Published in final edited form as:

Exp Brain Res. 2006 January ; 168(1-2): 131–142.

Control of aperture closure during reach-to-grasp movements in parkinson's disease

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Abstract

This study examined whether the pattern of coordination between arm-reaching toward an object (hand transport) and the initiation of aperture closure for grasping is different between PD patients and healthy individuals, and whether that pattern is affected by the necessity to quickly adjust the reach-to-grasp movement in response to an unexpected shift of target location. Subjects reached for and grasped a vertical dowel, the location of which was indicated by illuminating one of the three dowels placed on a horizontal plane. In control conditions, target location was fixed during the trial. In perturbation conditions, target location was shifted instantaneously by switching the illumination to a different dowel during the reach. The hand distance from the target at which the subject initiated aperture closure (aperture closure distance) was similar for both the control and perturbation conditions within each group of subjects. However, that distance was significantly closer to the target in the PD group than in the control group. The timing of aperture closure initiation varied considerably across the trials in both groups of subjects. In contrast, aperture closure distance was relatively invariant, suggesting that aperture closure initiation was determined by spatial parameters of arm kinematics rather than temporal parameters. The linear regression analysis of aperture closure distance showed that the distance was highly predictable based on the following three parameters: the amplitude of maximum grip aperture, hand velocity, and hand acceleration. This result implies that a control law, the arguments of which include the above parameters, governs the initiation of aperture closure. Further analysis revealed that the control law was very similar between the subject groups under each condition as well as between the control and perturbation conditions for each group. Consequently, the shorter aperture closure distance observed in PD patients apparently is a result of the hypometria of their grip aperture and bradykinesia of hand transport movement, rather than a consequence of a deficit in transport-grasp coordination. It is also concluded that the perturbation of target location does not disrupt the transport-grasp coordination in either healthy individuals or PD patients.

Keywords

Arm; Finger; Prehension; Coordination; Kinematics; Human

Introduction

The functional basis for coordination between the kinematics of hand transport (arm-reaching movement toward an object) and grasp formation remains a controversial issue in research on reach-to-grasp movements. There have been numerous observations indicating that the moment of the maximum grip aperture (the time at which the distance between the thumb and index fingers is maximized) is precisely timed with respect to hand transport (Jeannerod 1984; Marteniuk et al. 1990; Rand et al. 2000; Wallace et al. 1990). For this reason, it has been suggested that those two processes are temporally linked (Hoff and Arbib 1993; Jeannerod 1981, 1984). In contrast, Haggard and Wing (1991, 1995, 1998) proposed the state-space control as a basis for reach-grasp coordination. Based on the results from their mechanical perturbation study (1991 (1995)), they suggested that the formation of grip aperture is adjusted to maintain the spatial relationship between the grasp and transport components. Similar implications were made in recent studies with neurologically healthy subjects (Alberts et al. 2002; Rand and Stelmach 2005; Rand et al. 2004; Wang and Stelmach 1998, 2001), and PD patients (Alberts et al. 2000; Wang and Stelmach 2000).

It has been demonstrated that the maximum grip aperture (and hence the onset of closing the grip aperture) occurs approximately at the time when the wrist deceleration is maximum, thereby suggesting that onset of aperture closure is triggered by the reduction of transport speed (Jeannerod 1984; Paulignan et al. 1991a, b). Similar findings were also made in PD patients, even when they modified reach-to-grasp movements on-line in response to perturbations (Castiello and Bennett 1994; Castiello et al. 1999). However, recent studies from our laboratory showed that aperture closure distance, defined as the distance of the hand location from the target at which grip aperture began to close, was stable under a variety of conditions, such as differences in reaching distance (Wang and Stelmach 2001), target size (Alberts et al. 2000; Wang and Stelmach 2001), and arm posture used for grasping (Rand and Stelmach 2005). Furthermore, this was also observed even when an external force perturbed a subject's arm while reaching toward a target (Rand et al. 2004). Such stability of the aperture closure distance strongly implies that the reach and grasp are coordinated in the spatial domain, specifically the spatial information on distance of the hand from the target.

Although the above recent results indicate that individuals with PD and neurologically healthy controls coordinate the reach and grasp in the spatial domain, it is not clear whether they do so in the same manner. In some studies PD patients initiated aperture closure based on spatial distance between the hand and the target in a manner similar to that observed in control subjects (Wang and Stelmach 2000). However, in other studies it was shown that the distance to target at which PD patients began aperture closure was significantly shorter than that of controls (Alberts et al. 2000; Schettino et al. 2004). Reasons for this difference between healthy individuals and PD patients are not clear. Schettino et al. (2004) suggested that PD patients rely on visual feedback to control aperture, so that the patients moved the arm until it reached the spatial area where both the hand and target were visible simultaneously, thereby shortening the closure distance.

Another possible explanation is that the initiation of aperture closure is governed by a certain control law defined as a function of specific parameters of arm-target dynamics, such as the hand distance to target, hand velocity, aperture, etc. The term "control law" is standard and central in the mathematical theory of control (e.g., Davis 2002). It describes the dependence of control action (expressed, e.g., in joint torques or muscle activity) on the parameters of the motor plant, which in our experimental paradigm includes the dynamics of the arm and its relationship with the reach target. This theory was successfully used for modeling neural control of arm movements (e.g., Shimansky et al. 2004). If the initiation of aperture closure is based on the neural computation of such a function, the observed shortening of aperture closure

distance in PD patients could be merely a result of slower transport and a smaller aperture. The purpose of the present study is to test the above assumptions and compare the control law for initiation of aperture closure between PD patients and healthy individuals. If the PD patients and the control subjects employ the same control law, the aperture closure distance of the PD patients would be predicted in a similar manner as that of the control subjects, based on the hand transport speed and acceleration, and grip aperture all measured at the time aperture closure is initiated.

A paradigm was selected that permitted the testing of this possibility in both pre-planned unperturbed movements and in movements requiring the on-line control of reach-to-grasp movements. The PD patients have been known to have difficulty coordinating multiple components of many actions (Alberts et al. 1998, 2000; Seidler et al. 2001; Swinnen et al. 1997) as well as reorganizing their behavior from one action to the other (Bennett et al. 1995; Castiello et al. 1993, 1999; Castiello and Bennett 1994; Plotnik et al. 1998). Consequently, differences in the control law employed by individuals with PD and control subjects could be expected when on-line reorientation of the reaching movements in response to perturbations is required. Based on these inferences, we compared the control law for initiation of aperture closure between PD subjects and neurologically healthy controls during reach-to-grasp movements in unperturbed and perturbed conditions.

Materials and methods

Subjects

Eight subjects with Parkinson's disease (mean age: 71.1 years, range: 64–79 years; six males, two females) and ten control subjects (mean age: 71.1 years, range: 60–79 years; five males, five females) participated in the study. The symptoms and severity of the PD patients are listed in Table 1. At the time of the experiment the PD patients were on medication. The controls showed no signs of neurological disease and self-reported no neurological history. All subjects were right-handed based on preferred hand for writing except for two PD patients who were ambidextrous. Participants in each group were screened for impaired cognitive function via the Mini-Mental State Exam (MMSE) (Folstein et al. 1975). The mean ($\pm$ SD) MMSE score was 28.9 ($\pm$ 0.8) for the controls and 28.5 ($\pm$ 0.9) for the PD subjects. This study was approved by the Institute's Internal Review Board, overseeing the use of human subjects in research, ensuring that all studies are performed in accordance with the 1964 Declaration of Helsinki. All subjects provided written informed consent prior to participation.

Apparatus and procedure

All subjects performed reach-to-grasp movements with their right hand. They were seated comfortably in front of a tabletop on which three target objects were placed. The start position was a push button located approximately 30 cm to the right of the subject's midline and placed at the end of an extended armrest. The targets were three dowels, with a diameter of 2.5 cm and a height of 10 cm. The targets were placed in a semi-circular manner centered with respect to the start position, each 55 cm from the start position. The center target was in front of the start position, and the other targets were 20 cm to the right or to the left of the center target. A red LED was attached to the top of each dowel. Twenty-four infrared light beams (Banner Mini-Array system, 19.1 mm beam spacing) were set 17.5 cm away from the start button, perpendicular to the line between the start button and the center target. This system detected when the beams were disrupted making it possible to identify the time at which the subject's hand reached this point during the transport.

Before each trial, the subjects pushed down the start button with the ulnar edge of their hand and closed the thumb and index finger. At the beginning of a trial, the LED on one of the three

targets was illuminated. After a short random delay (the range between 1000 and 1500 ms), a tone signal (1000 Hz, 200 ms duration) was delivered. In response to the tone, subjects were asked to reach for and grasp the lit dowel with only the index finger and thumb at any location along its vertical extent and lift it a few centimeters off the table. The LED remained lit until the end of the trial.

The experiment consisted of two successive sets of trials: a set of control conditions and a set of perturbation conditions. The control set consisted of 60 trials and was completed first, followed by a short break; then the perturbation set was performed. Another break was taken midway through the 120 perturbation trials.

Of the 60 trials in the control set, there were 20 trials to the center target, 20 to the left and 20 to the right, presented in a random order, all considered “control” trials. In the perturbation set, the 120 trials consisted of 40 unperturbed trials and 80 perturbed trials. The center target was always lit at the beginning of the trial. The perturbation consisted of a shift of the illuminated LED during movement from the center target to either the left or right target, which remained lit until the end of the trial. Perturbations were applied at two different times: (1) 50 ms after release of the start button (early perturbation); and (2) at the time when the subject’s hand broke the light beams 17.5 cm away from the start button (late perturbation) [Note that in similar studies the onset of perturbation occurred simultaneously with the release of the start button (Castiello et al. 1999; Gentilucci et al. 1992; Paulignan et al. 1991a). In the present study, the early perturbation timing was set 50 ms after the start button release because our preliminary study on healthy subjects showed that this timing produced a more distinct and consistent modification of hand transport movement in response to the perturbation.] The two perturbation directions and two times produced four perturbation conditions, with 20 trials per condition. The 40 unperturbed and 80 perturbation trials were presented in a pseudorandom fashion. The unperturbed trials in the perturbation set were not utilized in the primary analyses; their function was to make the perturbation more unexpected.

The subjects were instructed to reach for and grasp the target as quickly as possible. This instruction was used to impose the maximum stress on the motor control system for examining the subject’s capacity to coordinate the grasp and transport components under movement perturbations. Fast reach-to-grasp movements were also examined for similar reasons in some previous studies (Paulignan et al. 1991a, b; Desmurget et al. 1996; Rand et al. 2004; Rand and Stelmach 2005). Before the perturbation set, the subjects were told that the perturbation would occur randomly across trials, but that they were to continue reaching for and grasping the target as quickly as possible in every trial. Before the recording session, the subjects practiced reach-to-grasp movements without perturbation for a few trials to each target.

Arm and finger positions during reach-to-grasp movements were recorded using an Optotrak 3D motion analysis system (Northern Digital). Infrared light emitting diodes (IREDS) were placed on the shoulder, elbow, wrist, proximal interphalangeal joint, and tip of the index finger and the interphalangeal joint and tip of the thumb. For all subjects, the location of the wrist IRED was shifted toward the elbow joint 12.2 ± 2.1 (SD) cm on average across subjects so that this IRED was visible to the Optotrak cameras at all time for all trials. This recorded wrist IRED position was adjusted to the level of the actual wrist position for each subject based on the wrist and elbow IRED data, as well as the distance information from the wrist IRED position to the actual wrist position. This adjusted wrist IRED position was used for data analyses. In addition, an IRED was placed on each dowel in order to record its position and movement. Positions of the IREDS were sampled at a rate of 100 Hz.

Data analysis

Kinematic characteristics of the reaching component and grip component were analyzed. The reaching component was assessed based on the wrist IRED. Wrist velocity during the reach was calculated as the first derivative of wrist position. Derivatives were calculated based on the sliding window technique, where the data points within the window were approximated with a quadratic polynomial and its coefficients were then used for calculating its analytic derivative at the window's center (or other points, when at the beginning or end of the data array representing the curve). Thus, calculating derivatives using this method also carried out data filtering. The end of the transport was simultaneous with the end of grasp. An automated movement-parsing algorithm calculated the onset of transport (Teasdale et al. 1993, algorithm B). The onset of the transport was verified by visual inspection by the experimenter; any errors were corrected. The grip component was assessed based on the position of IREDS on the tips of the index and thumb. Grip aperture was defined as the distance between these two IREDS. The end of the grasp was identified as the time when both fingers came in contact with the object, namely, when the decrease of grip aperture during the aperture closure was halted.

The following general parameters of the movement were calculated for each trial: (1) transport time: the duration from reach onset to the end of grasp; (2) total wrist trajectory length: the resultant distance of the wrist path from reach onset to the end of the grasp; (3) amplitude of maximum grip aperture.

For assessing the general characteristic of perturbed trials, the grip aperture and wrist velocity profiles were classified into either a single-peak profile or a multiple-peak profile. The number of trials that had a multiple-peak profile for both the aperture and wrist velocity profiles was counted and expressed as a percentage of all trials within each perturbed condition.

To examine whether maximum grip aperture occurred at a consistent time relative to reach onset or to the grasping of the target object, two variables were identified: aperture opening time, defined as the duration from reach onset to maximum grip aperture (multiple-peak situations are addressed below) and aperture closure time, defined as the duration from maximum grip aperture to the end of grasp. Then, changes in the timing of aperture opening/closure in relation to the total transport time across trials were assessed using regression analysis.

Similarly, to examine if maximum grip aperture occurred at a consistent location relative to the hand location at reach onset and object location, aperture opening distance and aperture closure distance were measured. Aperture opening distance was defined as the distance from the hand location at reach onset to the hand location at maximum grip aperture. Aperture closure distance was defined as the distance from the hand location at the time of maximum grip aperture to the hand location at the end of grasp. These distances were calculated as the resultant distance between two positions of the wrist IRED at which the two events occurred (reach onset and maximum grip aperture; maximum grip aperture and the end of grasp). Subsequently, the changes of the aperture opening/closure distances in relation to the total trajectory length across trials were assessed using a regression analysis.

These parameters of aperture opening and closure time/distance were measured for all trials in the control set and in the unperturbed trials of the perturbation set. In the case of perturbed trials, the event of maximum grip aperture was replaced with the event of the last grip aperture peak for the calculation of these parameters. The reason for this was that the second peak was often produced in response to the perturbation, resulting in a two-peak grip aperture profile together with a two-peak wrist velocity profile (Castiello et al. 1998; Gentilucci et al. 1992; Paulignan et al. 1991a). In addition, a small percentage of perturbed trials (4.9%) had a three-peak grip aperture profile, primarily observed when subjects reached toward the initial target

(and sometimes grasped it), briefly withdrew the hand toward their body, and then reached again toward the new target, producing a three-peak wrist velocity profile (This occurred more frequently in the late perturbation condition.) In this case, as well as the two-peak grip aperture profiles, the last grip aperture peak was the movement made toward the new target. Thus, we used this last peak for analyses.

To examine the relationship between the aperture closure distance and parameters related to the transport and grasp components, wrist velocity and acceleration were measured at the time of maximum grip aperture (and hence the initiation of the aperture closure). Subsequently, a linear regression analysis was performed for estimating the dependence of aperture closure distance on these two parameters and the amplitude of maximum grip aperture.

To verify whether the relationship between the above parameters (aperture closure distance, the amplitude of maximum grip aperture, and wrist velocity and acceleration at the time of maximum grip aperture) estimated in healthy subjects in the control set trials was significantly different from those in the perturbation set for the same subject group or for the PD patients, a residual error analysis was performed for each of the left and right target directions. A residual error was calculated for each subject for each condition as follows: (1) based on each control subject's mean values across all trials, a multiple linear regression analysis was applied for the aperture closure distance as a function of the three parameters for the control set left-target (or the control set right-target) condition; (2) an intercept constant (k_0) and slopes (k_1 , k_2 , and k_3) were calculated from the regression analysis involving the three parameters (aperture, wrist velocity, and wrist acceleration); (3) by using this constant and the slopes, the residual error (E) was calculated for each subject by using the equation $E = k_0 + k_1 x_1 + k_2 x_2 + k_3 x_3 - D$, where x_1 was the mean aperture amplitude across all trials, x_2 the mean wrist velocity, x_3 the mean wrist acceleration and D was the mean aperture closure distance; (4) the intercept constant and slope coefficient values obtained in the control left-target (or right-target) condition were used for the calculation of the residual errors for the early-perturbation and late-perturbation conditions with the left (or right) target; and (5) the same constant and slope values were also used to calculate the residual errors in PD patients. These residual errors were compared between groups as well as across conditions.

For statistical analysis, a mean value across all trials within each subject was calculated for each of the conditions. For the control set, a 2 (group) $\times$ 3 (target) ANOVA with repeated measures, group as a between-subject factor and target as a within-subject factor, was performed to identify any group and target location effects. For the perturbation set, a 2 (group) $\times$ 2 (target location: left or right) $\times$ 3 (perturbation timing: none (from the control set), early, late) ANOVA with repeated measures, group as a between-subject factor and target location and perturbation timing as within-subject factors was performed. The ANOVA results were adjusted with the Huynh-Feldt epsilon (ϵ) correction when necessary. When significant, the value of ϵ is reported together with the adjusted P -value and the corresponding uncorrected degrees of freedom. When needed, a post hoc comparison with Bonferroni correction was performed ($\alpha = 0.05$) to identify significant differences between individual cell means.

Furthermore, the variability between the values of aperture closure time and aperture closure distance were compared as follows: (1) the normalized aperture closure time was calculated as a percentage of transport time, (2) the normalized aperture closure distance was calculated as a percentage of total wrist trajectory length, (3) the variance across all trials in the control set was calculated for each subject for each of the normalized aperture closure times and distances, and (4) based on these variance values, comparisons between the variances of these two types of measurements (time or distance) were carried out for each group by using the Wilcoxon matched-pairs signed-rank test.

Results

Parameters relating to aperture closure initiation

Control set—The subjects performed pre-planned reach-to-grasp movements toward one of the three targets. Means standard errors, and F values of the kinematic measures are shown in Table 2. In agreement with numerous studies that reported bradykinetic movements in PD patients (Alberts et al. 2000; Castiello et al. 1999; Majsak et al. 1998; Tresilian et al. 1997), the PD patients produced significantly slower transport movements than controls ($P<0.05$). As for the grasp component, PD group had a significantly smaller amplitude of maximum grip aperture than controls ($P<0.001$), showing the hypometric movement features that are typical for individuals with PD (Castiello and Bennett 1994; Castiello et al. 1999; Gentilucci and Negrotti 1999).

For the purpose of examining if maximum grip aperture (hence the initiation of aperture closure) occurred at a stable time relative to reach onset or to grasping the object, the aperture opening time, and aperture closure time were examined. Figure 1a and c shows scatter plots of these times as a function of total transport time across all trials in the three control conditions. As seen in the figure, both groups increased the aperture opening time as the total transport time increased (Control—Panel a upper regression line: slope=0.83, $r=0.95$, $P<0.0001$; PD—Panel c upper regression line: slope=0.79, $r=0.97$, $P<0.0001$) and aperture closure time (Control—Panel a lower regression line: slope=0.17, $r=0.55$, $P<0.0001$; PD—Panel c, lower regression line: slope=0.21, $r=0.75$, $P<0.0001$). Thus, the initiation of aperture closure occurred at variable times relative to both reach onset and grasping the object.

Similar to the temporal measures, in order to assess if maximum grip aperture occurred at a stable distance relative to reach onset location or to the object, aperture opening distance and aperture closure distance were examined. Figure 1b and d are scatter plots of these distances as a function of total hand transport distance (trajectory length). The plots show that both groups similarly increased opening distance as the total transport distance increased (Control—Panel b upper regression line: slope=1.00, $r=0.79$, $P<0.0001$; PD—Panel d upper regression line: slope=0.86, $r=0.87$, $P<0.0001$). In contrast to the opening distance, the PD and control subjects began to close aperture at a stable distance from the target across different trials (Fig. 1b and d, lower regression line). There was no correlation between closure distance and total transport distance for the control subjects (Panel b, slope=0, $r=0.107$). The PD patients, however, showed a very slight positive relation between the closure distance and the total transport distance (Panel d, slope=0.13, $r=0.27$, $P<0.0001$).

Thus, among parameters of aperture opening and closure times and distances, aperture closure distance was stable across trials while others varied. This indicates that the aperture closure initiation occurred at a stable distance relative to the target, suggesting that the initiation of aperture closure was controlled based on this spatial information.

To confirm statistically that the aperture closure distance measurements had less variability than the aperture closure time measurements, normalized closure distance and closure time measurements were calculated and expressed as a percentage of reaching distance and time, respectively. The mean and variance of normalized closure distance across subjects was 10.8 and 7.6%, respectively, for the control group, and 6.7 and 4.6%, respectively, for the PD group. The mean and variance of normalized closure time across subjects was 23.9 and 15.6%, respectively, for the control group and, 20.9 and 23.5%, respectively, for the PD group. The variance of normalized closure distance was significantly smaller than that of the normalized closure time for both groups (Control: ($Z(10)=2.59$, $P<0.01$; PD: ($Z(10)=2.52$, $P<0.05$), emphasizing that the spatial parameters were less variable than the temporal parameters for

both groups. This finding supports the notion that the distance from the hand to the target is a critical factor in initiating the aperture closure for both PD and control subjects.

Each group's mean values for the aperture opening and closure times and distance were summarized in Table 2. Both mean aperture opening time and mean closure time were significantly longer for the PD patients than for the controls ($F(1, 16)=8.24$, $P<0.05$ for opening time, $F(1, 16)=6.47$, $P<0.05$ for closure time). As for the spatial measures, PD patients tended to travel for a greater distance to the maximum grip aperture than the controls ($F(1, 16)=3.72$, $P<0.1$). Mean closure distance of the PD patients was significantly shorter than that of the controls ($F(1, 16)=8.12$, $P<0.05$). This indicates that PD patients traveled to a point much closer to the target before they began aperture closure. In this set, the illumination of the target suddenly moved from the center target to either the left or right target during the reach, requiring the subjects to re-orient their arm to a new location. As expected from previous studies that examined the effects of target location perturbations (Castiello et al. 1999; Paulignan et al. 1991a; Scarpa and Castiello 1994), the subjects showed a biphasic wrist velocity profile and a biphasic aperture profile for the majority of the perturbation trials regardless of the time of perturbation. In a small number of trials subjects even made more than two peaks in the aperture and/or transport profiles. Between two groups, the controls produced a higher percentage of trials with multiple-peaks for both the velocity and aperture profiles (early-perturbation: 61.4%; late-perturbation: 87.2%) than the PD patients (early-perturbation: 10.7%; late-perturbation: 67.8%). The above observations are supported by the results of the total wrist trajectory length during the reach (Table 3). A $2 \times 2 \times 3$ ANOVA revealed that the group and perturbation timing interaction was significant for this measurement ($F(2, 32)=6.28$, $\eta^2=0.91$, $P<0.01$). A post hoc analysis revealed that controls increased the trajectory length from the control trials to the early-perturbation condition ($P<0.001$) and from the early-perturbation to the late-perturbation condition ($P<0.001$). Conversely, PD patients increased the trajectory length only for the late-perturbation condition from the control condition ($P<0.05$). The means and standard errors for total wrist trajectory length, transport time, and the amplitude of maximum grip aperture are presented in Table 3.

For the purpose of examining the stability of spatial and temporal coordination between the transport and grasp component, aperture opening/closure times and distances were measured for the perturbation trials. Mean values across subjects for these parameters are shown in Table 3. To determine whether the aperture closure distance, which was found to be stable in the control set, was changed with perturbations, a $2 \times 2 \times 3$ ANOVA was applied. The PD patients made a significantly shorter aperture closure distance than the control subjects ($F(1, 16)=9.33$, $P<0.01$). However, there was no perturbation timing main effect and no target location main effect. Thus, the aperture closure distance was relatively stable within each group regardless of perturbations, again supporting the notion that the distance from the hand to the target is a critical factor in initiating the aperture closure for both groups.

In contrast to the stability of aperture closure distance, other parameters underwent significant changes in the perturbation conditions. Both the time and distance of aperture opening increased under the perturbations compared to the control conditions (perturbation timing main effect: $F(2, 32)=86.16$, $\eta^2=0.96$, $P<0.01$ for opening time; $F(2, 32)=65.69$, $P<0.001$ for opening distance). In terms of the aperture closure time, the PD patients spent a slightly longer time for aperture closure in the perturbed conditions than in the control conditions (Table 3), while the control subjects spent a slightly shorter time. Accordingly, the group and perturbation timing interaction was significant ($F(2, 32)=3.63$, $\eta^2=0.95$, $P<0.05$), and a post-hoc analysis revealed that the difference between both groups was significant for the perturbed conditions ($P<0.01$ for both early-perturbation and late-perturbation conditions).

Data supporting the existence of a control law for initiating aperture closure

It is not immediately clear why the distance to the target at which the PD patients initiated aperture closure was significantly shorter than that of the controls. One possible explanation is that the above distance could depend on wrist velocity. If so, since the PD patients moved more slowly, they would not initiate aperture closure until the wrist distance to the target was proportionally shorter. Based on this conjecture, we hypothesized that the initiation of aperture closure is governed in general by a certain control law, a function defined based on certain state parameters. The set of relevant parameters apparently should include distance to target, grip aperture, wrist velocity, and wrist acceleration. Then, the condition for initiation of aperture closure can be presented formally as $F(x_1, x_2, x_3, x_4) \geq 0$, where x_1, x_2, x_3 , and x_4 are the above state parameters, respectively. The onset of aperture closure would correspond to a state where $F(x_1, x_2, x_3, x_4)=0$. This equation can be solved with respect to a certain state parameter (e.g., wrist distance to target), and that parameter therefore can be presented as a function of the other parameters: $x_1=F_1(x_2, x_3, x_4)$. Assuming that the region of state-space explored experimentally is sufficiently small for linear approximation of $F_1(x_2, x_3, x_4)$ to be sufficiently accurate, we can test the above hypothesis by presenting x_1 as $x_1=k_2 x_2+k_3 x_3+k_4 x_4+k_0$ and estimating the slope coefficients k_2, k_3 and k_4 , and the intercept constant k_0 based on linear regression analysis. To illustrate, a schematic diagram of the regulation of aperture closure initiation is shown in Fig. 2. Only two state parameters, hand distance to target (D) and hand velocity (V), constitute a function $F(D, V)$ in the figure for simplification. Based on the law described in the figure, it is predicted that the hand distance to the target at which PD patients initiate aperture closure is shorter than that of control subjects, because the PD patients move their hand more slowly than that of the controls.

The results of the regression analysis for the control (non perturbation) set are illustrated in Fig. 3. Data points in the plots reflect parameter values averaged across the control condition trials for individual subjects. For the control group (Fig. 3a–c, open circles), there are significantly high positive correlations between the closure distance and grip aperture ($r=0.83$, $P<0.01$), velocity ($r=0.96$, $P<0.001$), and acceleration ($r=0.94$, $P<0.001$) measures. The PD group (Fig. 3a, b, solid circles) also produced a significantly high correlation between the closure distance and wrist velocity ($r=0.86$, $P<0.01$), and a trend of correlation between closure distance and grip aperture ($r=0.69$, $P=0.054$). However, contrary to the control group, there was no significant correlation between the closure distance and wrist acceleration (Fig. 3c, solid circles, $r=0.57$). Despite the fact that the PD patients had both shorter closure distance and smaller values for all three parameters than the controls, the relationship between the closure distance and each of the parameters followed similar linear correlations across groups. The results obtained from the center and right target conditions were similar to those of the left target condition. Furthermore, the perturbation set exhibited similar results to the ones in the control set.

If the data of PD patients are on a continuum with those of the control subjects as suggested in Fig. 3, the PD patients likely used the same law as the control subjects in triggering the aperture closure based on the information of finger aperture, wrist velocity and acceleration. To test this interpretation, we examined whether the data of PD patients were distributed along the same regression line defined by the data of control subjects. We applied a multiple linear regression analysis based on each subject's mean values across trials to identify the regression line that predicted the aperture closure distance in terms of the amplitude of maximum grip aperture, wrist velocity and wrist acceleration for the control subjects. With all three parameters included, the regression coefficient was very high for both the left-target control condition ($r=0.96$, $P<0.001$) and the right-target control condition ($r=0.96$, $P<0.001$). Based on the intercept constant and slopes of the regression line obtained in the control conditions, the residual errors were calculated for each subject for each condition (see Methods section). These

residual values were submitted to a $2 \times 2 \times 3$ ANOVA. The main effect showed that there was neither group difference ($P > 0.05$), nor perturbation timing condition difference ($P > 0.05$). Thus, the data points related to the PD patients were distributed along the regression line based on the control subjects' data. These results imply that the PD patients and control subjects used a similar control law for triggering the aperture closure based on the aperture, wrist velocity and acceleration during the reach, and that both groups used similar control laws under both control and perturbation conditions.

We conducted a regression analysis to assess how the three variables that were measured at the time of maximum grip aperture were related to the aperture closure distance based on each trial. First, the regression coefficients between the aperture closure distance and each of the three parameters were calculated across all trials for each subject. Based on individual values, average regression coefficients across conditions and across subjects were calculated. The average regression coefficient ($\pm$ SE) for the amplitude of maximum grip aperture was 0.349 ± 0.063 for the controls and 0.229 ± 0.071 for the PD patients. The value for the wrist velocity was 0.725 ± 0.037 for the controls and 0.590 ± 0.041 for the PD patients. The value for the wrist acceleration was 0.378 ± 0.042 for the controls and 0.192 ± 0.047 for the PD patients. For both groups, wrist velocity exhibited the highest coefficient among the three parameters, indicating that the wrist velocity is the best predictor of the aperture closure distance. Furthermore, including all three parameters into the regression analyses produced high regression coefficients in relation to the aperture closure distance (control: 0.810 ± 0.028 and PD patients: 0.696 ± 0.031). A $2 \times 2 \times 3$ ANOVA revealed that the PD patients showed significantly smaller coefficients than the controls subjects for the correlation between the closure distance and wrist velocity ($F(1, 16) = 5.99$, $P < 0.05$), wrist acceleration ($F(1, 16) = 8.75$, $P < 0.01$), and all three parameters included ($F(1, 16) = 7.56$, $P < 0.05$). In summary, the closure distance in a given trial depended on the grip aperture amplitude as well as hand velocity and acceleration. Although the PD patients employed the same control law for initiating aperture closure, they relied less on hand velocity and acceleration, compared to the control subjects. Finally, there was no perturbation timing main effect for all comparisons. Thus, both groups performed similarly under all conditions, regardless of the perturbations.

Discussion

Initiation of aperture closure in PD and healthy subjects governed by same control law

A clear difference between PD and control groups in initiating aperture closure to grasp an object was that the PD patients initiated aperture closure at a shorter distance to the target. This abnormal characteristic in PD patients was in agreement with previous studies (Alberts et al. 2000; Schettino et al. 2004). Despite this difference, the present results support a conclusion that PD patients and control subjects initiate aperture closure based on essentially the same control law defined by the kinematic state parameters of hand distance to target, hand velocity and acceleration, and grip aperture magnitude.

As a first step to support this conclusion, the present results provide evidence that the initiation of aperture closure occurred at a consistent distance along the reach from the target (Fig. 1b, d), but at a variable time (Fig. 1a, c). Thus, it is suggested that the spatial information plays a dominant role in triggering the aperture closure in both groups of subjects rather than the temporal information. These results support findings of previous studies (Alberts et al. 2000, 2002; Rand and Stelmach 2005; Rand et al. 2004; Wang and Stelmach 1998, 2001). The PD and control groups showed similar results, suggesting that PD patients were the same as control subjects in terms of using spatial rather than temporal information in initiation the grip aperture closure.

As a second step to support the above conclusion, the linear regression analysis of aperture closure distance averaged across trials for each subject showed that the distance was highly predictable based on the following three parameters of arm dynamics: amplitude of maximum grip aperture, hand velocity, and hand acceleration (Fig. 3). This result implies that a control law, the arguments of which include the above parameters, governs the initiation of aperture closure. The results further showed that the PD patients were able to use a similar law as that used in control subjects, suggesting that the patients produced typical patterns of coordination between the hand transport and the initiation of the aperture closure. Thus, PD does not seem to impair this coordination during the reach-to-grasp movements, despite that PD patients are known to have difficulty in coordinating multiple components of many other actions (Alberts et al. 1998,2000;Seidler et al. 2001;Swinnen et al. 1997).

Previously, Schettino et al. (2004) suggested that PD patients' strategy of applying visual feedback-based control was a possible reason for the shorter aperture closure distance in PD patients. They argued that, by the time of maximum grip aperture, the PD patient's hand is already within the region of space where both hand and target object are visible simultaneously, thereby enabling visual feedback-based control for determining formation of the grasp. However, in the current study, the aperture closure distance of the controls was only about 2 cm greater than that of the PD patients, and initiation of aperture closure for the controls occurred at about 5 cm away from the target (Table 2). Consequently, it is likely that the controls were also able to see the target object and hand simultaneously at the time of initiation of aperture closure. Thus, whether their argument can be exclusively applied to PD patients is questionable. Therefore, the visual feedback-based control may not be the only reason for the shorter aperture closure for PD patients.

The experimental fact that PD patients initiate aperture closure at a shorter distance to target can be explained using our finding that closure initiation is based on a control law based on kinematic parameters that include positively correlated hand distance to target, grip aperture amplitude, hand velocity and hand acceleration. Since the PD patients exhibited a smaller grip aperture and moved their hand significantly more slowly than the control subjects, the control law predicts that the distance to target at which they initiated aperture closure should also be shorter. Thus, the shorter aperture closure distance observed in PD patients can be viewed as resulting from hypometria of their grip aperture (Castiello and Bennett 1994; Castiello et al. 1999; Gentilucci and Negrotti 1999) and bradykinesia of their hand transport (Alberts et al. 2000; Castiello et al. 1999; Majsak et al. 1998; Tresilian et al. 1997), rather than being a result of a deficit in transport-grip coordination in terms of the initiation of aperture closure.

Weaker dependence of aperture closure initiation on velocity and acceleration in PD patients

An important result of the present study is that the PD patients scored significantly smaller regression coefficients between aperture closure distance and hand speed (velocity and acceleration) than the control subjects did. This fact, together with the finding that the aperture closure initiation is governed by the same control law in both PD patients and healthy controls, indicate that the PD patients rely less on those kinematic parameters when initiating aperture closure, compared with the control subjects. There are two possible explanations for this difference. First, it may be a consequence of the slowness characterizing the patients' movement (Fig. 1, Tables 1, 2). The PD patients are well known to be bradykinetic, caused in part by a smaller-than-normal agonist burst due to basal ganglia impairments associated with PD (Farley et al. 2004;Flament et al. 2003;Hallett and Khoshbin 1980;Wierzbicka et al. 1991). The slower the movement, the smaller the range of velocity and acceleration values, which could lead to a decrease in sensory perception accuracy. It also could result in a data analysis artifact due to an increase in the relative contribution of noise related to data registration and processing (e.g., digital differentiation). Second, assuming that sensory

information about velocity and acceleration is derived mainly from proprioception rather than vision, the reduced correlation between the aperture closure distance and hand velocity and acceleration in PD patients may reflect patients' abnormality in the processing of proprioceptive information regarding hand velocity and acceleration during the reach-to-grasp movements as well as the utilization of that information. It was previously documented that PD patients exhibited a deficit in the processing of proprioceptive information during aiming movements (Adamovich et al. 2001; Khudados et al. 1999; Rickards and Cody 1997). Although the first explanation seems to be more likely, the second possibility cannot be excluded at this time. It is consistent with the results of a different study in which we tested young adults who performed reach-to-grasp movements in four different speed conditions (slow, comfortable, fast, and as fast as possible, Squire et al. 2004). The result showed that the regression coefficient between aperture closure distance and hand velocity as well as acceleration did not change with the speed conditions. Dissociation between the above two possibilities is an important problem; to address it adequately, further studies with specifically designed experimental conditions are required.

Control of aperture closure initiation is similar for pre-planned and re-planned movements

Little effect of perturbing target position was observed in the control of aperture closure initiation in the current study. Both the PD and control groups produced a similar aperture closure distance for the pre-planned movements (control conditions) and on-line re-planned movements (perturbation conditions). At the same time, the PD patients utilized essentially the same control law for aperture closure initiation as that employed by the control subjects even under perturbation conditions with two different perturbation timings. Together, these results suggest that the initiation of the aperture closure in relation to the hand transport is mediated by a mechanism that is used in both pre-planned movements and those re-planned in response to perturbation. Thus, the differences between the PD patients and controls in such parameters as end-point trajectory length and the number of peaks observed in grip aperture and hand velocity profiles should be attributed to the patients' bradykinesia (Castiello and Bennett 1994; Castiello et al. 1999; Gentilucci and Negrotti 1999), rather than a deficit in transport-grasp coordination either in unperturbed or perturbed trials. Furthermore, the PD patients, apart from being bradykinetic, did not demonstrate any impairment specific to the control of grasp initiation. Therefore, it is unlikely that the basal ganglia are significantly involved in this aspect of controlling reach-to-grasp movements.

Should aperture closure be considered a self-initiating movement?

It has been reasonably well established that PD patients experience considerable difficulty with self-initiation of motor actions (Debaere et al. 2003; Jackson et al. 1995; Morris et al. 1996; Oliveira et al. 1997; Schenk et al. 2003). For the initiation of aperture closure during reach-to-grasp, there is no explicit sensory cue. Hence, grasp initiation requires an internally generated signal, which is not a part of conscious control, but originates from the progress of arm transport with relation to the reach target. Therefore, initiation of the grasp may be considered a self-initiated, automatic motor act linked to the context of an ongoing goal-directed movement. As our results indicate, PD patients utilized essentially the same control law for aperture closure initiation as that employed by the control subjects, suggesting that the performance of this specific motor act is not significantly impaired in PD patients. Consequently, it can be hypothesized that PD patients are impaired in self-initiation of a specific motor action only if the initiation is made by a conscious effort. This is an important question to address in future studies.

The results of the present study support the conclusion that, despite the bradykinesia of arm transport and the hypometria of grip aperture, the coordination between arm transport and aperture closure is not significantly impaired in PD patients. These findings improve our

understanding of the specific nature of the deficit in goal-directed control of arm movements in those with PD, which is important for developing reliable PD-related diagnostic tools and intervention methods.

Acknowledgements

This study was supported by NIH grants NS 36752 and NINDS NS 39352, NS 40266. We are grateful to Mr. Richard Bauer, Ms. Quinn Emerson and Ms. Linda M. Squire for their technical support. We also thank Dr. Todd Ajax and Dr. Michael Kitchell for their help with subject recruitment. Portions of the results of this study were presented at the Society for Neuroscience 34th Annual Meeting, San Diego, USA, 2004.

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Fig. 1.

Grip aperture opening (*open squares*) and grip aperture closure (*filled squares*) for the control set. **a** and **c** plot the aperture opening/closure time as a function of total transport time. **b** and **d** plot the aperture opening/closure distance as a function of total transport distance. Panels **a** and **b** represent individual trials for control subjects and Panels **c** and **d** represent individual trials for PD patients

Fig. 2.

Schematic diagram of the regulation of aperture closure initiation. The condition for initiating the control action is described based on a function $F(D, V)$ defined on the hand's distance to the target (D) and hand velocity (V) as state parameters. Aperture closure onset corresponds to a state where $F(D, V) = 0$. The condition for aperture closure in progress is described as a state where $F(D, V) \geq 0$. The arrows depict small segments of hand trajectory in state-space coordinates D and V . The distance to the target at which PD patients initiate aperture closure is shorter than that of healthy subjects, because the PD patients move their hand more slowly than that of the controls

Fig. 3.

Scatter plots for the aperture closure distance as a function of the amplitude of aperture (a), the wrist velocity (b) and wrist acceleration (c) at the time of maximum grip aperture. The data from the left-target control condition are presented. Mean values for each subject are plotted for the control group (open circles) and the PD group (filled circles). The error bars indicate the standard deviations

Table 1

Description of Parkinson’s disease patients

Patient Number	Age (years)	Gender	Duration (years)	H and Y	Bradykinesia	Resting tremor	Rigidity	Dyskinesia	Affected side	Medications
1	74	M	15	3	Yes	No	Yes	Mild	B	Sinemet, Amantadine, Comtan, Mirapex
2	64	M	15	2	Yes	No	No	Moderate	R	SinemetCR, Mirapex, Amantadine
3	79	M	5	2	Yes	No	Yes	No	B	Sinemet, Mirapex
4	65	F	1	1	Yes	Yes	Yes	No	R	None
5	71	F	10	3	Yes	Yes	Yes	No	B	Sinemet
6	73	M	10	2	Yes	Yes	Yes	No	B	Sinemet, SinemetCR, Requip
7	66	M	2	2	Yes	Yes	No	No	B	Mirapex, Selegiline, Eldepryl
8	77	M	16	2.5	Yes	No	Yes	No	B	Sinemet, Amantadine, Mirapex, Comtan

Table 2
Mean (SE) of kinematic parameters for control conditions for the control subjects and Parkinson’s disease patients

	Controls (n=10) target location			PD patients (n=8) target location			Group effects
	Center	Left	Right	Center	Left	Right	
Transport time (ms)	690 (68)	667 (64)	695 (68)	1148 (157)	1157 (160)	1154 (171)	$F=8.38^*$
Total wrist trajectory length (mm)	502 (8)	498 (9)	487 (8)	504 (9)	504 (7)	493 (12)	ns
Amplitude of maximum grip aperture (mm)	79 (5)	80 (5)	80 (5)	50 (4)	50 (4)	52 (4)	$F=22.26^{***}$
Aperture opening time (ms)	532 (61)	515 (57)	530 (60)	916 (129)	924 (132)	898 (136)	$F=8.24^*$
Aperture closure time (ms)	159 (11)	152 (11)	165 (13)	232 (30)	233 (32)	256 (40)	$F=6.47^*$
Aperture opening distance (mm)	450 (10)	445 (10)	432 (10)	472 (8)	472 (5)	456 (10)	ns
Aperture closure distance (mm)	53 (6)	53 (6)	55 (6)	33 (3)	32 (4)	36 (3)	$F=8.12^*$

ns not significant, *df*. 1,16,
* $P \leq 0.05$,
** $P \leq 0.01$,
*** $P \leq 0.001$

Table 3
Mean (SE) of kinematic parameters for the perturbed conditions for the control subjects and Parkinson’s disease patients

	Controls (n=10)						PD patients (n=8)					
	Unperturbed			Perturbed			Unperturbed			Perturbed		
	Left			Right			Left			Right		
	Early timing	Late timing		Early timing	Late timing		Early timing	Late timing		Early timing	Late timing	
Transport time (ms)	819 (37)	957 (39)		834 (40)	988 (51)		1247 (185)	1462 (186)		1359 (213)	1527 (185)	
Total wrist trajectory length (mm)	581 (17)	644 (22)		574 (23)	639 (21)		520 (7)	585 (15)		515 (14)	580 (23)	
Amplitude of maximum grip aperture ^a (mm)	90 (5)	93 (5)		88 (4)	90 (4)		50 (5)	52 (6)		52 (5)	53 (5)	
Aperture opening time ^a (ms)	681 (32)	813 (38)		688 (32)	858 (49)		1002 (146)	1195 (137)		1075 (166)	1278 (148)	
Aperture closure time ^a (ms)	138 (6)	144 (10)		147 (10)	130 (9)		245 (42)	266 (53)		284 (62)	249 (48)	
Aperture opening distance ^a (mm)	523 (13)	580 (16)		523 (22)	593 (21)		481 (6)	544 (13)		477 (12)	546 (21)	
Aperture closure distance ^a (mm)	58 (7)	65 (10)		51 (3)	45 (3)		39 (5)	40 (4)		38 (4)	34 (3)	

^aValues are obtained based on the last aperture peak