Still functional but limited postural adaptation for individuals with Parkinson's Disease in goal-directed visual tasks

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Short running title: PD's postural control in goal-directed task

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Abstract

Patients with Parkinson's disease (PD) notably exhibit impairments in posture and visual attention. The objective of the present study was to determine whether PD patients were able to exhibit adaptive postural control in a goal-directed visual task. We hypothesized that the patients would reduce their centre of pressure (COP) movement and/or postural sway to a lesser extent than age-matched controls in the goal-directed visual (search) task, compared with the control free-viewing task (i.e. a lower degree of relative postural adaptation). We also expected the PD patients to sway more than controls in the goal-directed task (i.e. a lower degree of absolute adaptive postural control). The study included 39 PD patients (mean age: 59; mean Hoehn and Yahr stage: 2.1; mean Movement Disorder Society-Unified Parkinson's Disease Rating Scale score: 22; mean Montreal Cognitive Assessment score: 28 (on-drug) and 40 age-matched adults (mean age: 62 years). The participants gazed domestic ecological images (visual angle: 100°). Movements of the COP, head, upper back and lower-back and variations in pupil dilatation were analysed. As expected, PD patients exhibited greater COP and body sway than controls in both tasks (p<0.05). Unexpectedly, the difference in COP and/or body sway between the two tasks was greater in PD patients than in controls (p<0.05). Our results showed that PD patients are able to exhibit adaptive postural control for goal-directed visual tasks. On a practical level and at a more general level, our findings emphasize the likely benefits of rehabilitation with goal-directed tasks requiring a visual attentional focus (walking on footprints on the ground, etc.).

Keywords

Postural adaptation – Parkinson's disease – goal-directed task – Attentional involvement – Visual task – Ecological environment – Relative postural adaptation

1. Introduction

Parkinson's disease (PD) is a neurodegenerative disease resulting in motor and cognitive impairments (Allen, Schwarzel, & Canning, 2013; Papagno & Trojano, 2018). These impairments worsen the person's quality of life and interfere with postural stability during suprapostural tasks (Bloem, Grimbergen, Dijk, & Munneke, 2006; Chen et al., 2018). Furthermore, people with PD fall over more often than age-matched controls do (Crouse, Phillips, Jahanshahi, & Moustafa, 2016; Fasano, Canning, Hausdorff, Lord, & Rochester, 2017). Researchers are therefore seeking to establish which impairment is responsible for postural instability and falls in PD patients (Bloem et al., 2006; Fasano et al., 2017). In the present study, we focused on a related question: can patients with early-stage PD spontaneously improve their postural control – reduce their postural sway, here – in goal-directed visual searching tasks requiring such an adaptation. We referred to this reduction in postural sway in a goal-directed task as "adaptive postural control". We hypothesize that an improvement in adaptive postural control in PD is relevant for neurorehabilitation.

Studies of situations with no external perturbation have highlighted the presence of adaptive postural control in people with PD. Indeed, it has already been reported that patients with early-stage PD (i.e. Hoehn and Yahr (H&Y) stage I or II only) (Caudron et al., 2014; Huang, Chen, Hwang, & Wu, 2018; Landers, Wulf, Wallmann, & Guadagnoli, 2005; Wulf, Landers, Lewthwaite, & Tollner, 2009) are able to reduce their postural sway when they focus their attention on external information (rather than internal information). Azulay et al.'s literature review (Azulay, Mesure, & Blin, 2006) showed that PD patients can use visual information to focus their attentional resources on balance and thus can improve their postural control. On the same lines, Caudron et al. (Caudron et al., 2014) showed that PD patients are able to improve their postural control when looking at a real-time, virtual representation of the body's position via a biofeedback technique. Furthermore, our team showed that PD patients (H&Y stage I and II) are able to adjust their postural coordination in a goal directed task to perform left/right gaze shifts both when off- and on-medication (Bonnet, Delval, & Defebvre, 2015; Bonnet, Delval, Szaffarczyk, & Defebvre, 2017). However, these studies were limited by (i) the absence of an age-matched control group (Caudron et al., 2014; Huang et al., 2018; Landers et al., 2005; Wulf et al., 2009) and (ii) a focus on impairments rather than adaptive postural control (Bonnet et al., 2015; Bonnet, Delval, et al., 2017).

The objective of the present study was to test adaptive postural control (a reduction in postural sway) in PD patients performing goal-directed visual tasks. 39 patients with early-stage PD (H&Y I/II) and 40 age-matched controls performed a goal-directed visual search task and a control free-viewing task. On the basis of previous results (Bonnet et al., 2015; Bonnet, Delval, et al., 2017), our primary hypothesis was that PD patients are able to reduce their postural sway in the goal-directed search (relative to the free-viewing control task) but to a lesser extent than age-matched controls do (see Figure 1A; the downward arrow is shorter for the PD patients than for age-matched controls). In other words, we analyzed *relative* adaptive postural control (for the goal-directed task vs. the control task) in each group. A secondary, more basic, hypothesis was to find that PD patients sway more than age-matched controls in all tasks (general standard deviation of both free-viewing and search tasks) and still in the search task (Figure 1A) because of the patients' various impairments (Figure 1A) (Ekker et al., 2017; Magrinelli et al., 2016; Rowe et al., 2002; Weil et al., 2016). We therefore analyzed *absolute* adaptive postural control, which we expected to be worse in PD patients than in age-matched controls. This distinction allowed us to assess both postural control (absolute sway) and functional adaptation (relative sway). To the best of our knowledge, the present study is the first to have investigated relative and absolute adaptive postural control - whether in PD patients or any population (Figure 1A).

Insert Figure 1A and 1B about here

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2. Materials & methods

2.1. Participants

G*power software (version 3.1; Faul et al., 2009) was used to calculate the minimum required sample size. We chose a repeated measures ANOVA within factors model. With a risk of 0.05, a power of 0.8, 2 groups, 2 measurements per group, G*power indicated that the required sample size was 34. In order to increase the statistical power of our analyses, we recruited thirty-nine PD patients without freezing and forty age-matched controls. In fact, we reanalyzed completely differently the data of two studies, i.e. (Bonnet, Delval, Singh, & Defebvre, 2021) including twenty PD patients and twenty age-matched controls and Bonnet et al. (send to publication) including nineteen PD patients and twenty age-matched controls. Physical characteristics of the PD patients and age-matched controls were not significantly different ($P>0.05$, cf. Table 1).

For inclusion criteria, all participants had to have normal or corrected-to-normal vision. Also, each person in the group of PD patients had to be diagnosed as PD patients by a neurologist. For non-inclusion criteria, participants were excluded if they had a history of or signs of vestibular, musculoskeletal or neurological disease (except for PD in the patient group), recurrent dizziness, dementia (according to Diagnostic and Statistical Manual - Revision IV), cognitive decline (Montreal Cognitive Assessment (MOCA) score lower than 27 (Nasreddine et al., 2005). Participants were also excluded if they had motor fluctuations, subclinical dyskinesia, known hip- and ankle-related diseases or injuries, if they had fallen in the previous six months (based on a simple question) and if they were taking any medication known to affect postural control.

For PD patients, the mean stage Hoehn and Yahr score, disease duration, MOCA score, usual treatment equivalent in levodopa and the section about the motor examination score (part III) of Movement Disorders Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) are also described in Table 1. Our experimental paradigm was performed in accordance with the tenets of the Declaration of Helsinki and validated by the French ethics committee n°2014-74. The PD patients performed the experimental tasks with their usual treatment. All the participants gave their written, informed consent to participate.

2.2. Experimental tasks

2.2.1. Apparatus

The experimental images (rooms of houses, such as the kitchen, the bedroom, etc.) were projected on a full panoramic display with three video projectors (HD83, Optoma UK, Hemel Hempstead, United Kingdom; resolution: 1024×768 pixels; frequency: 60 Hz; visual angle: 100°) (Figure 2A). A dual-top force platform (AMTI, Watertown, MA, USA) was used to record centre of pressure (COP) sway with a sampling frequency of 200 Hz. A one-eye oculometer (SensoMotoric Instruments, Teltow, Germany) recorded pupil dilatation and movements of the right eye, at a frequency of 50 Hz. Three electromagnetic markers (Polhemus Liberty 240/8-8 System, Colchester, VT 120 Hz) were used to record movements of the lower back, upper back (7^{th} cervical) and head (on top of the head) with a sampling frequency of 240 Hz. A French version of the National Aeronautics and Space Administration Task Load Index (NASA-TLX) questionnaire was used to record the subjective mental workload. During trials, the participants held a computer mouse in their preferred hand. A MATLAB script had been designed (MathWorks Inc., Natick, MA, USA, 2010; version 7.10.0; R2010a) to control and synchronize the recordings from our devices. Thus, the triggering of the image display (test), the start of postural and ocular data acquisition, the presentation of the targets to be located and the recording of mouse clicks were managed by a main computer.

2.2.2. Tasks and instructions

In the present study, we reanalyzed data on the free-viewing and search tasks previously described by Bonnet, Delval, et al. (2021) for 20 PD patients and 20 age-matched controls. We also analyzed new data recorded with 19 PD patients and 20 age-matched controls. There were five trials per task, and each trial lasted 45 sec. In the search task, the participants had to locate as many targets as possible (a pen, an alarm clock, an oven, a

chair, etc.) in the image (Figure 2B). When the participant was confident that he/she had located the correct target, he/she had to find another target. In the study by Bonnet, Delval, et al. (2021), five targets were displayed all the time at the top of the image. For the new 19 PD patients and 20 age-matched controls, one target was visible in the red square, and the participants had to click with a mouse to see the next target to be found (Figures 2C). We verified the accuracy of the objects found by looking at the video of the eye-tracker to verify the gaze position when the participants clicked on the mouse. Our customized MATLAB script marked the moment of the click on the recorded time-series of eye movement and we used this signal to verify correspondence between the target to be found and the target found. Participants were instructed several times to look at the object found exactly when they clicked on the mouse. In the free-viewing task, the participants were instructed to visually explore the image (Figure 2B) but were not given any specific instructions. The participants had to stand in relaxed stance and behave as naturally as possible when performing the visual tasks.

Insert Figure 2A, 2B and 2C about here

2.2.3. Procedures

Patients were recruited through the neurological service at Roger Salengro Hospital (Lille University Hospital, Lille, France), and age-matched controls were recruited through the university hospital's Clinical Investigation Centre. Once the PD patients had arrived at the study site, they were examined by an experienced neurologist (in order to check compliance with inclusion and non-inclusion criteria) (see 2.1. Participants section) and signed the informed consent form. The age-matched controls were examined in the Clinical Investigation Centre. After the instructions had been given, the participants performed a training trial in the experimental room. The experimenter then installed and calibrated all the devices. In all trials, the participants stood barefoot on the force platform (Figure 2A). The participants performed the five trials in one task before the five trials in the other task. The order of task, target and images were randomized for each participant. In each trial, the experimental image was different (one image per trial). The order of image for each task was also randomized. The participants were invited to sit down and rest after the five trials in each task. NASA-TLX questionnaire was administered during this resting time.

2.3. Dependent variables

We analyzed the amplitude of COP, lower back, upper back, and head on both mediolateral (ML) and anteroposterior (AP) axes. To analyze these dependent variables, we differentiated between absolute adaptive postural control and relative adaptive postural control. In each group of participants, absolute adaptive postural control was defined as the magnitude of COP and/or postural sway in the goal-directed search task (regardless of differences between tasks), whereas relative adaptive postural control referred to the difference between COP movement or/and lower back, upper back and head amplitude when searching vs. when free-viewing in both groups of participants. We sought to determine whether absolute and relative levels of adaptive postural control were greater in PD patients than in age-matched controls.

Search task performance was evaluated as the number of objects found per trial. We measured variations in the participants' attentional resources objectively (as the participants' pupil diameter, in pixels) and subjectively (the overall mental workload score in the NASA-TLX questionnaire). Kahya et al. (2021) have confirmed the reliability and validity of the pupillary response in PD patients. Furthermore, the NASA-TLX questionnaire has already been used several times in studies with PD patients (Bank, Cidota, Ouwehand, & Lukosch, 2018; Hoang et al., 2019; Kahya et al., 2021). It has been shown that the overall NASA-TLX score is significantly correlated with objective measurements of attentional involvement in healthy adults and in PD patients (Hoang et al., 2019; Kahya et al., 2021).

2.4. Statistical analyses

The data from the Polhemus system and force platform were resampled at 50 Hz. We used repeated measures ANOVAs with the type of task (search or free-viewing) as a repetition factor and the group (PD patients or age-matched controls) as a cross-subject variable. We performed analyses of COP/body sway through two repeated measure analyses of variance (ANOVAs) on the movement amplitude on both anteroposterior (AP) and mediolateral (ML) axes. For theses analyses, the main effects tested the absolute postural adaptation while the interaction tested the relative postural adaptation. For both variables of attentional resources (pupil diameter, global score of the NASA-TLX questionnaire), we performed two repeated measure ANOVAs. Furthermore, we conducted a one-way ANOVA on the search task performance (number of objects found). Our main analyses (including several factors) were performed initially without correction but we applied a Bonferroni correction (which divides the significance threshold by the number of factors used, in this case two) to assess the type I error. We also applied a correction with the Benjamini-Hochberg method to control the possibility of false results, i.e. to control for type I error. The results showed that our data did not suffer from either type I error or a significant false relationship. Outliers were removed from the datasets in considering values outside the mean ± 3 SD, which is a conservative method (Berger & Kiefer, 2021). In our study, less than 3% of data were removed. All analyses were performed with Statistica (Statistica 10 software, Statsoft Inc., Tulsa, OK, USA) with an original alpha level at $p<0.05$.

3. Results

3.1. Characteristics of the study participants

Overall, the PD patients and age-matched controls did not differ significantly with regard to their physical characteristics ($p>0.05$, Table 1). For the PD patients, the H&Y stage, disease duration, MOCA score, levodopa equivalent dose, and the MDS-UPDRS part III score are summarized in Table 1.

Insert Table 1 about here

3.2. Amplitude of movement

3.2.1. On the ML axis

The relative reduction in the amplitude of ML movement between the free-viewing and search task was greater in the PD patients than in the age-matched controls ($F_{1,71} = 14.9$, $P < 0.001$, Figure 3). Post-hoc analyses with Tukey's correction showed that sway was greater in the PD patients than in the age-matched controls for the free-viewing task ($t_{71} = 3.0$, $P < 0.05$) but not for the search task ($t_{71} = 0.21$, $P > 0.05$; Figure 3). Furthermore, the PD patients showed a significant relative reduction in their oscillation between the free-viewing and search tasks ($t_{71} = 4.36$, $P < 0.001$), which was not observed in the age-matched controls ($P > 0.05$). For all participants, the absolute amplitude of movement was greater in the free-viewing task than in the search task ($t_{71} = 2.50$, $P < 0.05$).

To detail Figure 3 further, PD patients reduced their sway magnitude from free-viewing to searching proportionally more (COP: -0.40 cm; lower back: -0.21 cm; upper back: -0.20 cm; head: -0.40 cm) than age-matched controls (COP: -0.26 cm; lower back: -0.12 cm; upper back: -0.06 cm; head: -0.39 cm).

Insert Figure 3 about here

3.2.2. On the AP axis

The relative reduction in the amplitude of AP movement between the free-viewing and search task was greater in PD patients than in age-matched controls ($F_{1,71}$ =14.99, P<0.001, Figure 4). Post-hoc analyses with Tukey's correction showed that absolute sway was greater in the PD patients than in the age-matched controls for the free-viewing task (t_{74} = 3.05, P<0.05) and the search task (t_{74} = 3.68, P=0.001). Furthermore, the PD patients showed a significant relative reduction in their sway between the free-viewing and search tasks ($t_{74.0}$ = 5.78, P<0.001), which was not found in the age-matched controls (P=0.833). We also observed a greater absolute amplitude of movement in the free-viewing task than in the search task, for all participants (t_{74} = 4.73, P<0.001).

To detail Figure 4 further, PD patients reduced their velocity of sway from free-viewing to searching (COP: -0.11 cm; lower back: -0.53 cm; upper back: -0.37 cm; head: -0.24 cm) while age-matched controls slightly increased them all (COP: 0.08 cm; lower back: 0.01 cm; upper back: 0.03 cm; head: 0.03 cm).

Insert Figure 4 about here

3.3. Number of targets found in the search task

Although the number of objects found in the search task was slightly higher in the control group (mean ± SD: 32.07±13.01) than in the patient group (27.46±13.01), the ANOVA did not show a main effect of group (P>0.05).

3.4. Additional analyses

3.4.1. Attentional focus in the free-viewing and search tasks

The variation in pupil dilation was significantly greater in the PD patients than in the age-matched controls, for all tasks ($F_{1;64}$ =6.52, P<0.05). For all participants, the variation in the pupil diameter was significantly greater in the search task than in the free-viewing task ($F_{1;64}$ =16.16; P<0.001). The interaction between the two factors was not significant (P>0.05).

The one-way ANOVA of the overall NASA-TLX questionnaire score showed a significant main effect of task, with a higher mean score in the search task (8.68±3.75) than in the free-viewing task (5.90±3.01; $F_{1,76}$ =37.42, P<0.01). However, the main effect of group and the task x group interaction were not significant (*ns*).

3.4.2. Head rotation and eye movement

We analyzed how quickly the participants rotated their body and moved their eyes, as indices of image exploration in the free-viewing and search tasks. The results showed that all the participants moved their head and body very slowly in both tasks. The mean velocity of head rotation was low in PD patients (1.95±0.60°/s for free-viewing and 2.09±0.62°/s for searching) and in age-matched controls (2.35±0.72°/s for free-viewing and 2.49±0.66°/s for searching). The mean velocity of eye movement was also low in PD patients (10.8±2.21°/s for free-viewing and 12.79±3.76°/s for searching) and in age-matched controls (11.01±2.37°/s for free-viewing and: 14.35±4.74°/ for searching).

4. Discussion

In the present study, we investigated the ability of PD patients to adapt their postural control to suit the visual task performed. We found that the PD patients were able to improve their postural stability in the search task relative to the free-viewing task. Unexpectedly, relative adaptive postural control was greater in PD patients

than in age-matched controls. However, the PD patients swayed more than the age-matched controls in the search task and thus showed worse absolute adaptive postural control.

4.1. Greater relative adaptive postural control in PD patients than in age-matched controls

Our first hypothesis (H1) was that relative adaptive postural control, i.e. the reduction of postural sway from free-viewing to searching would be lower in the PD patients than in the age-matched controls (Figure 1A) due to their cognitive and attentional impairments caused by the disease. This hypothesis was not validated because the PD patients reduced their postural sway more from free-viewing to searching than the age-matched controls did (Figures 1B, 3 and 4). Firstly, several published studies have shown that postural control in PD patients can be modulated by visual information (J. P. Azulay, Mesure, Amblard, & Pouget, 2002; J.-P. Azulay et al., 2006; Bronstein, Hood, Gresty, & Panagi, 1990; Bronstein, Yardley, Moore, & Cleeves, 1996; Davidsdottir, Wagenaar, Young, & Cronin-Golomb, 2008; Stuart, Galna, Delicato, Lord, & Rochester, 2017). Secondly, we are aware of studies showing that PD patients are able to improve their postural control when they focus their attention on external information rather than internal information (Huang et al., 2018; Landers et al., 2005; Wulf et al., 2009) or when they look at a real-time virtual representation of the body's actual position via a biofeedback technique (Caudron et al., 2014). Our present results are also in line with our previous findings. In fact, we had already studied PD patients (also at H&Y stage I/II) and age-matched controls perform a fixation task and two left-right gaze shift tasks at 100° at 0.125 Hz or 0.25 Hz when standing (Bonnet, Delval, et al., 2017). The PD patients were better than the age-matched controls in strengthening their postural control in the search task requiring precise gaze shifts. Furthermore, the PD patients reinforced their postural control more in the on-drug state than in the off-drug state. In one study (Bonnet, Delval, et al., 2017), the main effect of group (the PD patients swayed significantly more than the age-matched controls) was especially evident in the on-drug condition. Hence, our present results are in line with those reported by Bonnet et al. (Bonnet, Delval, et al., 2017) in several ways.

The relative adaptive postural control in on-drug PD patients was greater in our study than in the literature (Caudron et al., 2014; Wulf et al., 2009) [1] . In fact, the significant main effect of task had *F*-values below 8 in two studies (Caudron et al., 2014; Wulf et al., 2009) and an *F*-value above 35 in our study. These high values were found in both of our groups, and the value was even higher in the PD patients than in the age-matched controls (Figure 1B). There are two possible explanations for the strong effect of task in the PD patients in our study. Firstly, we used only visual tasks, whereas other researchers (Caudron et al., 2014; Wulf et al., 2009) used tasks that did not specifically modify visual attention. Analyses of visual tasks and the associated visual attention might accentuate differences between PD patients[2] and age-matched controls because the former are known to use their vision more when controlling posture (Bonnet, Delval, Singh, Kechabia, & Defebvre, 2020; Caudron et al., 2014; Hill, Stuart, Lord, Del Din, & Rochester, 2016; Park, Kang, & Horak, 2015; Rinalduzzi et al., 2015). Secondly, we compared postural control in goal-directed vs. control tasks, whereas other researchers (Caudron et al., 2014; Wulf et al., 2009) compared postural control in two goal-directed tasks (i.e. a task with an external focus and a task with an internal focus). Overall, the manipulation of control and goal-directed visual tasks is a powerful method for highlighting differences in postural control between PD patients and age-matched controls.

Although the PD patients showed a *greater* degree of relative adaptive postural control than the age-matched controls (Figure 1B; 3 and 4), their adaptive postural control was not *better*. Indeed, this overall result was mostly due to the fact that the PD patients swayed notably more than the age-matched controls in the control free-viewing task (Figure 1B). If the PD patients had swayed to the same extent as the age-matched controls in the free-viewing task and had shown a larger reduction in their postural sway than the age-matched controls, we would have considered that the patients' relative adaptive postural control in the search task was better.

[1] In fact, the significant main effect of task in both (Caudron et al., 2014; Wulf, Landers, Lewthwaite, & Tollner, 2009) had *F*-values lower than 8 while our main effect of task had a *F*-value higher than 35. Our finding was found in both groups and it was even higher in the PD patients than in the age-matched controls (cf. Figure 1B).

[2] The PD patients in these studies were diagnosed between Hoehn and Yahr stage I and III.

However, this was not the case because the PD patients still swayed more than the age-matched controls in the search task. We discuss this result further below.

4.2. Worse absolute adaptive postural control in PD patients than in age-matched controls

As expected, we found that the PD patients swayed more on the AP axis in the search task than the age-matched controls (Figure 4); the PD patients therefore had an impairment in *absolute* adaptive postural control, which confirmed our second hypothesis. Hence, PD patients showed "impaired control of action stability" (Falaki, Huang, Lewis, & Latash, 2016; Freitas et al., 2020; Latash & Huang, 2015; Ricotta & Latash, 2021) or "maladaptive adjustments" (Ferrazzoli, Ortelli, Zivi, et al., 2018).

We expected the differences in COP and body sway between the PD patients and age-matched controls to be higher in the search task than in the free-viewing task; in fact, as evidenced by the contrast between Figure 1A and 1B, we found that the opposite was true. We did not expect to see any intergroup differences in COP sway and body sway because PD patients usually do not sway more than age-matched controls in an easy task in quiet stance (Bonnet, Delval, & Defebvre, 2014; Bonnet et al., 2015; Bonnet, Delval, et al., 2017; Marchese, Bove, & Abbruzzese, 2003; Rinalduzzi et al., 2015). In fact, our additional analyses showed that the free-viewing task was not challenging at all for postural control in either group; all the participants moved their eyes and head extremely slowly when exploring images. Usually, external perturbations of balance are needed to reveal PD-related impairments in postural control (Frenklach, Louie, Koop, & Bronte-Stewart, 2009; Horak, Dimitrova, & Nutt, 2005). So why did the PD patients sway much more than the age-matched controls in the easy free-viewing task, in particular? In theory, young adults do not need to closely control their balance in a free-viewing task because the latter does not have a goal (Bonnet, Barela, & Singh, 2021; Bonnet, Davin, & Baudry, 2019; Bonnet, Szaffarczyk, & Baudry, 2017).

Balance control does not have to be exaggerated and/or goal-directed in any free-viewing task, it simply has to be automatic. As a fact, our finding (Figure 3 and 4) means that PD patients did not control well their balance when they visually explored their environment with no goal (e.g. free-viewing), and may more easily destabilize their balance in this free-viewing task. It seems that when the PD patients did not have to adapt their balance in goal-directed manners, they let their body moves with less control than age-matched controls. Overall, and in line with a distinction between automatic vs. goal-directed postural control, our finding thus showed a greater PD-related impairment in automatic postural control (difference between the two white barres in Figure 1B) than in goal-directed postural control (difference between the two black barres in Figure 1B)."

In previous work (Bonnet et al., 2020), we described PD-related impairments in automatic postural control. The PD patients and age-matched controls performed two types of fixation task: one with a totally blank background behind the fixation cross and another with an image of a room in a house around the cross (Bonnet et al., 2020). We showed that PD patients were more perturbed (in terms of postural control, eye movement and visual attention) by the presence of the surrounding environment than age-matched controls were (Bonnet et al., 2020). Accordingly, our present results (greater sway by PD patients in the free-viewing task; Figures 3 and 4) provide new evidence of impairments in automatic postural control mechanisms. However, it should be borne in mind that some other studies of postural control did not highlight any PD-related impairments in automatic postural control (Caio F. Cruz, Genoves, Doná, Ferraz, & Barela, 2020; Caio Ferraz Cruz et al., 2018; Feller, Peterka, & Horak, 2019). All of the latter studies were well designed and rigorous, and so we cannot explain the difference with our results. We can only highlight that the literature data show that automatic motor control is impaired in PD (Ferrazzoli, Ortelli, Madeo, et al., 2018; Gao & Wu, 2016; Redgrave et al., 2010, 2010; Wu, Hallett, & Chan, 2015). The loss of dopaminergic innervation is greatest and earliest in the basal ganglia's sensorimotor circuits (i.e. the putamen) responsible for automatic behaviour. So, why would automatic motor control (but not automatic postural control) be impaired? Our present results suggest that in PD patients', postural control could be improved by adopting a visual search strategy in a natural environment, even over a relatively short lasting.

The results in Figure 1B show PD-related impairments not only in the automatic postural control in the free-viewing task but also in goal-directed postural control in the search task. Other researchers have found that goal-directed postural control is impaired in PD (Ewenczyk et al., 2017; Janssen et al., 2020; Mi, Zhang, McKeown, & Chan, 2021), albeit to a lesser extent than automatic control (Redgrave et al., 2010). Alternatively, goal-directed processes might be impaired because they interfere with automatic processes. In fact, (Redgrave et al., 2010; Takakusaki, 2017) considered that both types of controls operate through a common final motor pathway; this might explain (at least in part) the impairments in goal-directed control observed in our study.

4.3. Limitations

Firstly, we were unable to differentiate between effects of PD and/or effects of medication because all the PD patients were assessed in the on-drug condition. In fact, we decided to use an ecological paradigm (the projection of large images of rooms) so that the PD patients' usual behaviour could be tested. In future research, it will be necessary to control for the possible effects of medication and differentiate between the latter and the effects of PD. Secondly, all the patients studied here had early-stage disease, and so we could not analyze the possible relationships between the severity of PD and the level of adaptive postural control. It will be necessary to perform a similar study of PD patients at stages I to IV. Finally, a third limitation of our study concerns the methodological differences in the set-up between the first experimental session published in (Bonnet, Delval, et al., 2021) and the second added one in Bonnet et al. (sent to publication), i.e. either five targets shown in a text format or a single target shown in one image. On average, the PD patients found less target objects than healthy controls but the difference was not significant. This is why these results are not discussed much, as they are not discriminating. These methodological differences could have changed the number of targets found and also prevented us from making temporal analyses of the evolution of postural behavior.

5. Conclusion

Our first main message is that our dichotomous approach between absolute and relative body sway allowed us to highlight a relatively preserved capacity for postural adaptation (relative body sway) despite a significant impairment in postural control (absolute body sway). In a large population of PD patients (39 PD patients), the PD patients' control of action stability was still functional in our goal-directed task. Although – or perhaps because – the PD patients swayed more than the age-matched controls in the free-viewing task, they were able to adapt their postural control. The relative adaptive postural control was even greater in PD patients than in age-matched controls. Hence, on-drug patients with early-stage PD can switch well from automatic control to goal-directed control. Our findings have practical implications for rehabilitation and confirm that the greater attentional focus in goal-directed visual tasks can improve postural control in the standing position. Our findings emphasize the likely benefits of rehabilitation with goal-directed tasks requiring a visual attentional focus (e.g. playing Wii games, walking on footprints on the ground, etc.). On the other hand, very slow body movements can challenge postural control in on-drug patients with early-stage PD – especially in a more automatic, free-viewing task. Indeed, the PD patients swayed significantly more than the age-matched controls in a free-viewing task, although all the participants rotated their body extremely slowly. We tentatively hypothesize that PD patients are posturally unstable and are exposed to a greater risk of falls when they perform non-constraining, free-viewing exploration. In the future, researchers could try to investigate further PD-related impairments in postural control found in our free-viewing task, with a temporal analysis of postural behavior as a function of the distance between the target and the center of the screen. This type of paradigm would help to better understand postural changes in goal-directed tasks in individuals with Parkinson's disease. It would also allow to study a more precise exploration of the link between gaze position movement amplitude and postural behavior. As we have already shown that PD patients are affected by the presence vs. absence of surrounding objects in a room (Bonnet et al., 2020), one could test the influence of the number and nature (e.g. size) of these objects and assess the potential negative influence that attentional focus on targets might have on postural control during cognitively demanding task protocols.

Competing Interests Statement

All authors have no conflicts of interest of any kind to declare.

Acknowledgment

We wish to thank France Parkinson for the grant (SHS research project support 2021) that allowed us to pay an engineer for 8 months to prepare the study. The participants were also compensated thanks to the France Parkinson grant.

Data availability statement

If requested, all data used from this study can be made available. Simply contact the principal author, Dr. Cédrick Bonnet. All data transmitted are totally anonymized and no information allowing the identification of participants will be transmitted.

Funding statement

We wish to thank France Parkinson for the grant (SHS research project support 2021) that allowed us to pay an engineer for 8 months to prepare the study. The participants were also compensated thanks to the France Parkinson grant.

Ethics approval statement

Our experimental paradigm was performed in accordance with the tenets of the Declaration of Helsinki and validated by the French ethics committee n°2014-74. The PD patients performed the experimental tasks with their usual treatment. All the participants gave their written, informed consent to participate.

Authors' contributions

Cédrick T. Bonnet contributed to all parts of the work. Arnaud Delval contributed in conception, inclusion of the patients with PD, analyses, writing and review of the manuscript. Luc Defebvre was the principal investigator and contributed to the conception, inclusion of the patients with PD and review of the manuscript. Yann-Romain Kechabia contributed to analyses, writing and review of the manuscript. All authors read and approved the final manuscript.

List of abbreviations

ANOVA: Analysis of Variance

AP: Anteroposterior

COP: Center Of Pressure

H&Y: Hoehn and Yahr

MDS-UPDRS: Movement Disorders Society-Unified Parkinson's Disease Rating Scale

ML: Mediolateral

MOCA: Montreal Cognitive Assessment

NASA-TLX: National Aeronautics and Space Administration Task Load Index

PD: Parkinson’s Disease

SD: Standard Deviation

6. Reference

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7. Table

Table 1 shows the number of participants in both the group of patients with Parkinson's Disease (PD patients) and age-matched controls, the gender, the mean age (in years), the mean height (in meters), the mean bodyweight (in Kilograms), the Montréal Cognitive Assessment score (MOCA score), the MDS UPDRS part III (Motor examination), the levodopa mean equivalent dosage (in mg per day) and the Hoehn and Yahr score and the axial subscore (calculated as in (Bejjani, 2000) and (Dimitrova, Horak, & Nutt, 2004) by summing MDS-UPDRS part III items 18, 22, 27, 28, 29, and 30).

8. Figure caption

Figure 1. Graphical representation of expected vs. found results specifically for center of pressure (COP) sway. A. Virtual data representing our expected results for the standard deviation (SD) of medio-lateral (ML) COP sway for age-matched controls and patients with Parkinson's Disease (PD patients) in the free-viewing and search tasks. The standard deviation around the means are also virtual, they are all the same in the four barre graphs. Originally, we expected similar results between PD patients and age-matched controls in the free-viewing task (horizontal dashed line). We expected a higher reduction of COP sway (between free-viewing and searching) in age-matched controls than in PD patients (black arrow longer for age-matched controls). B Results found for ML SD mean of the COP sway in both groups. The PD patients exhibited higher COP sway in free-viewing than the age-matched controls (inclined dashed line). The reduction of COP sway (between free-viewing and searching) was higher in PD patients than in age-matched controls (black arrow longer for PD patients).

Figure 2. Experimental set up. A. The participants stood 3.72 m in front of a visual display (diameter: 4.08 m) and could see images with a visual angle of 100°. The experimental images (designed in an ecological way) were projected on this panoramic screen. The participants wore an onboard SMI oculometer (attached on a helmet) and three Polhemus markers attached at the level of the head, upper back and lower back. In their preferred hand, the participants held a computer mouse that they pushed against their lateral lower body part. B. One experimental image here shown in the free-viewing task. In this task, the participants simply looked at the image with no specific goal. C. One experimental image here shown in the search task. In this task, the participants could see a target in the red square (top middle center of the image). Once they had found and looked at this found object, they had to click on one button on the mouse they kept in their hand. This click recorded their finding and automatically changed the target presented in the red square. In this search task, the participants had to locate as many targets as possible.

Figure 3. Box-and-whisker plot representing the standard deviation (SD) mean oscillations in cm on the mediolateral (ML) axis, split by group (Parkinson's Disease patients (PD patients) vs. age-matched controls) and task (search vs. free-viewing). A significance threshold of $p<0.05$ is marked with *, and a threshold of $p<0.001$ is marked with **. Red boxplots represent PD patients, and green boxplots represent controls, with hatched patterns corresponding to one specific task and solid boxes to another. The crosses (×) indicate the means, while the whiskers show the interquartile ranges and extreme values.

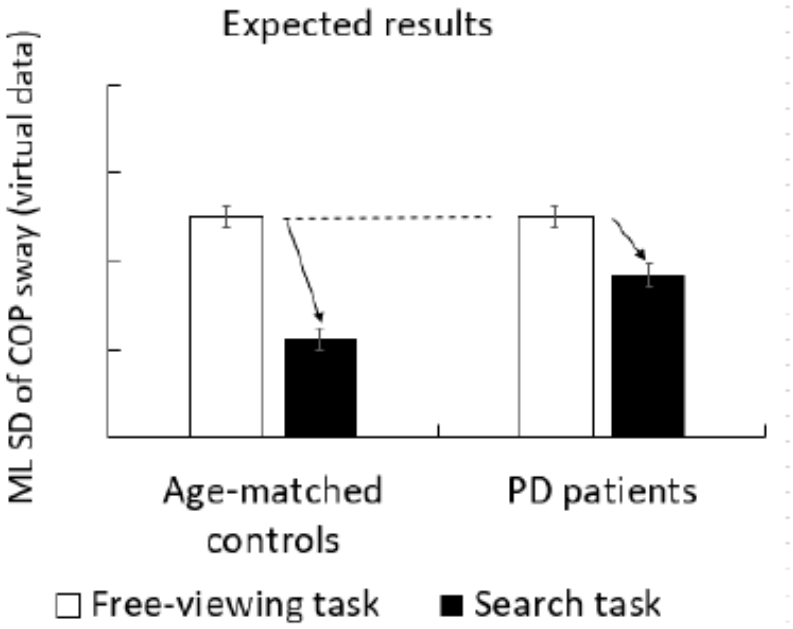
Figure 4. Box-and-whisker plot representing the standard deviation (SD) mean oscillations in cm on the anteroposterior (AP) axis, split by group (Parkinson's Disease patients (PD patients) vs. age-matched controls) and task (search vs. free-viewing). A significance threshold of $p<0.05$ is marked with *, and a threshold of $p<0.001$ is marked with **. Red boxplots represent PD patients, and green boxplots represent controls, with hatched patterns corresponding to the free-viewing task and solid boxes to the search task. The crosses (×) indicate the means, while the whiskers show the interquartile ranges and extreme values.

Table 1. Demographical data of the 79 participants

	PD patients	Controls
n	39	40
Gender	28 males/11 females	27 males/13 females
Mean age	59.08 ± 7.57	61.56 ± 6.39
Mean height	1.73.62 m ± 6.87	1.71 m ± 6.16
Mean bodyweight	78.15 kg ± 12.37	80.89 kg ± 11.61
MOCA score	27.82 ± 1.16	
Disease duration	5.68 ± 2.33 years	
MDS UPDRS part III	22.41±7.84	
levodopa mean equivalent dosage	658.6 ±239.04 mg/day	
Hoehn & Yahr score	2.08±0.19 (range: 1–2)	
Axial rigidity	3.35± 1.59	

Figure 1

A


Expected results
ML SD of COP sway (virtual data)
Age-matched controls
PD patients
Free-viewing task
Search task

B

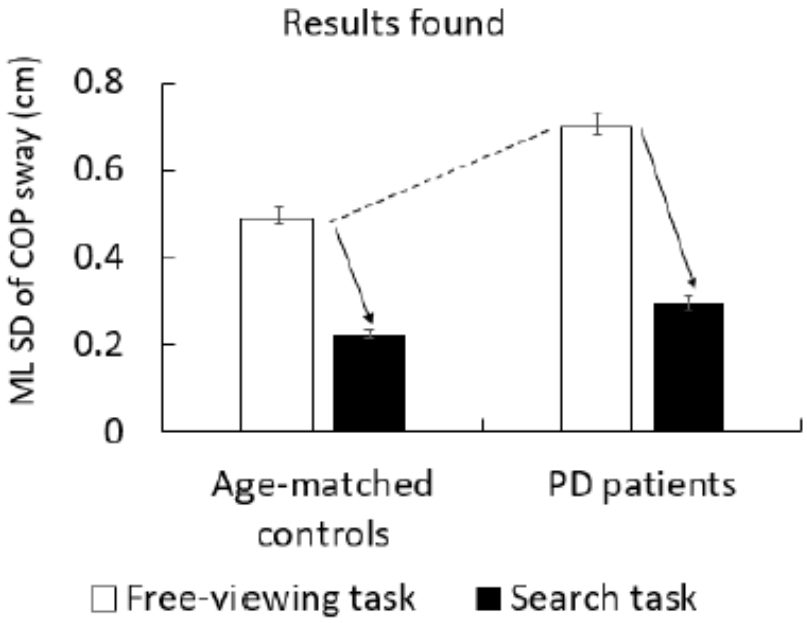
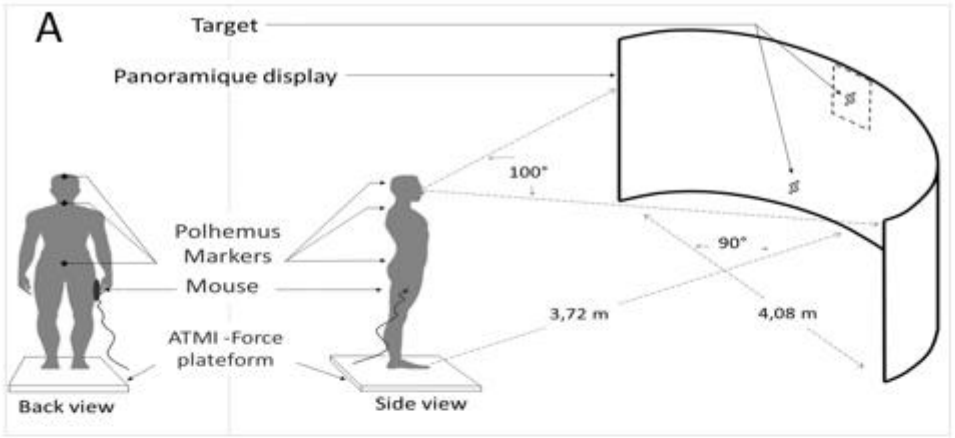

Results found
ML SD of COP sway (cm)
0.8
0.6
0.4
0.2
0
Age-matched controls
PD patients
Free-viewing task
Search task

Figure 2


A
Target
Panoramique display
100°
90°
Polhemus
Markers
Mouse
ATMI -Force
plateform
3,72 m
4,08 m
Back view
Side view


B


C

Figure 3

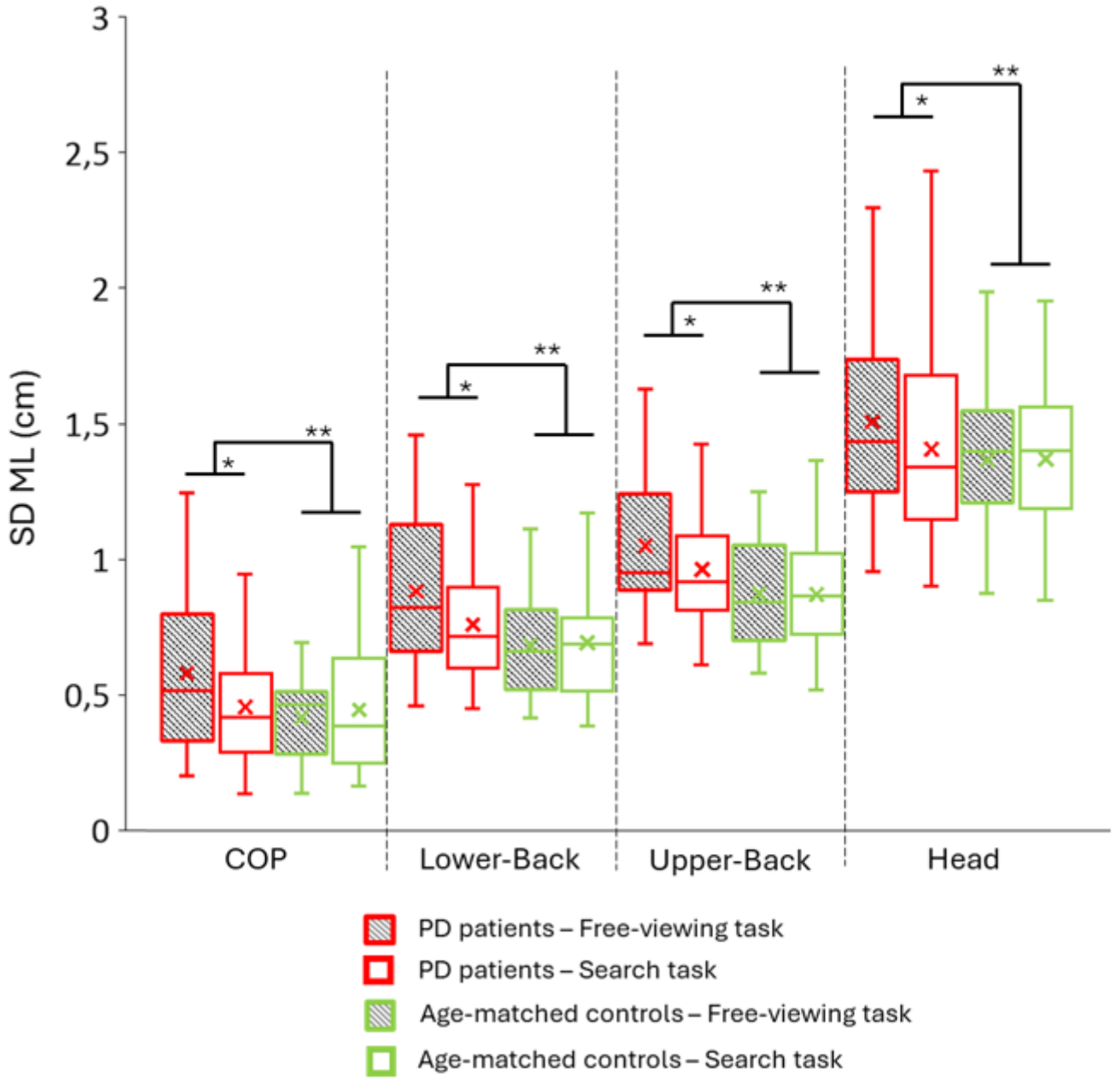
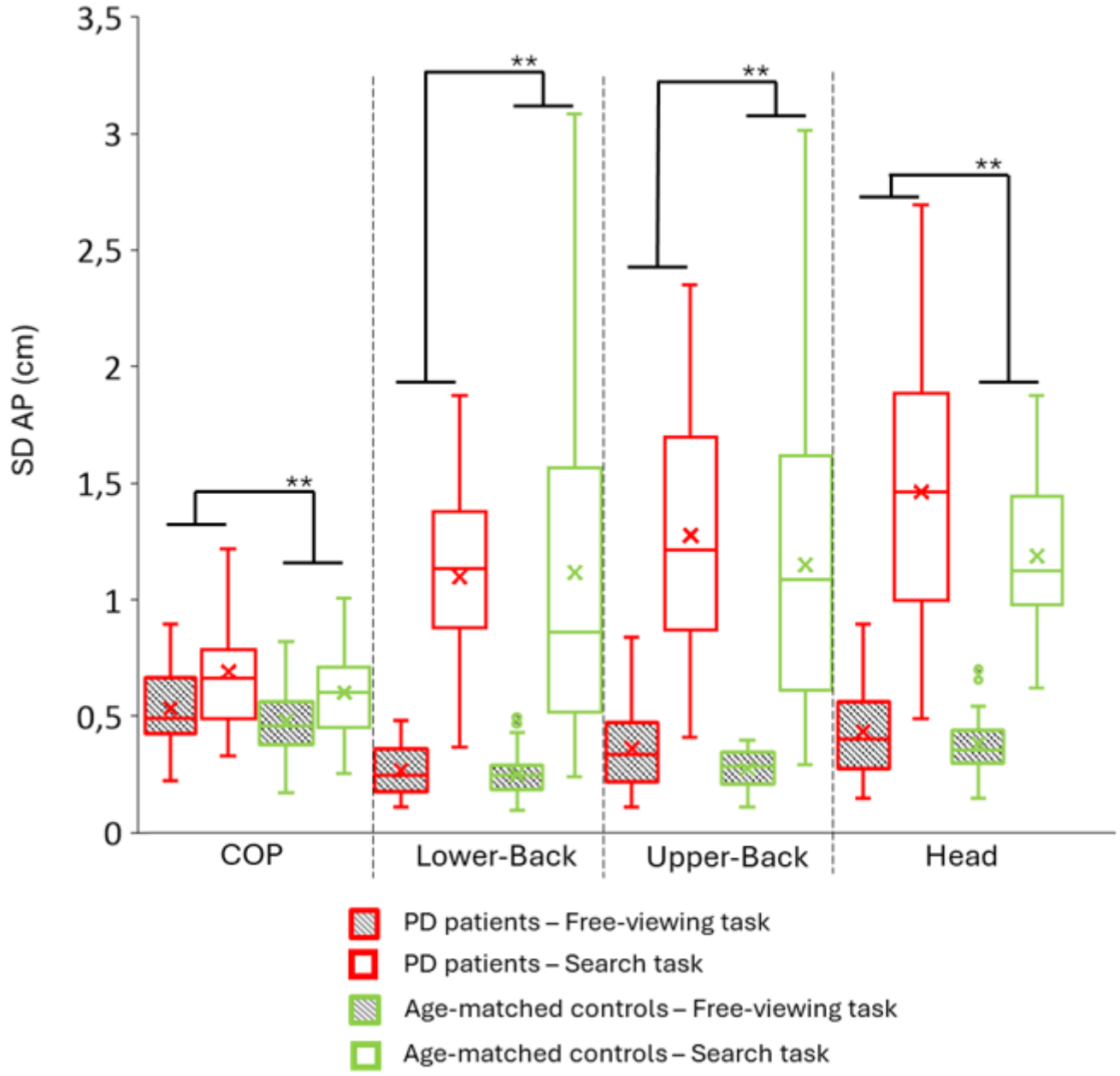

SD ML (cm)
3
2,5
2
1,5
1
0,5
0
COP
Lower-Back
Upper-Back
Head
*
**
PD patients – Free-viewing task
PD patients – Search task
Age-matched controls – Free-viewing task
Age-matched controls – Search task

Figure 4


3,5
3
2,5
2
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SD AP (cm)
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COP
Lower-Back
Upper-Back
Head
PD patients – Free-viewing task
PD patients – Search task
Age-matched controls – Free-viewing task
Age-matched controls – Search task