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Effects of Parkinson's disease on proprioceptive control of posture and reaching while standing

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3 **E f f e c t s of Parkinson’s Disease on Proprioceptive Control of**
4 **Posture and Reaching while Standing**
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List of Abbreviations:

- CoM: center of mass
- CoP: center of pressure
- CTR: control
- EO: eyes open
- EC: eyes closed
- LCoM: lower center of mass
- PCA: principal component analysis
- PD: Parkinson's disease
- R: coefficient of correlation
- UCoM: upper center of mass

1
2
3 **Abstract**
4

5
6 Although previous studies have shown pointing errors and abnormal multijoint coordina-
7 tion in seated subjects with PD who cannot view their arm, the extent to which subjects
8 with PD have problems using proprioception to coordinate equilibrium maintenance and
9 goal-oriented task execution has not been adequately investigated. If a common motor
10 program controls voluntary arm pointing movements and the accompanying postural
11 adjustments, then impairments of proprioceptive integration in subjects with PD should
12 have similar effects on pointing and body center of mass (CoM) control with eyes
13 closed. Ten standing subjects with PD (OFF-medication) and 10 age-matched control
14 subjects pointed to a target with their eyes closed and open. Although pointing accuracy
15 was not significantly different between groups, body CoM displacements were reduced
16 in subjects with PD, but not in controls, when eyes were closed. In addition, with eyes
17 closed, PD subjects showed reduced temporal coupling between pointing and CoM ve-
18 locity profiles and reduced spatial coupling between pointing and CoM endpoints. This
19 poor coupling with eyes closed could be related to the PD subjects' increased jerkiness
20 of CoM displacements. The different effects of eye closure between control and PD sub-
21 jects on the CoM displacements, but not pointing accuracy, are consistent with separate
22 motor programs for the pointing and postural components of this task. Furthermore, the
23 decoupling between the two movement components in subjects with PD when they
24 could not use vision, suggests that the basal ganglia are involved in the integration of
25 proprioceptive information for posture-movement coordination.
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Keywords: Motor control · Pointing · Posture · Whole body · Basal ganglia · Complex movement

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3 Patients with severe Parkinson's disease (PD) have problems maintaining balance
4
5 and coordinating complex goal-directed movements. Previous studies have shown that
6
7 postural adjustments that accompany voluntary movements are bradykinetic (i.e. slow
8
9 and weak) in subjects with PD (Horak et al. 1992; Gantchev et al. 1996; Frank et al.
10
11 2000; Rocchi et al. 2006). Subjects with PD also have smaller than normal limits of sta-
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13 bility when asked to lean to their maximum limits (Mancini et al. 2008). Undershooting
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15 intended targets for arm pointing, locomotion, and stepping by subjects with PD with
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17 eyes closed has been hypothesized to be due to an underestimation of the motor com-
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19 mand because of difficulty integrating proprioceptive information (Poizner et al. 1998;
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21 Adamovich et al. 2001b; Schubert et al. 2005; Almeida et al. 2005; Jacobs and Horak
22
23 2006). In contrast to smaller than normal intended movements, however, impaired up-
24
25 per-lower body coordination for axial movements during stance in subjects with PD often
26
27 results in larger than normal center of mass (CoM) displacements, both in response to
28
29 external perturbations and during voluntary axial movements (Alexandrov et al. 1998;
30
31 Horak et al. 2005). Thus, although abnormal proprioceptive-motor integration in PD re-
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33 sults in smaller than normal voluntary body CoM displacements during leaning and walk-
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35 ing, it can also result in larger than normal CoM movements with reduced equilibrium
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37 control. It is unknown whether body CoM trajectories would be smaller or larger than
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39 normal when PD subjects are performing a voluntary, target-directed, arm pointing task
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41 requiring simultaneous control of axial postural coordination and postural equilibrium in
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43 stance (Stapley et al. 1999; Pozzo et al. 2002). Previous studies suggest that subjects
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45 with PD may have more difficulty coordinating multiple joints and multiple tasks than sin-
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47 gle joint single tasks (Poizner et al. 1998). Therefore, in the current study we asked
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3 standing subjects with PD and age-matched control subjects to point to a remembered
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5 visual target beyond their arm reach with their eyes open and eyes closed. Based on
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7 previous studies investigating movements to a target, we hypothesize that subjects with
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9 PD would undershoot their voluntary pointing endpoint and that the errors in endpoint
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11 will be greater in the subjects with PD when their eyes were closed, because they would
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13 need to depend on their impaired use of proprioceptive integration to estimate body mo-
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15 tion (Jacobs and Horak 2006; Zia et al. 2000; Adamovich et al. 2001b). However, the
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17 analogies between the present experimental protocol and previous studies on axial syn-
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19 ergies in subjects with PD would predict larger than normal body CoM displacements
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21 (Alexandrov et al. 1998).
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26
27 Analysis of the conflict between hypometric voluntary (focal) arm movements and
28
29 hypermetric postural (CoM) movements with loss of visual feedback in subjects with PD
30
31 is especially interesting because this opposite prediction for the focal and postural com-
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33 ponents is not compatible with the hypothesis of a tightly coupled link between both the
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35 spatial (Stapley et al. 1999; Pozzo et al. 2002) and temporal (Frank et al. 2000; Patron
36
37 et al. 2005) parameters of voluntary pointing and postural displacement in healthy sub-
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39 jects. If a single motor program controls the voluntary and postural components of a
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41 complex movement, it would not be possible for subjects with PD without visual feed-
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43 back to decouple the close relationship between these two components (Massion 1992;
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45 Schepens and Drew 2003). However, a previous study suggests that subjects with PD
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47 show a less consistent coupling between the postural and voluntary components of a
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49 task (Frank et al. 2000). Specifically, unlike healthy subjects who consistently couple the
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51 offset of their preparatory postural, tibialis muscle activity with the onset of their focal,
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3 gastrocnemius muscle activity during a voluntary rise-to-toes task, subjects with PD
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5 showed late, inconsistent delays between the postural and the focal components (Frank
6
7 et al. 2000). If PD decouples the normal tight link between the postural and voluntary
8
9 components of a goal-directed pointing task, this is consistent with the hypothesis that
10
11 the basal ganglia participate in this linkage and that posture and voluntary control are
12
13 organized independently and then coupled downstream in subcortical areas (Massion
14
15 1992; Latash et al. 1995; Prentice and Drew 2001). If this uncoupling occurs only with
16
17 loss of vision during the task, this is consistent with use of proprioceptive feedback in
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19 coupling postural with movement synergies (Adamovich et al. 2001a; Poizner et al.
20
21 2000).

22 23 24 25 26 27 28 **1 Methods**

29 30 31 32 33 **1.1 Subjects**

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36 Ten subjects with idiopathic PD and 10 age-and sex-matched subjects gave in-
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38 formed consent to participate in the protocol approved by the institutional review board
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40 of Oregon Health & Science University. Subjects with neurological, muscular, or psychia-
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42 tric disorders other than PD were excluded. All PD subjects showed bradykinesia and
43
44 rigidity but little dyskinesia or tremor. Table 1 summarizes the characteristics of the PD
45
46 subjects. To determine the effects of PD without the influence of dopaminergic medica-
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48 tion, PD subjects were tested in the morning, at least 12 hours after their last consump-
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50 tion of anti-PD medication (OFF). There was no significant difference between the ages
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3 (PD: 61±7 vs CTR: 63±9 years) or weights (PD: 82±13 vs CTR: 85±11 kg) of subject
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5 groups.

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7 [Table 1 about here.]
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10 11 **1.2 Experimental protocol**

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14 The subjects performed whole-body pointing movements to a 2 cm diameter, re-
15 flective ball target suspended directly in front of them at a height from the floor and dis-
16 tance from their ankles of 50% of their body height (See Fig. 1). Subjects stood with their
17 hands clasped together to point with both index fingertips at the target. Subjects re-
18 peated the task 5 times with their eyes closed, followed by 5 repetitions with their eyes
19 open. For the eyes closed (EC) condition, subjects were asked to memorize the position
20 of the target, close their eyes for approximately 3 seconds and then to reach to the tar-
21 get location, keeping the eyes closed. In order to avoid tactile feedback of task accom-
22 plishment, the target was moved aside once the subjects closed their eyes (the subjects
23 were acquainted with it). The subjects held their final fingertip endpoint position for 3
24 seconds before returning to the starting position with eyes still closed. For the eyes open
25 (EO) condition, the subjects touched the target with the tip of their fingers. Subjects were
26 asked to move at their natural speed.
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45 [Fig. 1 about here.]
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50 51 **1.3 Data Collection**

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53 To quantify the subjects' kinematic strategies for whole body pointing, 21 reflective
54 markers were placed on the following anatomical landmarks: nasion, occipital ridge,
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3 chin, 7th cervical segment of the spine, apex of index fingers, bilateral acromions, hum-
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5 eral lateral epicondyles, ulnar styloids, anterior superior iliac spines (ASIS), iliac crests,
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7 posterior superior iliac spines (PSIS), femoral lateral epicondyles, and lateral malleoli.
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9 The three-dimensional position of the markers were recorded using a Motion Analysis
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11 system (Santa Rosa, CA, USA) with eight Falcon video cameras sampling at 60 Hz.
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13 Ground reaction forces and position of the center of foot pressure (CoP) were recorded
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15 with an AMTI force platform sampling at 480 Hz.
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22 **1.4 Data Analysis**

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24 The spatial coordinates of markers were projected onto the sagittal plane. For bila-
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26 teral markers, their midpoints were projected onto this plane. In order to verify that
27
28 whole-body pointing was actually constrained to the sagittal plane, a principal compo-
29
30 nent analysis (PCA) was performed on the three-dimensional trajectories of all markers.
31
32 PCA showed that the direction of minimal variability of the marker displacements was in
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34 the medio-lateral direction and the variability along this direction was negligible com-
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36 pared to the variability in the sagittal plane. Since the angle between the medio-lateral
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38 direction and the 3rd eigen-vector (i.e. the direction of minimal variability of the data) was
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40 less than 5 degrees, and the variability along this direction represented only 1.3% of the
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42 variability of the markers trajectories, we restricted the analysis to the sagittal plane.
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48 A biomechanical model of the whole body was implemented and validated for each
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50 subject using the force platform data (Tagliabue et al. 2008). This 7-segment model was
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52 used to estimate the anterior-posterior position of the whole body CoM as well as the
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54 upper and lower body CoM (UCoM, LCoM, respectively). The upper-body consisted of
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3 head, trunk, arms, forearm and hands. The lower-body included pelvis, thighs, shanks
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5 and feet. To decouple the upper-and lower-body contributions, the position of the whole-
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7 body CoM and LCoM were calculated as the distance from the lateral malleolus, whe-
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9 reas the UCoM position was calculated as the distance from the lumbar spine midway
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11 between bilateral PSIS. All CoM displacements are reported as a percentage of foot
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13 length to compensate for between-subject differences in the length of base of support.
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17 For each trial, movement onset was defined as the last motion capture frame when
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19 the velocity of all markers was less than 5% of their peak velocity. Task execution time
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21 was defined as the difference between the frame when the fingertip endpoint reached its
22
23 final position and the movement onset.
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26 The primary dependent measures were displacement of the fingertip endpoint (vo-
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28 luntary movement) and of the whole body CoM (postural adjustment) and the temporal
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30 and spatial relationship between them. The subjective pointing performances were eva-
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32 luated with two types of endpoint errors: constant error and variable error (Adamovich et
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34 al. 2001b). Constant error (accuracy) and variable error (precision) are, respectively, the
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36 mean and the standard deviation of the length of the vector connecting the target with
37
38 the final, pointing endpoint position. Pointing errors were calculated individually for each
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40 subject on the five trials performed in the EC condition. Endpoint error was not calcu-
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42 lated for the EO condition because the fingertip of every subject accurately reached the
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44 target.
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50 To determine whether control of the endpoint-or CoM-trajectory was impaired by
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52 lack of visual feedback, we calculated their mean jerk (i.e. the 3rd time derivative of posi-
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54 tion). Increased jerk (more frequent changes of acceleration) reflected increased correc-
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3 tions of the movement trajectory. Before the jerk was calculated, the fingertip and CoM
4 trajectories were normalized in time and amplitude to compensate for the effects of dif-
5 ferent movement durations among trials and different displacement magnitudes between
6 fingertip and CoM trajectories. In addition, the coefficient of correlation (R) between the
7 velocity profiles of the pointing trajectories and CoM trajectories for each subject was
8 taken as index of temporal coupling between the focal and postural components of the
9 movement.

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12 Spatial coupling between the focal and postural components was evaluated across
13 subjects in each group. Spatial coupling was calculated as the R between the individual
14 changes in horizontal pointing errors of the fingertip endpoint between the EO and EC
15 conditions and the changes in horizontal body CoM displacement between the EO and
16 EC conditions.

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19 To address the hypothesis that pointing errors in the EC condition differed between
20 groups, the nonparametric Mann-Whitney U test with group as a factor and the horizon-
21 tal and vertical components of the pointing errors (in the sagittal plane) as dependent
22 variables was used. For the other parameters describing the movement features, the
23 Mann-Whitney U test was performed in both EO and EC conditions. The p values re-
24 ported in the results section for the U test are exact probabilities for small samples.

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27 To verify whether the lack of vision affects movement execution, the non-
28 parametric Wilcoxon matched pairs test was performed for both CTR and PD subjects
29 with vision condition (EO, EC) as factor and the parameter of interest as dependent va-
30 riable. To determine possible differences in the effects of vision between the two groups,
31 the difference between the median values of each parameter in the two visual conditions

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3 was computed for each subject and used as the dependent variable in a non-parametric
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5 Mann-Whitney U test, where the group was the independent factor.
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7 To test whether the fatigue could affect the performances of the subject with PD
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9 the parameters a non-parametric Friedman test (χ^2) and the Kendall's Coefficient of
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11 Concordance (Kcc) were performed on the analyzed movement parameters with the trial
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13 number as independent variable, in both EC and EO conditions.
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18 19 **2 Results**

20 21 22 **2.1 Effects of PD and Vision on Pointing Errors**

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24 Although the bar graph in Fig. 2A shows that apparently the subjects with PD tend
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26 to take longer than CTR to complete the reach in both visual conditions, the differences
27
28 between groups in pointing speed are not statistically significant. Fig. 2B shows that both
29
30 groups of subjects had longer execution time in the EC, than in EO, condition ($Z=2.80$,
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32 $p<0.01$; $Z=2.80$, $p<0.01$ for CTR and PD respectively) and that the increases in the ex-
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34 ecution times without vision are not different for the two groups. The trial number does
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36 not affect the execution time of PD subjects either with EC ($\chi^2(10,4)=1.52$, $p<0.82$;
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38 $Kcc=0.04$) or with EO ($\chi^2(10,4)=0.88$, $p<0.93$; $Kcc=0.02$).
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46 [Fig. 2 about here.]
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48 Fig. 3 shows that the constant and variable components of the pointing errors in
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50 the EC condition are not statistically different between groups.
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53 [Fig. 3 about here.]
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3 These results are also supported by the error ellipse representation shown in Fig.
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5 4, in which the CTR subjects appear to overshoot the target slightly more than the PD
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7 subjects with EC and the shape of the error ellipses appears a bit different between
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9 groups.

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11 [Fig. 4 about here.]

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14 Significant differences between the two groups were not found even when the ver-
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16 tical and anteroposterior components of the constant and variable pointing endpoint er-
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18 rors were considered separately.
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24 **2.2 Effects of PD and Vision on Body CoM control**

25 26 27 28 **Whole-body CoM**

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30 While pointing to the target with EO, the subjects with PD and the CTR subjects
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32 moved their body CoM forward the same distance. However, Figure 5A shows that in the
33
34 EC condition, 7 out of 10 subjects with PD decreased their forward CoM displacements,
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36 whereas the CTR group slightly increased the forward CoM displacement. Fig. 5B com-
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38 pares the effect of EC on CoM displacement for the CTR and PD groups. EC did not
39
40 significantly alter the CTR groups final CoM position. In contrast, EC significantly re-
41
42 duced the PD groups final CoM displacement ($Z=2.60$, $p<0.01$). The different effect of
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44 the lack of vision on the two groups is statistically significant ($Z=2.04$, $p<0.05$). However,
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46 the differences among subjects with PD shown in Fig. 5A does not depend on the sever-
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48 ity of the disease. There is no significant correlation between the CoM displacement or
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50 change in displacement with eyes closed and either UPDRS or Hoehn & Yahr scores.
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3 The trial number does not affect the CoM displacement of PD subjects either with EC
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5 ($\chi^2(10,4)=5.84$, $p<0.21$; $K_{cc}=0.15$) or with EO ($\chi^2(10,4)=3.2$, $p<0.52$; $K_{cc}=0.08$).
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7 [Fig. 5 about here.]
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10 Panel A and B of figure 6 show that the jerkiness of the CoM trajectory increased
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12 when both CTR and PD subjects executed the pointing movement with EC (CTR:
13 $Z=2.08$, $p<0.05$; PD: 2.70 , $p<0.01$), but the increase observed for the subjects with PD
14
15 was significantly greater than for CTRs ($Z=2.72$, $p<0.01$).
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18 [Fig. 6 about here.]
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21 Panel C and D of Fig. 6 show that, unlike CoM jerk, the jerk of the pointing end-
22
23 point trajectory was not significantly affected by visual condition or by group and the ef-
24
25 fect of the lack of vision was similar for the two groups.
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28 29 30 31 **Upper-versus lower-body CoM** 32

33 The similar forward displacements of the whole body CoM for both CTR and PD
34
35 subjects in the EO condition are due to similar control of upper-and lower-body masses.
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37 Despite a stooped posture in the PD subjects, there was no significant difference in for-
38
39 ward displacements of the upper body CoM or in backward displacements of the lower
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41 body CoM in the EO condition (Fig. 7 A and C).
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44 Although both groups similarly increased the amplitude of the backward lower-body
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46 CoM displacement with EC (see Fig. 7D), only the CTR subjects compensated for this
47
48 backward motion by increasing the forward displacement of their upper-body CoM (Fig.
49
50 7B). The difference of the effect of vision on the upper-body CoM replacement for the
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52 two groups is statistically significant ($Z=2.27$, $p=0.02$).
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3 [Fig. 7 about here.]
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7 **2.3 Coordination of Pointing with Posture**

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10 No differences were observed between CTR and PD groups' temporal correlation
11 between pointing- and CoM-trajectory velocities in the EO or EC conditions (Fig. 8A).
12 However, the effect of visual deprivation on the temporal coupling between the voluntary
13 and postural components of the task was significantly different between groups. That is,
14 while CTR subjects tended to increase the correlation between the pointing and CoM-
15 trajectory velocity in the EC condition, the subjects with PD showed a decrease of this
16 coordination (Fig. 8B).
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26 [Fig. 8 about here.]
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29 Spatial coupling between the voluntary and postural components of the task were
30 affected by eye closure in the PD, but not the control subjects. The relative effect of eye
31 closure on fingertip and CoM displacement were significantly correlated across the CTR,
32 but not the PD, subjects. As shown in Figure 9, the more each control subject increased
33 their pointing endpoint displacement with EC, the more they also increased their CoM
34 displacement ($R=0.83$, $p=0.003$). In contrast, the correlation between the effects of vi-
35 sion on pointing endpoint and CoM displacements was not significant for the subjects
36 with PD ($R=0.31$, $p=0.38$). For example, of the 3 PD subjects who moved their CoM
37 backward 10% more with EC than EO, one subject increased endpoint displacement,
38 one decreased endpoint displacement and one did not change endpoint displacement.
39 Besides, Figure 9 shows that the decline of the coupling between the effect of the eye
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3 closure on the voluntary and postural components of the movement can not be ascribed
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5 to the PD severity.
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7 [Fig. 9 about here.]
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10 11 12 **3 Discussion**

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14 This study demonstrates the importance of an intact basal ganglia and propriocep-
15 tive feedback for the precision and coordination of the postural (body CoM) with the vo-
16 luntary (fingertip pointing) components of a whole-body pointing task while standing. The
17 key effects of PD were: (1) no deterioration in precision of pointing to targets with eyes
18 closed and with eyes open; (2) undershooting of whole body CoM displacement with
19 eyes closed; (3) impaired temporal coordination between the fingertip endpoint and body
20 CoM velocity profiles; (4) increased jerkiness of CoM displacement with eyes closed;
21 and (5) poor spatial coupling between effects of eyes closure on body CoM and pointing
22 error across subjects with PD. The significant effects of removing visual feedback on
23 postural control and postural-voluntary movement coordination, but not on pointing accu-
24 racy in subjects with PD suggest that the basal ganglia are more important for propri-
25 oceptive mapping of whole-body coordination than for visual-proprioceptive mapping for
26 pointing to a remembered endpoint.
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47 **3.1 Pointing movement**

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49 Previous studies of pointing by sitting PD subjects with similar disease severity
50 have reported significantly more slowing and significantly larger than normal constant
51 and variable pointing errors (Flowers 1975; Poizner et al. 1998; Adamovich et al. 2001b;
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3 Schubert et al. 2002; Maschke et al. 2003; Keijsers et al. 2005). Decrements in perfor-
4
5 mance of PD subjects with eyes closed have been ascribed to impairment of propriocep-
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7 tive integration for precise, voluntary movements (Adamovich et al. 2001b; Maschke et
8
9 al. 2003). Analogous observations of impaired performance with eyes closed, compared
10
11 to eyes open, in subject with PD have also been reported recently for compensatory
12
13 stepping and locomotion (Almeida et al. 2005; Jacobs and Horak 2006). In the present
14
15 study, however, even in the eyes closed condition, when PD subjects could not com-
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17 pensate with vision for unreliable proprioception, the subjects with PD were able to point
18
19 to the target with similar slowing, accuracy and precision as then control subjects. How
20
21 is this possible?
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26 The most likely explanation for excellent pointing performance by moderately se-
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28 vere PD subjects with eyes closed in the Off state is that our subjects with PD formed
29
30 accurate internal representation of target location from visual-spatial maps memorized
31
32 prior to the movement. Consistent with our study, a previous study in sitting subjects
33
34 who could view both their initial hand position and the position of the target, showed no
35
36 larger pointing errors in subjects with PD than in controls (Poizner et al. 1998). Further-
37
38 more, the large head displacements associated with pointing allowed subjects to use
39
40 vestibular information, instead of proprioception, to track the visual representation of the
41
42 target. This hypothesis is consistent with recent studies suggesting that subjects with PD
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44 have an increased gain of vestibulospinal and visual control of posture, secondary to
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46 impaired proprioceptive control (Pastor et al. 1993; Smiley-Oyen et al. 2002; Maurer et
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48 al. 2004). Better than normal use of vestibular inputs for postural control to compensate
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50 for impaired use of proprioception also explains why subjects with PD show increased
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3 sway during quiet stance on a firm surface, but better than normal sway on an unstable
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5 surface (Chastan et al. 2008). In fact, our results are consistent with another study in
6
7 which trunk and head movements were involved when subjects with PD pointed from a
8
9 seated position (Poizner et al. 2000). Even while sitting, the vestibular information pro-
10
11 duced by the head movements associated with pointing could be used to update the
12
13 visual representation of the target. Alternatively, the subjects with PD may have used
14
15 preprogrammed trunk-arm movement synergies to compensate for the body displace-
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17 ments (Poizner et al. 2000; Adamovich et al. 2001a).
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22 The lack of differences in the pointing endpoint accuracy between groups suggests
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24 that this task did not represent a particular challenge for subjects with moderately severe
25
26 PD. In fact, the need to control stance equilibrium simultaneously while pointing did not
27
28 seem to impair the voluntary pointing movement, as would be expected if the task was
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30 associated with fear of falling (Adkin et al. 2003) or required divided attention between
31
32 the postural and voluntary components (Woollacott and Shumway-Cook 2002).
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38 **3.2 Equilibrium control**

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41 Despite the relative lack of effects of PD on the voluntary, pointing component of
42
43 the movement, the postural strategy was affected by PD, but only when visual feedback
44
45 was not allowed. With eyes closed, PD but not CTR subjects showed increased jerk in
46
47 their CoM trajectory, consistent with increased active corrections to their movement. In
48
49 addition, whereas control subjects tended to slightly increase the forward displacement
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51 of their body CoM when they closed their eyes, subjects with PD showed a reduction
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53 (undershooting) of their forward CoM displacement with eyes closed. This difference in
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3 whole body CoM displacement between groups was due to the fact that the CTR, but
4
5 not the PD subjects, changed kinematic strategies when closing their eyes. With eyes
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7 closed, the controls increased the backward displacement of their lower-body CoM while
8
9 concomitantly increasing the forward displacement of their upper-body CoM. In contrast,
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11 the subjects with PD increased the backward displacement of their lower-body CoM, but
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13 did not compensate by increasing the forward displacement of their upper-body CoM.
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15 Similar inflexibility of postural strategies with changes in support, instruction, and envi-
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17 ronmental conditions in subjects with PD has been demonstrated previously for res-
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19 sponses to external perturbations (Horak et al. 1992; Chong et al. 1999-2000).
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24 With eyes closed, the subjects with PD may have exaggerated their backward
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26 postural adjustments to increase their equilibrium safety margin from the front of foot
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28 support (Mancini et al. 2008). Without visual feedback, PD subjects' proprioceptive defi-
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30 cits become more relevant and, thus, a more conservative postural strategy may be de-
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32 sirable (Jacobs and Horak 2006). Alternatively, the undershooting of forward CoM dis-
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34 placement in the EC condition may be because PD subjects were not able to accurately
35
36 use proprioception to map how far their body CoM was moving forward. In fact, under-
37
38 shooting of intended limb and body motion associated with the bradykinesia of PD sub-
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40 jects has been proposed to be due to overestimation of movements due to impaired
41
42 proprioception (Adamovich et al. 2001b; Almeida et al. 2005). Subjects with PD also un-
43
44 dershoot body CoM movements while walking to remembered targets in the dark but
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46 improve their locomotion endpoint positions to remembered targets when they can view
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48 their bodies (Almeida et al. 2005). Similarly, the PD subjects undershoot their compen-
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3 satory, postural stepping in response to external perturbations and increased their step-
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5 ping accuracy to a visual target if they could view their legs (Jacobs and Horak 2006).
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7 Surprisingly, the postural deficits of subjects with PD in this pointing task were not
8
9 related to disease progression, although postural problems increase with severity of dis-
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11 ease (Bloem et al. 2004). The inability to integrate proprioception for control posture
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13 could be a very early symptom of Parkinson's disease, consistent with increased postur-
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15 al sway in newly-diagnosed, untreated subjects with PD (Chastan et al. 2008).
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22 **3.3 Movement-posture coordination**

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24 A coupling of the voluntary, with the postural, components of the whole body point-
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26 ing movement could be seen in the control subjects by the strong temporal relationship
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28 between the velocity profiles of the pointing endpoint and body CoM displacement and
29
30 by the strong correlation between the effects of vision on both the endpoint pointing and
31
32 CoM displacements. Specifically, loss of visual feedback resulted in the same amount of
33
34 over-shooting of the pointing endpoint and the forward CoM displacement in the control,
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36 but not the PD subjects. Similarly, control, but not PD subjects, kept the same temporal
37
38 synergy between the finger and CoM displacement with eyes closed. These results are
39
40 consistent with the hypothesis that the voluntary (focal pointing) and postural (body
41
42 CoM) components of the whole-body pointing task are normally tightly coupled (Stapley
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44 et al. 1999; Kerlirzin et al. 1999; Pozzo et al. 2002), but they also suggest that this coupl-
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46 ing can be disrupted by PD when subjects need to rely on proprioception (Massion
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48 1992; Frank et al. 2000).
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3 The lack of relation of the UPDRS with the decrease in focal-postural coupling
4 suggests that these coordination problems are not simply rooted in rigidity, bradykinesia
5 or tremor, since all of these symptoms were related to the UPDRS. Since PD subjects
6 with mild or more severe symptoms could show just as disordered posture-voluntary
7 coordination, this may suggest a problem in pontomedullary postural integration sites
8 (Massion 1992; Schepens and Drew 2004, Braak and Tredici 2008) or in the mesocor-
9 tical pathway (Owen 2004) that are affected early in the disease.
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19 Although the substantial heterogeneity of disease severity in the patients involved
20 in this study could be considered as a potential issue for the interpretation of the results,
21 it allowed to show that fundamental aspects of the motor behavior, such as the coordina-
22 tion between movement and posture, can be affected independently from the classic
23 symptoms used to classify the stage of Parkinson's disease.
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31 Disruption of focal-postural coupling in the subjects with PD occurred only when
32 they closed their eyes, suggesting that this coupling depends, at least partly, upon pro-
33 prioceptive feedback, which is impaired by PD. When visual information is not available,
34 healthy subjects could still use proprioceptive control for this coupling, whereas subjects
35 with PD must depend upon memorized visual information and vestibular inputs to com-
36 pensate for their difficulty integrating proprioceptive information. Many studies have
37 demonstrated impaired joint, force, and cutaneous kinesthesia as well as impaired motor
38 coordination with eye closure in patients with PD, consistent with poor use of propopri-
39 oception (Zia et al. 2000; Poizner et al. 2000; Adamovich et al. 2001a; Maschke et al.
40 2006; Konczak et al. 2007). It is possible that the disruption in coupling between the
41 CoM and finger pointing components of the task is due to the role of the basal ganglia in
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3 using proprioceptive feedback to formulate internal representation of body maps to help
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5 control multisegmental movements. Studies on human and animal subjects with propri-
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7 oceptive loss and lack of visual feedback are consistent with an important role of propri-
8
9 oceptive pathways for multisegmental coordination when the body cannot be seen (Fung
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11 and Macpherson 1999; Horak 2001; Cordo and Gurfinkel 2004; Vaugoyeau et al. 2007).
12
13 The poor temporal coordination between the voluntary and postural components of the
14
15 movement in our standing subjects with PD was not related to any degradation of syn-
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17 chrony between pointing and postural movement onsets however, as suggested for
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19 pointing from a seated position involving the trunk (Poizner et al. 2000). In the present
20
21 study, the impaired voluntary-postural coupling in PD appeared due to increasing jerk of
22
23 the CoM trajectory without similar effects of loss of vision on pointing endpoint trajectory.
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25 The difference between the present and previous findings reflects a fundamental differ-
26
27 ence in the motor control involved in executing a pointing movement while seated or
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29 standing. While standing, the CNS must coordinate movement execution with balance
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31 maintenance, so we can investigate the effects of PD and vision on the coordination be-
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33 tween movement and posture.
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41 Although proprioceptive feedback aids voluntary-postural coupling, central nervous
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43 system coupling of voluntary-postural components is also involved, consistent with the
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45 hypothesis of Massion (1992). In fact, recently, separate populations of brainstem neu-
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47 rons have been identified that are active in relation to either the postural or the voluntary
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49 component of a paw lift in cats (Schepens and Drew 2004). Since the brainstem reticular
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51 formation in which these neurons can be found receive descending projections from the
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3 basal ganglia, it is not surprising that PD may disrupt this coupling between the postural
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5 and voluntary components of the task.
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8 9 10 **4 Conclusions**

11
12 The effect of vision deprivation on the postural, but not the voluntary, component of
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14 the movement and disruption of the posture-movement coupling by a basal ganglia dis-
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16 ease, such as PD, could be explained by the existence of separate pathways for pro-
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18 gramming the voluntary and postural components of whole-body goal-oriented tasks,
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20 (Massion 1992; Slijper et al. 2002, Massion et al. 2004, Drew et al. 2004, Robert et al.
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22 2007), and by a role of basal ganglia in coordinating program selection and coupling
23
24 (Massion 1992; Grasso et al. 1999; Poizner et al. 2000). The fact that the decoupling
25
26 was observed in subjects with PD only when they could not use visual feedback sug-
27
28 gests that coordination between the voluntary and postural motor commands involves
29
30 not only the basal ganglia, but also proprioceptive pathways, critical for postural control
31
32 (Pigeon and Feldman 1998; Poizner et al. 2000; Maurer et al. 2006). In contrast, when
33
34 subjects have prior visual spatial information about hand and target location, the volunta-
35
36 ry component of whole-body pointing movement did not seem to require proprioceptive
37
38 integration, but could be carried out via remembered visual-motor transformations, as-
39
40 sisted by vestibular feedback.
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3 **References**

4 Adamovich S, Archambault P, Ghafouri M, Levin M, Poizner H, and Feldman A (2001a). Hand trajectory
5 invariance in reaching movements involving the trunk. *Exp Brain Res*, 138(3):288–303.

6
7 Adamovich S. V, Berkinblit M. B, Hening W, Sage J, and Poizner H (2001b). The interaction of visual and
8 proprioceptive inputs in pointing to actual and remembered targets in parkinson's disease. *Neuroscience*,
9 104(4):1027–1041.

10
11 Adkin A. L, Frank J. S, and Jog M. S (2003). Fear of falling and postural control in parkinson's disease.
12 *Mov Disord*, 18(5):496–502.

13
14 Alexandrov A, Aurenty R, Massion J, Mesure S, and Viallet F (1998). Axial synergies in parkinson pa-
15 tients during voluntary trunk bending. *Gait and Posture*, 8:124–135.

16
17 Almeida Q, Frank J, Roy E, Jenkins M, Spaulding S, Patla A, and Jog M (2005). An evaluation of senso-
18 rimotor integration during locomotion toward a target in parkinson's disease. *Neuroscience*, 134:283–293.

19
20 Bloem B. R, Hausdorff J. M, Visser J. E, and Giladi N (2004). Falls and freezing of gait in parkinson's dis-
21 ease: a review of two interconnected, episodic phenomena. *Mov Disord*, 19(8):871–884.

22
23 Braak H and Tredici K. D (2008). Invited article: Nervous system pathology in sporadic Parkinson dis-
24 ease. *Neurology*

25
26 Chastan N, Debono B, Maltte D, and Weber J (2008). Discordance between measured postural instability
27 and absence of clinical symptoms in parkinson's disease patients in the early stages of the disease. *Mov*
28 *Disord*, 23(3):366–372.

29
30 Chong R. K, Horak F. B, and Woollacott M. H (2000). Parkinson's disease impairs the ability to change
31 set quickly. *J Neurol Sci*, 175(1):57–70.

32
33 Chong R. K, Jones C. L, and Horak F. B (1999). Postural set for balance control is normal in alzheimer's
34 but not in parkinson's disease. *J Gerontol A Biol Sci Med Sci*, 54(3):M129–M135.

35
36 Cordo P. J and Gurfinkel V. S (2004). Motor coordination can be fully understood only by studying com-
37 plex movements. *Prog Brain Res*, 143:29–38.

38
39 Drew T, Prentice S, and Schepens B (2004). Cortical and brainstem control of locomotion. *Prog Brain*
40 *Res*, 143:251–261.

41
42 Flowers K (1975). Ballistic and corrective movements on an aiming task. intention tremor and parkinso-
43 nian movement disorders compared. *Neurology*, 25(5):413–421.

44
45 Frank J. S, Horak F. B, and Nutt J (2000). Centrally initiated postural adjustments in parkinsonian patients
46 on and off levodopa. *J Neurophysiol*, 84(5):2440–2448.

47
48 Fung J and Macpherson J. M (1999). Attributes of quiet stance in the chronic spinal cat. *J Neurophysiol*,
49 82(6):3056–3065.

50
51 Gantchev N, Viallet F, Aurenty R, and Massion J (1996). Impairment of posturo-kinetic co-ordination dur-
52 ing initiation of forward oriented stepping movements in parkinsonian patients. *Electroencephalogr Clin*
53 *Neurophysiol*, 101(2):110–120.

54
55 Grasso R, Peppe A, Stratta F, Angelini D, Zago M, Stanzione P, and Lacquaniti F (1999). Basal ganglia
56 and gait control: apomorphine administration and internal pallidum stimulation in parkinson's disease. *Exp*
57 *Brain Res*, 126(2):139–148.

- 1
2
3 Horak F. B (2001). Postural ataxia related to somatosensory loss. *Adv Neurol*, 87:173–182.
- 4
5 Horak F. B, Dimitrova D, and Nutt J. G (2005). Direction-specific postural instability in subjects with parkinson's disease. *Exp Neurol*, 193(2):504–521.
- 6
7
8 Horak F. B, Nutt J. G, and Nashner L. M (1992). Postural inflexibility in parkinsonian subjects. *J Neurol Sci*, 111(1):46–58.
- 9
10
11
12 Jacobs J. V and Horak F. B (2006). Abnormal proprioceptive-motor integration contributes to hypo-metric postural responses of subjects with parkinson's disease. *Neuroscience*, 141(2):999–1009.
- 13
14
15
16 Keijsers N. L. W, Admiraal M. A, Cools A. R, Bloem B. R, and Gielen C. C. A. M (2005). Differential progression of proprioceptive and visual information processing deficits in parkinson's disease. *Eur J Neurosci*, 21(1):239–248.
- 17
18
19 Kerlirzin Y, Pozzo T, Dietrich G, and Vieilledent S (1999). Effects of kinematics constraints on hand trajectory during whole-body lifting tasks. *Neurosci Lett*, 277(1):41–44.
- 20
21
22 Konczak J, Krawczewski K, Tuite P, and Maschke M (2007). The perception of passive motion in parkinson's disease. *J Neurol*, 254(5):655–663.
- 23
24
25
26 Latash M. L, Aruin A. S, Neyman I, Nicholas J. J, and Shapiro M. B (1995). Feedforward postural adjustments in a simple two-joint synergy in patients with parkinson's disease. *Electroencephalogr Clin Neurophysiol*, 97(2):77–89.
- 27
28
29 Mancini M, Rocchi L, Horak F. B, and Chiari L (2008). Effects of parkinson's disease and levodopa on functional limits of stability. *Clin Biomech*, 23(4):450–458.
- 30
31
32 Maschke M, Gomez C. M, Tuite P. J, and Konczak J (2003). Dysfunction of the basal ganglia, but not the cerebellum, impairs kinaesthesia. *Brain*, 126(Pt 10):2312–2322.
- 33
34
35 Maschke M, Tuite P. J, Krawczewski K, Pickett K, and Konczak J (2006). Perception of heaviness in parkinson's disease. *Mov Disord*, 21(7):1013–1018.
- 36
37
38 Massion J (1992). Movement, posture and equilibrium: interaction and coordination. *Prog Neurobiol*, 38(1):35–56.
- 39
40
41 Massion J, Alexandrov A, and Peterka R. J (2004). Why and how are posture and movement coordinated? *Prog Brain Res*, 143:13-27.
- 42
43
44 Maurer C, Mergner T, and Peterka R. J (2004). Abnormal resonance behavior of the postural control loop in parkinson's disease. *Exp Brain Res*, 157(3):369–376.
- 45
46
47 Maurer C, Mergner T, and Peterka R. J (2006). Multisensory control of human upright stance. *Exp Brain Res*, 171(2):231–250.
- 48
49
50 Owen A. M (2004). Cognitive dysfunction in parkinson's disease: the role of frontostriatal circuitry. *Neuroscientist*, 10(6):525-537.
- 51
52
53 Pastor M. A, Day B. L, and Marsden C. D (1993). Vestibular induced postural responses in parkinson's disease. *Brain*, 116 (Pt 5):1177–1190.
- 54
55
56 Patron J, Stapley P, and Pozzo T (2005). Human whole-body reaching in normal gravity and micro-gravity reveals a strong temporal coordination between postural and focal task components. *Exp Brain Res*, 165(1):84–96.
- 57
58
59
60
61
62
63
64
65

- 1
2
3 Pigeon P and Feldman A. G (1998). Compensatory arm-trunk coordination in pointing movements is pre-
4 served in the absence of visual feedback. *Brain Res*, 802(1-2):274–280.
- 5
6 Poizner H, Feldman A. G, Levin M. F, Berkinblit M. B, Hening W. A, Patel A, and Adamovich S. V (2000).
7 The timing of arm-trunk coordination is deficient and vision-dependent in parkinson's patients during
8 reaching movements. *Exp Brain Res*, 133(3):279–292.
- 9
10 Poizner H, Fookson O. I, Berkinblit M. B, Hening W, Feldman G, and Adamovich S (1998). Pointing to
11 remembered targets in 3-d space in parkinson's disease. *Motor Control*, 2(3):251–277.
- 12
13 Pozzo T, Stapley P. J, and Papaxanthis C (2002). Coordination between equilibrium and hand trajectories
14 during whole body pointing movements. *Exp Brain Res*, 144(3):343–350.
- 15
16 Prentice S. D and Drew T (2001). Contributions of the reticulospinal system to the postural adjustments
17 occurring during voluntary gait modifications. *J Neurophysiol*, 85(2):679–698.
- 18
19 Robert G, Blouin J, Ruget H, and Mouchnino L (2007). Coordination between postural and movement
20 controls: effect of changes in body mass distribution on postural and focal component characteristics. *Exp*
21 *Brain Res*, 181(1):159-171.
- 22
23 Rocchi L, Chiari L, Mancini M, Carlson-Kuhta P, Gross A, and Horak F. B (2006). Step initiation in parkin-
24 son's disease: influence of initial stance conditions. *Neurosci Lett*, 406(1-2):128–132.
- 25
26 Schepens B and Drew T (2003). Strategies for the integration of posture and movement during reaching
27 in the cat. *J Neurophysiol*, 90(5):3066–3086.
- 28
29 Schepens B and Drew T (2004). Independent and convergent signals from the pontomedullary reticular
30 formation contribute to the control of posture and movement during reaching in the cat. *J Neurophysiol*,
31 92(4):2217–2238.
- 32
33 Schubert M, Prokop T, Brocke F, and Berger W (2005). Visual kinesthesia and locomotion in parkinson's
34 disease. *Mov Disord*, 20(2):141–150.
- 35
36 Schubert T, Volkman J, Miller U, Sturm V, Voges J, Freund H.-J, and Cramon D. Y. V (2002). Effects of
37 pallidal deep brain stimulation and levodopa treatment on reaction-time performance in parkinson's dis-
38 ease. *Exp Brain Res*, 144(1):8–16.
- 39
40 Slijper H, Latash M. L, and Mordkoff J. T (2002). Anticipatory postural adjustments under simple and
41 choice reaction time conditions. *Brain Res*, 924(2):184-197.
- 42
43 Smiley-Oyen A. L, Cheng H.-Y. K, Latt L. D, and Redfern M. S (2002). Adaptation of vibration-induced
44 postural sway in individuals with parkinson's disease. *Gait Posture*, 16(2):188–197.
- 45
46 Stapley P. J, Pozzo T, Cheron G, and Grishin A (1999). Does the coordination between posture and
47 movement during human whole-body reaching ensure center of mass stabilization? *Exp Brain Res*,
48 129(1):134–146.
- 49
50 Tagliabue M, Pedrocchi A, Pozzo T, and Ferrigno G (2008). A mathematical tool to generate complex
51 whole body motor tasks and test hypotheses on underlying motor planning. *Med Biol Eng Comput*,
52 46(1):11–22.
- 53
54 Vaugoyeau M, Viel S, Assaiante C, Amblard B, and Azulay J. P (2007). Impaired vertical postural con-
55 trol and proprioceptive integration deficits in parkinson's disease. *Neuroscience*, 146(2):852–863.
- 56
57 Woollacott M and Shumway-Cook A (2002). Attention and the control of posture and gait: a review of
58 an emerging area of research. *Gait Posture*, 16(1):1–14.
- 59
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50
51
52
53
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56
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58
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61
62
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Zia S, Cody F, and O'Boyle D (2000). Joint position sense is impaired by parkinson's disease. *Ann Neurol*, 47(2):218–228.

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3 **Figure Captions**
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5

6 **Fig. 1**
7

8 Whole body pointing protocol. Subjects reached with the apex of their joined index fin-
9 gers to a target located at a distance and height proportional to their body height. Ref-
10 lective markers (white circles) were placed at the following anatomical landmarks: na-
11 sion, occipital ridge, chin, 7th cervical segment of the spine, apex of index fingers, bila-
12 teral acromions, humeral lateral epicondyles, ulnar styloids, anterior superior iliac spines
13 (ASIS), iliac crests, posterior superior iliac spines (PSIS), femoral lateral epicondyles,
14 and lateral malleoli.
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22 **Fig. 2**
23

24 Execution time. A. Median values of pointing execution times for Eyes Open (EO) and
25 Eyes Closed (EC) conditions and for CTR and PD subjects. B. Median value of the indi-
26 vidual differences between EC and EO conditions for the CTR and PD groups. Zero on
27 the ordinate axis corresponds to no effect of eyes closure.
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31 In A and B and following figures, upper and lower whiskers represent the 25th and 75th
32 percentile of the data distribution respectively. The ** indicate significant ($p < 0.01$) ef-
33 fects of eyes closure on the execution time for both groups.
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38 **Fig. 3**
39

40 Median values of the constant and variable components of the pointing error for the
41 CTR and PD groups in the EC condition.
42
43
44

45 **Fig. 4**
46

47 Distribution of pointing errors in the sagittal plane. The gray and black ellipses represent
48 the 95% confidence interval of the pointing endpoint performed with eyes closed for the
49 control (gray) and PD (black) groups. The black circle represents the target location.
50 The 'x' represents the center of the error ellipse. In this representation, subjects are lo-
51 cated to the left of the target (see Fig. 1), therefore rightward and downward endpoints
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3 represent pointing overshoots, whereas upward and leftward endpoints represent un-
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represent pointing overshoots, whereas upward and leftward endpoints represent undershoots.

Fig. 5

A. Comparison of final anterior-posterior position of the CoM in front of the ankle joints, CoMx, for the CTR and PD groups. Data are reported as percentage of foot length for the EC and EO conditions, so that the ordinate 0 value corresponds to the ankle position and 100 represents the limit of the base of support. On the right, the UPDRS score of each PD subject is related to their corresponding CoM displacement. B. Median values of the individual differences between the EC and EO condition for CTR and PD subjects. Zero on the ordinate axis corresponds to no effect of eyes closure. ** indicates a significant effect ($p < 0.01$) of eyes closure for the subjects with PD. * indicates significant difference ($p < 0.05$) in the effect of the eyes closure between the groups.

Fig. 6

Normalized Jerk of CoM and finger trajectory. A and C represent the median Jerk of the CoM and finger endpoint (EP) in the EO and EC conditions for controls (CTR) and subjects with PD. Because of the time and amplitude normalization the values are dimensionless. B and D illustrate the median of the individual differences between EC and EO conditions of the CoM and EP Jerk. The zero value indicates no effect of eyes closure. The upper and lower whiskers represent the 25th and 75th percentile of the data distribution respectively. In lower part of B, * and ** indicate significant ($p < 0.05$ and $p < 0.01$ respectively) effects of eyes closure on the Jerk of the CoM for both groups. In the upper part of B, ** indicates a significant difference ($p < 0.01$) between the effects of the eyes closure on the CoM Jerk in CTR and PD subjects.

Fig. 7

Final position of the Upper and Lower body CoM. A and C represent the median anterior-posterior position of the Upper body CoM (UCoM) and Lower body CoM (LCoM) in the EO and EC conditions for controls (CTR) and subjects with PD. The CoM position is reported as percentage of the foot length with zero corresponding to the pelvis position

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3 for the UCoM and ankle position for the LCoM. B and D illustrate the median of the indi-
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5 vidual differences between EC and EO conditions of the UCoM and LCoM. The zero
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7 value indicates no effect of eyes closure. * indicates a significant difference ($p < 0.05$) be-
8
9 tween the effects of the eyes closure on the UCoM in CTR and PD subjects.

10
11 **Fig. 8**

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13 Temporal coupling between postural and voluntary components of the task. A. Median
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15 values of correlation between CoM and fingertip velocity profile in EO and EC conditions
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17 for controls and subjects with PD. Values equal to 1 indicate a perfect correlation. B.
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19 Median values of the individual differences in correlation between the EC and EO condi-
20
21 tions for CTR and subjects with PD. Zero on the ordinate represents no effect of eye
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23 closure. * indicates significant difference ($p < 0.05$) in the effect of eyes closure between
24
25 the groups.

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27 **Fig. 9**

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29 The effect of eyes closure on spatial coupling between the final horizontal CoM position,
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31 CoM_x , and on the pointing error, EP_x . Both variables are represented as percentage of
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33 subject foot length. Each point represents a subject. The UPDRS score is reported for
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35 each subject with PD. The coefficient of correlation, R , between the vision effect on
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37 CoM_x and EP_x , as well as the p -values for testing the hypothesis of no correlation are
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39 reported for the PD and CTR groups in black and in gray respectively.

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4 **List of Tables**
5

6 **Table 1**

7 Patient Characteristics. For each subject with PD the table reports the age, the years elapsed since the
8 diagnosis of the PD, the score in the Hoehn & Yahr scale, the total and the axial score in the Unified Par-
9 kinson's Disease Rating Scale and the Dyskinesia score in the off-medication state.
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14 Subject	15 Age	16 Since 17 Diagnosis	18 H&Y	19 Motor 20 UPDRS	21 Axial 22 UPDRS	23 Dyskinesia
24 S1	25 55	26 5	27 2	28 19	29 10	30 0
31 S2	32 65	33 7	34 2	35 25	36 10	37 0
38 S3	39 52	40 8	41 2	42 28	43 14	44 4
45 S4	46 65	47 8	48 2	49 34	50 18	51 0
52 S5	53 69	54 9	55 2	56 27	57 12	58 0
59 S6	60 71	61 10	62 2	63 58	64 24	65 0
66 S7	67 50	68 10	69 3	70 27	71 13	72 0
73 S8	74 62	75 15	76 4	77 59	78 28	79 4
80 S9	81 60	82 16	83 2	84 39	85 23	86 0
87 S10	88 58	89 18	90 4	91 60	92 34	93 0

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Figure 1
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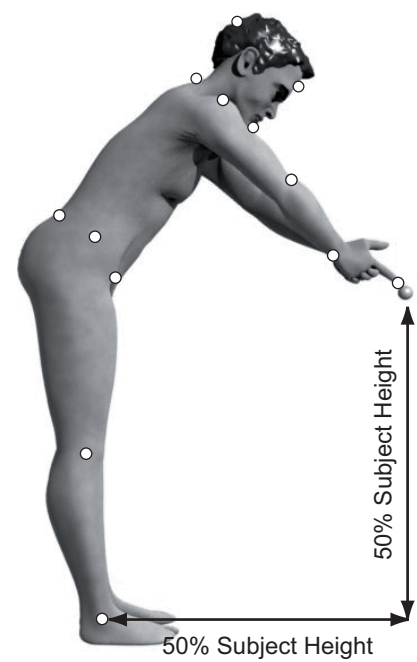


Figure 2 Execution Time [sec]
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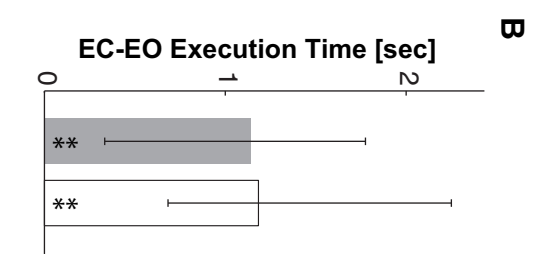
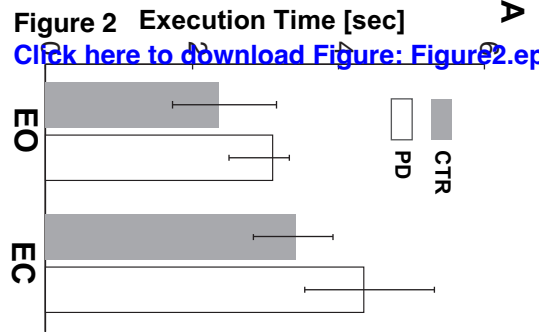


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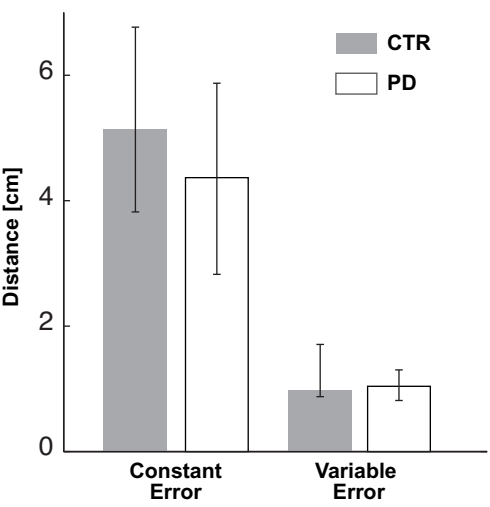


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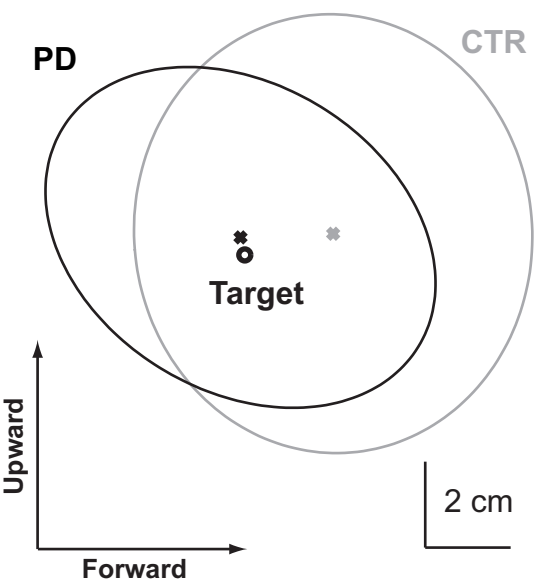


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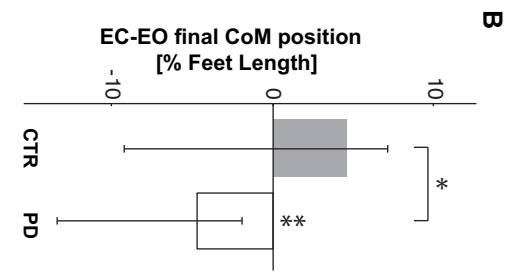
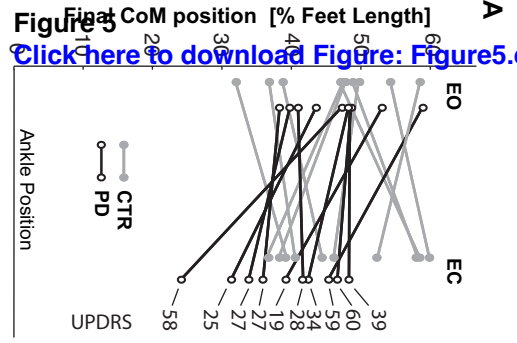
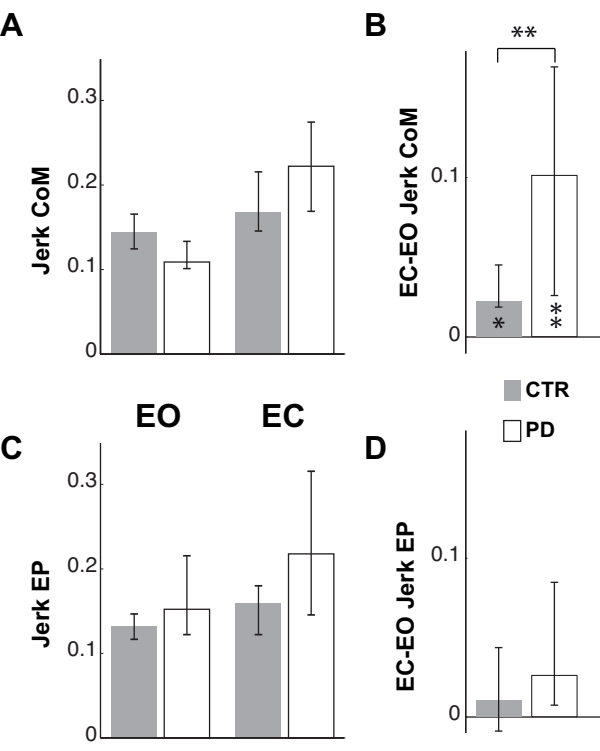


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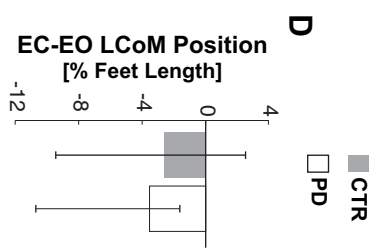
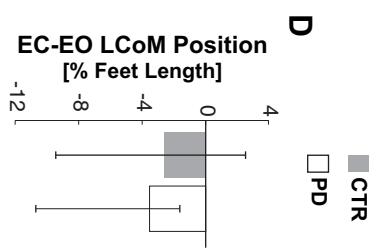
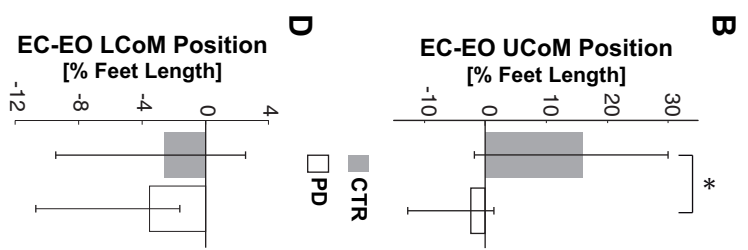
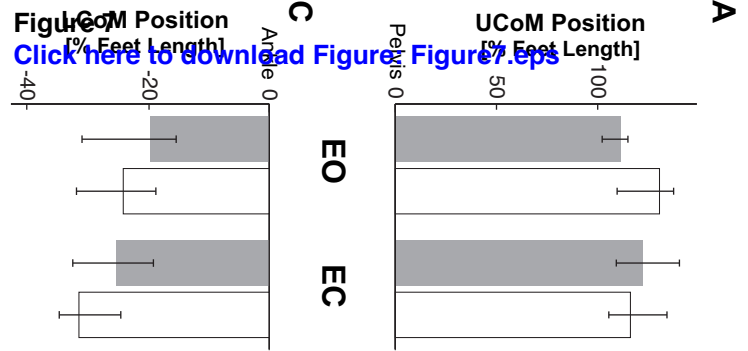


Figure 8
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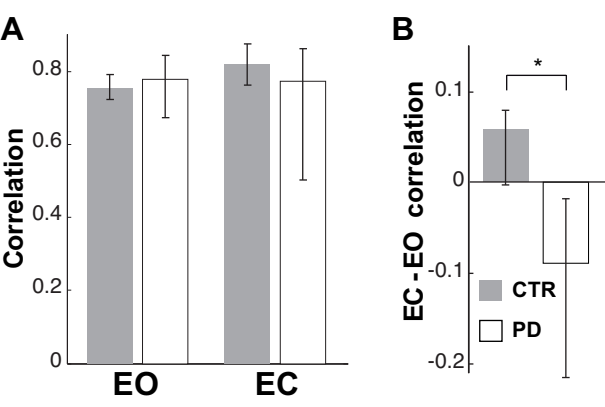
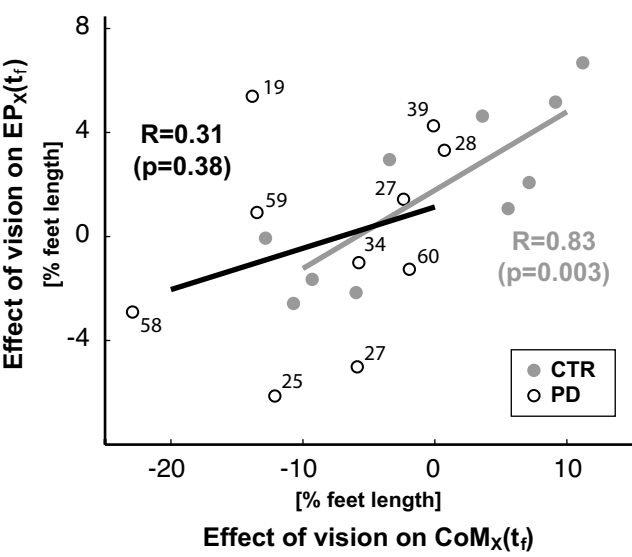


Figure 9

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