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Interest of active posturography to detect age-related and early Parkinson's disease related impairments in mediolateral postural control

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Running head: Parkinson and age-related issues in postural control

Abstract

Patients with Parkinson's disease display impairments of postural control most particularly in active challenging conditions. The objective of the present study was to analyze early signs of disease-related and also age-related impairments in mediolateral body extension and postural control. Fifty-five participants (18 Hoehn and Yahr stage 2 patients in the off-drug condition, 18 healthy elderly controls and 19 young adults) were included in the study. The participants performed a quiet stance task and two active tasks that analyzed the performance in mediolateral body motion: a limit of stability and rhythmic weight shift tasks. As expected, the patients displayed significantly lower and slower body displacement (head, neck, lower back, center of pressure) than elderly controls when performing the two body excursion tasks. However, the behavioral variability in both tasks was similar between both groups. Under these active conditions, the patients showed significantly lower contribution of the hip postural control mechanisms compared with the elderly controls. Overall, the patients seemed to lower their performance in order to prevent a mediolateral postural instability. However, these patients, at an early stage of their disease, were not unstable in quiet stance. Complementarily, elderly controls displayed slower body performance than young adults, which therefore showed an additional age-related impairment in mediolateral postural control. Overall, the study illustrated markers of age-related and Parkinson's disease impairments in mediolateral postural control that may constrain everyday activities in elderly adults and even more in patients with Parkinson's disease.

Keywords: Parkinson's disease, Limits of stability, Rhythmic weight shift, Postural control mechanisms, Mediolateral axis

Footnote: PD = Parkinson's disease; ML = mediolateral; AP = anteroposterior; LOS = limit of stability; RWS = rhythmic weight shift; UPDRS = unified Parkinson's disease rating scale; DSM IV = part IV of the diagnostic and statistical manual of mental disorders; SD = standard deviation; COP = center of pressure; COP_v = center of pressure vertical; COP_c = center of pressure change; COP_{net} = resultant COP displacement; COP_r and COP_l = COP displacement under the right and left foot, respectively; R_{vr} and R_{vl} = vertical reaction forces under the left and right foot, respectively; $MeanCOP_l$, $meanCOP_r$, $meanR_{vl}$ and $meanR_{vr}$ are the mean of each time-series

INTRODUCTION

Parkinson's disease (PD) is a degenerative disease that causes problems in motor control. Falls are a common problem in patients with PD (Allen et al. 2013; Pickering et al. 2007) and when they occur in the mediolateral (ML) axis, they can cause hip fractures (Hayes et al. 1996; Rogers and Mille 2003). Patients with PD have about four times more chance than elderly controls to get a hip fracture (Walker et al. 2013). Hence, there is a necessity to understand the causal factors of ML postural instability in patients with PD.

The quiet stance condition may be limited to reveal deficiencies in postural control because postural control is not challenged enough (Winter, 1995). Hence, researchers have used complex tasks (e.g., dual tasks versus quiet stance; platform perturbation vs. quiet stance) to better detect and understand age-related and disease-related deficiencies in postural control. For example, older adults have been shown to sway more than younger adults, especially when the tasks performed were more challenging (Bonnet et al., 2010; Maki and McIlroy, 1996). One very challenging condition is the ML limit of stability (LOS) task (Brauer et al. 1999). This task shows the boundaries that the centre of mass cannot cross if stability is to be maintained (Mancini et al. 2008). An alternative of the LOS task is the rhythmic weight shift (RWS) task (Owings et al. 2000). Both tasks are relevant to unveil deficiencies in ML postural control because they challenge postural control until the maximum values of the stability limits (see Methods). These tasks are also relevant because they can test the dynamic nature of postural control (e.g., maximum amplitude and velocity of body motions) that cannot be analyzed in quiet stance. In the literature, rare are the reports of ML LOS and ML RWS performances in patients with PD (Ganesan et al. 2010; Rossi et al. 2009; Vervoort et al. 2013; Yang et al. 2008). Mostly, these studies showed disease-related impairments in the performance in both tasks (amplitude, velocity) and in the variability of performance in the ML LOS task. However, these four studies did not analyze causal factors such as disease-related impairments in ML postural control mechanisms. Kim et al. (2009) and Mancini et al. (2008) suggested to test and detect disease-related impairments in postural control. In the present study, we did so in analyzing deficiencies of ML postural control mechanisms as potential causal factor of reduced performance in ML active tasks.

Our objective was to build knowledge on Parkinson's disease-related impairments in ML body excursion and ML postural control mechanisms beyond age-related impairments. We studied patients with PD at stage 2 (Hoehn and Yahr 1967: bilateral involvement without impairment of balance) and in an off-drug condition to detect early signs of ML postural impairments. In the comparison between patients and elderly controls, we expected to find disease-related impairments when performing the ML RWS and ML LOS tasks (amplitude, velocity, and/or directional control; cf. Ganesan et al. 2010; Rossi et al. 2009; Vervoort et al. 2013; Yang et al. 2008) and in the contribution of the ML postural control mechanisms, as causal factors. These disease-related effects should be detected because the LOS and RWS tasks are very challenging. Alternatively, we were not sure to find disease-related impairment in ML postural stability in quiet stance because the patients with PD were at a low stage of

their disease and because of the conflicting results in the literature (Frenklach et al., 2009; Mancini et al., 2012; Nantel et al., 2012; Termoz et al., 2008). Moreover in the comparison between young adults and elderly controls, we expected to find age-related reductions when performing the ML RWS and ML LOS tasks and in the contribution of the ML postural control mechanisms (Bonnet et al. 2014b; Brauer et al. 1999; Owings et al. 2000).

METHODS

Participants

Physical characteristics of the participants

Eighteen patients with PD and eighteen elderly controls (twelve males in each group) were included in the study. Their mean age, bodyweight and height were 60.39 ± 0.07 years and 61.61 ± 5.73 years, 78.58 ± 12.69 kg and 77.88 ± 18.73 kg, 1.71 ± 0.07 m and 1.69 ± 0.09 m, respectively. There was no group difference in these three variables ($P > 0.42$). Nineteen young, healthy adults were also included. They were 21.87 ± 2.87 years, 63.05 ± 11.43 kg and 1.72 ± 0.10 m, respectively.

The patients with PD were diagnosed in accordance with the criteria of the United Kingdom Parkinson's Disease Brain Bank. They were all at a stage 2 on the Hoehn and Yahr's (1967) scale (bilateral involvement without impairment of balance). The mean time since disease onset averaged 3.94 years (± 2.34). The mean motor Unified Parkinson's Disease Rating Scale (UPDRS) score (part III) analyzed in off-drug condition averaged 16.22 (± 6.89). None of the patients presented motor fluctuation or dyskinesia. Patients with PD had an axial UPDRS III score of 3.94 ± 2.31 and a postural stability UPDRS score of 1.28 ± 1.02 , calculated as in Bejjani et al. (2000) and Dimitrova et al. (2004). The mean axial score was calculated by summing UPDRS III items 18, 22, 27, 28, 29, and 30 and the mean postural stability score was calculated by summing UPDRS III items 18, 27, 28, 29, and 30.

In their usual life, the patients were receiving a mean daily total levodopa equivalent dose of 420 ± 168 mg. The study was accepted by legal authorities in the University of Lille 2 and was performed in accordance with the tenets of the Declaration of Helsinki. All participants signed an inform consent to participation.

Exclusion – inclusion criteria

The patients with PD had not taken their medication in the 12h prior to their participation. The participants were included if they scored more than 25 in the Mini-Mental State Examination. They were included if they had correct or corrected visual acuity and if they had not fallen in the last 6 months. The participants were excluded if they had any neurological, musculoskeletal (especially at the hip and ankle), vestibular pathologies and recurrent dizziness. They were excluded if they presented signs of dementia (DSM IV criteria).

Apparatus

A dual-top force platform (AMTI, Watertown, MA; 120 Hz) was used to record the forces and moments under each foot. A two-camera video motion analysis system (Version 7.5 from SIMI Reality Motion Systems GmbH, Munchen; 15 Hz) was used to record the displacement of the markers. The reflective markers were attached to the back of a chest belt (lower back marker), of the neck (neck marker) and of a headset (head marker).

Conditions, instructions and procedure

The three conditions were the quiet stance, ML LOS (left and right) and ML RWS tasks. In quiet stance, the participants were instructed to refrain from making any voluntary movements. They were told to relax. In the ML RWS task, the participants were instructed to oscillate as far as possible along the ML direction (Figure 1). They were told to achieve the greatest possible head displacement during oscillatory movements. The participants were only allowed to flex their hips at the end of each semi-cycle of oscillation in order to extend their head displacement. The trials lasted 30 seconds in both quiet stance and ML RWS tasks. The ML LOS task was performed as follows: after 15 seconds, a start signal was given and the participants leaned their body as far as possible (Figure 1). Once the participants had achieved a stable, maximum ML body lean position, they had to hold it for 15 seconds as timed by the investigator.

In both the ML LOS and ML RWS tasks, the participants had to keep both heels in full contact with the force platform (Brauer et al. 1999; Owings et al. 2000). They were not allowed to flex their knees. The two tasks were demonstrated once by an investigator and practiced once by the participants. In all trials, the participants looked at the black dot in front of them. The order of the tasks was randomized.

The participants were bare foot and the foot position was standardized: stance width of 14 cm and stance angle of 17° (McIlroy and Maki 1997).

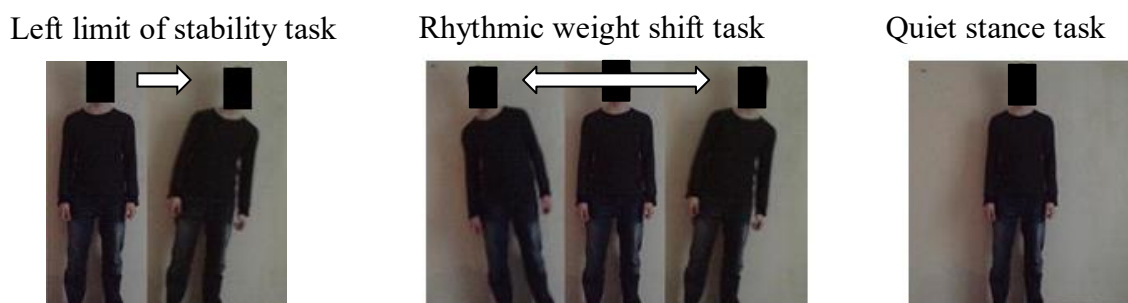


Figure 1. Illustration of the three tasks: the limit of stability task (here shown on the left), the rhythmic weight shift task and the quiet stance task. For the limit of stability task, the first and second figures represent the initial and final body positions, respectively. For the rhythmic weight shift task, the three figures represent the mediolateral (ML) body oscillations performed throughout the trial.

Dependant variables

The variables were analyzed with the mean of the two trials in the three conditions (quiet stance, LOS, RWS). We analyzed the mean of the left and right LOS performance to control the influence of any asymmetry in the participants. In the LOS task also, the variables were computed with two means per trial, one in a first period (10 sec) just before extension and one in a second period after extension and during the maximum extension (10 sec; Figure 2A). The second period did not begin at the first lower value just after extension but at the second one (see Figure 2A) to reduce the behavioural variability of the extension period in each participant.

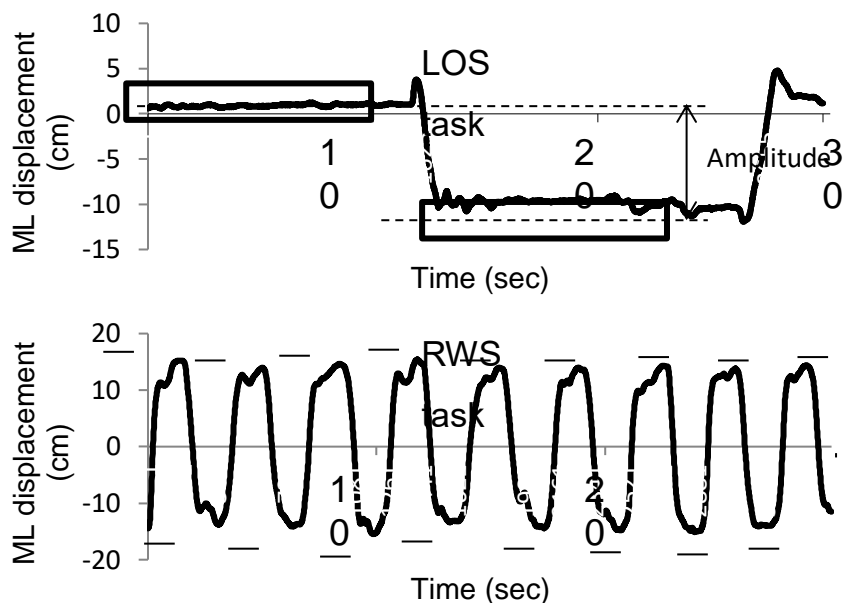


Figure 2. Representation of the mediolateral (ML) displacement of a marker (COP, lower back, neck or head) in the limit of stability (LOS) task (upper figure) and rhythmic weight shift (RWS) task (lower figure) for 30 seconds. In the LOS task, the two rectangles represent the 1st period (10 sec) just before extension and one in the 2nd period after extension and during the maximum extension (10 sec). As can be seen on the figure, the 2nd period began in the second lower minimum peak and not in the first minimum peak. This methodology allowed lower the variability of the marker displacement within that 2nd period. The amplitude performance was calculated between the mean displacement of the two periods. In the RWS task, the ML amplitude performance was calculated in averaging and then subtracting the higher and lower oscillation peaks marked by a light horizontal bar on the figure.

Performance variables in the RWS and LOS tasks

In the LOS task, the ML amplitude and velocity performances were the distance and velocity between the mean position of the first and second periods (Figure 2A). In the RWS task, the ML amplitude performance was calculated by averaging the maximum left and right oscillation peaks reached by the marker (COP, head, neck, lower back; Figure 2B). The mean ML velocity was the ML distance travelled divided by the duration of the trial. The two tasks were performed in the ML axis and the performance variables were therefore computed in the ML axis.

Behavioural variability variables in the three tasks

In the RWS and LOS tasks, the variability of behavioural performance was calculated as the standard deviation (SD) of the mean ML amplitude performance. In the quiet stance task, the SD, maximum displacement (range) and mean velocity (distance/time) were used to analyze the marker displacements (COP, lower back, neck and head) in the ML axis. In addition, the SD, range and mean velocity of marker displacements (COP, lower back, neck and head) were calculated in the AP axis in the three tasks, as complementary signs of behavioural variability, or instability, in these conditions.

Postural control variables

In their manuscripts, Winter et al. (1993, 1996) showed that the control of ML stance was not performed primarily at the level of the ankles by inversion/eversion but instead at the level of the hip by loading more bodyweight under one leg and thus unloading bodyweight under the other leg. Loading/unloading the bodyweight under each foot is referred to as the bodyweight distribution mechanism. Muscular activities of inversion/eversion at the ankle play a secondary role in the control of ML stance and the related mechanism is referred to as the COP location mechanism.

In the present study, the contribution of the ML bodyweight distribution mechanism (denoted as COP_v in the model calculation, v for vertical) and COP location mechanism (denoted as COP_c in the model calculation, c for changes) were calculated by using an updated version (Rougier 2007, 2008) of Winter et al.'s (1993, 1996) model. In a first step of analysis, we used three equations to obtain the COP displacement of the three time series ($COP_{net}(t)$, $COP_c(t)$ and $COP_v(t)$):

$$COP_{net}(t) = COP_l(t) \frac{R_{vl}(t)}{R_{vl}(t) + R_{vr}(t)} + COP_r(t) \frac{R_{vr}(t)}{R_{vl}(t) + R_{vr}(t)} \quad (1)$$

$$COP_c(t) = COP_l(t) \times meanR_{vl} + COP_r(t) \times meanR_{vr} \quad (2)$$

$$COP_v(t) = meanCOP_l \frac{R_{vl}(t)}{R_{vl}(t) + R_{vr}(t)} + meanCOP_r \frac{R_{vr}(t)}{R_{vl}(t) + R_{vr}(t)} \quad (3)$$

$COP_l(t)$ and $COP_r(t)$ are the COP displacement under the left and right foot. $R_{vl}(t)$ and $R_{vr}(t)$ are the vertical reaction forces under the left and right foot. $COP_v(t)$ and $COP_c(t)$ are the COP displacement under the control of the body weight distribution and COP location mechanisms, respectively (Rougier 2007, 2008). $meanCOP_l$, $meanCOP_r$, $meanR_{vl}$ and $meanR_{vr}$ are the mean of each time-series.

Equation (1) simply shows how to calculate the resultant COP_{net} displacement, classically known as COP displacement in the literature (Winter et al. 1996). In equation (2), the COP_{net} displacement explained by the COP location mechanism was calculated in controlling – that is in keeping constant throughout the trial – the COP_{net} displacement explained by the bodyweight distribution mechanism. In equation (3) the COP_{net} displacement explained by the bodyweight distribution mechanism was calculated.

Once we had found the COP_{net} , COP_v and COP_c time series, we computed the contribution of each mechanism to explain the COP_{net} displacement. The amplitude contribution, or strength, of each mechanism was calculated by analyzing the variability in SD of $COP_c(t)$, $COP_v(t)$ and $COP_{net}(t)$ (Rougier, 2007, 2008). Additionally, we computed cross-correlations for COP_v vs. COP_{net} , and COP_c vs. COP_{net} as in all previous studies (Bonnet et al. 2013; Lafond et al. 2004; Rougier 2007, 2008; Termoz et al. 2008; Winter et al. 1993, 1996). In line with the study by Bonnet et al. (2013, 2014b, in press), we assumed that the degree of similarity between $COP_c(t)$ and $COP_v(t)$ on one hand and $COP_{net}(t)$ on the other hand could show the degree of active contribution of that mechanism to control $COP_{net}(t)$. We assumed that the higher the cross-correlation coefficient, the higher the active contribution of the postural mechanism to controlling ML COP displacement. In brief, two kinds of analysis were used to analyze the amplitude and active contributions of the ML bodyweight distribution and ML COP location mechanisms.

The bodyweight distribution and COP location mechanisms were computed in the ML axis because the RWS and LOS tasks challenged the ML equilibrium specifically. They were not analyzed in the AP axis because the participants had their feet side by side. A recent study

by Bonnet et al. (2014a) indeed explained and demonstrated that Winter et al.'s (1993,1996) model should not be used with the feet side by side to compute the AP mechanisms. According to this study, the AP mechanisms should only be studied when one foot is completely forward the other, not otherwise (Bonnet et al., 2014a).

Data analysis

To control spurious sources of between-subjects variability in postural control, the data were detrended to keep the principal component of displacement straight within trials (cf., Bonnet et al., in press). Then, the confounding influence of bodyweight and height, was removed by applying the normalization procedure recommended by O'Malley (1996) and briefly explained by Bonnet et al. (in press).

Most of our time-series presented outliers. Hence, non-parametric Kruskal-Wallis ANOVA were used to analyze differences between groups for all the dependent variables. Mann-Whitney U-tests were performed for post-hoc analyses (P -value <0.05).

RESULTS

Main effects of group for the performance in the RWS and LOS tasks

In the RWS task, the ANOVA was significant for the mean amplitude reached by the head ($H(2,55)=7.88, P<0.05$), neck ($H(2,55)=8.96, P<0.05$), lower back ($H(2,55)=11.44, P<0.05$) and COP displacement ($H(2,55)=7.24, P<0.05$). The amplitude performance was significantly lower in patients with PD than in elderly controls and young adults for the head, lower back and COP displacement ($U_s<93, p<0.05$; Figure 3A) and significantly lower in patients with PD than in elderly controls for the neck displacement ($U=76, p<0.05$). The ANOVA was also significant for the mean velocity of lower back displacement ($H(2,55)=6.63, P<0.05$) but not of the head, neck and COP displacement ($P>0.13$). The velocity performance was lower in patients with PD than in young adults ($U=87, p<0.05$; Figure 4A).

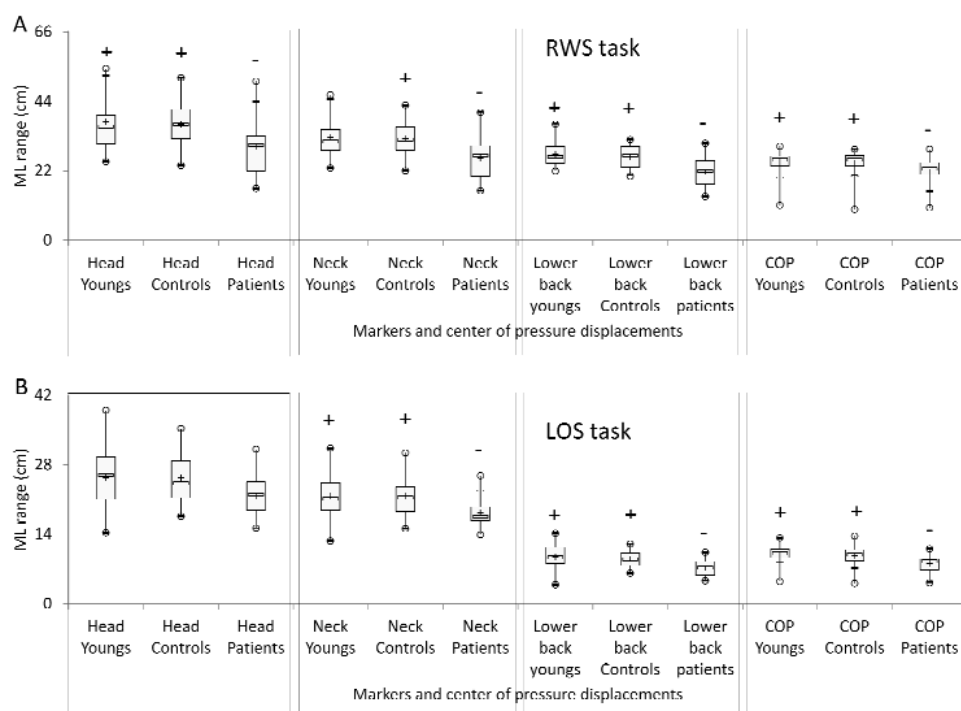


Figure 3. Box plot for the mediolateral (ML) range of the head, neck, lower back and center of pressure (COP) displacements in A) the rhythmic weight shift (RWS) and B) limit of stability (LOS) tasks. The range is displayed in centimeters (cm). Within the box plot, the + represents the mean, the \square represents the median, the higher and lower end of the box represent the first and third quartiles, the higher and lower whiskers represent the mustache and the higher and lower o represent the max and min values of the box plot. Significant main effects of group in the non-parametric Kruskal-Wallis ANOVA for the rank were found only when there are + and – signs above the box plots ($P < 0.05$). Results of the Mann-Whitney U-tests are shown by the signs + (meaning significantly higher rank) and – (meaning significantly lower rank; $P < 0.05$). When there is no sign, the Mann-Whitney U-test was *ns*.

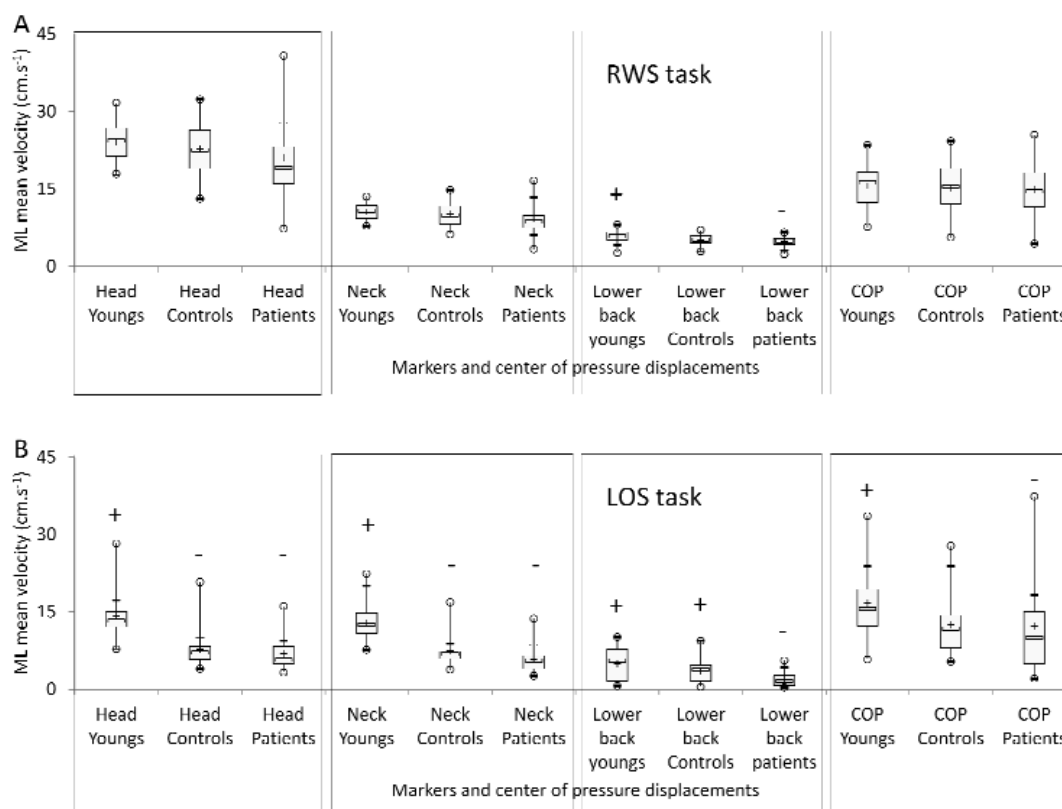


Figure 4. Box plot for the mediolateral (ML) mean velocity of the head, neck, lower back and center of pressure (COP) displacements in A) the rhythmic weight shift (RWS) and B) the limit of stability (LOS) tasks. Within the box plot, the + represents the mean, the \square represents the median, the higher and lower end of the box represent the first and third quartiles, the higher and lower whiskers represent the mustache and the higher and lower o represent the max and min values of the box plot. The mean velocity is displayed in centimetres per second (cm.s⁻¹). Significant main effects of group in the non-parametric Kruskal-Wallis ANOVA for the rank were found only when there are + and – signs above the box plots ($P < 0.05$). Results of the Mann-Whitney U-tests are shown by the signs + (meaning significantly higher rank) and – (meaning significantly lower rank; $P < 0.05$). When there is no sign, the Mann-Whitney U-test was *ns*.

In the LOS task, the ANOVA was significant for the mean amplitude reached by the neck ($H(2,55)=8.73, P<0.05$), the lower back ($H(2,55)=9.53, P<0.05$) and COP ($H(2,55)=9.15, P<0.05$) but not by the head ($P=0.10$). Each time, the amplitude performance was lower in patients with PD than in elderly controls and young adults ($U_s<94, p<0.05$; Figure 3B). The ANOVA was also significant for the mean velocity to reach the LOS with the head ($H(2,55)=25.03, P<0.05$), neck ($H(2,55)=27.25, P<0.05$), lower back ($H(2,55)=10.35, P<0.05$) and COP displacement ($H(2,55)=6.30, P<0.05$). The velocity of lower back displacements was significantly lower in patients with PD than in elderly controls and young adults ($U_s<88, p<0.05$; Figure 4B). The velocity of the head and neck displacements was significantly lower in both patients with PD and elderly controls than in young adults ($U_s<40, p<0.05$; Figure 4B). Moreover, the velocity of the COP displacement was significantly lower in patients with PD than in young adults ($U_s<98, p<0.05$; Figure 4B).

Main effects of group for the behavioural variability in the RWS and LOS (second part) tasks

In the RWS task, the ANOVAs for the ML SD mean amplitude of the head, neck, lower back and COP displacements were not significant ($H(2,55)<3.17, P>0.05$). In the LOS task, the ANOVAs for the AP and ML range, standard deviation and mean velocity of the head, neck, lower back and COP displacements were not significant ($H(2,55)<5.42, P>0.05$).

Main effects of group for the contribution of the bodyweight distribution and COP location mechanisms in the RWS and LOS tasks

In the RWS task, the ANOVA was significant for SD COP_v ($H(2,55)=7.79, P<0.05$; Figure 5A) and SD COP_c ($H(2,55)=7.06, P<0.05$; Figure 5B). The SD COP_v was significantly lower in patients with PD than young adults ($U=84, p<0.05$) and almost significantly lower in patients with PD than in elderly controls ($U=103, p=0.06$). The SD COP_c was significantly lower in elderly controls than in young adults ($U=85, p<0.05$) and almost significantly lower in patients with PD than in young adults ($U=107, p=0.06$). In the LOS task, the ANOVA was significant for SD COP_v ($H(2,55)=8.67, P<0.05$; Figure 5C). The SD COP_v was significantly higher in elderly controls than in both PD than young adults and young adults ($U_s<91, p<0.05$). In both RWS and LOS tasks, there was no significant effect in the cross-correlation analyses, *ns*.

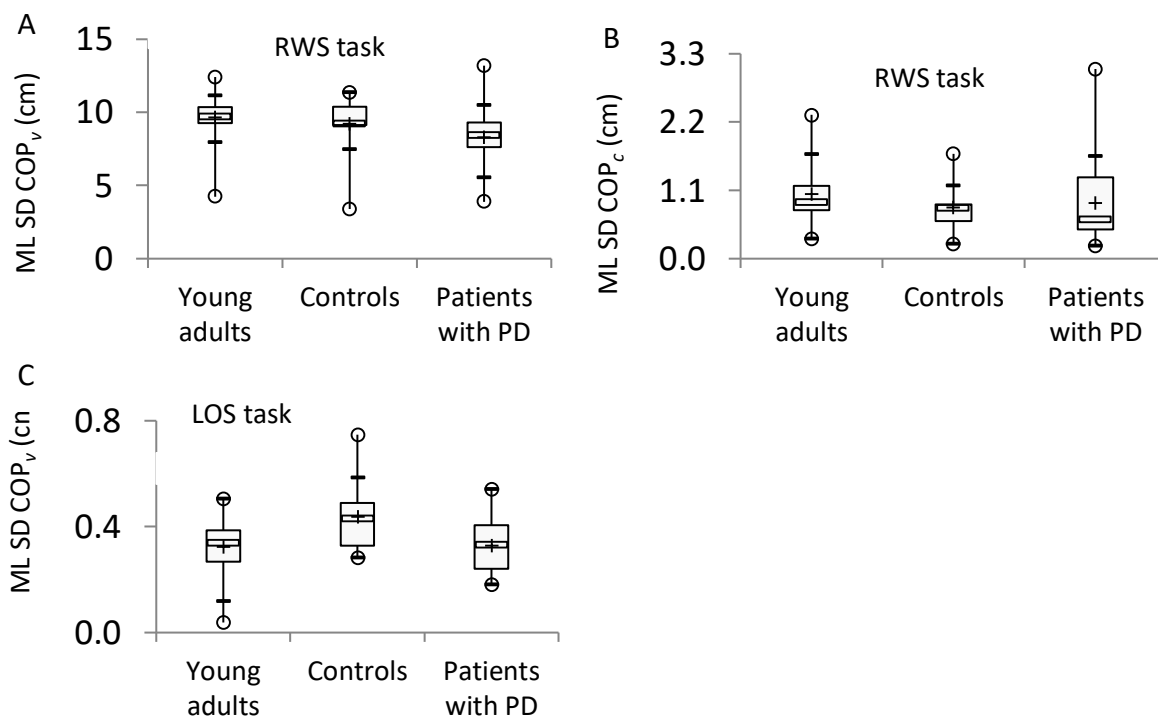


Figure 5. A. Significant main effect of group ($P < 0.05$) in the non-parametric Kruskal-Wallis ANOVA for the rank of the mediolateral (ML) standard deviation (SD) of COP_v (center of pressure vertical; abbreviation of the bodyweight distribution mechanism in the model computation) in the rhythmic weight shift (RWS) task. B. Significant main effect of group ($P < 0.05$) in the non-parametric Kruskal-Wallis ANOVA for the rank of the ML SD COP_c (COP_c changes; abbreviation of the COP location mechanism in the model computation) in the limit of stability (LOS) task. C. Significant main effect of group ($P < 0.05$) in the non-parametric Kruskal-Wallis ANOVA for the rank of the ML SD COP_v in the LOS task. Within the box plot, the + represents the mean, the \equiv represents the median, the higher and lower end of the box represent the first and third quartiles, the higher and lower represent the mustache and the higher and lower o represent the max and min values of the box plot. The COP_v and COP_c displacements are displayed in centimeters (cm). Results of the Mann-Whitney U-tests are shown by the signs + (meaning significantly higher rank) and - (meaning significantly lower rank; $P < 0.05$). When there is no sign, the Mann-Whitney U-test was *ns*.

Additional analyses

In quiet stance, the ANOVA was not significant for any variable ($H(2,55) < 5.20, P > 0.05$). In the first part of the LOS task, the ANOVA was significant for the AP and ML velocity of the COP displacement ($H_s(2,55) > 6.24, P < 0.05$). The AP COP velocity of elderly controls (1.59 ± 0.43) was significantly lower than the one in young adults (1.80 ± 0.29 ; $U = 97, p < 0.05$) but not the one in patients with PD ($U = 161, p > 0.05$; 1.78 ± 0.82). The ML COP velocity of patients with PD (1.48 ± 0.61) and elderly controls (1.30 ± 0.33) were lower than the one in young adults (1.53 ± 0.23 ; $U_s < 97, p < 0.05$). The ANOVA was also significant for SD COP_c ($H(2,55) = 8.52, P < 0.05$). SD COP_c was higher in patients with PD (0.044 ± 0.041) and elderly controls (0.039 ± 0.024) than in young adults (0.024 ± 0.013 ; $U_s < 92, p < 0.05$). However, there was no significant effect in SD COP_v and in COP_v vs. COP_{net} and COP_c vs. COP_{net} .

For the patients with PD, none of the relationships between ML performances in the RWS and LOS tasks and clinical variables (UPDRS motor score, axial score and postural stability score) was significant ($P>0.13$). These results thus showed that the patients with PD were at an early stage of their disease.

Seven and eleven patients with PD were more affected by the disease on the right and left parts of their body, respectively. We performed two additional analyses to control if the performance in the LOS task was lower in the affected side compared with the other side of the body. For both performances (amplitude, velocity), the Wilcoxon test was not significant ($Z_s<0.81, p>0.05$). Hence, patients performed equally on both sides.

DISCUSSION

The present manuscript studied Parkinson's disease-related and age-related impairments in ML body excursion and ML postural control mechanisms. Overall, the main results showed lower performances in the ML body excursion tasks and lower contribution of the ML postural control mechanisms in patients with PD than in healthy controls and also in healthy controls than in young adults.

Disease-related impairments in ML LOS and RWS performances

In past reports, Yang et al. (2008) showed Parkinson's disease-related impairments in maximum extension, velocity and directional control in the ML LOS task. Rossi et al. (2009) also showed that patients with PD performed the ML RWS task slower than elderly controls. No other significant difference in ML performance was found in other studies (Ganesan et al. 2010; Vervoort et al. 2013). Stronger than these previous reports and consistent with the first hypothesis, we found disease-related reduction in the ability to extend the body in both amplitude and velocity at different levels of the body (head, neck, lower back and/or COP) in both ML LOS and ML RWS tasks (Figures 3A, 3B, 4A, 4B). Therefore, even at an early stage of their disease, patients with PD show unambiguous reduction in their ability to extend their body laterally. However, in contrast to some previous reports (Ganesan et al. 2010; Yang et al. 2008), the patients with PD displayed identical AP and ML variability in postural behavior than elderly controls (see the second part of the results section). Hence, at an early stage of their disease, the patients with PD were not unstable in both ML and AP axis in performing the active tasks but simply limited in their ML performance. At minimum, we can conclude that patients with PD have reduced body extension capabilities when they try to lean or oscillate as far as possible in the ML axis.

Disease-related impairments in ML postural control mechanisms

In the literature, Termoz et al. (2008) showed a significantly lower contribution of the ML bodyweight distribution mechanism in patients with PD (Hoehn and Yahr stage: 2.7 ± 0.3) than in their elderly controls who intentionally adopted a stooped posture. Our results also showed a lower contribution of the ML bodyweight distribution mechanism in patients with PD. In our study, this disease-related deficiency was found in the RWS (Figure 5A) and LOS tasks (Figure 5C). On one hand, this disease-related impairment was not so strong because it was not significant in the quiet stance task. On the other hand, this significantly lower contribution of the ML bodyweight distribution mechanism was present in the RWS and LOS tasks even in patients at an early stage of their disease. Hence, this result confirmed previous reports evidencing physiological disease-related impairments at the hip level (Bridgewater and Sharpe 1998; Wright et al. 2007) and impairments in trunk movement and axial rotation

(Adkin et al. 2005; Carpenter et al. 2004; Horak et al. 2005). Our results showed that the ML bodyweight distribution mechanism was weaker in patients with PD than in controls. It may be so because patients with PD display a higher trunk rigidity (Adkin et al. 2005; Horak, et al. 2005; Wright et al. 2007). As a consequence, this insufficiency in the ML bodyweight distribution mechanism may explain the lower and slower ML performances in the LOS and RWS tasks in patients with PD. Indeed, the ML bodyweight distribution mechanism is fundamental to control ML stance (Bonnet et al. 2013; Lafond et al. 2004; Rougier 2007, 2008; Termoz et al. 2008; Winter et al. 1993, 1996).

In complement to our study results, Shen and Mak (2012) showed slower and smaller LOS performance in patients with PD (Hoehn and Yahr stage: 2.3 ± 0.5 ; duration of the disease: 5.8 ± 2.2 years; on-drug condition) in the AP axis. These authors explained that the patients may have perceived a greater difficulty of moving their center of mass than elderly controls, thus favoring their postural stability. Therefore, Shen and Mak's (2012) finding validated their hypothesis of a disease-related change in the speed-accuracy trade-off (reduced performance to keep the variability safe). Our results also validated this hypothesis in the ML axis. With our model, we suggest that the disease-related change in the speed-accuracy trade-off may be due to weaker contribution in ML postural control mechanisms, essentially so in the ML bodyweight distribution mechanism. It should be borne in mind that we found disease-related impairment when the patients with PD performed the tasks in the off-drug condition.

Disease-related impairments in quiet stance

In Termoz et al. (2008), patients with PD were at a higher stage of their disease than in the present study (Hoehn and Yahr stage: 2.7 ± 0.3 ; duration of the disease: 5 ± 3.3 years; off-drug condition). Like Termoz et al. (2008), we could not observe Parkinson's disease-related impairments in postural control mechanisms and in the displacement of the COP and markers in quiet stance. Also, we could not identify any significant disease-related differences in the first part of the LOS task. In the literature, some other authors did not find disease-related deficiencies in ML postural control in patients with PD at an early stage of their disease (Frenklach et al., 2009) while others did (Mancini et al., 2012; Nantel et al., 2012). We agree that more and more evidences show that patients with PD at an early stage of the disease are unstable in quiet stance but this is not systematically the case. Hence, for clinicians, the quiet stance task may not be the best condition to detect early signs of disease-related impairments in ML postural control, especially when there is no significant relationship between clinical signs (UPDRS motor score, axial score and postural stability score) and postural control as in the present study. In contrast, the LOS task is a good test that was already shown to dissociate fallers from nonfallers (Behrman et al. 2002). The present study complementary showed that the RWS might turn out to be a valuable test, even better than the LOS task in the ML axis. Therefore overall, active tasks are relevant to detect early signs of postural control impairments in patients with PD. However, at a later stage of their disease, patients with PD definitely can be found to be unstable and show disease-related deficiencies in ML postural control simply in quiet stance (e.g., Mitchell et al., 1995).

Age-related impairments

The significant age-related difference in SD COP_c in the first part of the LOS but not in quiet stance is remarkable although unexpected. Indeed, young adults did not change the amplitude contribution of their COP location mechanism between both conditions (quiet stance: 0.024 ± 0.013 vs. LOS: 0.026 ± 0.016) while elderly controls (0.030 ± 0.019 vs;

0.039±0.024) and patients with PD (0.032±0.033 vs. 0.044±0.041) did so. Therefore, the simple fact of anticipating a challenging ML task induced elderly controls and patients to strengthen their ankle mechanism (COP location mechanism) before performing that task. This should only be a preparatory effect as Bonnet et al. (2013) showed a lower age-related contribution in the ML COP location mechanism in quiet stance condition, not a higher one. The age-related significant reduction in the velocity of the AP and ML COP displacements in the first part of the LOS task (cf., additional analyses) may be due to the increased strength in the ankle mechanism just discussed. Indeed, in quiet stance no such significant effects could be found (cf., additional analyses).

In performing the LOS task, elderly controls were significantly slower in velocity of body motion than young adults (Figure 4B). However, we could not find any age-related reduction in the amplitude performance in both LOS and RWS tasks (Figure 3A and B). Therefore in our study, the age-related change in ML body excursion was thus only captured in the velocity of body motion. This effect is remarkable because elderly controls tried harder than young adults to lean their body as far as possible. Indeed, they used a stronger COP_v mechanism than young adults when they performed the LOS task (Figure 5C). This is the only way we can understand the result displayed in Figure 5C – greater engagement to perform the task in elderly adults – as the literature does not mention that elderly adults have a stronger hip mechanism than young adults do.

Conclusion and perspectives

The present study assessed novel findings in many respects. Most importantly, previous studies who analyzed impairments in ML LOS and ML RWS performances did so with patients in their ‘on’ state only (Ganesan et al. 2010; Rossi et al. 2009; Vervoort et al. 2013; Yang et al. 2008). Antiparkinsonian medications may influence the results. Three of these studies imposed the amplitude and/or velocity of body motion (Ganesan et al. 2010; Rossi et al. 2009; Vervoort et al. 2013) while we analyzed disease-related impairments in ML self-initiated maximum excursions of body motion. Moreover, our study analyzed the contribution of postural control mechanisms in addition to movement related variables to analyze causal relationships. These types of analysis were suggested by Kim et al. (2009) and Mancini et al. (2008) to go beyond the limitation of usual variables to understand disease-related impairments in postural control.

In conclusion patients with PD displayed significantly lower amplitude and velocity in the performance of the ML RWS and ML LOS tasks, and changes in the contribution of the ML bodyweight distribution mechanism. These results were found at an early stage of their disease (Hoehn and Yahr stage 2) even after controlling many confounding variables. Thus, we identified early disease-related markers of ML insufficiency in postural control that did not directly translate into postural instability (*ns* in quiet stance) and lack of control (*ns* in behavioural variability in performing the LOS and RWS tasks). The message is important for clinicians because our methodology with an active posturography study could help them to detect early signs of ML postural impairments in patients with Parkinson’s disease and also in elderly individuals. In more advanced stage of the disease, we would expect patients with PD to overestimate their self-perceived LOS (Kamata et al. 2007) and to lower their directional control. This would show an inadequate and risky behaviour. Further research should examine this hypothesis with patients at a more advanced stage of the disease than in the present study and also with/without the effect of the medication. Future studies also have to identify which physiological variables, especially at the trunk level, could explain the lower contribution of the ML bodyweight distribution mechanism in patients with PD in the active RWS task. The

question is relevant since ML postural control at the hip is fundamental if ML instability and ML falls are to be prevented (Hayes et al. 1996).

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Conflict of Interest

None

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