Effects of disease progression and L-dopa therapy on the control of reaching-grasping in Parkinson’s disease

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Abstract

The present study aimed to determine whether the bradykinesia of Parkinson’s disease (PD) patients during the execution of reaching-grasping movements (i) is related to an impaired implementation of movement parameters and (ii) selectively involves the control of reach and/or grasp movements. We compared the kinematics of reaching to grasp of differently sized objects placed at different positions, among PD patients in the early stage of disease (ESPD), in the advanced stage of disease (ASPD) without L-dopa medication (off-state), and in healthy controls. In addition, we analysed the effects of L-dopa replacement therapy by comparing the kinematics of the patients in the advanced stage of disease after L-dopa administration with those of the other groups. Bradykinesia increased with disease progression, but only in the initial phases of the reach and grasp components. However, at both stages of the disease, the kinematics of reaching and grasping responded to extrinsic and intrinsic object properties just as in controls. L-dopa administration improved the performance of PD patients, though this was more evident for the reach than for the grasp. We suggest that the basal ganglia (BG) are involved in implementing kinematic parameters, but neither (or only marginally) in the initial movement parameterization itself, nor in the on-line control of movement. Specifically, the BG dysfunction in PD induces a slowed implementation of movement parameters. The lack of effect of L-dopa administration on grasp kinematics may be because the motor control of distal effectors is less represented in the motor circuitry formed by the supplementary motor area (SMA), thalamus and BG.

Keywords: Parkinson’s disease; Reaching-grasping kinematics; Bradykinesia; L-dopa therapy; Disease progression

1. Introduction

Bradykinesia is considered one of the cardinal manifestations of Parkinson’s disease (PD). At clinical examination, a slowing of movement, affecting all (axial, proximal, and distal) effectors is observed. Disease progression enhances this slowing, whereas therapy with L-dopa ameliorates it (Sian, Gerlach, Youdim, & Riederer, 1999). However, the exact nature of bradykinesia is not yet well understood (Berardelli, Rothwell, Thompson, & Hallet, 2001; Valls-Solé & Valdeon-riola, 2002). Is the movement slowing caused by errors in the initial scaling of movement parameters as a function of object features? Movement slowing might be an adaptive response to such errors. Alternatively, does PD cause an inefficient use of feedback during on-line control of movement? Such a difficulty might occur because PD patients are slower than healthy people in comparing visual and kinaesthetic information from their moving arm with visual information from the target. If so, the kinematics of the final phase of the movement should show most slowing, since this is believed to be the time when on-line control comes mainly into operation (Meyer, Abrams, Kornblum, Wright, & Smith, 1988; Woodworth, 1899).

Previous experiments analysing the arm kinematics of PD patients indicated that both initial and late kinematics are affected by the disease (Tressl, Stelmach, & Adler, 1997; Weiss, Stelmach, & Heller, 1997). However, Gentilucci &
Negrotti (1999a, b) analysed both reaching and grasping movements, and found that the initial parameters of both components in PD patients were scaled as a function of position and distance (extrinsic properties) and size (intrinsic properties) of the object, respectively, just as in healthy controls. In the case of the reach component, they observed normal changes both in the initial parameters (arm peak acceleration, APA and arm peak velocity, APV) and in the late parameters (duration of deceleration). It should be noted that these parameters are chiefly sensitive to extrinsic (i.e. position and distance) properties, though also to a lesser extent to intrinsic (i.e. size) properties of the target object (Gentilucci et al., 1991; Gordon, Ghilardi, & Ghez, 1994; Jeannerod, 1988).

In contrast, a deficit in the on-line control (i.e. movement parameterization, on-line control deficit) may be due to a differential difficulty in controlling movements of varying amplitude. Amplitude, in the reaching-grasping movements, was determined as a function of target features just like those of healthy people. This would be accompanied by a global movement slowing, along with movement corrections made as an adaptive response to the errors. Finally, a disruption of on-line movement control should imply a lengthening of the final movement phase. In the present study, we tested the three hypotheses, i.e. implementation, parameterization, and on-line control deficit, by examining the kinematics of reaching-grasping movements as a function of both the progression of PD and L-dopa therapy, in comparison with healthy people.

A second problem concerning bradykinesia is whether the reach and grasp components are equally or differently affected by the disease. It is commonly accepted that axial-proximal movements are impaired in PD patients (Marsden, 1984). Conversely, however, in clinical practice, examination of distal movements is often used (Fahn et al., 1987) in order to assess severity of the PD motor impairment, and previous kinematic studies have shown that both the reach and the grasp components are slowed down.

The nature and the exact degree of impairment of the two components inducing the observed slowness are not well understood. First, it is unclear whether only the strength of proximal and/or distal effectors, or also the control (movement parameterization and/or on-line control) is impaired, or whether differences in reach and grasp impairment might be due to a differential difficulty in controlling movements of varying amplitude. After all, the amplitude of the finger-thumb aperture is usually smaller than the reaching movement amplitude.

One way to determine the relative degree of reach and grasp bradykinesia in PD is to study its evolution with disease progression and its amelioration after L-dopa administration. First, if the impairment lies simply in a weakness of proximal and/or distal effectors, both initial and final kinematic landmarks should decrease with disease progression, and should ameliorate after L-dopa administration. In contrast, if visuomotor control (i.e. movement parameterization, parameter implementation, or on-line control) is impaired, then disease progression and L-dopa administration might specifically affect some phases of the reach and/or the grasp more than others. Second, any differential difficulty in controlling movements of different amplitude (as in grasp versus reach movements) must presumably affect the parameterization and/or the on-line control of movement. A deficit in parameterization would imply an inability to scale initial parameters as a function of object features, for either small or large movement amplitudes. A deficit in the on-line control of movement, however, would imply an inability to compare kinaesthetic and visual information from the moving hand with visual information from the target. It is known that kinaesthetic and visual information on the moving arm is different for movements of different amplitude since the effector velocity differs (Chieffi & Gentilucci, 1993). Thus, the final kinematics of either the reach or the grasp should be
affected. Finally, if there is a differential difficulty in controlling the strength needed for movements of different amplitudes, then the kinematic parameters of the grasp or the reach should show decreased or increased effects of changes in object properties during disease progression and with L-dopa administration, respectively.

In the present study, we compared the prehension of objects of different sizes placed at different locations between PD patients in the early stage of disease (ESPD, L-dopa-naive), in the advanced stage of disease (ASPD) without L-dopa medication (off-state), and in control healthy participants. In addition, the degree of amelioration of ASPD patients after L-dopa administration (on-state) was evaluated by comparing their kinematics with those of ESPD, off-state ASPD patients, and healthy control participants.

2. Methods

2.1. Participants

Eight PD patients (six males, two females, median age 63.5 years, range 49–73 years) in the early stage of disease (ESPD), L-dopa-naive, and eight PD patients (seven males, one female, median age 61.0 years, range 52–67 years) in the advanced stage of disease (ASPD), experiencing L-dopa motor complications of the “wearing-off” type, participated in this study. Diagnosis of PD was made according to the criteria of the UK Parkinson’s Disease Society Brain Bank (Gibb & Lees, 1988). Duration of the symptoms of the ESPD group was not longer than 5 years (median 3.5 years). Median duration of symptoms of the ASPD group was 9.5 years (range 7–12 years) and median L-dopa treatment duration was 6.7 years (range 2–10 years). The daily cumulative dose of L-dopa ranged from 325 to 825 mg (median 700 mg). The clinical characteristics of each ESPD and ASPD patient are summarized in Tables 1 and 2.

The ESPD patients were tested in one experimental session, in the morning after overnight PD medication withdrawal. The ASPD patients were tested in two sessions. In the first session each patient was tested early in the morning after at least 12 h withdrawal of all antiparkinsonian medications (off-state). In the second session the same patient was tested 1–2 h after administration of the first morning dose of L-dopa plus peripheral-decarboxylase inhibitor, at a time when he/she reported being in the best motor condition (on-state). The interval between the first and the second session was at least 2 weeks, in order to minimize practice effects. A clinical assessment using the motor section (part III) of the Unified PD rating scale (UPDRS, Fahn et al., 1987) and Hoehn & Yahr (1967) scale was performed (by the same neurologist, A.N.) every time at the end of the session in both groups of patients. Therefore, the ASPD patients were assessed twice, i.e. in both off- and on-state (Tables 1 and 2). Four patients of the ASPD group exhibited clinically evident dyskinesias when in on-state, but these were of mild severity (corresponding to a score of 1 on the dyskinesia rating scale by Goetz et al., 1994) and did not interfere with the voluntary motor acts involved in the task.

Eight age-matched healthy volunteers (one male, seven females, median age 62.5 years, range 51–73 years) formed the control group. None of them had any history of neurological disease and their neurological examination was normal. Patients and controls all showed right-handed dominance and did not differ significantly on the Mini Mental State Examination (MMSE, Folstein, Folstein, & McHugh, 1975) (means: controls 29.0, ESPD group 28.8, ASPD group 28.9). All participants gave their informed consent to participate in the study.

2.2. Apparatus and procedure

In a dark and soundproof room the participant sat in front of a table. He/she placed his/her right thumb and index finger, held in the pinch position, on a disk (starting position). Target objects to be reached and grasped were square red wooden parallelepipeds of three sizes: small (sides 2 cm × 2 cm, height 1 cm), medium (sides 4 cm × 4 cm, height 1 cm), and large (sides 6 cm × 6 cm, height 1 cm). One parallelepiped was placed at random on either the right or the left side of the participant’s midline (inclination by 30°), at a distance of either 15 cm (near target) or 30 cm (far target) from the hand starting position. The participant was required to reach and grasp the parallelepiped with her/his right thumb and index finger and to lift it, as quickly as possible while maintaining accuracy. Objects were grasped by the sides parallel to the
Table 2

<table>
<thead>
<tr>
<th>Patients</th>
<th>Age (y)</th>
<th>Sex</th>
<th>Duration of symptoms (y)</th>
<th>More affected hemibody at the initial stage of disease</th>
<th>Section III UPDRS total score (off state)</th>
<th>H&amp;Y stage (off state)</th>
<th>Section III UPDRS total score (on state)</th>
<th>H&amp;Y stage (on state)</th>
<th>Duration of L-dopa therapy (y)</th>
<th>L-dopa dosage (mg/die)</th>
<th>Other anti-PD drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>A.G.</td>
<td>63</td>
<td>M</td>
<td>8.5</td>
<td>Left</td>
<td>57</td>
<td>III</td>
<td>39</td>
<td>III</td>
<td>2</td>
<td>12.5</td>
<td>375</td>
</tr>
<tr>
<td>C.B.</td>
<td>67</td>
<td>M</td>
<td>10</td>
<td>Left</td>
<td>38.5</td>
<td>III</td>
<td>35</td>
<td>II</td>
<td>10</td>
<td>825</td>
<td>D,P</td>
</tr>
<tr>
<td>E.C.</td>
<td>59</td>
<td>M</td>
<td>11</td>
<td>Left</td>
<td>52</td>
<td>IV</td>
<td>23.5</td>
<td>II–III</td>
<td>8</td>
<td>762.5</td>
<td>D,P</td>
</tr>
<tr>
<td>C.C.</td>
<td>66</td>
<td>F</td>
<td>9</td>
<td>Right</td>
<td>46</td>
<td>IV</td>
<td>35.5</td>
<td>III–IV</td>
<td>7.5</td>
<td>675</td>
<td>P</td>
</tr>
<tr>
<td>P.T.</td>
<td>55</td>
<td>M</td>
<td>12</td>
<td>Left</td>
<td>49.5</td>
<td>III</td>
<td>20</td>
<td>II–III</td>
<td>6</td>
<td>725</td>
<td>D,P</td>
</tr>
<tr>
<td>L.C.</td>
<td>52</td>
<td>M</td>
<td>7</td>
<td>Left</td>
<td>41</td>
<td>III</td>
<td>31</td>
<td>III</td>
<td>2</td>
<td>325</td>
<td>B,P</td>
</tr>
<tr>
<td>T.L.</td>
<td>54</td>
<td>M</td>
<td>37</td>
<td>Right</td>
<td>54</td>
<td>I</td>
<td>33</td>
<td>II</td>
<td>3</td>
<td>255</td>
<td>D,P</td>
</tr>
</tbody>
</table>

UPDRS: Unified Parkinson’s Disease Rating Scale; H&Y: Hoehn and Yahr; B = biperiden; D = deprenyl; L = lysuride; P = pergolide.  

Participants’ transverse axis. When the object was not correctly grasped, the trial was repeated at the end of the session. Illumination of the room, controlled by a PC, was the signal to commence the movement. Five trials for each of the two positions and distances, and three sizes of the target, were randomly administered. In total, 60 trials were run. Before starting the experimental session, all participants performed 10 practice trials, in order to familiarize themselves with the experimental procedure.

2.3. Movement recording and data analysis

Movement of arm and hand were recorded using the optoelectronic ELITE system (B.T.S. Milan, Italy). This system consists of two TV-cameras detecting infrared-reflecting markers at a sampling rate of 50 Hz. Details of the recording system, movement reconstruction, and computation of kinematic parameters are reported elsewhere (Gentilucci, Toni, Chieffi, & Pavesi, 1994). In the present study four markers were used. The first marker was placed on the styloid process of the radius of the wrist; the second and third markers were placed on the base of the nail of the thumb and the index finger, respectively. The fourth marker was a reference point. It was placed on the plane of the table at a distance of 1.5 cm from the starting position. The marker placed on the participant’s wrist served to measure the reach component. The following kinematic parameters were analysed: arm peak acceleration, arm peak velocity, percentage of deceleration time with respect to reach time (%DT), and reach time (RT). APA and APV are the maximum values of the wrist acceleration and tangential velocity vectors, respectively. The time course of the distance between the thumb and the index finger was analysed in order to study the grasp component. Peak velocity of finger opening, the maximal finger aperture, and the percentage of time to maximal finger aperture with respect to grasp time (%TMFA) were analysed. The time course of the grasp component is constituted by a hand opening phase until a maximum (MFA), and a phase of finger closure onto the object. PVFO is the maximum value of the velocity of opening the finger-thumb aperture.

APA and APV (reach), and PVFO and MFA (grasp) are considered to be initial movement parameters and, consequently, were used as measures of movement parameterization. The %DT (reach) and %TMFA (grasp) were used to determine whether disease progression and L-dopa administration induced changes either in the early movement phase duration (and, consequently, in duration of program implementation) or in the late movement phase duration (and, consequently, in duration of on-line movement control). Overall RT was used to measure the global effects of disease progression and L-dopa administration on the action.

The procedure for calculating the beginning and end of the prehension movement is described elsewhere (Gentilucci et al., 1994). The kinematic parameters of the reach and the grasp were submitted to the following three series of ANOVAs. In the first series the ASPD patients in off-state
were compared with the ESPD patients and the control participants. In the second series the ASPD patients in on-state were compared with the ESPD patients and the control participants. In the third series of ANOVAs the experimental design included one between-subjects factor with three levels (groups: off-state ASPD or on-state ASPD versus ESPD versus controls) and three within-subjects factors: object position (left versus right target), object distance (near versus far target), and object size (small versus medium versus large target). In the third series of ANOVAs the experimental design included the following four within-subjects factors: state (off- versus on-state), object position (left versus right target), object distance (near versus far target), and object size (small versus medium versus large target). In all analyses the Newman–Keuls post hoc test was used with $P = 0.05$ accepted as significant.

3. Results

3.1. Reaching

3.1.1. Arm peak acceleration

APA decreased significantly moving from the controls to the off-state ASPD (Table 3). Administration of L-dopa significantly improved APA, which was not significantly different between the ESPD and the on-state ASPD groups. APA of all groups was significantly higher for movements directed to right and far targets (Table 3).

3.1.2. Arm peak velocity

The velocity profiles were characterized by an absence of multiple peaks, including in the off-state ASPD group. APV of the PD patients significantly decreased with respect to the controls and with disease progression (Table 3). L-dopa administration significantly improved APV, which was not significantly different between the ESPD and the on-state ASPD groups. APV of all groups was significantly higher when reaching larger, left, and far targets (Table 3).

3.1.3. Percentage deceleration time

The %DT was always shorter in the groups of PD patients with respect to the controls, although only a trend to significance was found (Table 3). A longer time was spent in the patients in acceleration than in deceleration. No differences were observed between the patient groups, though there was a trend for %DT to increase in the on-state ASPD group with respect to the off-state ASPD group. The %DT significantly increased for small, right, and far targets (Table 3).

3.1.4. Reach time

The factor of group was not significant in any of the analyses (Table 3), although there was a trend for the overall duration of movements to be slowed in the patients and for this to be reversed by L-dopa. In the comparisons among controls, ESPD group, and on-state ASPD group (F(4, 42) = 4.2, $P = 0.006$) and between on-state and off-state ASPD groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>Target position</th>
<th>Target distance</th>
<th>Target size</th>
</tr>
</thead>
<tbody>
<tr>
<td>APA</td>
<td>(2, 21) = 11.1, $P = 0.0005$</td>
<td>(2, 21) = 4.8, $P = 0.04$</td>
<td>n.s.</td>
</tr>
<tr>
<td>APA</td>
<td>(2, 21) = 3.7, $P = 0.04$</td>
<td>(2, 21) = 4.8, $P = 0.04$</td>
<td>n.s.</td>
</tr>
<tr>
<td>APA</td>
<td>(2, 21) = 12.8, $P = 0.002$</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>APA</td>
<td>(2, 21) = 3.2, $P = 0.06$</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>APA</td>
<td>(2, 21) = 9.0, $P = 0.002$</td>
<td>(2, 21) = 92.8, $P = 0.0001$</td>
<td>(2, 21) = 625.3, $P &lt; 0.0001$</td>
</tr>
<tr>
<td>APA</td>
<td>(2, 21) = 7.4, $P = 0.07$</td>
<td>(2, 21) = 135.5, $P &lt; 0.0001$</td>
<td>(2, 21) = 118, $P &lt; 0.0001$</td>
</tr>
<tr>
<td>APA</td>
<td>(2, 21) = 7, $P = 0.02$</td>
<td>(2, 21) = 63.1, $P = 0.0001$</td>
<td>(2, 21) = 4.1, $P = 0.04$</td>
</tr>
<tr>
<td>APA</td>
<td>(2, 21) = 6.9, $P = 0.04$</td>
<td>(2, 21) = 183.5, $P &lt; 0.0001$</td>
<td>(2, 21) = 3.2, $P &lt; 0.0001$</td>
</tr>
<tr>
<td>APA</td>
<td>(2, 21) = 9, $P = 0.06$</td>
<td>(2, 21) = 124, $P = 0.0001$</td>
<td>n.s.</td>
</tr>
<tr>
<td>APA</td>
<td>(2, 21) = 9.1, $P = 0.008$</td>
<td>(2, 21) = 16.5, $P &lt; 0.0001$</td>
<td>(2, 21) = 16.6, $P &lt; 0.0001$</td>
</tr>
<tr>
<td>APA</td>
<td>(2, 21) = 7, $P = 0.04$</td>
<td>(2, 21) = 10.5, $P &lt; 0.0001$</td>
<td>(2, 21) = 10.5, $P &lt; 0.0001$</td>
</tr>
<tr>
<td>APA</td>
<td>(2, 21) = 15.2, $P = 0.0001$</td>
<td>(2, 21) = 28.5, $P &lt; 0.0001$</td>
<td>(2, 21) = 9.4, $P = 0.06$</td>
</tr>
<tr>
<td>APA</td>
<td>(2, 21) = 6.8, $P = 0.0005$</td>
<td>(2, 21) = 28.7, $P &lt; 0.0001$</td>
<td>(2, 21) = 2.4, $P = 0.0004$</td>
</tr>
<tr>
<td>APA</td>
<td>(2, 21) = 7, $P = 0.04$</td>
<td>(2, 21) = 10.4, $P &lt; 0.0001$</td>
<td>(2, 21) = 7.9, $P &lt; 0.0001$</td>
</tr>
<tr>
<td>APA</td>
<td>(2, 21) = 9, $P = 0.0009$</td>
<td>(2, 21) = 11.9, $P &lt; 0.0001$</td>
<td>(2, 21) = 7.4, $P = 0.01$</td>
</tr>
<tr>
<td>APA</td>
<td>(2, 21) = 16.9, $P &lt; 0.0001$</td>
<td>(2, 21) = 9.1, $P = 0.0007$</td>
<td>(2, 21) = 2.4, $P = 0.0001$</td>
</tr>
<tr>
<td>APA</td>
<td>(2, 21) = 9.9, $P = 0.0009$</td>
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</tr>
<tr>
<td>APA</td>
<td>(2, 21) = 16.9, $P &lt; 0.0001$</td>
<td>(2, 21) = 11.9, $P &lt; 0.0001$</td>
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<tr>
<td>APA</td>
<td>(2, 21) = 9.9, $P = 0.0009$</td>
<td>(2, 21) = 11.9, $P &lt; 0.0001$</td>
<td>(2, 21) = 3.0, $P = 0.0001$</td>
</tr>
</tbody>
</table>

First row: comparisons among controls, PD patients in the early stage of disease, and PD patients in the advanced stage of disease in off-state. Second row: comparisons among controls, PD patients in the early stage of disease, and PD patients in the advanced stage of disease in on-state.

APA: arm peak acceleration; APV: arm peak velocity; %DT: percentage of deceleration time; RT: reach time; PVFA: peak velocity of finger aperture; MFA: maximal finger aperture; %TMFA: percentage of time to maximal finger aperture.
Fig. 1. Changes in reach time (RT) of PD patients and controls with changing object size, object position, and object distance. Circle refers to mean values of controls, whereas diamond, square, and triangle refer to mean values of PD patients in the early stage of disease (ESPD) and in the advanced stage of disease (ASPD) in off- and in on-state, respectively. Bar markers are S.E.

(F(2, 14) = 6.0, P = 0.04), however, the interaction between group and object size reached significance (see Fig. 1).

3.2. Grasping

3.2.1. Peak velocity of finger opening
PVFO significantly decreased moving from the controls to the off-state ASPD (Table 3, Fig. 2). Improvement with L-dopa administration rendered the ASPD group no longer significantly different from the ESPD group (Table 3, Fig. 2). PVFO significantly increased with object size (Table 3). This sensitivity to object size was higher in the controls than in the patients (interaction between group and object size: F(4, 42) = 5.1, P = 0.002; F(4, 42) = 3.9, P = 0.009, Fig. 5). PVFO was significantly higher when grasping rightward and nearer objects (Table 3, Fig. 2).

3.2.2. Maximal finger aperture
MFA of the PD patients was significantly less than in the controls, and decreased with disease progression (Table 3, Fig. 3). Unlike the other parameters, L-dopa administration produced no significant improvement (Table 3, Fig. 3). MFA significantly increased when grasping larger, leftward, and far objects (Table 3, Fig. 3). The effect of distance was observed only when grasping small objects (interaction between object distance and object size: F(2, 42) = 6.4, P = 0.004; F(2, 42) = 4.9, P = 0.001; F(2, 14) = 5.1, P = 0.002).

3.2.3. Percentage of time to maximal finger aperture
The %TMFA of the PD patients was higher than the controls and increased with disease progression, whereas no significant improvement was observed after L-dopa administration (Table 3). This parameter significantly increased when grasping larger, far, and left objects (Table 3).

3.3. Summary of results

Fig. 4 shows a summary of the effects of disease progression and L-dopa administration on the reaching and grasping parameters of the controls and the PD patients. The disease and its progression induced a not significant increase in overall RT, but there were significant decreases in all the other parameters except in percentage of deceleration time. In ASPD patients, L-dopa administration produced a significant improvement in all parameters of the reach, though for percentage of deceleration time only a trend toward significance was found. In contrast, only the very initial phase of grasp significantly improved after L-dopa administration. In general, the effects of object size, object position, and object distance on reaching-grasping parameters did not differ between the controls and the PD patients. However, reach time of off-state ASPD group showed a greater effect of object size as compared with the other groups, and peak velocity of finger opening of controls was more sensitive to object size as compared with the PD groups. Finally, no obviously increased or decreased effect as a function of object properties was observed in any of the parameters, either as a result of disease progression or of L-dopa administration.
4. Discussion

The data of the present study confirm a progressive slowing of velocity parameters (though not of overall RT) with PD progression (Lee et al., 1994; Louis et al., 1999), affecting both the reach and the grasp components. Slowing was observed for both the initial and late phases of the reach and the grasp, although a greater effect was observed in the initial phase of both components. In addition, the kinematic parameters of the reach and the grasp were affected by extrinsic and intrinsic object properties, just as in healthy controls, even in the advanced stage of disease.
Fig. 4. Changes in reach and grasp parameters of controls and of PD patients with disease progression and after L-dopa administration. APA: arm peak acceleration, APV: arm peak velocity, %DT: percentage of deceleration time, RT: reach time, PVFO: peak velocity of finger opening, MFA: maximal finger aperture, %TMFA: percentage of time to maximal finger aperture. In each panel moving from left to right mean values of controls, ES PD patients, off-state ASPD patients, and on-state ASPD patients are represented by each bar, respectively. Asterisks: significance in the ANOVAs. Other conventions as in Fig. 1.
The PD disorder seems not to lie in the transformation of object features into movement parameters. This is supported by the finding that most reach and grasp parameters of PD patients in all stages of disease showed normal scaling as a function of both extrinsic (distance, Jeannerod, 1988; and position, Gordon et al., 1994, i.e. right versus left target in our study) and intrinsic (size, Chieffi & Gentilucci, 1993) object properties.

The first exception was peak velocity of finger opening, which turned out to be more sensitive to object size in the controls than in the PD groups. The explanation of this result could be either that in PD patients the neural circuitry involved in transforming visual information of object size into initial grasp parameters was partially damaged, or that the disorder in implementing initial grasp parameters was greater for larger than for smaller objects. It is possible that the implementation difficulty increases for greater movement amplitudes, causing slower finger opening for larger objects, and consequently, the observed lower sensitivity to object size. A finding in favour of this latter interpretation is the abnormal increase in time to maximal finger aperture compared with finger closure time, especially in ASPD patients in off-state (79.1%). These patients may have continued to open their fingers because the information on how far to open them, and when to stop doing so, decayed during the execution of the movement. This would occur especially for larger objects, which would require longer times for finger opening.

The second exception was the overall reach time of the off-state ASPD patients, who, unlike the other groups, showed an increased RT when reaching for larger objects. A possible explanation is that the finger velocity during grasping of these patients decreased when grasping larger objects, producing longer grasp times (see above). Consequently, reach time might also increase because of the temporal co-ordination between the two components (Chieffi & Gentilucci, 1993).

The effect of disease progression and L-dopa administration affected neither the movement as a whole nor the final movement phase in particular. Consequently, neither muscle weakness nor a disruption of on-line movement control can easily explain the results of the present study. Decrease in %DT was due to lengthening of duration of the acceleration phase relative to the deceleration phase. Decrease in percent deceleration time was observed in the early stage of disease, while progression of the disease did not affect it. In contrast, the increasing durations of the acceleration and deceleration phases with disease progression were of a similar order of magnitude, since %DT did not vary. The finding that the duration of the acceleration phase increased in the early PD patients, can be interpreted as due to an impairment in implementing movement parameters (Gentilucci & Negrotti, 1999a, b; Gentilucci et al., 2000) rather than in transforming visual information about object features into movement parameters, since initial reach parameters of PD patients were affected by intrinsic and extrinsic object properties just like those of controls (see above). However, the final phase of movement also lengthened with disease progression. According to previous proposals (Meyer et al., 1988; Woodworth, 1899), the final reach is considered to be especially related to on-line control of movement. Consequently, a deficit in on-line control of movement as well as in parameter implementation may be hypothesized in the advanced stage of the disease.

We suggest that the increase in the initial temporal parameters and the decrease in values of the kinematic landmarks of PD patients were due to a slowing of a process that stores movement parameters in a buffer, prior to their execution. We previously proposed that the motor loop formed by SMA, BG, and thalamus may be involved in the sequencing and synchronization of the kinematic events of an action (Gentilucci & Negrotti, 1999a, b; Gentilucci et al., 2000). In particular, SMA may be involved in establishing the progression of the kinematic events. These are stored in a buffer in the BG, which provides for their implementation by means of connections to the primary motor cortex via the thalamus. The SMA, during implementation of the kinematic parameters, plans and temporally links successive kinematic events (Gentilucci & Negrotti, 1999a, b; Gentilucci et al., 2000).

The data of the present study are in favour of the hypothesis that this motor loop is involved also in the organization of the phases of a single motor act (for example for the grasp motor act, the finger opening phase and the finger closing phase, and for the reach motor act the acceleration phase and the deceleration phase) using a mechanism similar to that proposed for a whole action. Disease progression affected both the grasp and the reach. However, L-dopa therapy selectively affected the reach parameters. The reach parameters were significantly ameliorated in ASPD patients in the on-state, whose motor behaviour was comparable with that of ESFD patients. In contrast, the grasp was little affected by L-dopa therapy, with only the increased peak velocity of finger opening reaching significance. Maximal finger aperture and time to maximal finger aperture (as a percentage) were not significantly improved. These results were not the result of a greater difficulty in controlling movements of smaller amplitude, because both initial grasp parameters were scaled as function of object properties, thus excluding a deficit in parameterization of small amplitude movements. Moreover, finger closure time did not increase with respect to finger opening time, thus excluding a deficit in on-line control of small-amplitude movements. Finally, no difference in grip scaling gain as a function of object size was observed among the groups. Summing up, the finding that L-dopa therapy differentially affected the reach and the grasp may support the hypothesis that in BG circuits the grasp component is less represented than the reach component (Rizzolatti, Luppino, & Matelli, 1998). Indeed, L-dopa therapy does not ameliorate functioning of the BG circuit involved in grasp control, probably because of the smaller neuronal grasping population whose partial restoration is not sufficient to achieve behavioural recovery. Another explanation moves from the finding that the reach and the grasp are partially coordinated (Chieffi & Gentilucci, 1993;
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