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Finger force changes in the absence of visual feedback in patients with Parkinson's disease

Hang Jin Jo[a], Satyajit Ambike[a], Mechelle M. Lewis[b,c], Xuemei Huang[a,b,c,d,e], Mark L. Latash[a,*]

[a] Department of Kinesiology, The Pennsylvania State University, University Park, PA 16802, USA
[b] Department of Neurology, Pennsylvania State University – Milton S. Hershey Medical Center, Hershey, PA 17033, USA
[c] Department of Pharmacology, Pennsylvania State University – Milton S. Hershey Medical Center, Hershey, PA 17033, USA
[d] Department of Radiology, Pennsylvania State University – Milton S. Hershey Medical Center, Hershey, PA 17033, USA
[e] Department of Neurosurgery, Pennsylvania State University – Milton S. Hershey Medical Center, Hershey, PA 17033, USA

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HIGHLIGHTS

- Patients with Parkinson's disease (PD) show an accelerated drop in total force in accurate two-finger force production tasks performed without visual feedback.
- Sharing of the total force between the two fingers drifts towards a 50:50 pattern without a difference between the PD patients and control subjects.
- The accelerated force drop in PD may reflect adaptive changes to the documented loss of action stability.

ABSTRACT

Objectives: We investigated the unintentional drift in total force and in sharing of the force between fingers in two-finger accurate force production tasks performed without visual feedback by patients with Parkinson's disease (PD) and healthy controls. In particular, we were testing a hypothesis that adaptation to the documented loss of action stability could lead to faster force drop in PD.

Methods: PD patients and healthy controls performed accurate constant force production tasks without visual feedback by different finger pairs, starting with different force levels and different sharing patterns of force between the two fingers.

Results: Both groups showed an exponential force drop with time and a drift of the sharing pattern towards 50:50. The PD group showed a significantly faster force drop without a change in speed of the sharing drift. These results were consistent across initial force levels, sharing patterns, and finger pairs. A pilot test of four subjects, two PD and two controls, showed no consistent effects of memory on the force drop.

Conclusions: We interpret the force drop as a consequence of back-coupling between the actual and referent finger coordinates that draws the referent coordinate towards the actual one. The faster force drop in the PD group is interpreted as adaptive to the loss of action stability in PD. The lack of group differences in the sharing drift suggests two potentially independent physiological mechanisms contributing to the force and sharing drifts.

Significance: The hypothesis on adaptive changes in PD with the purpose to ensure stability of steady states may have important implications for treatment of PD. The speed of force drop may turn into a useful tool to quantify such adaptive changes.

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* Corresponding author at: Department of Kinesiology, Rec.Hall-268N, The Pennsylvania State University, University Park, PA 16802, USA. Tel.: +1 814 863 5374; fax: +1 814 863 4424.

E-mail address: mll11@psu.edu (M.L. Latash).

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1. Introduction

Stability of action is paramount given the unpredictable external conditions typical of natural everyday motor behavior. The idea of task-specific stability (Schöner, 1995) implies that the central nervous system (CNS) is able to organize redundant (actually, abundant, Latash, 2012) sets of elements taking part in all natural movements into groups (synergies, Latash et al., 2007; Latash, 2008) that provide stability with respect to salient, task-specific variables. Analysis of inter-trial variance within the space of elemental variables has been used to provide a quantitative index of stability: Assuming that individual trials start from somewhat different internal states, variance in directions of low-stability is expected to be large whereas variance in directions of high stability is expected to be low. Within the uncontrolled manifold (UCM) hypothesis (Scholz and Schöner, 1999), the difference between the former (variance within the UCM, V_{UCM}) and the latter (variance orthogonal to the UCM, V_{ORT}) has been used as an index of synergy (ΔV) stabilizing the corresponding performance variable.

Problems with stability of posture and movement are among the most common consequences of Parkinson's disease (PD), and postural instability is one of the cardinal features of PD (Fahn and Jankovic, 2007). In a recent series of studies, we used the framework of the UCM hypothesis to quantify stability of multi-finger pressing and prehensile actions (Park et al., 2012, 2013; Jo et al., 2015). Across tasks and analyses, patients with early-stage PD showed significantly lower synergy indices, ΔV, stabilizing the multi-finger steady-state actions compared to controls.

Recently, a complementary mechanism of ensuring stability of action has been hypothesized based on the observations of unintentional changes in the motor output when subjects were instructed to keep the output constant (Vaillancourt and Russell, 2002; Zhou et al., 2014; Ambike et al., 2015). In particular, when a healthy person is asked to press with a finger and maintain constant force, turning the visual feedback off leads to a slow drop in the produced force, up to 40% of the initial force level over 20 s (Slifkin et al., 2000; Vaillancourt and Russell, 2002; Shapkova et al., 2008; Ambike et al., 2015). Active force production may be viewed as a consequence of a discrepancy between the actual (AC) and referent (RC) coordinates of the finger multiplied by a gain (apparent stiffness, cf. Latash and Zatsiorsky, 1993). Within this view, the unintentional force drop reflects a slow drift of RC towards AC, which is fixed in isometric conditions. This drift reduces the difference between the AC and RC and hence moves the effector closer to the minimum of its potential energy (reached when AC = RC), which is also a state of high stability.

A recent study explored accurate total force production by the two index fingers pressing simultaneously while the shares of the total force produced by the two fingers varied across trials within a broad range (Ambike et al., 2015). Turning the visual feedback off led to two phenomena: The aforementioned drift of the total force was accompanied by a drift in the sharing pattern towards more equal force distribution between the two fingers. The time profiles of the two drifts were similar leading to a conclusion that they reflected a single neurophysiological mechanism.

In this study, we explored the unintentional force drift during accurate force production without visual feedback in patients in early-stage PD. Our main hypothesis was that PD patients could use an adaptive strategy to compensate, at least partially, for their loss of stability reflected in the reduced synergy index (Park et al., 2013, 2014). Hence, we expected the patients to show a stronger coupling between the AC and RC of the fingers resulting in a faster unintentional drop in the finger force when the visual feedback was turned off (cf. Vaillancourt et al., 2001). We also explored the effects of varying the initial sharing pattern of force between the two fingers based on the mentioned observations that the sharing drifts towards a preferred pattern, close to 50:50 (Ambike et al., 2015). In that study, Ambike and colleagues suggested that a single neurophysiological process could be responsible for the observed drifts of finger forces to lower values and sharing towards a preferred pattern. Both were supposed to reflect a drift within the UCM, which also affected total force because of the coupling between the UCM and orthogonal to the UCM sub-spaces. Therefore, our second hypothesis for the present study was that the adaptive changes leading to a faster drop in forces in PD patients (as in the first specific hypothesis) would also lead to a faster drift in the sharing pattern.

2. Methods

2.1. Subjects

Ten patients with PD (aged 63.1 ± 4.6 years; 6 males) and 10 age-matched control subjects (CS; aged 63.3 ± 3.1 years; 7 males) were tested. The participants were selected from a larger pool of subjects of an ongoing clinical and neuroimaging correlation study in which all PD subjects were recruited from a movement disorder clinic and diagnosed by movement disorder specialists. CS were recruited from spouses and friends of the patients, as well as through flyers posted in the local community. All participants were right-handed according to their preferential hand use during writing and eating. None of the CS had any known neurological disorders or arthritis in their upper extremities.

Descriptive data for all subjects are presented in Table 1. For PD subjects, Unified PD Rating Scale part III – motor scores (UPDRS-III) ranged between 3 and 24. The median duration of illness since diagnosis was 2.2 years (ranging from 0.1 to 8.1 years); none of the patients showed postural instability and/or signs of drug-induced dyskinesia. PD subjects were tested while on their prescribed anti-parkinsonian medication. The levodopa equivalent daily dose (LEDD) was estimated for PD subjects according to a published formula (Tomlinson et al., 2010). The study protocol followed the Helsinki principles and was reviewed and approved by the Pennsylvania State University-Hershey Medical Center Institutional Review Board. Written informed consent was obtained from all subjects.

2.2. Apparatus and procedure

Subjects were seated comfortably in a chair with their forearms resting on top of a table and facing a 19-in. computer monitor positioned at eye level. They performed a set of tasks with two fingers pressing on individual force sensors (1) right and left index fingers (*BOTH* condition); (2) right index and middle fingers (*RIGHT* condition); and (3) left index and middle fingers (*LEFT* condition). Two piezoelectric force sensors (model 208A03; PCB Piezotronics, Depew, NY) were used to measure the vertical forces produced by the fingers. Each sensor was covered with sandpaper (100-grit) to increase the friction between the fingertips and the top surface of the sensors. Prior to each trial, all sensor signals were set to zero when subjects placed their fingertips on the sensor centers and relaxed their hands. As a result, the sensors measured only active downward forces. A customized LabVIEW program was used for the data acquisition at 100 Hz with 16-bit resolution and for subject feedback.

For the *BOTH* condition, subjects' shoulders were flexed at approximately 30°, abducted at approximately 30° and internally rotated approximately 45° with the elbows flexed approximately at 90° (Fig. 1A). The mid-point between the two sensors was aligned with the midline of the body, and the distance between

Table 1
Description of study participants.

Subject	Sex, M/F	Age, year	Handedness, R/L	Symptom onset	Years since diagnosis	HY stage	UPDRS motor score	Medication, on/off	Total LEDD, mg
PD group									
1	M	49	R	R	4.9	II	10	On	300
2	F	72	R	R	4.1	II	11	On	400
3	F	47	R	Both	0.9	II	12	On	160
4	M	76	R	Both	1.0	II	24	On	350
5	F	48	R	L	1.7	I	10	On	380
6	F	79	R	L	2.0	I	16	On	250
7	M	43	R	R	0.1	I	12	Off	0
8	M	67	R	L	8.1	I	3	On	737.5
9	M	79	R	R	2.3	II	8	On	500
10	M	71	R	R	3.2	II	21	On	400
CS group									
1	F	59	R						
2	M	47	R						
3	F	77	R						
4	M	56	R						
5	F	54	R						
6	M	69	R						
7	M	64	R						
8	M	77	R						
9	M	70	R						
10	M	60	R						

Abbreviations: M/F, male/female; R/L, right/left; HY, Hoehn and Yahr stage defined in the "on-drug" stage; UPDRS, Unified Parkinson's Disease Rating Scale; LEDD, levodopa equivalent daily dose.

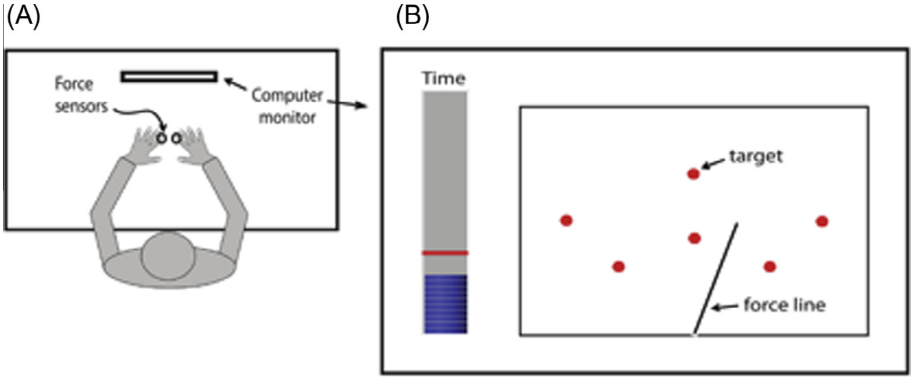

Fig. 1. (A) Experimental setup (for *BOTH* hands condition). (B) Visual feedback provided to the subject. Only one of the red targets was shown on the screen for each trial. The six target points are combinations of two force levels (15% and 25% MVC) and three sharing ratios of the left and right fingers (1:3, 1:1, and 3:1). The blue bar represents time, and takes 30 s to reach the top. The red line indicates the 10-s point, when the visual feedback (force line) disappears. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

the midpoints of the two sensors was 3 cm. For the *RIGHT* and *LEFT* conditions, the configuration of the corresponding upper limb was similar to that in the *BOTH* condition. The position of the sensor for the middle finger was adjusted in the anterior–posterior direction according to each subject's individual hand and finger anatomy in order to achieve a comfortable hand posture.

Within each of the three conditions described above, subjects performed a maximum voluntary contraction (MVC) task and the main, accurate force production task. In the MVC task, subjects were instructed to press on the sensors as hard as possible using both task fingers simultaneously to achieve maximal total force level within 8 s. They were instructed to relax immediately after reaching maximal force. Feedback presented to the subjects showed the sum of the forces from both fingers. Each subject performed two consecutive attempts and the trial with the higher MVC was selected to set the main task.

Fig. 1B shows the visual feedback screen provided to the subject during the main task. As the subject pressed on the two sensors, real time feedback on finger force appeared on the screen as a black line. The total force was depicted as the length of the line. One end of the line was always in the center of the *X*-axis and the angle of the line with the *X*-axis reflected the force-sharing ratio of the two fingers. For example, the line would be vertical when the finger forces were equal (the sharing ratio was 1:1); it tilted towards the left or right side of the screen when the corresponding finger force share was larger. The task was to reach a red target with the far end of the force line, which could be accomplished by applying the prescribed amount of total force with the prescribed force sharing between the two fingers. The subjects had 10 s to reach the target point. Time was represented on the screen with a blue bar, with the 10-s point clearly marked. The force line showing the subject's force level and sharing ratio disappeared after 10 s. The subjects were instructed to "continue producing the same finger forces" for an additional 20 s without visual feedback. Thus, each trial duration was 30 s.

There were six target points (all six points are shown in Fig. 1B) and only one was shown on the screen for each trial. The six target points were combinations of two total force levels (15% and 25% MVC) and three sharing ratios between the left and right task fingers (1:3, 1:1, and 3:1). The sharing ratio corresponds to the fraction of total force produced by the left-most task finger: left index finger in the *BOTH* condition, the middle finger in the *LEFT* condition, and the index finger in the *RIGHT* condition. The visual locations of the targets on the screen were the same for all subjects and all conditions, although the actual amount of force needed to reach each target was scaled to the subject's MVC. Subjects performed two consecutive trials for each target. Each subject performed 36 trials (3 hand conditions × 2 force levels × 3 sharing ratios × 2 repetitions) in total. The three hand conditions (*BOTH*, *RIGHT*, and *LEFT*) were randomized. The order of six targets for each hand condition also was randomized. Subjects had 1–2 practice trials before each condition. The interval between trials was about 10–15 s and there were 5-min breaks between conditions. Subjects were offered rest at any time if they felt fatigued during testing. The entire experiment lasted ~1 h.

Two subjects in each group performed additional pilot trials for the *RIGHT* hand condition to explore possible memory effects. Subjects were instructed to reach the 25% MVC target with the 1:1 sharing ratio for the first 10 s with visual feedback. To test memory effects (cf. Vaillancourt and Russell, 2002), subjects were asked to relax for the following 10 s and then to reproduce the initial target level of force for the last 10 s without visual feedback. Each subject performed five consecutive trials with 10 s intervals between trials.

2.3. Data analysis

Force data were digitally low-pass filtered with a zero-lag, fourth-order Butterworth filter at 5 Hz. Data processing was performed using a customized MATLAB code. Two repetitions for each target were averaged for further analysis. The task variables, normalized total force (F_T) and force sharing (F_S), were computed from the finger forces for each hand condition as follows:

$$\textit{BOTH}\text{ condition}: F_T = (F_{RI} + F_{LI})/\text{MVC}_{BOTH} \times 100 \quad F_S = F_{LI}/(F_{RI} + F_{LI})$$

$$\textit{RIGHT}\text{ condition}: F_T = (F_{RI} + F_{RM})/\text{MVC}_{RIGHT} \times 100 \quad F_S = F_{RI}/(F_{RI} + F_{RM})$$

$$\textit{LEFT}\text{ condition}: F_T = (F_{LI} + F_{LM})/\text{MVC}_{LEFT} \times 100 \quad F_S = F_{LM}/(F_{LI} + F_{LM})$$

The subscripts of the force variables (F) refer to the following: *RI*, right index finger; *RM*, right middle finger; *LI*, left index finger; *LM*, left middle finger. Total force was normalized using the corresponding MVC value for comparisons across subjects. The variables for the left fingers were selected as the numerator in F_S computations in each hand condition for consistency.

The change in total force (ΔF_T) was calculated for the 20 s period without visual feedback. The first and last 0.5-s intervals were averaged and used as initial ($F_{T,\text{initial}}$) and final ($F_{T,\text{final}}$) values to compute ΔF_T.

$$\Delta F_T = F_{T,\text{initial}} - F_{T,\text{final}}$$

The magnitude of the force change was re-calculated separately for two time intervals to compare the rate of force change. The changes in force during the first 10-s interval (ΔF_{0-10}) and during the second 10-s interval (ΔF_{10-20}) were quantified. The first and last 0.5-s intervals were used for computing averages as in the computation of ΔF_T.

The change in force sharing (ΔF_S) was calculated for the 20-s period without visual feedback. The first and last 0.5-s intervals were averaged and used as initial ($F_{S,\text{initial}}$) and final ($F_{S,\text{final}}$) values. For F_S starting at 0.75 (3:1 *Sharing* condition), ΔF_S was defined as

$$\Delta F_{S\_0.75} = F_{S,\text{initial}} - F_{S,\text{final}}$$

and for F_S starting at 0.25 (1:3 *Sharing* condition), ΔF_S was defined as

$$\Delta F_{S\_0.25} = F_{S,\text{final}} - F_{S,\text{initial}}$$

This method of computation was based on the general observation that the sharing tended to drift towards 50% across all conditions. Thus, the method yields positive values for initial conditions, 3:1 and 1:3. Data averaged across subjects also were fit with exponential functions for each group and each condition separately.

2.4. Statistics

Standard descriptive statistics were used and the data are presented as means and standard errors (SE). Mixed-design ANOVAs with repeated measures were used to explore how outcome variables (ΔF_T, ΔF_{0-10}, ΔF_{10-20} and ΔF_S) were affected by factors *Group* (PD and CS), *Hand* (*BOTH, RIGHT* and *LEFT*), *Force* (15% and 25% MVC), *Sharing* (1:3, 1:1, and 3:1 for ΔF_T comparisons; 1:3 and 3:1 for ΔF_S comparison) and *Time* (0–10 s and 10–20 s). The data were checked for violations of sphericity and Greenhouse–Geisser criterion was used to adjust the degrees-of-freedom when necessary. Pair-wise comparisons were performed with Bonferroni corrections to explore significant effects of ANOVAs. Pearson correlation coefficients were used to determine significant relationships between variables. All statistical tests were performed with SPSS 19.0 (SPSS Inc, Chicago, IL, USA).

3. Results

3.1. Magnitude of drop in the total force

The two groups did not differ significantly in the maximal voluntary contraction (MVC) force; on average, the MVC force was 55.8 ± 16.8 N for the PD group and 55.0 ± 14.2 N for the control group. During the accurate force production trials, after the visual feedback disappeared, all subjects showed a drop in total force across all finger conditions and sharing ratios. This force drop was consistently larger in the PD group. Since this was true across the three sharing patterns, we illustrate the result with the time profiles of normalized total force (F_T) averaged across the sharing conditions and subjects (Fig. 2). Note that PD subjects (dashed lines) showed a faster drop in F_T compared to CS (solid lines).

The curves shown in Fig. 2 suggest an exponential force drop with time for the 25%MVC task and also for the 15%MVC task performed by the PD group (less so for the CS). The exponential function regression, $F(t) = a \times \exp(t/b) + c$, where a, b, and c are constants, accounted for over 99% of the total variance for the 25%MVC task in both groups and all three conditions. For the 15%MVC task, the regressions accounted for over 98% of the variance for the PD group, whereas the fit was poor for the CS group in the RIGHT and LEFT conditions. Across all regression analyses, there was a relatively small group difference between the a parameters (6.2 vs. 6.6 for PD and CS) and between the c parameters (13.7 vs. 16.0 for PD and CS), whereas the difference between the b parameters was more than two-fold (9.9 vs. 21.6 for PD and CS). This difference suggests a much faster drop in force in the PD group, which was explored quantitatively using another method (see below).

We tried running similar analyses on individual trials but, in some cases, very small force changes resulted in unrealistically large exponential time constants. The resulting distributions of the outcome variables were very far from normal, and this prevented us from using across-subjects ANOVA.

The magnitude of force drop (ΔF_T) is shown in Fig. 3. In the *BOTH* condition, ΔF_T was significantly larger in the PD group. This was confirmed by a three-way ANOVA on ΔF_T with factors *Group*, *Force*, and *Sharing*. There was a significant effect of *Group* [$F_{[1,18]} = 6.55$, $p < 0.05$]. There also were significant effects of

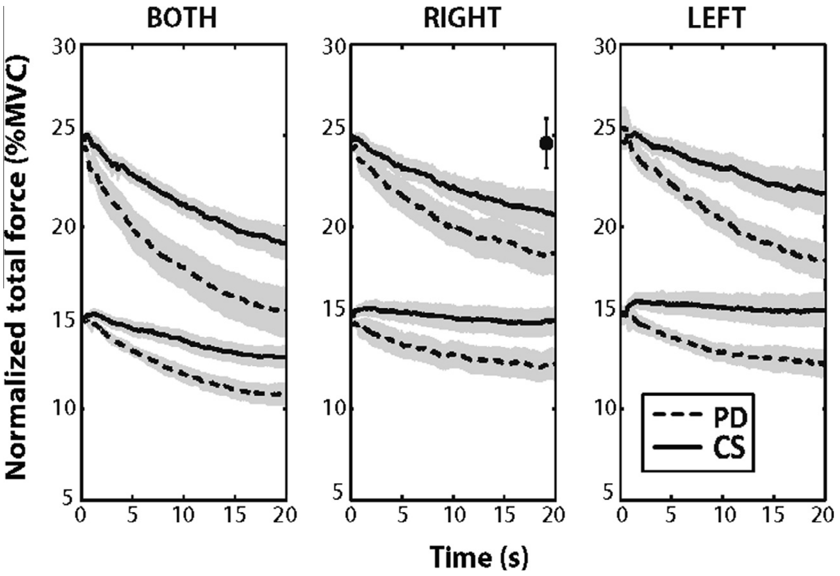

Fig. 2. The across-subject means of the total force (F_T) trajectory are presented with SE shades. The traces are for the 20 s without visual feedback. Three sharing ratios (1:3, 1:1, and 3:1) are averaged within subjects at each force level to show the overall trend of change in force. For the memory pilot trials, the average value of total force across four subjects is shown with SE bars in the middle panel.

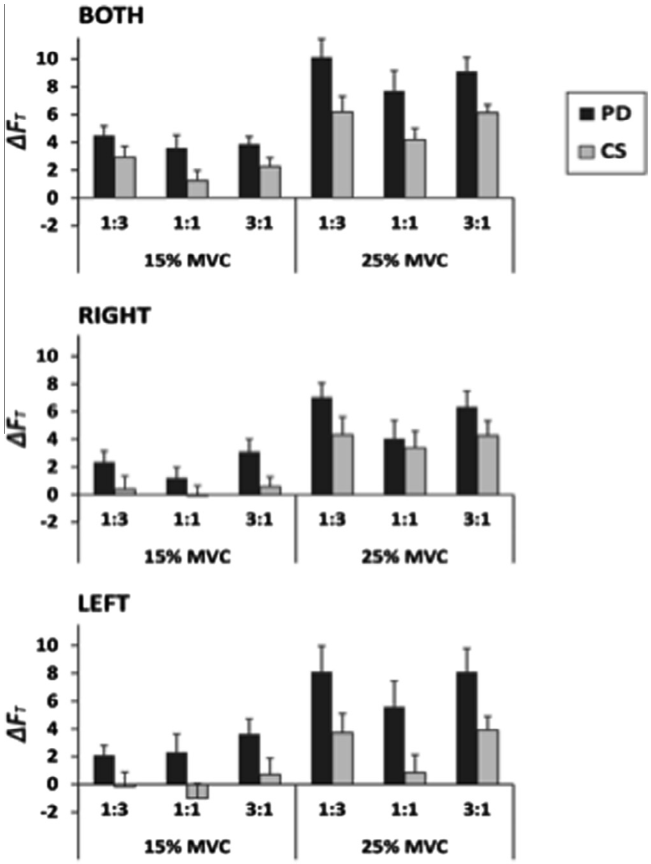

Fig. 3. The change in total force (ΔF_T) was calculated at the end of the 20-s time interval without visual feedback. The across-subject means for each group, force level, and sharing pattern are presented with SE bars. Note the consistently larger ΔF_T for the PD group.

Force [$F_{[1,18]} = 70.71$, $p < 0.001$] and *Sharing* [$F_{[2,17]} = 8.02$, $p < 0.05$] with no interaction effects. The effect of *Force* reflected the larger magnitudes of ΔF_T for the higher initial force level (25%MVC). Post-hoc analysis for *Sharing* revealed that 1:3, 3:1 > 1:1.

Although ΔF_T showed a similar pattern in the *RIGHT* and *LEFT* conditions to that in the *BOTH* condition, the effect of *Group* on ΔF_T was significant in the *LEFT* condition [$F_{[1,18]} = 4.74$, $p < 0.05$] but did not reach significance in the *RIGHT* condition [$F_{[1,18]} = 2.35$, $p = 0.14$]. The effects of *Force* [$F_{[1,18]} > 52.0$, $p < 0.001$] and *Sharing* [$F_{[2,17]} > 6.45$, $p < 0.05$] were significant in the LEFT and RIGHT conditions, reflecting the same differences as those described earlier for the *BOTH* condition. For the *LEFT* condition, there also was a significant *Force* × *Sharing* interaction [$F_{[2,17]} = 5.23$, $p < 0.05$] indicating the lack of a difference between the 1:3 and 1:1 sharing conditions at the low force level that was present at the high force level.

To explore the effect of *Hand* in ΔF_T, we averaged 12 trials (2 Force levels × 3 Sharing ratios × 2 repetitions) within each *Hand* condition for each subject. Two-way ANOVA showed significant effects of *Group* [$F_{[1,18]} = 6.19$, $p < 0.05$] and *Hand* [$F_{[2,17]} = 11.49$, $p < 0.05$] with no interactions. Post-hoc analysis for *Hand* revealed that *BOTH* > *RIGHT*, *LEFT*.

Pilot trials for the memory effect showed no trend for a drop in total force. The average value of the four subjects (24.58 ± 1.35%MVC) is shown in Fig. 2 as a large dot with standard error bars in the bottom middle panel.

3.2. Rate of force drop

To explore the rate of drop in total force, ΔF_{0-10} and ΔF_{10-20} were compared (Fig. 4). Overall, the PD group showed a faster rate of force drop reflected in the larger differences between ΔF_{0-10} and ΔF_{10-20} compared to the CS group. For the *BOTH* condition, two-way ANOVA showed significant effects of *Group* [$F_{[1,18]} = 6.16$, $p < 0.05$], *Time* [$F_{[1,18]} = 23.69$, $p < 0.001$] and an interaction of *Group* × *Time* [$F_{[1,18]} = 5.81$, $p < 0.05$]. For the *RIGHT* condition, only *Time* [$F_{[1,18]} = 11.07$, $p < 0.05$] showed a significant effect (for *Group*, $p = 0.149$; for *Group* × *Time*, $p = 0.098$). For the *LEFT* condition, the factors *Group* [$F_{[1,18]} = 4.94$, $p < 0.05$] and *Time* [$F_{[1,18]} = 5.04$, $p < 0.05$] were significant. There also was an interaction of *Group* × *Time* [$F_{[1,18]} = 5.65$, $p < 0.05$]. The significant interactions for the *BOTH* and *LEFT* conditions reflected the larger differences between ΔF_{0-10} and ΔF_{10-20}, i.e., the faster drop of F_T, in the PD group.

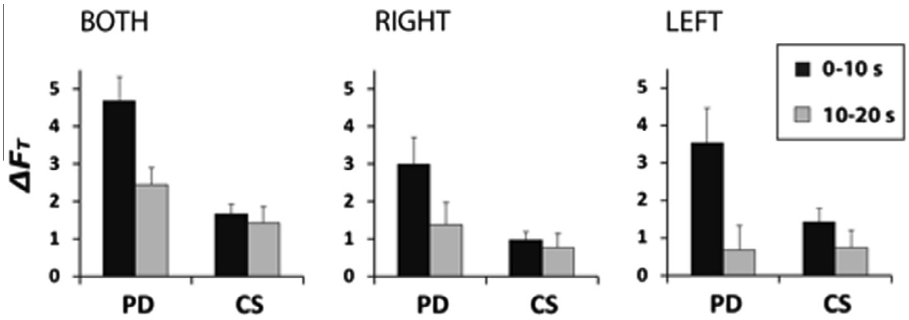

Fig. 4. The across-subject means of the change in total force (ΔF_T) for the two time intervals (0–10 s and 10–20 s) are presented with SE bars. The data represent averages across the three sharing ratios (1:3, 1:1, and 3:1) and two force levels (15% and 25% MVC).

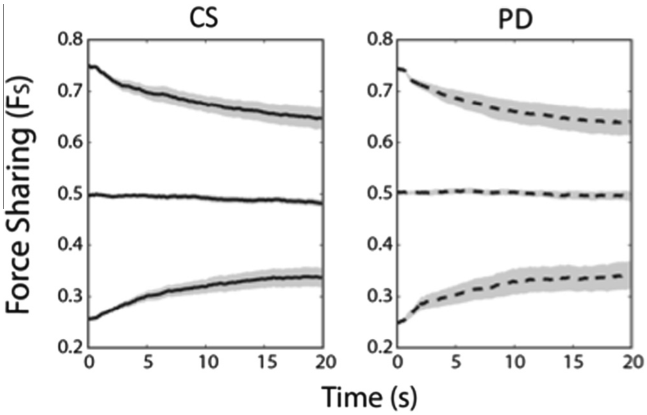

Fig. 5. The across-subject means of the force sharing (F_S) are presented with SE shades for the control (left, CS) and PD (right) groups. The traces are shown for the 20-s time interval without visual feedback. Three *Hand* conditions and two *Force* levels were averaged within a subject. Three lines within each group for each graph represent the three sharing ratios (3:1, 1:1 and 1:3).

Changes in individual finger forces for the first 10-s and the second 10-s intervals were consistent with the total force changes. Three-way ANOVA (*Group* × *Time* × *Finger*) for each hand condition showed similar statistical effects as the above two-way ANOVA (*Group* × *Time*). The effect of *Finger* was significant only in the *BOTH* condition [$F_{[1,18]} = 16.83$, $p < 0.05$], reflecting $\Delta F_{LI} > \Delta F_{RI}$, with no other effects.

There were no significant correlations between the UPDRS motor score and any of ΔF values. Also no correlations were seen between ΔF values and LEDD as well as between ΔF values and disease duration (see the data in Table 1).

3.3. Force sharing

There was a clear trend of the two finger shares towards more equal values over the 20-s time interval when the subjects produced force without visual feedback. This trend was present across conditions in both groups, with ΔF_S values significantly larger than zero ($p < 0.001$). A three-way ANOVA (*Hand* × *Force* × *Sharing*), however, showed no significant effects in either group. Hence, the data for the three *Hand* conditions and two *Force* levels were averaged within a subject to compare $\Delta F_{S\_0.25}$ and $\Delta F_{S\_0.75}$ between the two groups (Fig. 5). A two-way ANOVA (*Group* × *Sharing*) revealed no significant effects. On average, $\Delta F_{S\_0.75}$ was 0.102 ± 0.016 and $\Delta F_{S\_0.25}$ was 0.086 ± 0.016 ($p = 0.217$) over the 20-s without visual feedback.

4. Discussion

The results provided support for our main hypothesis formulated in the Introduction. Indeed, while both subject groups showed an unintentional drop in the finger force after the visual feedback had been turned off, the PD patients showed a significantly faster force drop (as in Vaillancourt et al., 2001). This was a robust result that was true across different finger combinations, involving fingers of one hand at a time or of both hands, and for both initial force magnitudes. Further, we offer and develop an interpretation of the observed unintentional finger force drop based on the idea that isometric force production is associated with setting a referent coordinate (RC) for the effector (cf. the referent configuration hypothesis, Feldman, 2009). Within this interpretation, a faster force drop is associated with a faster RC drift that moves the system to a minimum of its potential energy. The faster RC drift in PD may be viewed as an adaptive strategy to compensate, at least partially, for the loss of stability documented for multi-finger force production and prehensile tasks in PD (Park et al., 2013, 2014; Jo et al., 2015).

The second hypothesis has been falsified. We expected the group differences in the total force drift (faster force drop for PD subjects) to be reflected in similar differences in the sharing pattern drift (faster drift towards 50:50) based on the interpretation that the drifts in total force and in sharing represent two peripheral outcomes of a single neurophysiological mechanism (Ambike et al., 2015). As in the previous study (Ambike et al., 2015), both groups showed a drift in the force sharing towards 50:50 in trials that had started with a significantly different sharing pattern. Contrary to our expectation, however, there were no group differences in the sharing drift speed. This result suggests that independent neurophysiological processes may be responsible for changes in total force and changes in sharing.

4.1. Stability of steady-state actions by abundant systems

Stability is a crucial feature of functional movements in the everyday environment with its unpredictable and variable forces. One of the central features of natural movements is their task-specific stability (Schöner, 1995). This term means that the same abundant set of elements (joints, digits, muscles, etc.) can be organized by the CNS to ensure stability of different performance variables depending on the task and intention of the actor.

An unexpected observation has been made in experiments with similar transient perturbations involving a time interval between the perturbation application and removal (dwell time): An increase in the dwell time led to larger violations of equifinality with respect to the performance variable (Zhou et al., 2015). These unintentional changes in the performance variable were observed despite the explicit instruction to the subjects “not to react to the perturbations." These observations have been interpreted as the consequence of a drift in the RC for the performance variable towards the actual coordinate (AC) for this variable. Note that the difference between AC and RC for a variable results in active force production directed towards moving the variable closer to RC due to the length-dependence of muscle forces, both peripheral and reflex-based (reviewed in Feldman, 1986; Feldman and Levin, 1995). In other words, all effectors at all times exist in elastic force fields produced by all of the participating muscles. For a given effector, a minimum of potential energy in such a field is reached when AC = RC. Hence, a drift in RC towards AC may be viewed as a natural behavior of the system moving towards a minimum of potential energy, which also is a state of high stability.

Thus, we conclude that two factors define stability of a motor system. The first is typical of abundant systems and reflects the task-specific neural organization stabilizing salient performance variables. A number of mechanisms have been suggested for this mechanism, from back-coupling loops within the CNS (Latash et al., 2005) and from peripheral receptors (Martin et al., 2009) to optimal feedback control schemes (Todorov and Jordan, 2002). The second factor acts in both single-element and multi-element systems. Its neurophysiological origin is unknown, although its physical origin seems to be straightforward: It reflects the natural tendency of any physical system to move to a minimum of its potential energy reflected in the motion of RC to AC.

4.2. Potential origins and causes of unintentional force changes

The hypothesis that RC may drift naturally towards AC also can be used to account for other phenomena. In particular, it has been known for years that turning visual feedback off during an isometric force production task leads to an unintentional drop in the force (Slifkin et al., 2000; Vaillancourt and Russell, 2002). This drop may be rather large, up to 40% of the initial force level, without the subject being aware that the performance has changed.

In the original papers (Slifkin et al., 2000; Vaillancourt and Russell, 2002), a hypothesis was offered that the unintentional force drop had been due to the limited capacity of working memory. Our observations of the faster force drift in the PD group seem to provide indirect support for this hypothesis. Indeed, PD is known to be associated with working memory dysfunction (Sagar et al., 1988; Sullivan and Sagar, 1991; Lee et al., 2010). We believe, however, that these results may have a different origin.

The working memory hypothesis has obvious limitations. In particular, forgetting the initial force level may be expected to lead to a force drift in both directions, up and down, whereas typically the force drops consistently. An increase in the force has been documented only for very low initial force levels (Ambike et al., 2015), interpreted as a reflection of adaptation of pressure-sensitive receptors in the fingertips. This observed increase also was consistent across trials and subjects, something not expected from working memory problems that are more likely to lead to high inter-trial variance and not a consistent force drift. In our experiment, only a few subjects performed the pilot trials designed to check whether memory played a significant role in force drift. In those trials, subjects were asked to stop producing force for a time interval sufficient to observe a force drop and then to reproduce the memorized force. If memory was involved, a comparable drift of the force level would be expected. This did not happen, however: The mixed group of subjects, two CS and two patients with PD, showed no visible force drift, suggesting that their memory on the initial force level did not drift to lower levels (see Fig. 2).

The hypothesis that the unintentional force drop reflects a drift of the corresponding RC towards the unchanging AC (fingertip coordinates that stay the same throughout the trial) offers a different explanation for the finding of the faster force drift in PD. This explanation is based on two important concepts: First, the loss of stability of multi-element action in PD, and second, the idea of neural adaptations to primary motor impairments leading to non-trivial behavioral consequences.

Recently, the concept of '*slacking*' has been suggested (Reinkensmeyer et al., 2009; Secoli et al., 2011) as the property of the human motor system to decrease levels of muscle activation when movement error is small. In particular, slacking was observed during practicing movements with robotic assistance after neurologic injury: Subjects sometimes reduced their effort in response to external assistance. Slacking and RC-back-coupling seem to be related; perhaps slacking is a manifestation of RC-back-coupling in the robot-assisted-rehabilitation setting.

4.3. Effects of Parkinson's disease on stability of action

Loss of postural stability commonly is mentioned as one of the cardinal features of PD (Fahn and Jankovic, 2007). It is not observed, however, in PD patients with Hoehn–Yahr stage II. A series of recent studies have documented that such patients demonstrate a significant drop in synergy indices during multi-finger accurate force production and prehensile tasks (Park et al., 2012, 2014; Jo et al., 2015). Moreover, patients with Hoehn–Yahr stage I that have clinical signs limited to only one half of the body, showed comparable synergy indices to those in PD patients with bilateral involvement. Given that synergy indices reflect stability of the performance variable (reviewed in Latash et al., 2007), these studies have demonstrated that stability loss of multi-finger action may be one of the earliest, even pre-clinical, signs of PD motor dysfunction.

In addition to low synergy indices during steady-state tasks, PD patients also show delayed and reduced adjustments in those synergies in preparation to a quick action (Park et al., 2012; Jo et al., 2015). Such adjustments (anticipatory synergy adjustments, ASAs, Olafsdottir et al., 2005; Shim et al., 2005) are functionally important as they destabilize the salient variable in preparation to a quick action. Without ASAs, the action would have to fight the pre-existing synergies. Taken together, PD subjects demonstrate impaired control of action stability that is seen early in the disease and involves two components: Low synergy indices and small ASAs.

4.4. Adaptive motor strategies to impaired stability of action

Neural adaptations to a variety of neurological disorders have been documented. Such adaptations commonly lead to motor patterns that look different from those seen in unimpaired persons. For example, persons with atypical development, healthy older persons, and persons with neurological disorders commonly show patterns of muscle activation characterized by increased co-contraction of agonist-antagonist muscle pairs (Woollacott and Shumway-Cook, 1990; Aruin and Almeida, 1996; Carpenter et al., 2004). These differences, however, still may be compatible with optimal motor function given the actual state of the body (reviewed in Latash and Anson, 1996, 2006).

Loss of stability of movement patterns is one of the least explored aspects of motor disorders (although see a review by Stergiou and Decker, 2011) even though it is expected to render actions associated with many everyday tasks unstable and, therefore, useless. The current study may be viewed as the first one providing evidence for an adaptive reaction to loss of action stability. Indeed, the documented impaired stability of action in PD is expected to make many hand actions within the everyday repertoire subjected to major disturbances from the natural variability in external forces and internal body states.

It is natural to expect the CNS of PD patients to search for alternative and/or complementary strategies to ensure action stability. One such strategy would be to facilitate motion of the involved motor system towards its most stable state, which is achieved when AC = RC. This can be done by an increase in the gain in hypothetical neural loops involved in the naturally occurring drift of motor systems to their respective RCs. Our observations of the accelerated force drop in PD corroborate this hypothesis.

4.5. More than one drift process during multi-finger force production

In an earlier study, two drifts were documented during two-finger accurate force production tasks without visual feedback (Ambike et al., 2015). First, in tasks with moderate force levels (between 7% and 30% MVC), the total force drifted to lower values. Second, the sharing pattern drifted towards a more equal force distribution between the fingers (close to 50:50) in trials that had started with significantly different proportions of the total force produced by the two fingers. Both drifts were fit with exponential functions with similar time constants, close to 15 s. The similarity of the time constants suggested a common source for these changes. This expectation also follows the fact that changes in the sharing are unambiguously related to changes in the finger forces (see Section 2.3). Indeed, the finger that started a trial with a higher force level was expected to show a larger force drop as compared with a finger that started the trial with a lower initial force level. This could lead to an effect on the sharing pattern drawing the two force magnitudes closer to each other.

In our current experiment, however, this interpretation failed to receive support. The significantly faster total force drift in the PD group (Fig. 2) was not accompanied by a faster sharing pattern drift (Fig. 5). In fact, no differences between the two groups in the sharing pattern drift were seen. These observations cast doubt on the hypothesis that a common neurophysiological mechanism generates the two drifts and suggest that the drift in the sharing pattern was a reflection of another mechanism, apparently unchanged in PD. At this time, we cannot offer a physiological mechanism that could bring about the sharing pattern drift, but such a mechanism is likely immune to PD-associated changes in the dopaminergic projections in the basal ganglia and to possible secondary (adaptive) changes.

4.6. Concluding comments

We would like to emphasize two potentially important findings. The first is the accelerated decline of the total force in PD, which is likely not related to problems with working memory. We offer an interpretation of this phenomenon based on the idea of RC-back-coupling and hypothetical adjustments within the central nervous system of PD patients possibly adaptive to the documented loss of action stability in PD. The second is the significant group differences in the force drift while no such differences were seen in the sharing drift. These results suggest that the two drifts, while similar in their timing characteristics for healthy individuals, are likely to reflect different physiological mechanisms. It is important to state that the findings were consistent across force levels and finger combinations.

As any study, ours is not without weaknesses. The first is the inclusion of only early-stage PD patients. Indeed, if the hypothesis on an adaptive origin of the accelerated force drift in PD is correct, one can expect stronger effects in PD patients at later stages of the disease that allow more time for development of adaptive reactions. Such a study is in our plans. The second is the pilot nature of the working memory tests. Partly, this was done to reduce the testing time for the participants. We offered this test only to a few participants who were not time constrained and willing to prolong the testing session. These results have to be confirmed in a larger cohort that would allow proper statistical analysis of the data.

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