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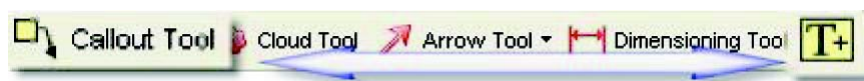
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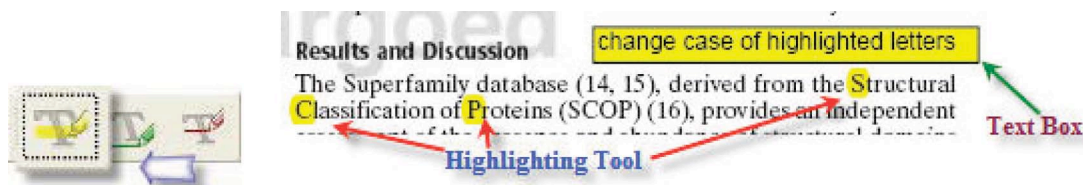
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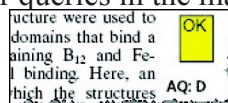
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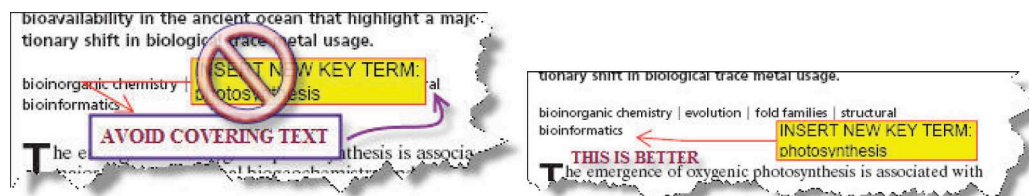
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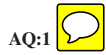


# Interest of active posturography to detect age-related and early Parkinson's disease-related impairments in mediolateral postural control

Cédric T. Bonnet,<sup>1</sup> Arnaud Delval,<sup>2</sup> and Luc Defebvre<sup>2,3</sup>

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Submitted 5 June 2014; accepted in final form 19 August 2014



AQ:1



AQ:2

**Bonnet CT, Delval A, Defebvre L.** Interest of active posturography to detect age-related and early Parkinson's disease-related impairments in mediolateral postural control. *J Neurophysiol* 112: 000–000, 2014. First published August 20, 2014; doi:10.1152/jn.00412.2014.—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 control subjects, 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 a rhythmic weight shift task. As expected, the patients displayed significantly lower and slower body displacement (head, neck, lower back, center of pressure) than elderly control subjects when performing the two body excursion tasks. However, the behavioral variability in both tasks was similar between the groups. Under these active conditions, the patients showed significantly lower contribution of the hip postural control mechanisms compared with the elderly control subjects. 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 control subjects 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.

Parkinson's disease; limits of stability; rhythmic weight shift; postural control mechanisms; mediolateral axis



AQ:3

**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 a four times greater chance than elderly control subjects to have a hip fracture (Walker et al. 2013). Hence, it is necessary to understand the causal factors of ML postural instability in patients with PD.

The quiet stance condition may be limited in revealing deficiencies in postural control because postural control is not challenged enough (Winter 1995). Hence, researchers have used complex tasks (e.g., dual tasks vs. 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 center 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 unveiling deficiencies in ML postural control because they challenge postural control up to 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, reports of ML LOS and ML RWS performance in patients with PD are rare (see Ganesan et al. 2010; Rossi et al. 2009; Vervoort et al. 2013; Yang et al. 2008). Mostly, these studies showed disease-related impairments in performance in both tasks (amplitude, velocity) and in 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. (2008) and Mancini et al. (2008) suggested testing and detection of disease-related impairments in postural control. In the present study, we did this by analyzing deficiencies of ML postural control mechanisms as a potential causal factor of reduced performance in ML active tasks.

Our objective was to build knowledge on PD-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 control subjects, 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. On the other hand, 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).



AQ:6

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Moreover, in the comparison between young adults and elderly control subjects, 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. 2014; Brauer et al. 1999; Owings et al. 2000).

## METHODS

### Participants

**Physical characteristics of participants.** Eighteen patients with PD and 18 elderly control subjects (12 men, 6 women in each group) were included in the study. Their mean age, body weight, and height were  $60.39 \pm 0.07$  and  $61.61 \pm 5.73$  yr,  $78.58 \pm 12.69$  and  $77.88 \pm 18.73$  kg, and  $1.71 \pm 0.07$  and  $1.69 \pm 0.09$  m, respectively. There was no group difference in these three variables ( $P > 0.42$ ). Nineteen young, healthy adults were also included. Their mean age, body weight, and height were  $21.87 \pm 2.87$  yr,  $63.05 \pm 11.43$  kg, and  $1.72 \pm 0.10$  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 stage 2 on Hoehn and Yahr's (1967) scale (bilateral involvement without impairment of balance). The mean time since disease onset averaged 3.94 yr ( $\pm 2.34$ ). The mean motor Unified Parkinson's Disease Rating Scale (UPDRS) score (part III) analyzed in the off-drug condition averaged 16.22 ( $\pm 6.89$ ). None of the patients presented motor fluctuation or dyskinesia. Patients with PD had an axial UPDRS III score of  $3.94 \pm 2.31$  and a postural stability UPDRS score of  $1.28 \pm 1.02$ , 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  $420 \pm 168$  mg. The study was approved by legal authorities in the University of Lille 2 and was performed in accordance with the tenets of the Declaration of Helsinki. All participants gave written informed consent to participation.

**Exclusion/inclusion criteria.** The patients with PD had not taken their medication in the 12 h prior to their participation. 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), or 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, Munich, Germany; 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 quiet stance and 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 (Fig. 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 semicycle of oscillation in order to extend their head displacement. The trials lasted 30 s in both quiet stance and ML RWS tasks. The ML LOS task was performed as follows: after 15 s, a start signal was given and the participants leaned their body as far as possible (Fig. 1). Once the participants had achieved a stable, maximum ML body lean position, they had to hold it for 15 s 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 a black dot in front of them. The order of the tasks was randomized.

The participants were barefoot, and the foot position was standardized: stance width of 14 cm and stance angle of  $17^\circ$  (McIlroy and Maki 1997).

### Dependent 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. Also in the LOS task, the variables were computed with two means per trial, one in a first period (10 s) just before extension and one in a second period after extension and during the maximum extension (10 s; Fig. 2A). The second period did not begin at the first lower value just after extension but at the second lower value (see Fig. 2A) to reduce the behavioral variability of the extension period in each participant.

### Performance Variables in 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 (Fig. 2A). In the RWS task, the ML amplitude performance was calculated by averaging the maximum left and right oscillation peaks reached by the marker [center of pressure (COP), head, neck, lower back; Fig. 2B]. The mean ML velocity was the ML distance traveled 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.

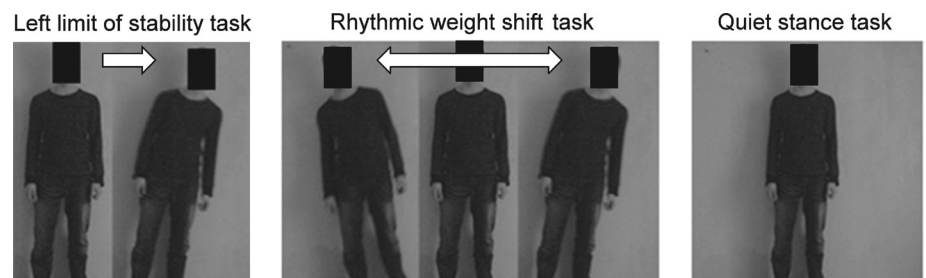


Fig. 1. Illustration of the 3 tasks: the limit of stability (LOS) task (here shown on the left), the rhythmic weight shift (RWS) task, and the quiet stance task. For the LOS task, the 1st and 2nd figures represent the initial and final body positions, respectively. For the RWS task, the 3 figures represent the mediolateral (ML) body oscillations performed throughout the trial.



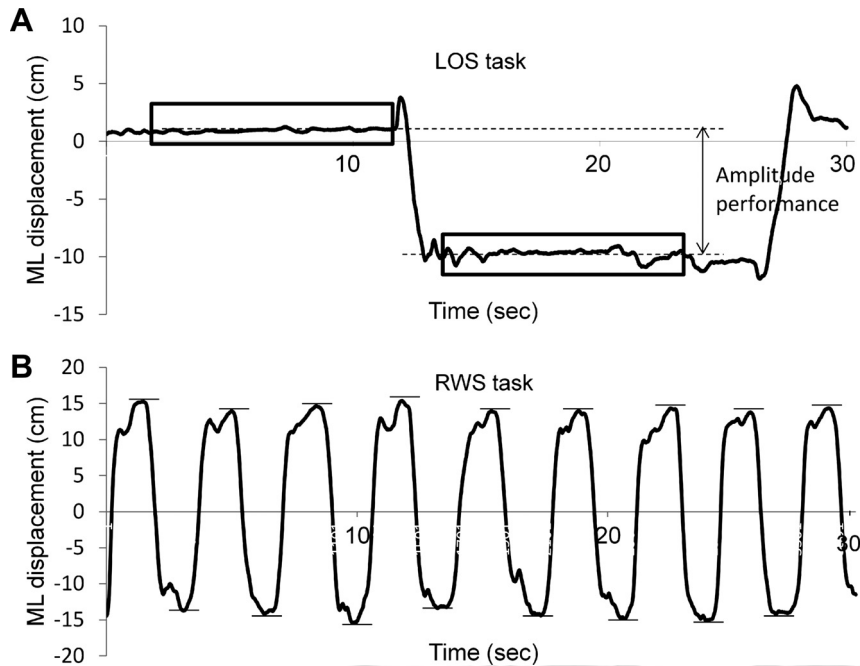


Fig. 2. Representation of the ML displacement of a marker [center of pressure (COP), lower back, neck, or head] in the LOS task (A) and the RWS task (B) for 30 s. In the LOS task, the 2 rectangles represent the 1st period (10 s) just before extension and the 2nd period after extension and during the maximum extension (10 s). As can be seen, the 2nd period began in the 2nd lower minimum peak and not in the 1st minimum peak. This methodology allowed lower variability of the marker displacement within that 2nd period. The amplitude performance was calculated between the mean displacement of the 2 periods. In the RWS task, the ML amplitude performance was calculated by averaging and then subtracting the higher and lower oscillation peaks marked with horizontal bars.

**Behavioral Variability Variables in the Three Tasks**

In the RWS and LOS tasks, the variability of behavioral 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 displacement (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 anteroposterior (AP) axis in the three tasks, as complementary signs of behavioral variability, or instability, in these conditions.

**Postural Control Variables**

In their studies, 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 body weight under one leg and thus unloading body weight under the other leg. Loading/unloading the body weight under each foot is referred to as the body weight 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 body weight distribution mechanism [denoted as  $COP_v$  in the model calculation (v for vertical)] and the COP location mechanism [denoted as  $COP_c$  in the model calculation (c for change)] 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 Eq. 2, the  $COP_{net}$  displacement explained by the COP location mechanism is calculated in controlling—that is, in keeping constant throughout the trial—the  $COP_{net}$  displacement explained by the body weight distribution mechanism. In Eq. 3, the  $COP_{net}$  displacement explained by the body weight distribution mechanism is calculated.

Once we had found the  $COP_{net}$ ,  $COP_v$ , and  $COP_c$  time series, we computed the contribution of each mechanism to explaining 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, 2014c), 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 control of ML COP displacement. In brief, two kinds of analysis were used to analyze the amplitude and active contributions of the ML body weight distribution and ML COP location mechanisms.

The body weight 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 of the other, not otherwise (Bonnet et al. 2014a).

Data Analysis

To control spurious sources of between-subject variability in postural control, the data were detrended to keep the principal component of displacement straight within trials (cf. Bonnet et al. 2014c). The confounding influence of body weight and height was then removed by application of the normalization procedure recommended by O'Malley (1996) and briefly explained by Bonnet et al. (2014c).

Most of our time series presented outliers. Hence, nonparametric Kruskal-Wallis ANOVAs 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 Performance in 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 [ $H(2,55) = 7.24, P < 0.05$ ] displacements. The amplitude performance was significantly lower in patients with PD than in elderly control subjects and young adults for the head, lower back, and COP displacements (all  $U < 93, P < 0.05$ ; Fig. 3A) and significantly lower in patients with PD than in elderly

control subjects for the neck displacement ( $U = 76, P < 0.05$ ). The ANOVA was also significant for the mean velocity of the lower back displacement [ $H(2,55) = 6.63, P < 0.05$ ] but not of the head, neck, and COP displacements ( $P > 0.13$ ). The velocity performance was lower in patients with PD than in young adults [ $U = 87, P < 0.05$ ; Fig. 4A].

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 the head ( $P = 0.10$ ). Each time, the amplitude performance was lower in patients with PD than in elderly control subjects and young adults (all  $U < 94, P < 0.05$ ; Fig. 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 [ $H(2,55) = 6.30, P < 0.05$ ] displacements. The velocity of lower back displacements was significantly lower in patients with PD than in elderly control subjects and young adults (all  $U < 88, P < 0.05$ ; Fig. 4B). The velocity of the head and neck displacements was significantly lower in both patients with PD and elderly control subjects than in young adults (all  $U < 40, P < 0.05$ ; Fig. 4B). Moreover, the velocity of the COP displacement was significantly lower in patients with PD than in young adults (all  $U < 98, P < 0.05$ ; Fig. 4B).

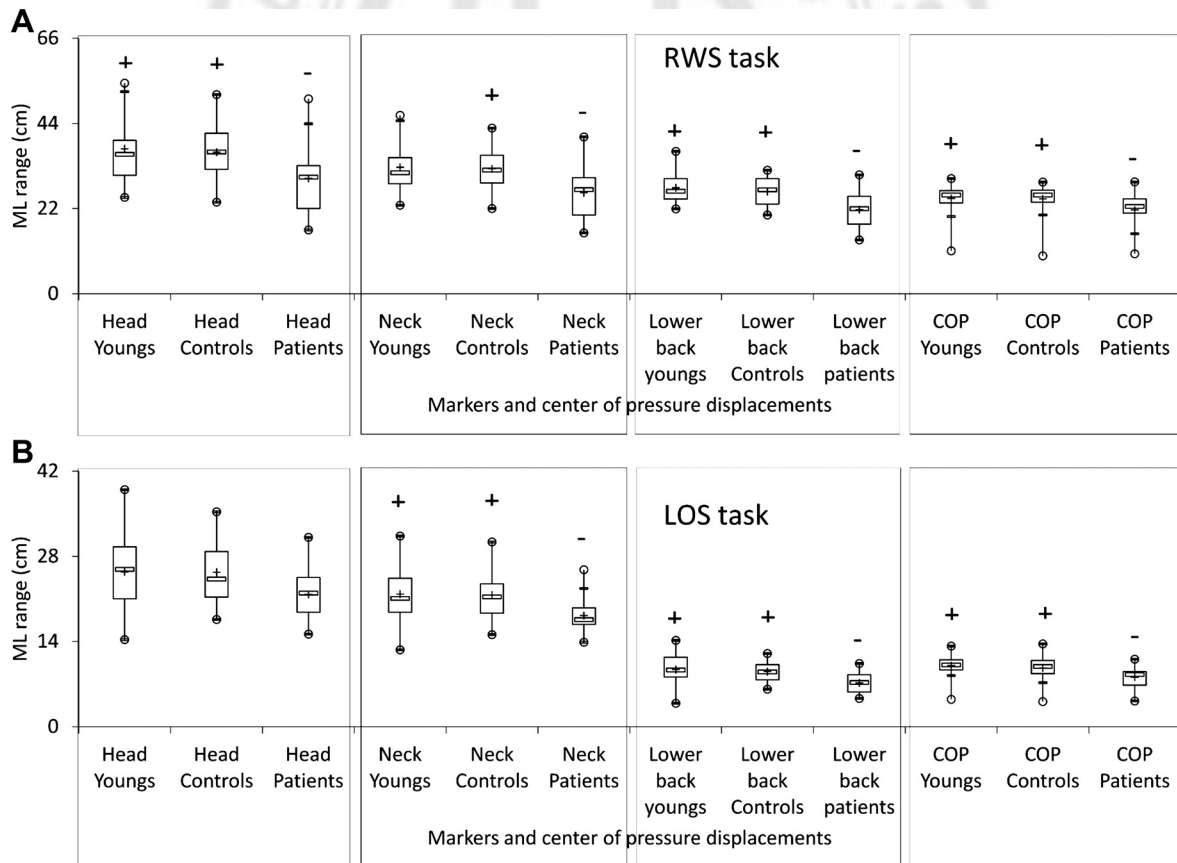


Fig. 3. Box plots for the ML range of the head, neck, lower back, and COP displacements in the RWS (A) and LOS (B) tasks. The range is displayed in centimeters (cm). Within the box plot, the + represents the mean, the open bar represents the median, the higher and lower ends of the box represent the 1st and 3rd quartiles, the higher and lower filled bars represent the mustache, and the higher and lower circles represent the max and min values of the box plot. Significant main effects of group in the nonparametric Kruskal-Wallis ANOVA by ranks 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 not significant (ns).

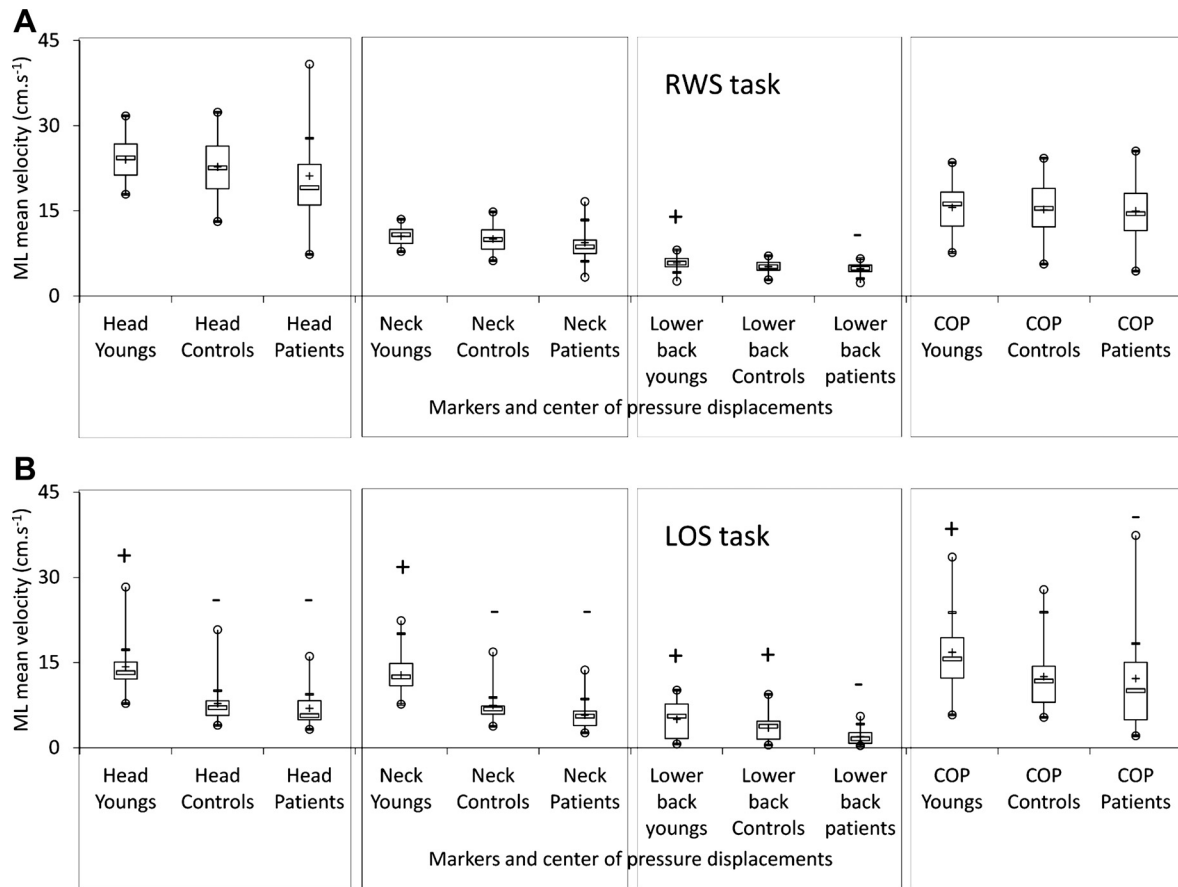


Fig. 4. Box plots for the ML mean velocity of the head, neck, lower back, and COP displacements in the RWS (A) and LOS (B) tasks. Within the box plot, the + represents the mean, the open bar represents the median, the higher and lower ends of the box represent the 1st and 3rd quartiles, the higher and lower filled bars represent the mustache, and the higher and lower circles represent the max and min values of the box plot. The mean velocity is displayed in centimeters per second (cm/s). Significant main effects of group in the nonparametric Kruskal-Wallis ANOVA by ranks 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.

*Main Effects of Group for Behavioral Variability in 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, SD, 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 Contribution of Body Weight Distribution and COP Location Mechanisms in RWS and LOS Tasks*

In the RWS task, the ANOVA was significant for SD COP<sub>v</sub> [ $H(2,55) = 7.79, P < 0.05$ ; Fig. 5A] and SD COP<sub>c</sub> [ $H(2,55) = 7.06, P < 0.05$ ; Fig. 5B]. The SD COP<sub>v</sub> 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 control subjects ( $U = 103, P = 0.06$ ). The SD COP<sub>c</sub> was significantly lower in elderly control subjects 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<sub>v</sub>

[ $H(2,55) = 8.67, P < 0.05$ ; Fig. 5C]. The SD COP<sub>v</sub> was significantly higher in elderly control subjects than in both patients with PD and young adults ( $U < 91, P < 0.05$ ). In both RWS and LOS tasks, there was no significant effect in the cross-correlation analyses (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 [both  $H(2,55) > 6.24, P < 0.05$ ]. The AP COP velocity of elderly control subjects ( $1.59 \pm 0.43$ ) was significantly lower than that in young adults ( $1.80 \pm 0.29; U = 97, P < 0.05$ ) but not that in patients with PD ( $U = 161, P > 0.05; 1.78 \pm 0.82$ ). The ML COP velocities of patients with PD ( $1.48 \pm 0.61$ ) and elderly control subjects ( $1.30 \pm 0.33$ ) were lower than that in young adults ( $1.53 \pm 0.23$ ; both  $U < 97, P < 0.05$ ). The ANOVA was also significant for SD COP<sub>c</sub> [ $H(2,55) = 8.52, P < 0.05$ ]. SD COP<sub>c</sub> was higher in patients with PD ( $0.044 \pm 0.041$ ) and elderly control subjects ( $0.039 \pm 0.024$ ) than in young adults ( $0.024 \pm 0.013$ ; both  $U < 92, P < 0.05$ ). However, there was no significant effect in SD COP<sub>v</sub> and in COP<sub>v</sub> vs. COP<sub>net</sub> and COP<sub>c</sub> vs. COP<sub>net</sub>.

F5



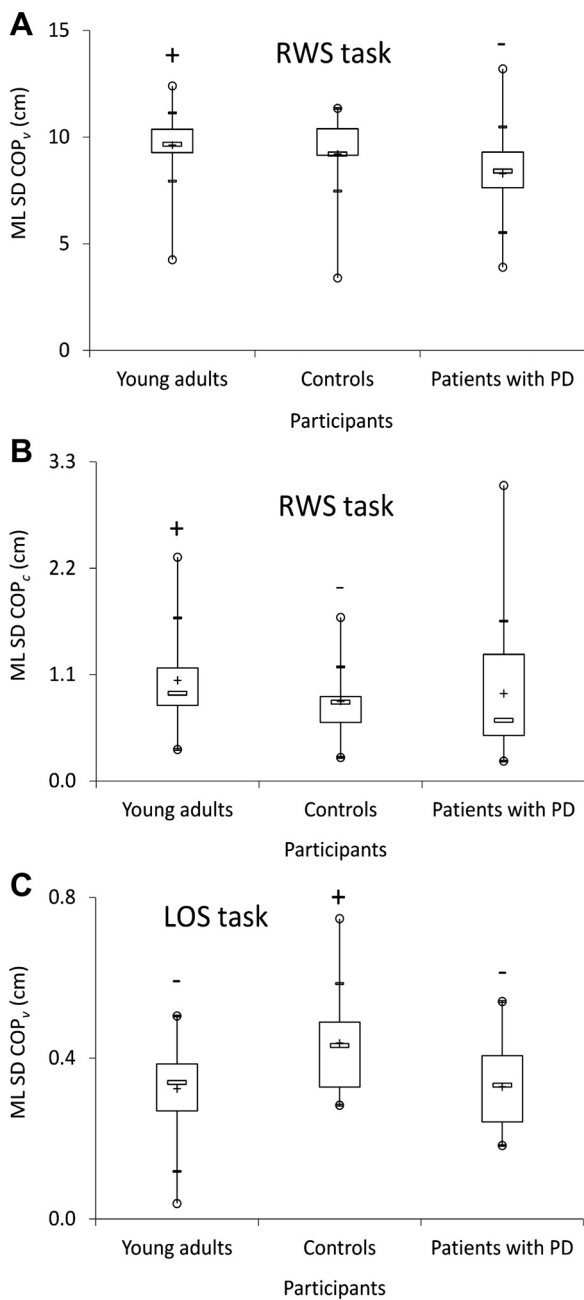


Fig. 5. *A*: significant main effect of group ( $P < 0.05$ ) in the nonparametric Kruskal-Wallis ANOVA by ranks of the ML standard deviation (SD) of center of pressure vertical (COP<sub>v</sub>; abbreviation of the body weight distribution mechanism in the model computation) in the RWS task. *B*: significant main effect of group ( $P < 0.05$ ) in the nonparametric Kruskal-Wallis ANOVA by ranks of the ML SD COP change (COP<sub>c</sub>; abbreviation of the COP location mechanism in the model computation) in the RWS task. *C*: significant main effect of group ( $P < 0.05$ ) in the nonparametric Kruskal-Wallis ANOVA by ranks of the ML SD COP<sub>v</sub> in the LOS task. Within the box plot, the + represents the mean, the open bar represents the median, the higher and lower ends of the box represent the 1st and 3rd quartiles, the higher and lower filled bars represent the mustache, and the higher and lower circles represent the max and min values of the box plot. The COP<sub>v</sub> and COP<sub>c</sub> 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.

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 whether 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 (both  $Z < 0.81$ ,  $P > 0.05$ ). Hence, patients performed equally on both sides.

### DISCUSSION

The present report studied PD-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 control subjects and also in healthy control subjects than in young adults.

#### *Disease-Related Impairments in ML LOS and RWS Performances*

In past reports, Yang et al. (2008) showed PD-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 control subjects. 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 (Fig. 3 and Fig. 4). 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 as elderly control subjects (see the second part of RESULTS). Hence, at an early stage of their disease, the patients with PD were not unstable in both ML and AP axes 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*

Termoz et al. (2008) showed a significantly lower contribution of the ML body weight distribution mechanism in patients with PD (Hoehn and Yahr stage:  $2.7 \pm 0.3$ ) than in their elderly control subjects who intentionally adopted a stooped posture. Our results also showed a lower contribution of the ML body weight distribution mechanism in patients with PD. In our study, this disease-related deficiency was found in the RWS (Fig. 5A) and LOS (Fig. 5C) tasks. 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 body weight 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 body weight distribution mechanism was weaker in patients with PD than in control subjects. 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 body weight distribution mechanism may explain the lower and slower ML performances in the LOS and RWS tasks in patients with PD. Indeed, the ML body weight distribution mechanism is fundamental to control of 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:  $2.3 \pm 0.5$ ; duration of the disease:  $5.8 \pm 2.2$  yr; 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 control subjects, 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 body weight 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:  $2.7 \pm 0.3$ ; duration of the disease:  $5 \pm 3.3$  yr; off-drug condition). Like Termoz et al. (2008), we could not observe PD-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 evidence shows 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 in which 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 has already

been shown to dissociate fallers from nonfallers (Behrman et al. 2002). The present study complementarily 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 detection of 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<sub>c</sub> 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 the conditions (quiet stance:  $0.024 \pm 0.013$  vs. LOS:  $0.026 \pm 0.016$ ), while elderly control subjects ( $0.030 \pm 0.019$  vs.  $0.039 \pm 0.024$ ) and patients with PD ( $0.032 \pm 0.033$  vs.  $0.044 \pm 0.041$ ) did so. Therefore, the simple fact of anticipating a challenging ML task induced elderly control subjects 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 the 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 control subjects were significantly slower in velocity of body motion than young adults (Fig. 4B). However, we could not find any age-related reduction in the amplitude performance in both LOS and RWS tasks (Fig. 3). 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 control subjects tried harder than young adults to lean their body as far as possible. Indeed, they used a stronger COP<sub>v</sub> mechanism than young adults when they performed the LOS task (Fig. 5C). This is the only way we can understand the result displayed in Fig. 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.

#### *Conclusion and Perspectives*

The present study assessed novel findings in many respects. Most importantly, previous studies that analyzed impairments in ML LOS and ML RWS performances did so with patients in the “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

the 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 body weight 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 behavioral 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 PD and also in elderly individuals. In a 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 behavior. 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 must identify which physiological variables, especially at the trunk level, could explain the lower contribution of the ML body weight 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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#### DISCLOSURES

AQ:5 No conflicts of interest, financial or otherwise, are declared by the author(s).

#### AUTHOR CONTRIBUTIONS

Author contributions: C.T.B. conception and design of research; C.T.B., A.D., and L.D. performed experiments; C.T.B. analyzed data; C.T.B., A.D., and L.D. interpreted results of experiments; C.T.B. prepared figures; C.T.B. drafted manuscript; C.T.B., A.D., and L.D. edited and revised manuscript; C.T.B., A.D., and L.D. approved final version of manuscript.

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1

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