurological conditions in which quantitative assessment of movement parameters and the extent of pathological changes are to be measured requires standardization of the movements chosen for study. This has often led to the use of externally imposed movement, or self-generated movements of a highly simplified and hence highly artificial nature. Given the complexity of our nervous system and of the motor tasks that have to be performed under functional conditions, it should not be automatically assumed that such studies will yield meaningful data about either the pathophysiology of motor disorders or, indeed, the problems facing affected patients on a day-to-day basis.

In the case of Parkinson's disease, for example, it is known that deficits in relatively simple motor tasks, such as scaling isometric forces (Stelmach and Worringham, 1988) and slow movements where accuracy and speed are not of cardinal importance (Montgomery and Nuessen, 1990), are relatively unaffected. This is in contrast to the situation with fast, accurate movements (Berardelli *et al.*, 1986, 1996) and in tasks involving a sequence of movements (Benecke *et al.*, 1987; Agostino *et al.*, 1992) or the simultaneous performance

of tasks (Schwab *et al.,* 1959; Benecke *et al.*, 1986). It has also been suggested (Currà *et al.*, 1997) that parkinsonian patients show greater abnormalities during internally generated movements than in movements made in response to external, environmental cues. Marsden (1989) has proposed that such a dichotomy may arise from the far greater involvement of the supplementary motor area (SMA) in the former mode. The SMA is thought to be a major projection area for the basal ganglia. Marsden has argued, therefore, that damage to the basal ganglia would disrupt the functioning of the SMA and particularly affect self-generated movements. When, however, a movement is made in response to and under the guidance of external cues, the SMA is thought to be much less involved (Goldberg, 1985), the major role now being played by the premotor cortex (PMA), which receives significantly less input from the basal ganglia. Thus deficits in such motor tasks might be thought to be much less affected in Parkinson's disease. It is thus desirable to study a paradigm which, while involving a meaningful degree of complexity and representing a normal part of our motor repertoire, may nevertheless be standardized to an extent that allows intersubject evaluation.

One such task is the lifting of an object in the hand using a precision grip. This paradigm has been investigated extensively in normal subjects by Johansson and his co-workers (for review see Johansson, 1996). They have shown that lifting in a precision grip is achieved by a complex but reproducible sequence of voluntary activity, which involves arm positioning, preparation of the fingers for gripping the object, and then the appropriate development of finger grip forces combined with lifting and bracing activity in the wrist, elbow and shoulder musculature. In addition it has been demonstrated that this task contains elements of memory, the grip force parameters being recalled as a set on a predictive basis with the assumption that object loading will have remained unchanged from the last encounter (Johansson and Westling, 1988; Gordon *et al.*, 1993). It has also been shown that such a parameter set can be modified automatically during an ongoing lift when sensory information (predominantly cutaneous afferent information from the hand and lower arm (Johansson and Westling, 1984, 1987) indicates that a change in loading has been encountered (Johansson, 1991).

In addition to these self-generated, 'internal' motor programmes, a further set of automatic motor responses acting to stabilize grip forces on an object have also been well characterized following slip of an object held in a precision grip, whether spontaneous or externally induced (Cole and Abbs, 1988; Johansson *et al.*, 1992*a*, *b*, *c*). Such responses might be considered to fall into the second class of 'responsive' motor tasks defined by Marsden (1989).

However, although precision grip has been studied extensively in normal subjects, its application to patient groups with motor disorders has been limited to a very few pilot studies (Müller and Abbs, 1990; Hermsdörfer *et al.*, 1994; Fellows *et al*., 1997). It was therefore decided in the present study to utilize the precision grip paradigm to investigate the motor deficits of patients with Parkinson's disease, using both the self-generated lifting paradigm and the automatic responses to object slippage.

Lifting was performed under three conditions. (i) The first condition used unpredictable changes in object load occurring between lifts. This part of the study was intended to reveal basic deficits in the performance of this internally generated task, as well as to investigate the extent to which predictive and adaptive changes in grip force were preserved in Parkinson's disease. Some evidence exists that while even complex patterns of movement can be learnt by parkinsonian patients, they are particularly impaired in switching between two such learnt tasks within a trial (Robertson and Flowers, 1990). The predictability of an object's behaviour (Bloxham *et al.*, 1984) and the visual control of an object (Cooke and Brown, 1979; Klockgether and Dichgans, 1994) have been suggested to lead to an improvement in the performance of parkinsonian patients, possibly due to the greater involvement of the PMA, for which the visual cortex is an important afferent source, under these conditions (Goldberg, 1985; Marsden, 1989). Therefore the lifting task was also studied (ii) with object load constant and known to the subject in advance and (iii) with predictable, unchanging load and, additionally, visual control of the hand and object. The possible expression of this SMA/PMA dichotomy in the motor behaviour of parkinsonian patients was further evaluated by studying the functional, automatic, but cortically mediated responses to an unexpected load change of an object held in a precision grip.

Method

Subjects

The present study involved 16 patients (aged 46–82 years; 11 male, five female) with Parkinson's disease who, at the time of examination, were being treated as in- or out-patients of the neurological clinic of the University of Aachen. Four patients with hemiparkinsonism (aged 42–73 years; all male) were also studied. All patients were examined in the 'on' condition. Clinical details are given in Table 1. Twelve age-matched subjects (aged 43–77 years; six male, six female) with no neurological abnormalities acted as a control group. All subjects gave their informed consent to the procedures, which had previously been approved by the Ethics Committee of the Universitätsklinikum, Aachen.

Apparatus

The experiments were performed in a quiet room with subdued lighting. The subjects were seated in a stable chair before a table on which the lifting apparatus (Fig. 1A) was placed. A curtain could be drawn between the subject and the apparatus when required in order to remove visual cues concerning hand position. The original Johansson paradigm, which involves lifting an object free to move in space, was

Table 1*Clinical details of patients*

Patient	Sex*	Age (years)	Duration of symptoms (years)	UPDRS score†
Clinical details of the parkinsonian patients				
1	M	65	9	63
2	M	72	4	75
3	M	82	11	57
4	M	76	4	29
5	M	72	4	45
6	F	76	5	25
7	F	74	9	59
8	M	73	9	19
9	M	64	8	37
10	M	58	2	23
11	M	65	12	33
12	M	59	5	111
13	F	74	5	45
14	F	66	6	49
15	M	74	<1	73
16	F	45	<1	35
Clinical details of the hemi-parkinsonian patients				
1	M	42	3	24
2	M	59	8	20
3	M	67	1	19
4	M	73	<1	22

*M = male; F = female. †Unified Parkinson's disease rating scale: activities of daily living and motor scores (items 5–31), maximum 160.

modified both to make the task more manageable for the patients and to obtain more accurate standardization of lifting and externally applied load changes in order to simplify the quantitative assessment of changes in Parkinson's disease. The device consisted of an aluminium block that was free to move in the vertical plane on a low-friction track. This change, by preventing lateral movement of the object, rendered the present paradigm less natural than the classical paradigm developed by Johansson, but nevertheless the task remained to a large extent functional, offering great advantages over the more artificial tasks usually employed in clinical studies, while still allowing a degree of standardization of the task. The block was in two parts, to each of which was attached a plastic disk that was contacted by the tip of the fully extended thumb and forefinger respectively. These disks were interchangeable in order to allow the frictional properties of the grip surface to be varied: in the present study two sets were used, one set covered with sandpaper, the other with silk. The subjects were required to keep the other fingers away from the apparatus while lifting the block (usually achieved by flexing these fingers) and to rest the elbow of the active arm on a padded support. A force transducer (9301B, Kistler, Winterthur, Switzerland), mounted between the two halves of the block, registered the grip force exerted on the block by the subject. The block was also connected, via a non-elastic band, to a servo-controlled torque motor, which varied the load the subject was required to lift. A second force transducer mounted between the block and this band registered the vertical load force acting on the block. With no extra torque from the motor, the block and transducers represented a load of 3.3 N. A laboratory computer (Macintosh IIvx, Apple, Cupertino, Calif., USA) controlled the output of the motor via the analogue outputs of an analogue-to-digital converter board (NB-MIO-16H, National Instruments, Austin, Tex., USA) and a servo device in order either to vary the static load of the device before a lifting trial or to apply rapid step increases in the load force during a maintained lift. This computer also generated trigger events to initiate sampling. A position signal was provided by a linear potentiometer (T60500, VAC, Germany) mounted as part of the track. EMG signals were obtained from the first dorsal interosseus (FDI) and thenar muscles using 8 mm diameter silver surface electrodes taped over the muscle belly and tendon. These signals were amplified, filtered (gain 1000, bandwidth 10 Hz to 10 kHz) and passed, together with trigger, grip force, load force and position signals, to the analogue-to-digital converter board (NI-PCI-MIO-16XE, National Instruments) of a second computer (Power Macintosh 7600/132, Apple), which, using the LabView 4 analysis package (National Instruments), sampled each channel at 2.5 kHz, displaying the data on-line and saving it to disk for later analysis.

Procedures

The total experimental time was between 45 and 55 min, depending on the attention span and stamina of the subjects. The study period was divided into three sections. The

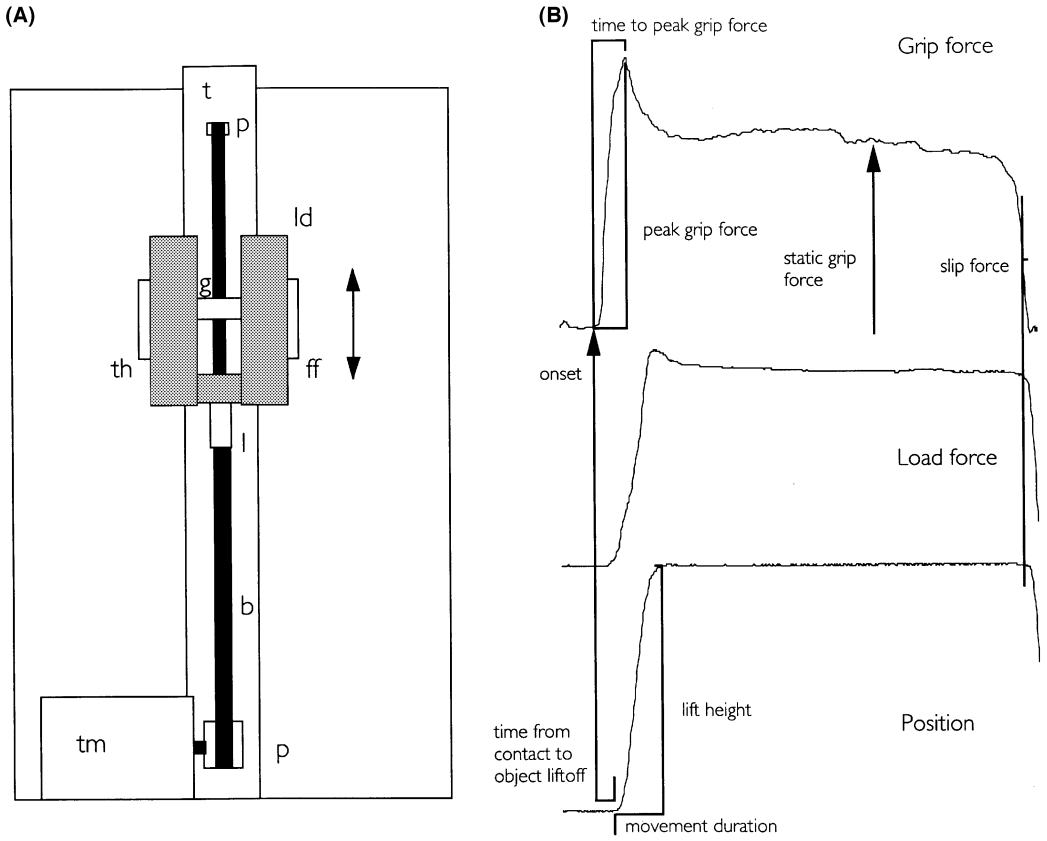

Fig. 1 (**A**) The lifting apparatus. β = connecting band; ff = forefinger grip; g = grip force transducer; l = load force transducer; ld = load; t = track; th = thumb grip; p = pulley; tm = torque motor. (**B**) Grip force, load force and position traces from a typical normal lift, illustrating the parameters measured for each lift.

first, 'unpredictable loading', examined the responses of the subjects to unexpected changes in the load of the object between two successive lifts. Under such conditions it has been demonstrated that a subject initiates a lift using the parameters (e.g. the grip force profile) appropriate to the load encountered in the previous lift (Gordon *et al.*, 1993). Should the load encountered differ from that expected, normal subjects are able to adjust their lifting parameters to appropriate values within the course of a lift (Westling and Johansson, 1984). In order to examine the extent to which this predictive and adaptive behaviour is preserved in Parkinson's disease, the following protocol was employed: the subjects were required to grasp and lift the block 4–8 cm above the table in one smooth action, hold the end position for 5–6 s, then, on command, to open the fingers slowly and let the block fall. The subject was unable to see the hand and had no pre-information on the loading of the block, which was varied pseudorandomly between one of two levels, namely 3.3 and 7.3 N. The grip surfaces were of sandpaper. A total of 21 lifts were performed, so that, discarding the first trial with no prehistory, five trials were obtained for each of the four conditions: light load following light load ('light'); light load following heavy load ('unload'); heavy load following light load ('load'); heavy load following heavy load ('heavy'). Each lift was separated by a 15–20 s pause.

In order to examine the effects of uncertainty and the importance of visual feedback about hand position on the lifting responses of the normal subjects and the patients, a second series of lifts, 'predictable loading', was then performed. This series consisted of 10 lifts. The subjects were informed at the outset that the block would be unloaded (i.e. 3.3 N) and were asked to make the series as consistent as possible in terms of lifting height and movement velocity. After five lifts the subjects were shown the height they had reached in the previous series and were asked to reproduce this in the remaining five lifts with full view of their hand.

The final series, 'unexpected loading', examined the grip force adjustments evoked by a situation simulating spontaneous slip of an object held in a precision grip. For this series the subjects were required to maintain the unloaded block (3.3 N) at a steady height 4–6 cm above the table. The grip surfaces for this section were of silk. Step increases in the load (2 N in 10 ms) were then randomly applied at intervals of 15–20 s. Subjects had been informed not to actively resist such loading events, in order to minimize voluntary contamination of reflex responses. Ten such trials were applied with and without visual control of the hand. Any trial in which the block escaped the patient's grasp was eliminated from later analysis and repeated, but this was a rare occurrence.

Analysis

For lifting trials a series of parameters was obtained for each lift, as shown in Fig. 1B, which represents a typical unloaded (3.3 N) lift from a normal subject. The starting point for the analysis was the first increase in the grip force signal, indicating contact of the finger and thumb with the block. Two timings were made from this point: that to the first increase in the position signal (initial grip to lift), and that to the peak value in the grip force signal (time to peak grip force). The magnitude of the peak grip force developed up to the attainment of a stable end position (peak grip force) and the static grip force at an arbitrary point 4 s after initial contact were also measured. In addition, the duration of the lifting phase and the height of the final hold position were measured. Finally, the grip force at which the block escaped the subject's grasp (slip force; Westling and Johansson, 1984) was estimated. From these parameters two further values were calculated: the difference between static grip force and slip force 'safety margin'), and the static grip force, expressed as a percentage of the peak grip force.

For the step load, changes during holding each sequence of 10 unexpected load changes were checked for artefacts and contaminated sweeps were eliminated; then, after rectification of the EMG signals, the changes were processed to yield the average response. Averaged EMG curves were then normalized by dividing them by the mean EMG level in the 200 ms period preceding the step load change. These curves were further processed to obtain the cusums, from which were obtained the total EMG activities in the intervals 70–140 and 140–210 ms after onset of the load step. In addition, after evaluating any differences between the subjects for initial position, load force or grip force, these initial values were subtracted from their respective curves to standardize their starting values and allow the construction of grand average responses.

Statistics

Non-parametric statistical analysis of the data was performed using the StatView 4.5 package (Abacus, Berkeley, Calif., USA). Group averages for the lifting section were obtained by combining the median value under a given condition of each subject. Where appropriate, data were evaluated using the Friedmann test, the Mann–Whitney *U* test, the Spearman rank correlation or the Wilcoxon signed rank test. Second-order polynomial regression modelling was performed using the same package.

Results

Unpredictable loading

As would be expected from the findings of Johansson and his co-workers (Gordon *et al.*, 1993), normal subjects showed clear evidence of selection of lifting parameters on the basis of the last lift experienced: that is, they began a lift with the assumption that conditions would be as in the last lift. Peak grip forces were significantly modulated according to the lifting conditions ($P < 0.0001$), significantly higher peak grip forces being developed when the heavier load was encountered compared with values for the lighter loading ($P = 0.0022$). In addition, however, peak grip force values for lifts under 'unload' conditions were slightly but significantly higher ($P = 0.0029$) than in lifts under 'light' conditions. This is indicative of a force profile selected with the assumption of a heavy load, but terminated at a lower value when sensory information indicated that a light load had in fact been encountered. Curves for the grip force for a typical normal subject are shown in Fig. 2A. Each trace is the average of five lifts under a given condition. The figure also displays the corresponding responses of a typical patient with Parkinson's disease. It may be seen that peak grip force levels were markedly higher under all conditions in the parkinsonian subject.

Figure 2B shows the group averages (± SEM) for the peak grip force under each of the four lifting conditions. It is apparent that the parkinsonian subjects developed significantly higher grip forces under all conditions. It is equally apparent, however, that they maintained the ability to scale force according to load, developing significantly higher forces during 'heavy' lifts than in those under the 'light' condition ($P = 0.0007$). Furthermore, the parkinsonian patients maintained the normal 'memory' strategy of assuming that load would remain unaltered from the last lift, as demonstrated by the significantly higher peak forces developed in the 'unload' than in the 'light' condition ($P = 0.0097$). But although peak forces in the unload condition were higher than those in the light condition, they were also significantly lower than those developed in the heavy condition ($P = 0.0008$). Thus the parkinsonian patients also retained the ability to modify a lift when sensory information indicated a change in loading.

Returning to Fig. 2A, it may be seen that normal subjects reduced grip force to a more or less stable level (the static grip force) once the object had attained the desired position. Figure 2C shows that the magnitude of the static grip force was also clearly dependent on load ($P < 0.0001$). This relationship was retained in the parkinsonian subjects ($P < 0.0001$), but they still produced inappropriately high grip forces for a given load ($P = 0.0004$). Figure 2D displays the static grip force represented as a percentage of the peak value during a lift. It may be seen that the relationship between the two parameters was normal in the parkinsonian patients under all lifting conditions. Thus, although the parkinsonian patients were able to correctly select and modulate grip forces according to the load encountered, they invariably employed an abnormally high level of grip force at all stages of their lifts.

From Fig. 2A it may also be seen that not only the magnitude but also the timing of the grip force change was abnormal in the parkinsonian patients, displaying a marked slowing. The graph on the left-hand side of Fig. 3A shows the grip force curves from the initial phase of a lift under

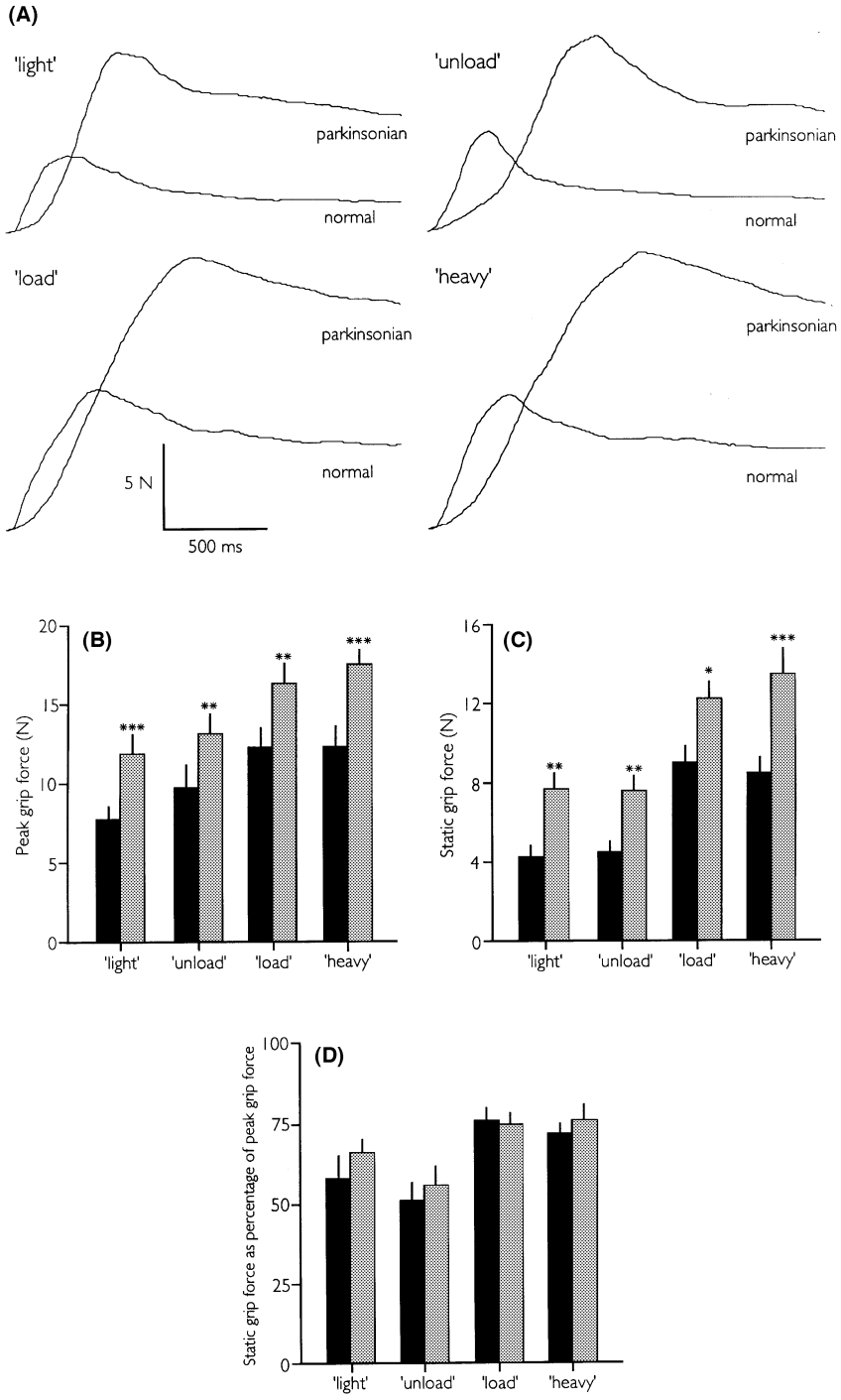

Fig. 2 (**A**) Mean grip force curves obtained from the five lifts performed under each of the four conditions for a representative normal subject and a parkinsonian patient. (**B**) Quantitative data for peak grip forces used under each of the four lifting conditions. Each bar represents the group mean ± SEM. Filled bars are normal subjects; shaded bars are parkinsonian patients. (**C**) Group means for static grip force obtained under each of the four lifting conditions. In **B** and **C** asterisks indicate statistically significant differences between the groups (*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$). (**D**) Group means for the static grip force expressed as percentages of the peak grip force in each of the four conditions.

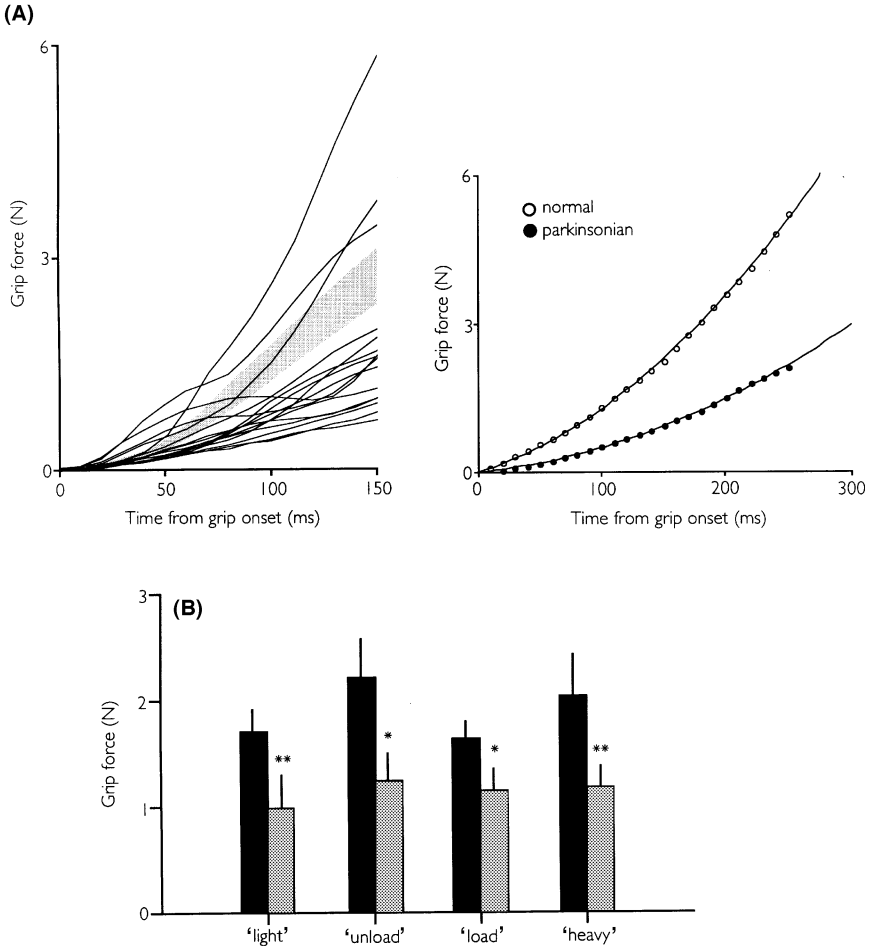

Fig. 3 (**A**) In the graph on the left the thin lines show grip force development from the early stages of a lift under 'light' conditions for the parkinsonian patients. The shaded area represents the normal mean (± SEM). The graph on the right-hand side illustrates the excellent fit of a second-order polynomial model to these curves for a representative normal subject and a parkinsonian patient. $y = a_{*}x + b_{*}x^2$. All $P < 0.0001$; $r^2 > 0.96$. (**B**) Group means (± SEM) for the predicted grip force after 100 ms obtained for each subject from this model, showing the significant reduction in the rate of grip force development in the parkinsonian patients (black bars). ($^{*}P < 0.05$; $^{**}P < 0.01$).

'light' conditions for each of the parkinsonian patients, along with the group mean (± SEM) for the normal subjects. It is apparent that all but three of the 16 patients lay below the normal range. The graph on the right-hand side of this figure illustrates that the initial phase of the grip force increase could be meaningfully modelled as a second-order polynomial in both the normal subjects and Parkinsonian patients.

Figure 3B displays the results of such a modelling: if the formula was used to predict the grip force developed after 100 ms, a significantly lower force than normal had been reached in the parkinsonian patients under all lifting conditions Thus the parkinsonian subjects not only developed higher peak grip and static hold forces, but showed greatly retarded rates of grip force development. Together, these factors had a marked effect on the timing of lifts performed by the parkinsonian patients.

The time from the initial contact between the fingers and the block to the first vertical displacement (that is, the time taken to get the block in motion) is given for each of the four lifting conditions in Fig. 4A. It may be seen that this time was significantly prolonged by ~50% in the parkinsonian subjects under all conditions. A similar prolongation was seen for the time taken to reach peak force value (Fig. 4B). These delays were matched by an increase in the duration of the movement phase (Fig. 4C), which was significantly longer in the parkinsonian patients than in the normal subjects under all conditions. Furthermore, the significant prolongation of movement duration seen in the normal subjects with heavier loads was lost in the parkinsonian subjects, due to a proportionally greater slowing of movement in lifts involving the lighter load. Figure 4D shows the lifting heights achieved by both groups under each of the four conditions. These were unchanged from normal values, indicating that the prolongation of the movement phase cannot be attributed to an increase in lifting height.

Due to the small number of patients studied, the responses

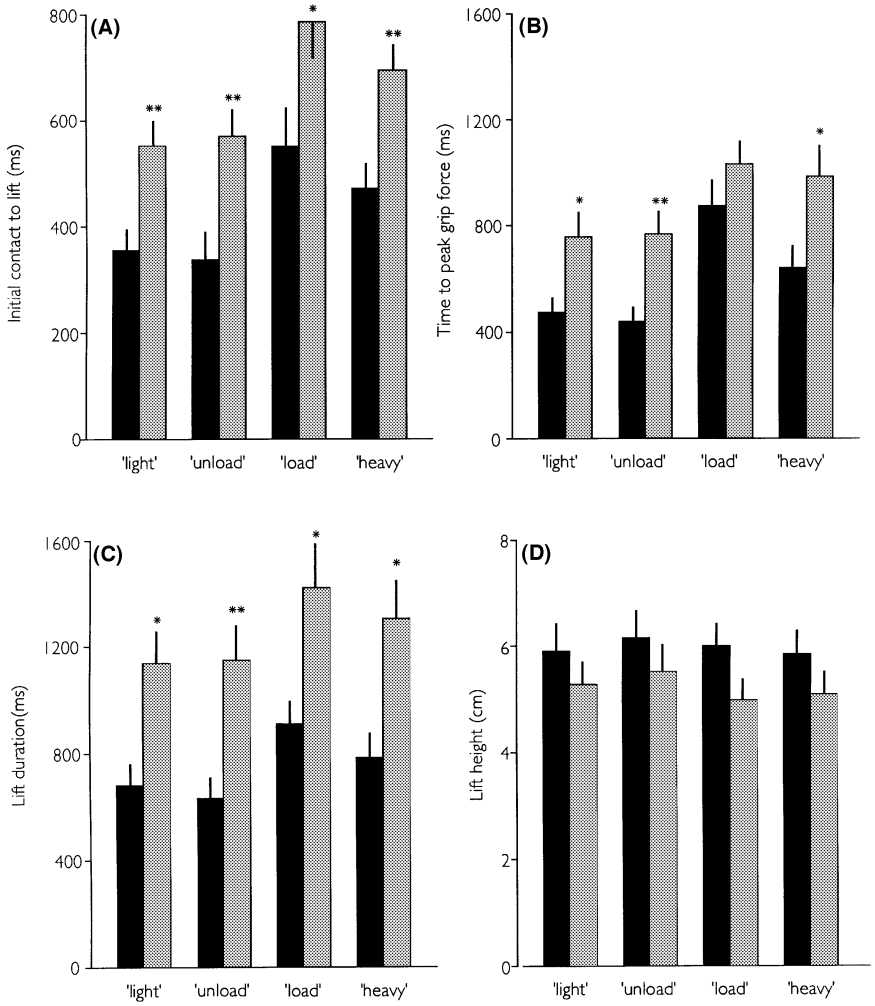

Fig. 4 Quantitative data for timings and amplitudes of lifts under each of the four conditions. Each bar represents the group mean ± SEM. Filled bars represent normal subjects; shaded bars represent parkinsonian patients. Asterisks indicate statistically significant differences between the groups (*$P < 0.05$; **$P < 0.01$).

of the hemiparkinsonian patients were not evaluated statistically. Qualitatively, however, it was apparent that the changes on their 'affected' side corresponded to those seen in the other parkinsonian patients. Figure 5 shows the grip force and position curves from a lift under 'light' conditions for both sides of one of the hemiparkinsonian subjects. A similar profile was obtained from the other three subjects. It may be seen that the 'affected' side showed both increased levels of grip force and a slowing of the rate of development, leading to a marked prolongation of the whole lifting task. On the 'unaffected' side the curves were more nearly normal, with lower levels of grip force and a faster rate of rise, so that the task was completed in a much shorter time. It should be noted, however, that the description 'unaffected' is not completely accurate: for instance, the grip force curves obtained from both sides of this patient revealed a small-amplitude action tremor. Nevertheless it is largely true that the hemiparkinsonian patients showed a typical pattern of changes predominantly on the 'affected' side.

Predictable and visual predictable loading

The performance of normal subjects in the lifting task was not discernibly affected either by providing the normal subjects with forewarning of the load to be lifted or by allowing visual control of finger position (for all parameters P was non-significant; Friedmann test). Similarly, no improvements in the timing deficits of lifts was observed in the parkinsonian patients. But, as may be seen in Fig. 6, providing parkinsonian patients with forewarning of the load to be lifted led to a reduction in the safety margin employed. This difference just failed to reach significance ($P = 0.057$), but additionally allowing the parkinsonian subjects to view their hand led to a further, highly significant reduction in the safety margin ($P = 0.0092$).

Unexpected loading

Under conditions of both visual and non-visual control, the parkinsonian patients were able to maintain the object at a

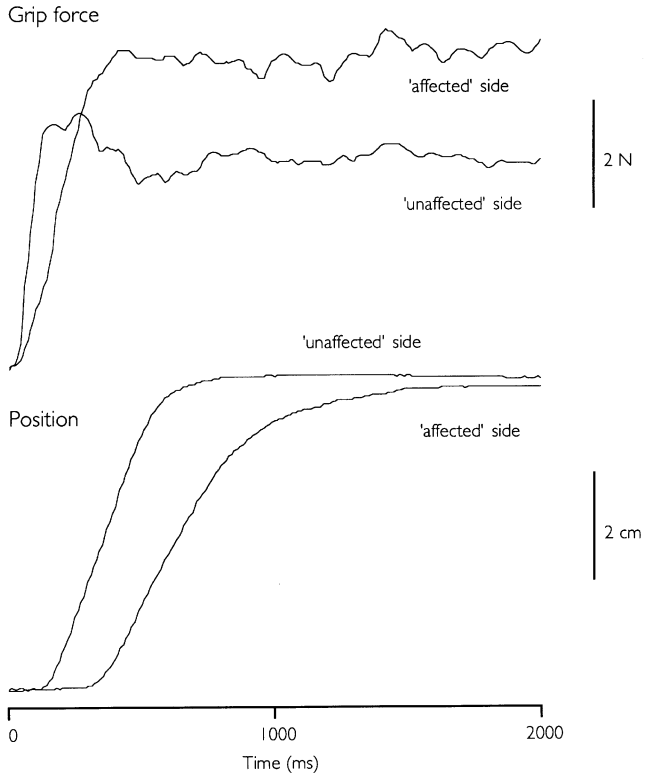

Fig. 5 Grip force and position curves obtained during a lift under the light loading condition on the affected and unaffected side of a typical hemiparkinsonian patient.

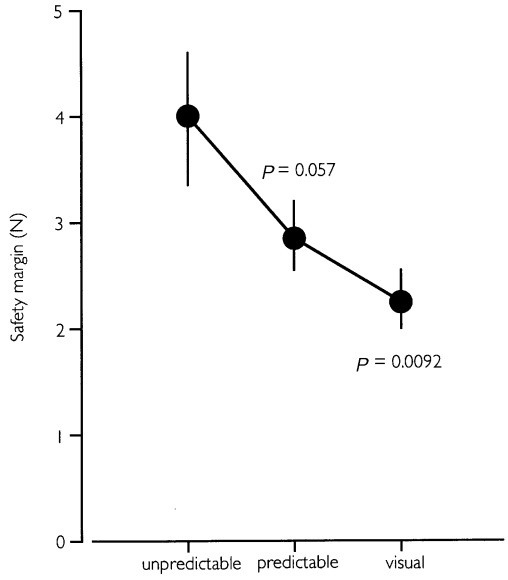

Fig. 6 The effect of foreknowledge of load, with or without visual control of hand position, on the safety margin employed while lifting a light load. Values are group means (± SEM) for the parkinsonian subjects. Overall significance with the Friedmann test, $P = 0.0136$. Significances are given for paired comparisons between unpredictable and predictable, and unpredictable and visual conditions.

stable height. In contrast to the situation in the shorter hold phases of the self-initiated lifts, where abnormally high grip forces were developed, the parkinsonian subjects were able to maintain position using grip forces within the range shown by the normal subjects. The unexpected load change displaced the block significantly further (2.5 mm) than was the case in normal subjects (non-visual control, $P = 0.0030$; visual control, $P = 0.0198$), but in all cases the parkinsonian subjects were able to retain their grip of the object. The reason for this larger displacement cannot be discerned from the data of the present study: the grip force curves in the first 100 ms after the load step, when most of the object displacement occurred, were identical in normal and parkinsonian subjects. As the fingers remained in contact with the block throughout this period, this displacement must have been induced at the wrist joint. It is possible, therefore, that the greater object excursion results from differences in the compliance of the wrist and forearm musculature (Hufschmidt *et al.*, 1991), which were not measured in the present study.

Figure 7 shows the grand average responses obtained without visual control in both groups. The onset latency of the response in parkinsonian patients was unchanged from normal values. Quantitative analysis of EMG activity was performed over several intervals, as follows: onset to 90 ms, in order to evaluate activity before any possible contribution from voluntary activity; 90–120 ms, to evaluate activity in the interval where voluntary activity, while possible, is unlikely to have played a role; and 120–140 ms, where a modulation of EMG activity was apparent in most subjects. No differences from normal values were seen in the parkinsonian patients in any of these intervals, or over the total interval from response onset until 140 ms, in either FDI or thenar muscles. Activity was also compared in the interval from 140 ms after loading until 210 ms, when the 'catch-up' response can be considered complete (Johansson, 1991). This later activity, which is likely to contain a sizeable voluntary contribution, was largely unchanged in the FDI, but was significantly reduced in the thenar muscle ($P = 0.0002$). This led to a flattening of the grip force curve in the parkinsonian subjects, although the peak value was not significantly lower than normal values. Later EMG activity (>210 ms) and the subsequent holding force were at normal levels.

Figure 8 shows the curves obtained from both groups under visual conditions. EMG activity in both the FDI and thenar muscles was normal in the parkinsonian patients in all intervals up to 140 ms. Again, however, a significant reduction ($P = 0.0098$) in the late (140–210 ms), voluntary-influenced EMG activity was apparent in the thenar but not in the FDI muscle. The peak of the grip force curve was also flattened, but again no significant differences from normal values were obtained. Similarly, later EMG activity (>210 ms) and the hold force in the plateau phase did not differ between parkinsonian subjects and normal subjects.

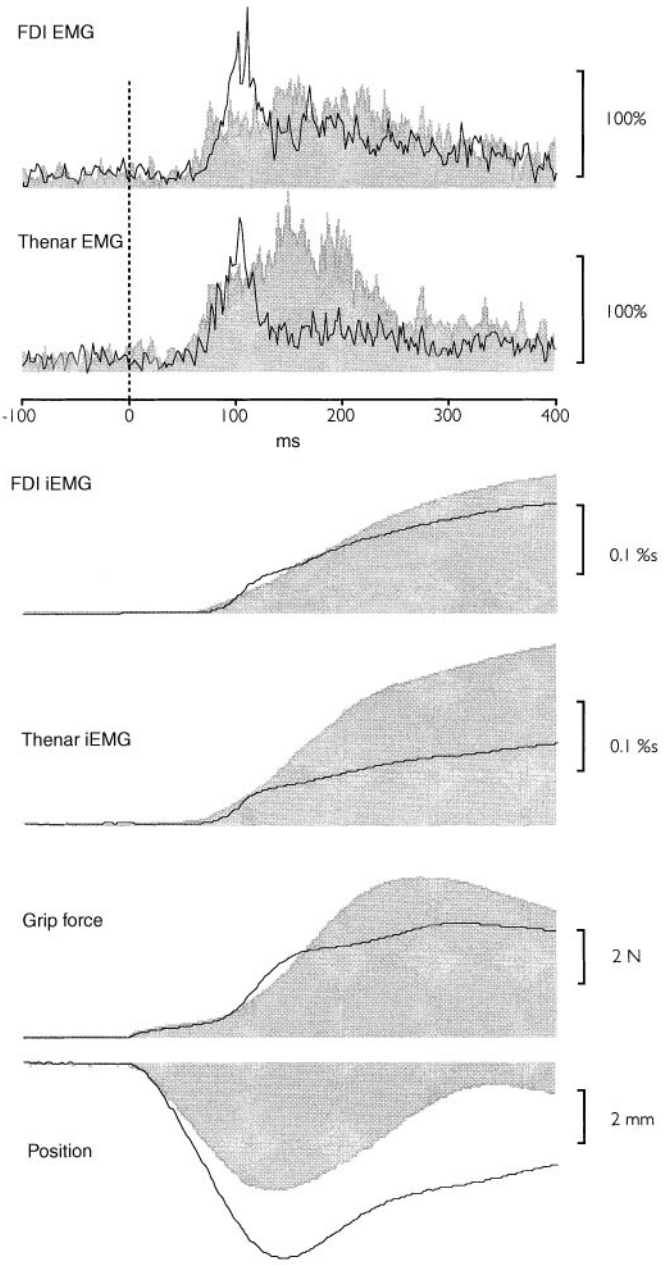

Fig. 7 Grand average responses to an imposed load change (2 N, 200 N/s) for the parkinsonian patients (lines) and normal subjects (filled shaded traces) without visual control of hand or object. The time axis applies to all traces. The dotted line arising from this axis indicates the point at which the load change was applied. From the top, the traces are: rectified and normalized first dorsal interosseus (FDI) EMG activity; rectified and normalized thenar EMG activity; integrated FDI EMG; integrated thenar EMG; grip force exerted on the object; object position.

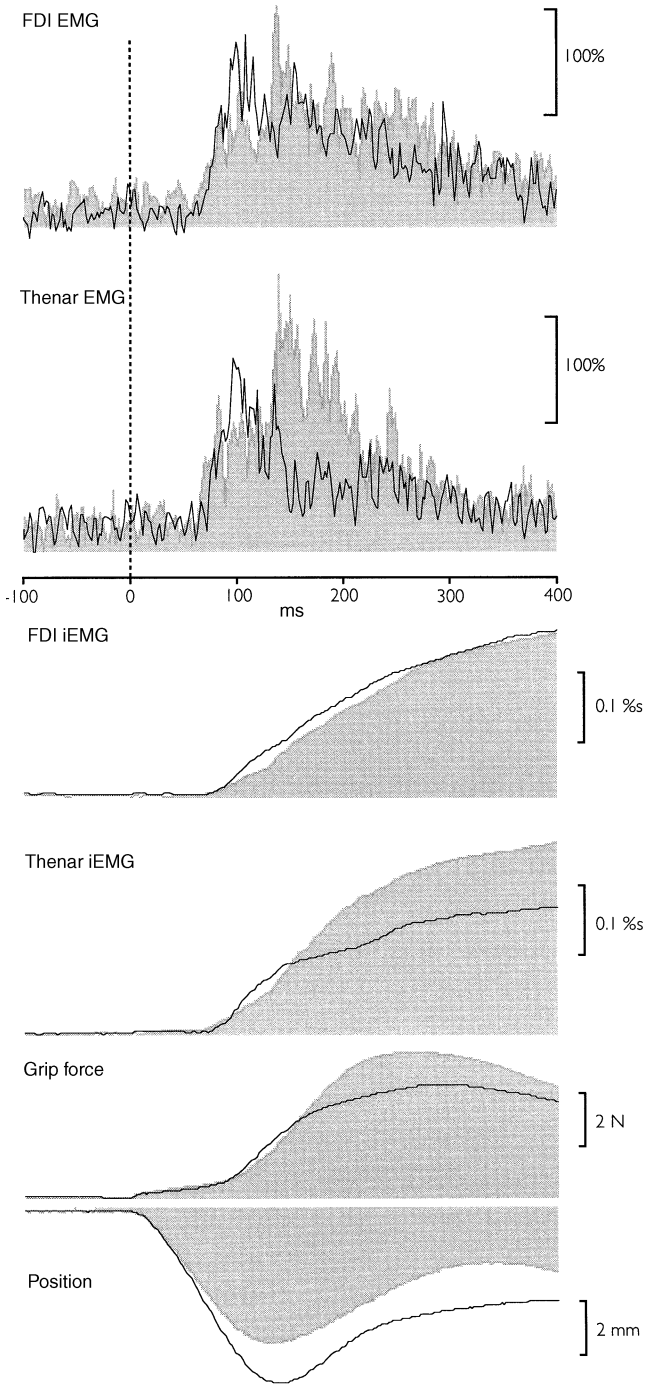

Fig. 8 Grand average responses to an imposed load change (2 N, 200 N/s) for the parkinsonian patients (lines) and normal subjects (filled grey traces) with visual control of hand and object. The time axis applies to all traces. The dotted line arising from this axis indicates the point at which the load change was applied. From the top, the traces are: rectified and normalized first dorsal interosseus (FDI) EMG activity; rectified and normalized thenar EMG activity; integrated FDI EMG; integrated thenar EMG; grip force exerted on the object; object position.

Discussion

Motor memory sets in Parkinson's disease

The grip force profiles employed by the normal subjects in the present study when lifting an object of unpredictable load clearly demonstrated the use of a memory 'set' based on the load encountered in the previous lift, confirming the findings of Johansson and his co-workers (Gordon *et al.*, 1993). The normal subjects generated significantly higher peak forces in the 'unload' than in the 'light' condition, but were still able to produce significantly lower peak forces in the 'unload'

condition than those employed for the heavier loading. This indicates that they could successfully modify lift parameters on the basis of somatosensory information obtained at the onset of the erroneously programmed lift attempt so that more or less appropriate levels of grip force were developed within one trial (Johansson and Westling, 1988). Both the prediction of load on the basis of the previous trial and the ability to correct grip forces during an ongoing lift were largely preserved in the parkinsonian patients. This finding is supported by that of Müller and Abbs (1990), obtained from a much smaller group of patients, and has two important implications. First, parkinsonian patients were able to maintain in memory and subsequently recall a set of parameters defining a complex voluntary motor task. Secondly, and in contradiction to Robertson and Flowers (1990), they were capable of storing more than one such set, and were able to switch between them at appropriate points in an ongoing motor trial. But although the parkinsonian patients were able to modulate their grip forces appropriately to the loads encountered, it was apparent that both grip force development and the movement phase of their lifts were profoundly slowed under all conditions and that they invariably employed abnormally high levels of grip force.

Bradykinesia and the precision grip

The pronounced increase in the time required to develop grip force seen in >80% of the parkinsonian patients in the present study was not so apparent in the earlier study of Müller and Abbs (1990), and was there attributed simply to the extra time required to reach the abnormally high grip forces generated by the parkinsonian patients. The results of the present study, however, demonstrate that, in addition to prolongation of the time required to reach peak grip force due simply to increased levels of grip force, a more important source of delay is the pronounced slowing in the rate at which the grip force was generated in the parkinsonian patients. Godaux *et al.* (1992) have reported a correlation between the rate of rise of arm muscle EMG and the slowness of reaching movements. Furthermore, a slowing of both force generation and, in particular, of force release, has been found for isometric contractions in Parkinson's disease (Jordan *et al.*, 1992). This delay seems likely to be central in origin because, at least for leg muscles, contractile properties appear to be unchanged in Parkinson's disease (Hufschmidt *et al.*, 1991). Indeed, Horak, reporting a failure to generate force rapidly in a postural task in parkinsonian patients, attributed this failure directly to basal ganglia dysfunction (Horak *et al.*, 1996).

Sensorimotor disturbances and elevated grip force levels

Although parkinsonian patients were capable of modulating grip forces to match changes in object loading and showed a normal relationship between the peak grip force during the lifting phase and the static grip force during the holding phase, they showed significantly higher levels of grip force than the normal subjects at all stages of lifting. Such an elevation in grip force during lifting in a precision grip has been associated with a variety of circumstances. In normal subjects it is known to occur when the cutaneous afferents of the fingers and lower arm are subject to local anaesthesia (Johansson and Westling, 1984; Häger-Ross and Johansson, 1996). A recent study of precision grip performance in a patient with chronic sensory demyelinating neuropathy (Thonnard *et al.*, 1997) has also reported elevated levels of grip force. These were observed to normalize when finger sensation was restored by intravenous immunoglobulin treatment, but returned to abnormally high levels when this treatment ceased to be effective. In recent years evidence has been increasing that parkinsonian patients suffer from a range of sensory deficits: it has been suggested in several studies (Schneider *et al.*, 1987; Klockgether *et al.*, 1995; Jobst *et al.*, 1997) that parkinsonian patients are significantly worse than normal subjects in sensing passively imposed movements. This loss of kinaesthetic sense has been attributed to increased gating of afferent input by basal ganglion structures (Schwarz *et al.*, 1992). Perhaps more relevant for the present findings are the results of a recent study of tactile perception of the fingers in Parkinson's disease (Sathian *et al.*, 1997), in which it was found that a significant increase (twofold) in the tactile threshold at the fingertips was present in parkinsonian patients. Given the vital role of the cutaneous afferents of the fingers in the control of precision grip (Johansson, 1996) and the increase in grip force associated with blockade of such fibres in normal subjects (Johansson and Westling, 1984; Häger-Ross and Johansson, 1996), the abnormally high levels of grip force seen in the parkinsonian patients in the present study may well represent a sensory deficit affecting cutaneous afferent input. Whether this deficit arises from a deficiency in peripheral receptors or from abnormal central processing due to disturbance in the basal ganglia cannot be decided on the basis of the present data. In line with the suggestion of Marsden (1989), however, it is tempting to attribute this deficit to inappropriate selection of force levels by the SMA due to misleading afferent information relayed from structures in the basal ganglia. That enough sensory discrimination was preserved in the patients of the present study to allow them to successfully modify grip force parameters in response to perceived load changes does not necessarily contradict this view: such adaptive programmes are automatic adaptive responses to external cues, and under the models of Marsden (1989) and Goldberg (1985) they would be mediated over pathways avoiding the SMA and, thus, the disruptive influence of the damaged basal ganglia. The largely normal levels of grip force generated by the parkinsonian patients during prolonged maintenance of an object in a precision grip might also be a reflection of this dichotomy: such a task may be considered to require much less conscious involvement than does the short hold

phase in a self-initiated lift, during which the subject was waiting for the order to release the object.

Visual effects on disturbed precision grip parameters in parkinsonian subjects

Although many reports have stressed the loss of the ability of parkinsonian patients to use predictive (usually visual) information in tracking and pointing tasks (Flowers, 1975, 1976, 1978*a*, *b*, *c*), others have shown that this is a function of task complexity, and that simple tracking, for example, can be performed predictively in Parkinson's disease (Day and Marsden, 1982; Bloxham *et al.*, 1984). In general, performance would seem to be inversely related to task complexity. One might expect, therefore, that when parkinsonian patients were provided with forewarning of object loading, thus simplifying the task, their lifting performance would improve. Furthermore it has been suggested that the importance of visual cues is increased in arm movements of parkinsonian patients (Cooke and Brown, 1979), indicating that a similar improvement might be expected when the parkinsonian patients were allowed visual control of the object and their hand. However, with the exception of the safety margin, none of the grip force parameters, whether of magnitude or of timing, were affected by either predictability of object loading or visual control. In terms of the forces generated this is perhaps not so surprising, as the object provided no visual cues of the load to be encountered. It has also been reported, however, that arm-pointing movements of parkinsonian patients performed without visual control are slower than normal and tend to overshoot the target (Klockgether and Dichgans, 1994). One might expect, accordingly, that movement duration and amplitude might change when the parkinsonian subjects of the present study were provided with visual control. Both parameters remained unchanged, however, which may represent differences in task between lifting an object in a precision grip and whole-arm pointing.

Reflex mechanisms in precision grip

It is now well established that longer-latency (presumably transcortical) components of the stretch reflex responses of hand and wrist muscles, in particular the M3 component occurring with a latency of ~75 ms, are abnormally enlarged in patients with Parkinson's disease (Lee and Tatton, 1975; Berardelli *et al.*, 1983; Cody *et al.*, 1986; Noth *et al.*, 1988). It remains questionable, however, how functional such stretch reflex responses are; it seems most likely that automatic responses of the hands during fine motor control, such as that elicited in the present study, are mediated largely by cutaneous afferent input (Johansson and Westling, 1984; Johansson and Westling, 1987; Johansson *et al.*, 1992*a*; Häger-Ross and Johansson, 1996). Thus activity occurring in the first stages (onset to 140 ms) of the response to imposed loading studied here might be considered more representative of the functional state of reflex control of the hand in Parkinson's disease. No changes in this activity were observed in the patients of the present study, which supports the hypothesis of Goldberg (1985) and of Marsden (1989) that automatic adaptive processes to external cues are largely preserved in Parkinson's disease. The clear reduction in late (140–210 ms) activity in the thenar muscle, in contrast, can be considered to arise from the known abnormalities in self-generated movements in the parkinsonian patients, expressed here through the likely voluntary nature of this later activity.

Changes in other basal ganglia disorders

It is interesting to note that in patients with Huntington's disease, in whom long-latency stretch reflexes are abolished (Noth *et al.*, 1985), the functional, cutaneous afferent-mediated responses to imposed load changes are preserved, albeit appearing after a delay (Fellows *et al.*, 1997). In this case the delay was attributed to reduction in the level of and/or the effectiveness of cutaneous afferent input due to disruption of processing by the damaged basal ganglia. Such a sensory deficit may play a role in the reduction in the later stages of the thenar EMG response seen in the parkinsonian patients in the present study, but with regard to the earlier components a clear difference exists between these two basal ganglion disorders in either the behaviour of peripheral receptors or the nature of the deficit in central processing.

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References

Agostino R, Berardelli A, Formica A, Accornero N, Manfredi M. Sequential arm movements in patients with Parkinson's disease, Huntington's disease and dystonia. Brain 1992; 115: 1481–95.

Benecke R, Rothwell JC, Dick JP, Day BL, Marsden CD. Performance of simultaneous movements in patients with Parkinson's disease. Brain 1986; 109: 739–57.

Benecke R, Rothwell JC, Dick JP, Day BL, Marsden CD. Disturbance of sequential movements in patients with Parkinson's disease. Brain 1987; 110: 361–79.

Berardelli A, Sabra AF, Hallett, M. Physiological mechanisms of rigidity in Parkinson's disease. J Neurol Neurosurg Psychiatry 1983; 46: 45–53.

Berardelli A, Accornero N, Argenta M, Meco G, Manfredi M. Fast complex arm movements in Parkinson's disease. J Neurol Neurosurg Psychiatry 1986; 49: 1146–9.

Berardelli A, Hallett M, Rothwell JC, Agostino R, Manfredi M,

Thompson PD, et al. Single-joint rapid arm movements in normal subjects and in patients with motor disorders. [Review]. Brain 1996; 119: 661–74.

Bloxham CA, Mindel TA, Frith CD. Initiation and execution of predictable and unpredictable movements in Parkinson's disease. Brain 1984; 107: 371–84.

Cody FW, MacDermott N, Matthews PB, Richardson HC. Observations on the genesis of the stretch reflex in Parkinson's disease. Brain 1986; 109: 229–49.

Cole KJ, Abbs JH. Grip force adjustments evoked by load force perturbations of a grasped object. J Neurophysiol 1988; 60: 1513–22.

Cooke JD, Brown JD. Increased dependence on visual information for arm movement in patients with Parkinson's disease. In: Poirier LJ, Sourkes TL, Bédard PJ, editors. Advances in neurology, Vol. 24. New York: Raven Press; 1979. p. 185–9.

Currà A, Berardelli A, Agostino R, Modugno N, Puorger CC, Accornero N. Performance of sequential arm movements with and without advance knowledge of motor pathways in Parkinson's disease. Mov Disord 1997; 12: 646–54.

Day BL, Marsden CD. Accurate repositioning of the human thumb against unpredictable dynamic loads is dependent upon peripheral feed-back. J Physiol (Lond) 1982; 327: 393–407.

Fellows S, Schwarz M, Schaffrath C, Dömges F, Noth J. Disturbances of precision grip in Huntington's disease. Neurosci Lett 1997; 226: 103–6.

Flowers K. Ballistic and corrective movements in an aiming task: intention tremor and parkinsonian movement disorders compared. Neurology 1975; 25: 413–21.

Flowers KA. Visual 'closed-loop' and 'open-loop' characteristics of voluntary movement in patients with parkinsonism and intention tremor. Brain 1976; 99: 269–310.

Flowers KA. The predictive control of behaviour: appropriate and inappropriate actions beyond the input in a tracking task. Ergonomics 1978a; 21: 109–22.

Flowers K. Some frequency response characteristics of parkinsonism on pursuit tracking. Brain 1978b; 101: 19–34.

Flowers K. Lack of prediction in the motor behaviour of parkinsonism. Brain 1978c; 101: 35–52.

Goldberg G. Supplementary motor area: structure and function: review and hypothesis. [Review]. Behav Brain Sci 1985; 8: 576–616.

Godaux E, Koulischer D, Jacquy J. Parkinsonian bradykinesia is due to depression in the rate of rise of muscle activity. Ann Neurol 1992; 31: 93–100.

Gordon AM, Westling G, Cole KJ, Johansson RS. Memory representations underlying motor commands used during manipulation of common and novel objects. J Neurophysiol 1993; 69: 1789–96.

Häger–Ross C, Johansson RS. Nondigital afferent input in reactive control of fingertip forces during precision grip. Exp Brain Res 1996; 110: 131–41.

Hermsdörfer J, Wessel K, Mai N, Marquardt C. Perturbation of precision grip in Friedreich's ataxia and late-onset cerebellar ataxia. Mov Disord 1994; 9: 650–4.

Horak FB, Frank J, Nutt J. Effects of dopamine on postural control in parkinsonian subjects: scaling, set, and tone. J Neurophysiol 1996; 75: 2380–96.

Hufschmidt A, Stark K, Lücking CH. Contractile properties of lower leg muscles are normal in Parkinson's disease. J Neurol Neurosurg Psychiatry 1991; 54: 457–60.

Jobst EE, Melnick ME, Byl NN, Dowling GA, Aminoff MJ. Sensory perception in Parkinson disease. Arch Neurol 1997; 54: 450–4.

Johansson RS. How is grasping modified by somatosensory input? In: Humphrey DR, Freund H-J, editors. Motor control: concepts and issues. Chichester (UK): John Wiley; 1991. p. 331–55.

Johansson RS. Sensory and memory information in the control of dexterous manipulation. In: Lacquaniti F, Viviani P, editors. Neural bases of motor behaviour. Dordrecht: Kluwer Academic Publishers; 1996. p. 205–60.

Johansson RS, Westling G. Roles of glabrous skin receptors and sensorimotor memory in automatic control of precision grip when lifting rougher or more slippery objects. Exp Brain Res 1984; 56: 550–64.

Johansson RS, Westling G. Signals in tactile afferents from the fingers eliciting adaptive motor responses during precision grip. Exp Brain Res 1987; 66: 141–54.

Johansson RS, Westling G. Co-ordinated isometric muscle commands adequately and erroneously programmed for the weight during lifting task with precision grip. Exp Brain Res 1988; 71: 59–71.

Johansson RS, Häger C, Bäckström L. Somatosensory control of precision grip during unpredictable pulling loads. III. Impairments during digital anesthesia. Exp Brain Res 1992a; 89: 204–13.

Johansson RS, Häger C, Riso R. Somatosensory control of precision grip during unpredictable pulling loads. II. Changes in load force rate. Exp Brain Res 1992b; 89: 192–203.

Johansson RS, Riso R, Häger C, Bäckström L. Somatosensory control of precision grip during unpredictable pulling loads. I. Changes in load force amplitude. Exp Brain Res 1992c; 89: 181–91.

Jordan N, Sagar HJ, Cooper JA. A component analysis of the generation and release of isometric force in Parkinson's disease. J Neurol Neurosurg Psychiatry 1992; 55: 572–6.

Klockgether T, Dichgans J. Visual control of arm movements in Parkinson's disease [see comments]. Mov Disord 1994; 9: 48–56. Comment in: Mov Disord 1996; 11: 115.

Klockgether T, Borutta M, Rapp H, Spieker S, Dichgans J. A defect of kinesthesia in Parkinson's disease. Mov Disord 1995; 10: 460–5.

Lee RG, Tatton WG. Motor responses to sudden limb displacements in primates with specific CNS lesions and in human patients with motor system disorders. Can J Neurol Sci 1975; 2: 285–93.

Marsden CD. Slowness of movement in Parkinson's disease. [Review]. Mov Disord 1989; 4 (Suppl 1): S26–37.

Montgomery EB Jr, Nuessen J. The movement speed/accuracy operator in Parkinson's disease. Neurology 1990; 40: 269–72.

Müller F, Abbs JH. Precision grip in parkinsonian patients. Adv Neurol 1990; 53: 191–5.

Noth J, Podoll K, Friedemann H-H. Long-loop reflexes in small hand muscles studied in normal subjects and in patients with Huntington's disease. Brain 1985; 108: 65–80.

Noth J, Schürmann M, Podoll K, Schwarz M. Reconsideration of the concept of enhanced static fusimotor drive in rigidity in patients with Parkinson's disease. Neurosci Lett 1988; 84: 239–43.

Robertson C, Flowers KA. Motor set in Parkinson's disease. J Neurol Neurosurg Psychiatry 1990; 53: 583–92.

Sathian K, Zangaladze A, Green J, Vitek JL, DeLong MR. Tactile spatial acuity and roughness discrimination: impairments due to aging and Parkinson's disease. Neurology 1997; 49: 168–77.

Schneider JS, Diamond SG, Markham CH. Parkinson's disease: sensory and motor problems in arms and hands. Neurology 1987; 37: 951–6.

Schwab RS, England AC, Peterson E. Akinesia in Parkinson's disease. Neurology 1959; 9: 65–72.

Schwarz M, Block F, Töpper R, Sontag K-H, Noth J. Abnormalities of somatosensory evoked potentials in the quinolinic acid model of Huntington's disease: evidence that basal ganglia modulate sensory cortical input. Ann Neurol 1992; 32: 358–64.

Stelmach GE, Worringham CJ. The preparation and production of isometric force in Parkinson's disease. Neuropsychologia 1988; 26: 93–103.

Thonnard J-L, Detrembleur C, Van den Bergh PY. Assessment of hand function in a patient with chronic sensory demyelinating neuropathy. Neurology 1997; 49: 253–7.

Westling G, Johansson RS, Factors influencing the force control during precision grip. Exp Brain Res 1984; 53: 277–84.

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