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Grip Force Abnormalities in De Novo Parkinson's Disease

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Abstract: In recent years it has been shown that a variety of movement disorders are associated with abnormalities of the fine motor control of the hand. In Parkinson's disease (PD), these changes consist of a slowing of the rate of grip force development and the use of abnormally large grip forces both during lifting and static holding of an object. It has been suggested, however, that these changes are a direct effect of the patient's levodopa medication or associated with levodopa induced dyskinesias. Accordingly, we examined the performance of de novo Parkinson patients in a precision lifting task. All patients (n = 6) were newly diagnosed and showed rigidity, bradykinesia, or both, but were unaffected by tremor or dyskinesia. None of the patients

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had received antiparkinson medication. Grip force was abnormally high in both the lifting and hold phases. This exaggeration was equal in magnitude to that observed previously in medicated patients. Thus we conclude that the abnormalities in grip force observed here are intrinsic features of PD and not the result of dopamine medication or its side effects. © 2003 Movement Disorder Society

Key words: Parkinson's disease; de novo; precision grip

In recent years it has been shown that a variety of movement disorders are associated with abnormalities of fine motor control of the hand.¹⁻⁷ In Parkinson's disease (PD), these changes consist of a slowing of the rate of grip force development⁸ and the use of abnormally large grip forces, during both lifting and static holding of an object.^{9,10} It has been suggested, however, that these changes were a direct effect of the patient's levodopa (L-dopa) medication.¹¹ This claim is somewhat surprising, given the improved quality of movement generally reported by the patients themselves, and indeed, L-dopa medication has been shown to markedly improve reach-to-grasp movements in patients with PD.¹² A more likely suggestion was that the exaggerated grip force levels resulted from L-dopa induced dyskinesias.¹³ Accordingly, we examined the performance of de novo Parkinson patients in a precision lifting task. These patients were in the early stages of the disease and did not exhibit tremor or dyskinesia as part of their symptoms. They had had no exposure to L-dopa or other dopaminergic medication, and so their performance clearly could not be influenced, directly or indirectly, by effects of L-dopa. We show that they demonstrated grip force abnormalities compatible with those of a group of parkinsonian patients on a stable L-dopa regime,⁹ indicating that the abnormalities are an intrinsic feature of the pathophysiology of PD. An alternative explanation for these deficits is discussed.

SUBJECTS AND METHODS

The study involved 6 patients who were referred to our outpatient clinic with a suspected and subsequently confirmed diagnosis of PD (Table 1). In cases of hemiparkinsonism, the affected hand was studied, whereas in the other cases the dominant hand was used. None of the patients was receiving or had received parkinsonian medication. A control group comprised 12 age-matched subjects (6 men, 6 women; mean age, 61 ± 3 years) with no history of neurological disorder. All subjects gave their informed consent to the procedures, which had been approved previously by the local ethics committee.

TABLE 1. Clinical details of the patients

Patient no.	Gender	Age (yr)	Main symptoms	H&Y stage ^a
1	F	61	Akinesia, rigor	1
2	M	70	Akinesia, bradykinesia	1.5
3	F	46	Akinesia, bradykinesia, rigor	2.5
4	M	49	Akinesia, bradykinesia	1
5	F	60	Akinesia, bradykinesia	1
6	M	73	Akinesia, bradykinesia	1.5

^aStage 0, no signs of disease; Stage 1, unilateral disease; Stage 1.5, unilateral plus axial involvement; Stage 2, bilateral disease without impairment of balance; Stage 2.5, mild bilateral disease with recovery on pull test; Stage 3, mild to moderate bilateral disease, some postural instability, physically independent; Stage 4, severe disability, still able walk or stand unassisted; Stage 5, wheelchair-bound or bedridden unless aided.

H&Y, Hoehn and Yahr.

Details of the apparatus and methods employed have been fully described elsewhere.⁹ Briefly, the investigation was carried out in a quiet room with subdued lighting. The subject was seated in a stable chair that supported the back (but not the head) before a table on which was situated the lifting device. Subjects were positioned so that they were able to grip the object between their forefinger and thumb and lift and hold the object at the wrist while their elbow remained fully supported on a padded rest. The measuring instruments built into the device registered the grip force exerted on the object (9301b; Kistler, Winterthur, Switzerland) and its vertical position (T60500; VAC, München, Germany). These signals were amplified and then passed to the analogue-to-digital converter board (NI-PCI-MIO-16XE; National Instruments, Austin, TX) of a laboratory computer (Macintosh PPC 7600/132; Apple, Cupertino, CA) sampling each channel at 2.5 kHz.

The subjects were required, without visual feedback concerning hand position, to grip and lift the object 4 to 6 cm above the table, then hold it steady for 6 to 8 seconds before replacing the object on the table and releasing it. The contact pads on the object for thumb and forefinger were covered with sandpaper (extra-fine, corn 400). A second laboratory computer (Macintosh IIVX; Apple) was used to control the load of the object via a servo-device. A torque motor attached via a nonelastic band to the object was used to alter object load between lifts without the subject's knowledge in a pseudo-random manner between two levels, namely 3.3 N (light) and 7.8 N (heavy), such that five lifts could be selected for each load where the load remained unaltered from the preceding lift. A 10- to 15-second pause was allowed between each lift.

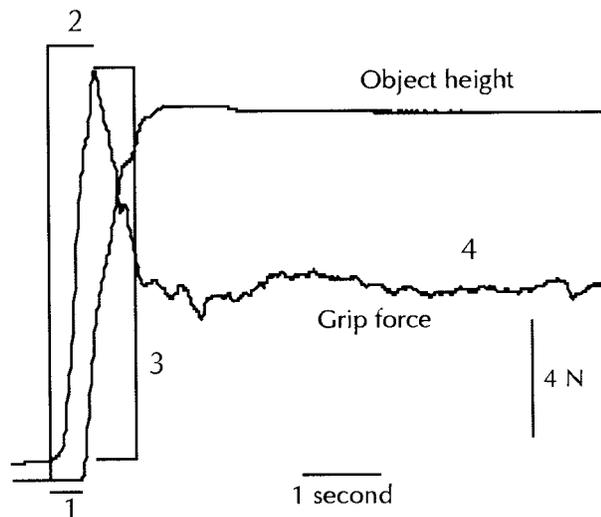


FIG. 1. The grip force and object position curves for a typical control subject lifting the light load. The parameters obtained from these curves are numbered. **1**, Time between onset of grip force development and object lift-off (IGL), a measure of finger/wrist co-ordination; **2**, time taken to achieve peak grip force (TPGF), a measure of the rate for grip force development; **3**, peak grip force (PGF) developed in the dynamic lifting phase, a measure of pre-planned matching of grip force to object properties; and **4**, static grip force (SGF), the grip force developed while holding the object steady above the table, a measure of grip force adaptation to actual conditions based on cutaneous afferent feedback.

The grip force curves obtained from each of the lifts carried out was measured subsequently (see Fig. 1) to yield a series of parameters: (1) IGL, the time between the onset of grip force and the lift-off of the object (msec); (2) TPGF, the time taken to reach the peak grip force (msec); (3) PGF, peak grip force magnitude (N); and (4) SGF, the stable grip force adopted while holding the object steady above the table (N). The IGL may be considered to provide a measure of the co-ordination between the fingers gripping the object and more proximal arm muscles responsible for the actual horizontal lift of the object. TPGF provides information about the rate of grip force development at the fingers. PGF provides information on the largely automatic processes of the selection from memory of motor sets matched to object properties,¹⁴ whereas the SGF is the result of modification of these stored commands by actual sensory feedback concerning object properties obtained during the lift itself.¹⁵

Statistical analysis was carried out using the *Statview 5.0* package (SAS Institute, Cary, NC). For this purpose, the median value obtained from five lifts with a given load were obtained for each parameter and compared between subjects using MANOVA analysis with clinical

status and object load as the main factors. Post-hoc testing was carried out using the Tukey-Kramer test.

RESULTS

All 6 de novo PD patients displayed obvious abnormalities in their grip force curves. Figure 2 shows 5 grip force profiles obtained while lifting a light load for a representative control subject (upper traces) and a patient with PD (lower traces). It is apparent that the patient developed grip force markedly slower than did the control subject, and consistently employed exaggerated levels of grip force, in both the dynamic and static phases of the lift.

The group values for the four lifting parameters are displayed in Figure 3. Each dot represents the value of a single parkinsonian patient, whereas the grey boxes represent the mean value for the control group (\pm SEM). The mean values for the patients with PD are shown as filled triangles. Figure 3A shows the data for the IGL. It may be seen that the parkinsonian patients all demonstrated timings outside or at the upper end of the range of values shown by the control group. On a group basis, this prolongation was highly significant ($P < 0.01$) and its magnitude was comparable with that observed in an

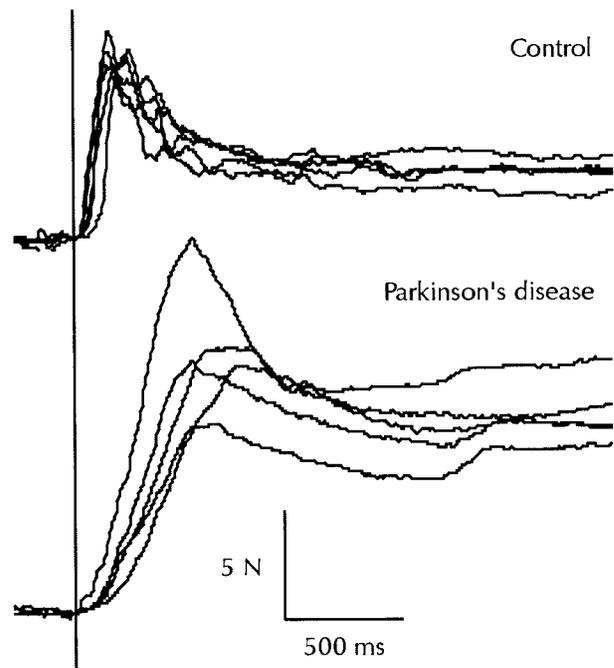


FIG. 2. The 5 grip force profiles obtained while lifting the light load by a typical control subject (upper traces) and a patient with PD (4, lower traces). Grip force development clearly was slower in the patient, who also developed consistently excessive force levels during both the dynamic lifting phase and the static hold phase.

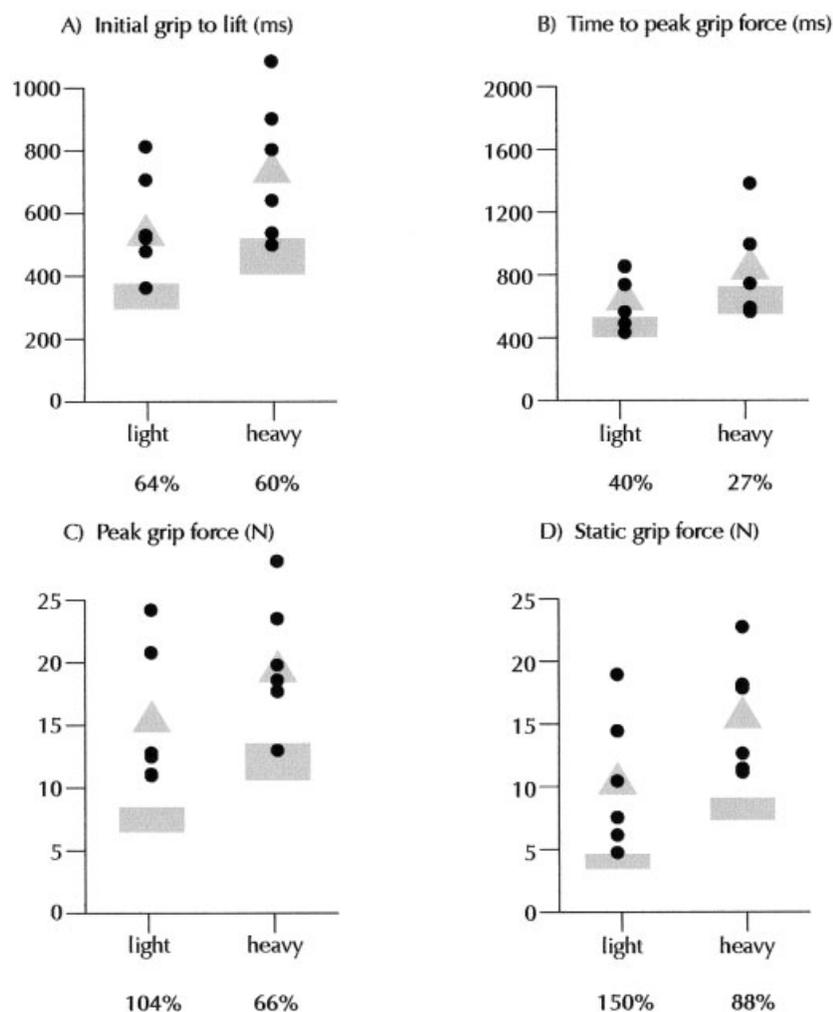


FIG. 3. Group values for the four lifting parameters. Each dot represents the value of a single parkinsonian patient, whereas grey boxes represent the mean value for the control group (\pm SEM). The parkinsonian mean is represented by a filled triangle. All four parameters showed a significant increase over control values in PD ($P < 0.01$, except TPGF, $P < 0.05$). The adaptation of the values according to load seen in the control group was maintained in PD, with the exception of TPGF (IGL, $P < 0.05$; PGF, SGF, $P < 0.01$). The percentage values under each load give the increase in the parkinsonian mean relative to the control mean. Abnormalities are more evident with the lighter load, and grip force is exaggerated especially in the static holding phase.

earlier study⁹ involving patients at a later stage of the disease who were on a stable regime of L-dopa medication. IGL modulation with load remained significant ($P < 0.05$) in the parkinsonian patients. The relative increase over control values ($\sim 60\%$) was equal for both loads.

TPGF values for the parkinsonian patients (Fig. 3B) were also prolonged relative to the control group ($P < 0.05$). This prolongation was less marked, however, than that observed previously in patients with a longer disease duration.⁹ The modulation of timing with load observed in the latter group of patients and in the control group was not significant in the group of de novo patients.

The most pronounced abnormalities shown by the de novo patients were observed in the exaggerated levels of grip force employed in both the dynamic and static phases of the lift. PGF values (Fig. 3C) for patients were significantly higher than control values ($P < 0.01$) for both the light and the heavy load, although the scaling of

grip force to load was retained ($P < 0.01$). It is interesting to note that the exaggeration was more marked for the light load (on average, twice the mean level of the control group) than for the heavy load (on average, an increase of two-thirds). The exaggeration was also more marked than that observed previously in the patients with a longer duration of disease,⁹ although the fact that the latter were receiving L-dopa medication must be borne in mind. Figure 3D shows the data for SGF and it can be seen that a significant exaggeration of grip force levels in de novo PD patients occurred ($P < 0.01$), even more marked than in the dynamic phase of the lift, particularly for the light load, where the exaggeration over control values was (in relative terms) almost twice as great as that observed with the heavy load. Scaling of grip force to load was retained ($P < 0.01$). Once again, the exaggeration was more marked than that observed previously in patients with a longer duration of disease.⁹

DISCUSSION

An unequivocal result of this study is that grip force abnormalities were present in the early stages of PD, in patients with no exposure to L-dopa medication. Furthermore, the greatest abnormalities were observed in grip force magnitude. Thus the hypothesis put forward by Gordon and Reilmann,¹¹ that exaggerated grip forces are a side effect of L-dopa medication, is contradicted by our findings. Another suggestion, namely that exaggerated grip force levels result from L-dopa-induced dyskinesia,¹³ can also be ruled out as an explanation for our findings, as none of the patients showed dyskinesia and as de novo patients had had clearly no chance to develop L-dopa-induced dyskinesia. Indeed, the grip force profiles of parkinsonian patients with L-dopa-induced dyskinesia (Wenzelburger and associates,¹³ Fig. 2C) resemble much more closely those of patients with Huntington's disease (see Hermsdörfer and colleagues,⁵ Fig. 2A) than the markedly slowed profiles obtained in the present study and in a group of PD patients on a stable L-dopa regime,⁹ indicating that a different pathophysiology may underlie the two phenomena.

Although this is more a matter of interpretation, we would also argue that the present results provide strong support for the hypothesis that grip force abnormalities in a variety of basal ganglia disorders result from a disturbance of sensorimotor processing.^{5,9,16} This idea arose in part from the similarities between exaggerated grip force profiles seen in basal ganglia disorders and those of neurologically normal subjects with a local anesthesia-induced block of the cutaneous receptors of the hand and wrist,¹⁷ or in patients with sensory neuropathy of the fingers.¹⁸ Peripheral sensory function, however, is largely normal in basal ganglia disorders, implying that disordered central processing of sensory input is the likely cause of any abnormalities. Reports of abnormal sensorimotor function in PD have appeared steadily in recent years. In particular, parkinsonian patients performing arm movements without visual guidance regularly underestimate the extent of a movement, either passively imposed or self-performed,^{19–22} and have difficulty in judging arm or finger position on the basis of proprioceptive information alone.²³ A similar deficit has been observed when patients replicating a movement imposed on the other hand must rely solely on kinesthetic information or receive visual cues designed to distract them from relevant kinesthetic input.²⁴ It was found recently that patients with PD lack the inhibition of responses in wrist muscles to transcortical magnetic stimulation seen normally during passive movement of the joint at which the target muscles operate.²⁵ Taken together, these results indicate

that patients with PD suffer a decreased sensitivity to sensory input acting on structures at a cortical level. We would argue that this is supported further by our findings. Firstly, although the scaling of grip force levels to load was maintained, a general shift to larger values was found. Secondly, the extent of the exaggerated grip force relative to the control values was significantly higher for the light load than for the heavy load. As more afferent input would be expected in the latter case, it could be argued that the exaggerated grip force levels result from a degree of insensitivity to afferent input caused by an upward shift in the threshold level at which sensory input can act effectively. The finding that the relative grip force abnormalities are most pronounced for the SGF, the control of which relies heavily on cutaneous feedback information, further supports this hypothesis.

In summary, we conclude that exaggerated grip force observed in patients with PD are intrinsic features of the pathophysiology of the disease, and not the result of dopamine medication or its side effects. Rather, we suggest that abnormalities arise from decreased efficiency in the utilization of sensory input concerning object properties and the performance of the motor apparatus.

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Verb and Noun Generation Tasks in Huntington's Disease

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Abstract: We compared noun- and verb-generation tasks in a demented group (n = 9, Dementia Rating Scale ≤ 129)

and in a non-demented group (n = 17, Dementia Rating Scale > 129) of Huntington's disease (HD) patients compared to 26 matched normal subjects. We did not find a specific deficit for verb production in non-demented patients who had a performance similar to but weaker than that of the controls across the four tasks. The profile of results was different in the demented group because, apart from a global deficit whatever the task in comparison with both non-demented and control groups, the demented patients exhibited increased difficulties in the two tasks implying verb production. The deficit of verb production observed in demented HD patients is discussed in relation to the damage to the motor loop in HD patients at later stages of disease. © 2003 Movement Disorder Society

Key words: Huntington's disease; language; word generation; verb

Besides motor deficiencies, Huntington's disease (HD) is characterized by several cognitive deficits in memory and executive functions such as problem solving, visuoperceptive processing, and spatial or arithmetical reasoning.¹ Language disorders mainly concern "frontal" aspects such as some features of syntactic abilities^{2,3} and verbal fluency.⁴ Ho and colleagues⁴ specified that this fluency deficit seems to concern specifically the ability to switch across subcategories, reflecting impairment of frontostriatal circuits, rather than the size of clusters within subcategories.

The frontal nature of language impairment in HD can be envisaged in another paradigm that concerns a differential deficit between verb and noun processing. Clinical evidence^{5–9} shows a relationship between object-naming deficit and damage to the left temporal lobe, and between action-naming deficit and large lesions in the left frontal cortex. Damasio and Tranel⁷ formulated the hypothesis that in the left hemisphere, noun retrieval is mediated preferentially by temporal regions, whereas verb retrieval is subserved by a large network including the prefrontal cortex; this hypothesis has received further support in studies devoted to degenerative diseases affecting the frontal cortex. A verb deficit was observed in frontotemporal dementia¹⁰ and in motor neuron disease associated with pathological changes in two frontal areas, namely Brodmann areas 44 and 45.¹¹ Language studies in Parkinson's disease (PD) have also revealed the existence of such dysfunction; Grossman and colleagues¹² showed a verb learning impairment in a group of early PD patients. Our group has shown recently that word generation tasks may be useful to unveil in non-demented PD patients a specific impairment of verb production compared with noun generation.¹³

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