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New insight into Parkinson's disease-related impairment of the automatic control of upright stance

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ABSTRACT

Parkinson's disease (PD) affects the automatic control of body movements. In our study, we tested PD-related impairments in automatic postural control in quiet upright stance. Twenty PD patients (mean age: 60±8 years; Hoehn and Yahr: 2.00±0.32, on-drug) and twenty age-matched controls (61±7 years) were recruited. We studied interrelations between center-of-pressure movements, body movements (head, neck, lower back), eye movements and variability of pupil size. Participants performed two fixation tasks while standing, during which they looked at: a) a cross surrounded by a white background; and b) a cross surrounded by a structured visual background (images used: rooms in houses). PD patients exhibited stronger and weaker correlations between eye and center-of-pressure/body movement variables than age-matched controls in the white and structured fixation tasks, respectively. Partial correlations, controlling for variability of pupil size showed that PD patients used lower and greater attentional resources than age-matched controls to control their eye and center-of-pressure/body movements simultaneously in the white fixation and structured fixation tasks, respectively. In the white fixation task, PD patients used attentional resources to optimize visuomotor coupling between eye and body movements to control their posture. In the structured fixation task, the salient visual stimuli distracted PD patients' attention and that possibly affected posture control by deteriorating the automatic visuomotor coupling. In contrast, age-matched controls were able to use surrounding visual background to improve the automatic coupling between eye and center-of-pressure movements to control their posture. These results suggest that cluttered environments may distract PD patients and deteriorate their postural control.

CONTRIBUTION OF THE AUTHORS

Cédrick T. Bonnet: all parts of the work

Arnaud Delval: conception, inclusion of the patients with PD, analyses, writing and review of the manuscript

Luc Defebvre: principal investigator, conception, inclusion of the patients with PD, review of the manuscript

Yann-Romain Kechabia: results sections, all parts concerned with pupil size, review of the manuscript

Tarkeshwar Singh: writing of the manuscript, discussion of the results, review of the manuscript

1. INTRODUCTION

Parkinson's disease (PD) is a disease that affects the basal ganglia. The basal ganglia are involved in the control of the upright stance (Magrinelli et al., 2016; Takakusaki, 2017) as well as in attentional processes (Gao & Wu, 2016; Redgrave et al., 2010). The putamen, in particular, is involved in the habitual control of automatic motor skills (Ferrazzoli et al., 2018; Redgrave et al., 2010; Takakusaki, 2017). The basal ganglia are also involved in visual processes such as the detection of optic flow (Putcha et al., 2014) and execution of stable fixations (Gitchel, Wetzel, & Baron, 2012). Dopamine depletion in the putamen appears very early in PD (Ferrazzoli et al., 2018; Gao & Wu, 2016; Wu, Hallett, & Chan, 2015) and likely impairs automatic posture control at an early stage of the disease (Gao & Wu, 2016).

The most likely cause for an impairment in automatic posture control is the reduction in the connectivity of corticostriatal motor pathways and an inability to send automated motor commands to the sensorimotor striatum (Gao & Wu, 2016). However, the literature is unclear if automatic postural control in quiet stance is impaired in PD patients. Some studies have shown that PD patients at early stages of the disease (Hoehn & Yahr stage I & II) sway more than age-matched controls (Cruz et al., 2018; Doná et al., 2016; Hill, Stuart, Lord, Del Din, & Rochester, 2016) while others have shown no difference in sway between the groups (Bonnet, Delval, & Defebvre, 2014, 2015; Bonnet, Delval, Szaffarczyk, & Defebvre, 2017; Frenklach, Louie, Koop, & Bronte-Stewart, 2009; Rinalduzzi et al., 2015). Clear differences in postural sway between PD patients and controls emerge only during the later stages of the disease (e.g. Hoehn & Yahr III and IV; Frenklach et al., 2009).

One explanation for the aforementioned discrepancy in quiet stance is that some PD patients may use compensatory mechanisms to perform as well as controls in the fixation task. For example, PD patients also use greater attentional resources than age-matched controls to perform automatic movements (Gao & Wu, 2016). In addition, in quiet stance, PD

patients may rely more on visual information than healthy controls to stabilize their posture (Hill et al., 2016; Park, Kang, & Horak, 2015; Rinalduzzi et al., 2015). However, it is unclear whether PD patients could automatically change their postural control in difficult fixation tasks.

To the best of our knowledge, only two studies on healthy old adults used various fixation tasks (Bonnet et al., 2010; Kinsella-Shaw, Harrison, Colon-Semenza, & Turvey, 2006). In both studies, old adults swayed significantly less when they performed a structured fixation task than the white fixation task. Hence, old adults are able to collect visual information from the visual background to improve their postural stability. We have previously shown that in old adults, the visual system is able to detect optic flow caused by postural sway and use it to reduce postural sway (Bonnet et al., 2010). Old adults flexibly and automatically improve their postural control when the visual environment is more structured.

Our group recently analyzed relations between eye and postural movements in a white fixation task performed by healthy young adults (Bonnet, 2019). For simplicity in the present manuscript, the term 'postural movements' here refers to center of pressure (COP) and/or body movements. In this previous study, participants looked at a black cross surrounded by a white background while standing upright. The results showed that this fixation task induced positive correlations between eye and postural movements (Bonnet, 2019). Pearson correlations showed that young adults automatically control their upright stance with respect to eye movements. This process was considered automatic because changes in attentional resources did not influence the relations between eye and postural movements (Bonnet, 2019).

The objective of the present study was to test PD-related impairment in automatic eye and postural movements in fixation tasks (white and structured) during the quiet upright stance. In the white fixation task, participants looked at a black cross surrounded by a white background. We did not expect any PD-related impairment in vision and/or posture because

of the simplicity of this task (see Fig.1). In the structured fixation task, the participants still looked at a black cross but this cross was surrounded by a structured image. In this task we predicted that PD patients would be unable to take advantage of the visual background to improve their automatic postural control (Figure 1). In contrast, we expected healthy participants to automatically control their upright stance more easily in the structured fixation task than in the white fixation task. In other words, healthy controls were expected to show a greater number of significant correlations between eye and postural movements in structured fixation than in white fixation (cf. Figure 1).

Insert Figure 1 about here

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2. MATERIALS AND METHODS

2.1 Participants

Twenty PD patients (12 males, 8 females) and 20 controls (12 males, 8 females) were included in the present study. The two groups were similar in terms of age (patients: 59.65 ± 8.31 years (range: 42-73 years); controls: 60.95 ± 6.78 years (range: 59-72 years)), weight (patients: 78.40 ± 16.88 kg (range: 45-107 kg); controls: 77.62 ± 12.79 kg (range: 55-105 kg)) and height (patients: 1.71 ± 0.06 m (range: 1.60-1.82 m); controls: 1.70 ± 0.08 m (range: 1.60-1.92 m); $F_s(1,38)<0.29$, $p>0.05$). The study was approved by the local independent ethics committee (n°2014-74). All the participants gave their written, informed consent to participation. The patients and age-matched controls were recruited during consultations at Lille University Hospital's Neurology Department (France) and by the Clinical Investigation Center of the Regional Hospital of Lille, respectively.

The PD patients were diagnosed according to the Movement Disorders Society clinical diagnostic criteria for Parkinson's disease (Postuma et al., 2015). The mean Hoehn and Yahr stage in the patient group was 2.00 ± 0.32 (range: 1–3). PD patients had a mean time since disease onset of 5.7 ± 2.7 years (range: 2-11 years) and a mean Movement Disorder Society's Unified Parkinson's Disease Rating Scale motor score (part III; (Hughes, Daniel, Kilford, & Lees, 1992) equal to 21.5 ± 7.5 (range: 10-39). The score on the Giladi et al.'s (Giladi et al., 2000) questionnaire was 5.7±4.7 (range: 0-15). The Stand Walk and Sit test was performed in 13.1 ± 2.2 sec (range: 9-18 sec) and with 21.2 ± 2.8 steps (range: 17-27 steps). PD patients were tested on-drug and their mean daily total levodopa equivalent dose was 659 ± 339 mg (range: 200-1580). None of the patients changed their medication in the three months leading up to their participation in the study.

The exclusion criteria for all participants were a history or signs of vestibular, musculoskeletal or neurological disease (except for PD in the patient group), a Montreal Cognitive Assessment score (MOCA) lower than 25 (Nasreddine et al., 2005), recurrent dizziness, dementia, motor fluctuations, subclinical dyskinesia or known hip- and ankle-related diseases or injuries, any medication known to affect postural control or pupil size and any falls in the previous six months. The inclusion criteria for all participants were normal or corrected-to-normal vision so they could clearly see the experimental images.

2.2 Apparatus

COP and body (head, neck, lower back) movements were recorded with a dual-top force platform (AMTI, Watertown, MA, USA) and a Polhemus system (Polhemus Liberty 240/8-8 System, Colchester, VT, USA) at 120 Hz and 240 Hz, respectively. The head and lower back markers were placed on a helmet and on a chest belt worn by the participants. The neck marker was placed at the seventh cervical vertebra. The platform only recorded linear

anteroposterior (AP), mediolateral (ML) movements while the Polhemus system recorded both linear (AP and ML) and angular (yaw (left-right), pitch (up-down)) movements.

Eye movements and variability (SD) of pupil size were recorded with a head mounted SMI eye-tracker (SensoMotoric Instruments, Teltow, Germany) at a sampling frequency of 50 Hz. This system was set up on the helmet. The platform, the Polhemus system and the SMI eye-tracker were synchronized with the images projected 3.75 m in front of the participants. The SMI eye-tracker inscribed "0-values" in data files for missing values during blinks and because of extra pupil dilation. This last issue occurred because the lights had to be switched off in the experimental room. A MATLAB script (MathWorks Inc., Natick, MA, USA) was used to cancel the missing "0-values" in the gaze time-series and at corresponding moments in the COP, head, neck and lower back time-series.

2.3 Conditions

The participants performed a total of 12 trials in the two tasks (the white task and the structured task with six trials per task; see below). They performed the six trials of each task in a block. The order of images presented in the structured task was randomized for each participant.

In the white task the participants were instructed to fixate on a black cross during the full trial (50 sec; see Fig. 2B). This cross was centered on the panoramic display in front of them and was surrounded by an entirely white panoramic display. This display subtended a visual angle of 100° when the participants stood 3.75 m behind the center of that panoramic display (Figure 2A). In the structured task, the participants were also instructed to fixate on a black cross during the full trial (50 sec), but this time the cross was surrounded by an image projected onto the full panoramic display (Figure 2B). The six projected images (one per trial) in front of the participants were of rooms inside a house (kitchen, living-room, see Fig. 2B).

Insert Figure 2A and 2B about here

2.4 Procedure

Once the participants arrived in the experimental room, they were briefly explained the experimental design. Then they took their shoes off to perform the trials barefoot. The various apparatus (platform, motion tracking system, eye tracker) were calibrated before starting the experimental session. During each trial, the participants had their feet placed along two normative lines with their heels 14 cm apart and their feet separated by 17° (McIlroy & Maki, 1997).

2.5 Variables

2.5.1 Choice of the variables

We focused on behavioural variability in the two groups. Variability is important because increased postural sway has been shown to be directly related to instability and increase in falls in old adults (Fernandes et al., 2018; Johansson, Nordström, Gustafson, Westling, & Nordström, 2017). For the COP, lower back, neck and head movements, the dependent variables were the standard deviation (SD), range (R) and mean velocity (V) along the AP and ML axes. These variables have been used by other authors (Roman-Liu, 2018) and by us in previous studies with PD patients and old adults (Bonnet et al., 2014, 2015, 2017). Path length and ellipse area were other dependent variables to provide the overall range of body and eye movements. For the eye movement time-series, we analysed the same dependent variables, i.e. SD, R, V but this time in the up/down and left-right directions. Additionally, the eye-

tracking software extracted the spatial characteristics of the fixations performed in the full trials before we calculated the R, SD, V of the fixations. Both types of eye movement variables were different. The characteristics of fixation concerned only a part of the full data excluding the saccades but the time-series concerned the full dataset. The software also extracted the mean pupil size in each trial. We used the variability (SD) of pupil size in each task to represent changes in attentional involvement as in other studies with healthy adults and/or PD patients (Ajasse, Benosman, & Lorenceau, 2018; Kahya et al., 2018; Wainstein et al., 2017; Wang, McInnis, Brien, Pari, & Munoz, 2016). For the pupil size measure, we did not consider the 5 first seconds of the trial (Naber, Alvarez, & Nakayama, 2013; Radzius, Welch, Cone, & Henningfield, 1989). For each variable, the data from the six trials (per task) were averaged to obtain a single score.

2.5.2 Selection of the variables

First, we used principal component analysis (PCA) to select the most relevant eye and postural movement variables for the Pearson correlation. We performed four PCAs, i.e. one for each group (PD and age-matched controls) and one for each task (white and structured). To identify the variables of interest in each of our four PCAs, we selected eye movement and postural movement variables that correlated significantly to the first and second principal components. These variables contained values that best explained maximum variability in eye and the postural movements (for more details about this technique, see Costa, Da-Silva, Almeida, & Infantosi, 2014; Ewenczyk et al., 2017).

Second, we separated the dependent variables into three groups: left-right (eye)/ML (postural) variables, up-down (eye)/AP (postural) variables and general (eye)/general (postural) variables. By doing this we avoided performing a large number of Pearson correlations.

Before analyses we checked the existence of outliers. Outliers were defined as extreme values that were more than 2 standard deviations outside the quartiles. Box plots were used to detect the presence of outliers in all the variables in the tables prepared for analyses. We deleted these outliers before performing any statistical analyses (Tabachnik, & Fidell, 2013, pp. 76-77, 92, 100).

2.6 Analyses

2.6.1 Correlation analyses and following analyses on these results

Pearson analyses were performed between eye and postural movement variables in each group and each task separately. They engaged the full time series of i) eye and ii) COP, lower back, neck and head time-series in both directions (up-down/AP and left-right/ML). To study the relation between eye movements and postural movements during performance of the fixation tasks, we only tested relations between angular eye and linear postural movements, and not relations between angular eye and angular body movements. This is because we were interested in the relation between visual functions and postural control and not in the coordination between angular eye and angular body movements. We selected two sets of eye and postural movement variables for analyses.

After Pearson correlations were performed, we obtained a certain number of significant correlation coefficients in both groups and both tasks. A Chi-square test was performed to test a population difference (PD patients vs. age-matched controls) in the number of statistically significant relations between eye and postural movements (absence or presence of significant correlations in both fixation tasks).

Cross-correlations were performed between eye and postural movement variables to test if eye and postural movements were coupled throughout each trial. Eight cross-correlations

were performed per group. Once cross-correlation coefficients were obtained, one-way ANOVAs were performed to test significant differences between these correlation coefficients in the two fixation tasks.

Partial correlations were performed to analyse whether changes in attention could influence the significant correlations found in Pearson correlations, and the cross-correlations between eye and postural movements. Hence, these partial correlations controlled for the effects the variability of pupil size could have had on the significant correlations.

In our previous study with healthy young adults (Bonnet, 2019), we proposed that positive correlations between eye and postural movements reflect a well-functioning automatic control of upright stance. If postural sways increase in the ML direction, then eye movement amplitudes would also have to increase in left-right direction to keep the eyes on the target. Significant positive correlations between eye and postural movements therefore show that eye movements are adaptively used for the automatic control of upright stance. Furthermore, we can also say that a greater number of significant correlations in one task and/or in one group would indicate more reliance on vision.

2.6.2 Singular analysis (ANOVA)

A two-way ANOVA was used to analyze the variability (SD) of eye movements between tasks and between groups. Before performing this analysis, we checked the normality with the Shapiro-Wilk test and homogeneity of variance of the data with the Mauchly's test.

2.6.3 Overall information for all analyses

The selection of variables with PCAs was performed in the open access statistical software, R. All (Pearson, ANOVA) analyses were performed with Statistica 10 Software

(Statsoft Inc., Tulsa, OK, USA) with an adjusted *p*-value ($p<0.01$). The alpha level was adjusted based on the test of several hypotheses and not on the number of correlations, as suggested by Rubin (2017). The Chi-square was performed at an alpha level of 0.05.

3. RESULTS

3.1 Results for the preparation of analyses

3.1.1 Choice of the variables

In all PCAs, only a subset of the eye movement variables were selected (Table 1). In contrast, most of the postural variables were present in the selected variables (Table 1). Overall, and based on our method of selection, we performed 205 Pearson correlations for a total of 1536 possible correlations in the full matrix. We thus selected the 13.34% a priori most relevant correlations.

Insert Table 1 about here

3.1.2 Missing data and outliers

We excluded 19.4% of eye movement files (13.1% for PD patients, 6.3% for age-matched controls) because these files were missing more than 20% of the data. On average, 94.5±5.4% of the data existed in the remaining files. The inspection of outliers in the final spreadsheets showed on average 1.3 % and 0.2 % of outliers per column of data in the white fixation and structured fixation tasks in the PD patients, and on average 0.1 % and 0.6 % of outliers per column of data in the age-matched controls, respectively. These data were removed before analyses.

3.2 Pearson correlations and cross-correlations between eye and postural movements in the two fixation tasks

The significant Pearson correlations between eye and postural movements were all positive in the PD patients and age-matched controls (100%) (Table 2A and B). This suggests that large postural sways were associated with large amplitude of eye movements to keep the gaze on the stationary target. There were also some differences between the two groups. Most of the significant correlations in the white and structured tasks were found at the head and neck levels in the patients (Table 2A) and exclusively at the COP level in the age-matched controls (Table 2B). Moreover, 100% of the correlations of the PD patients were related to the UD/AP directions in both the white and structured tasks. In contrast, only 50% of the correlations of the age-matched controls were related to the UD/AP directions in both tasks (Table 2B). Additionally, for the age-matched controls, 40% (4/10 of the correlations) were related to the LR/ML directions and 10% (1/10) were related to general variables (Table 2B). Four examples of significant correlations are showed in Figure 3A, B, C and D, with the highest coefficients in both groups and both tasks.

The two-way ANOVAs (group and task as factors) for the cross-correlation coefficient between eye and COP, head, neck, lower back movement were all non-significant.

Insert Table 2A and B about here

Insert Figure 3A, 3B, 3C and 3D about here

3.3 The Chi-square test show a difference in correlations for the two tasks between the two groups

Overall, the PD patients showed a slightly greater number of significant correlations in the white task than in the structured task (9 vs. 5), while the age-matched controls showed a lower number of significant positive correlations in the white task than in the structured task (2 vs. 8; Table 2A and B). The χ^2 showed that the PD patients exhibited more significant correlations than healthy controls in the white task and fewer significant correlations than age-matched controls in the structured task ($\chi^2 = 4.04$, p=0.03).

3.4 Partial correlations show the effects of attention on gaze posture coupling

To perform partial correlations, we used all significant correlations shown in Table 2A and 2B after controlling for the influence that variability of pupil size could have had on these correlations. Below, we report the correlations between eye and postural movements that were not significant after we controlled for the influence of variability of pupil size.

For PD patients. In the white fixation task, 4 of the 9 correlations in Table 2A (44.44 %) became non-significant after controlling for the influence of variability of pupil size, i.e. the correlations between Eye $SD_{UD}F$ and head $R_{AP,}$ between Eye $SD_{UD}F$ and head SD_{AP}, between Eye V_{UD} and Head V_{AP}, between Eye V_{UD} and Neck SD_{AP} (p>0.01). In the structured fixation task, all 5 out of 5 correlations in Table 2A (100%) became non-significant in the partial correlations (p>0.01).

For age-matched controls. In the white fixation task, 2/2 correlations in Table 2B (100%) became non-significant in the partial correlations (p>0.01). In the structured fixation task, 3 of the 8 correlations in Table 2B (37.5%) became non-significant after the partial correlations, i.e. correlations between Eye $R_{UD}F$ and COP R_{AP}, between Eye $R_{UD}F$ and COP $SD_{AP,}$ between Eye $R_{LR}F$ and COP R_{ML} (p>0.01).

3.5 ANOVA for the performance in the fixation tasks

The SD of eye movements for PD patients and the age-matched controls were 0.57°±0.19° and 0.53°±0.20° in the white task and 0.66°±0.21° and 0.55°±0.17° in the structured task, respectively (means calculated on the time-series, not on the characteristics of fixation). The ANOVA did not show any significant effect (F_s<2.15, p>0.05).

4. DISCUSSION

Our results show that PD patients were unable to use information from the visual background to improve automatic control of their upright stance. Specifically, a structured visual environment deteriorated their ability to control their posture. In contrast, age-matched controls were able to improve their postural control in the structured environment.

In a previous study with healthy young adults (Bonnet, 2019), the fixation task induced significant positive correlations between eye and postural movements. This showed that the eyes moved more in the left-right and up-down directions when the body moved more in the ML and AP direction, respectively. We also found that additional attentional resources were not needed to perform simultaneous control of eye and postural movements in this fixation task (Bonnet, 2019). This suggests that the visuomotor networks synergistically work with the vestibulo-ocular reflex networks to keep gaze fixated onto the target (Mossman, Mossman, Purdie, & Schneider, 2015).

The results in the age-matched controls were not surprising because they showed an improvement in automatic postural control during the structured fixation task compared to the white fixation task. Age-matched controls exhibited a greater number of significant positive correlations between eye and postural movements in the structured fixation task than in the

white fixation task (Table 2B). They also shared more overall variance in eye and postural movements in the structured fixation task than in the white fixation task (75.16% vs. 66.46%, Table 1). Furthermore, fewer attentional resources were engaged in the structured fixation task than in the white fixation task (37.5% vs. 100%; cf. partial correlations). Hence, age-matched controls could use background visual information to automatically control their upright stance with fewer attentional resources. Overall, these findings suggest that the presence of structured backgrounds around the fixation cross helped age-matched controls to improve automatic postural control. This finding is consistent with our previous studies (Bonnet et al., 2010; Kinsella-Shaw et al., 2006) and with our hypothesis (Figure 1). The real-life implication of these results is that age-matched controls may use visual information from objects and their orientations in the environment to control their upright stance efficiently in a complex and furnished environment.

For PD patients our prediction was that we would find appropriate automatic postural control in the white fixation task but no improvement in the structured fixation task (Figure 1). In the white fixation task, PD patients showed a greater number of significant positive correlations between eye and postural movements than age-matched controls (9 vs. 2, Table 2A and 2B). This suggests that PD patients relied more heavily on vision than age-matched controls to control their posture in the white fixation task; this result is consistent with previous reports (Hill et al., 2016; Park et al., 2015; Rinalduzzi et al., 2015). Partial correlations controlling for the influence of attentional resources (changes in variability of pupil size) showed that PD patients did not engage as many attentional resources as age-matched controls (44.44 % vs. 100 %). Therefore, it appears that by increasing reliance on visual information, PD patients performed automatic postural control better than age-matched controls. This suggests that PD patients can automatically control their posture well when the visual environment is simple.

In the structured fixation task, we predicted that PD patients would be unable to adapt their automatic postural control (flat line expected in Figure 1). Our results supported this prediction and were even stronger than expected. Indeed, PD patients exhibited fewer significant correlations between eye and postural movements in structured vs. white fixation (5 vs. 9; Table 2A; Figure 1 vs. 4). PD patients also showed fewer significant correlations between eye and postural movements than age-matched controls in the structured fixation task (5 vs. 8; Table 2B; Figure 4 vs. 4). Therefore, PD patients' automatic postural control was more compromised when they performed the structured fixation tasks than the white fixation task.

Partial correlations that controlled the role of attentional resources between eye and postural movements provided additional information. These analyses suggested that in the structured fixation task, PD patients engaged more attentional resources to significantly couple eye and postural movements (100 % of the time for these significant correlations), while age-matched controls only engaged 37.5 % of attentional resources (cf. Results section 3.4). Accordingly, in the structured fixation task, PD patients used more attentional resources to couple eye and postural movements.

The most important difference between white fixation and structured fixation is that PD patients were potentially distracted by peripheral objects, which interfered with the main (fixation) task (Weil et al., 2016). Norton et al. (2016) explained that basal ganglia, and particularly the substantia nigra, are responsible to selectively inhibit activity in the superior colliculus, a structure responsible for eye movements. In the structured fixation task, PD patients may have had a conflict between keeping the eyes on the stationary target and moving the eyes toward salient properties of the image. PD patients therefore needed to engage more attentional resources than age-matched controls to keep their eyes fixated on the target. This PD-related compensation has been reported in the literature (e.g. D'Ostilio,

Cremers, Delvaux, Sadzot, & Garraux, 2013; Gao & Wu, 2016) and may have contributed to the deterioration of automatic control of the upright stance in the structured fixation task. Thus, the novel finding in the current study is that environments with many visually salient and distracting stimuli may compel PD patients to shift from automatic to attention-assisted postural control. Since attentional resources are limited in patients with PD, this may explain why these patients become prone to falls with disease progression (Rowe et al., 2002).

Finally, we will also like to contrast our results with other studies. Recently, Cruz et al. (2018) and Feller, Peterka, & Horak (2019) showed that PD may not impair the automatic control of upright stance. However, these studies had a smaller sample size and may not have been sufficiently powered. Our results challenge Cruz et al.'s (2018) and Feller et al.'s (2019) findings and show that in patients with PD, automatic visuomotor coupling acts to control posture in fixation tasks in simple environments, while in complex environments, the control strategy shifts to an attention-assisted visuomotor coupling. If attentional resources are deficient in PD patients, then this may compromise their posture.

One of the limitations of our study is that variability of pupil size was not the most robust variable to measure changes in attentional resources in both groups and both tasks. However, variability of pupil size has been chosen as an index of attentional resources in many studies (Kahya et al., 2018; Naber et al., 2013; Wang et al., 2016). Future studies should measure EEG or fNIRS data to confirm our findings (e.g. (Ewenczyk et al., 2017). A second limitation relates to the fact that our participants were not involved in a 3D visual environment but only in a 2D environment. This should be tested in the future.

A direct practical recommendation from our study is that PD patients should avoid furnishing their home with too many distracting salient visual stimuli. One solution may be to change interior design in reducing as much as possible small decorative objects placed on pieces of furniture. Another important factor in our study was that PD patients were on-drug

during the study. A future study also should test the influence of medication on PD-related impairments of the automatic control of the upright stance.

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LIST OF ABBREVIATIONS: AP = antero-posterior; COP = center of pressure; LR = left-right; ML = medio-lateral; MOCA = Montreal Cognitive Assessment score; NASA-TLX = National Aeronautics and Space Administration Task Load Index; PCA = Principal Component Analysis; PD = Parkinson Disease; R = range; SD = standard deviation; UD = up/down; V = mean velocity; F = fixation (abbreviation only used when variables were related to characteristics of fixation; e.g. $R_{AP}F$ = range of locations of fixations on the AP axis).

CONFLICT OF INTEREST

There is no conflict in the present manuscript.

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Table 1. Results of the PCA for PD patients and healthy controls

	Percentage of variance in dimension 1	Percentage of variance in dimension 2	Percentage of variance in both dimensions	Eye movement variables selected in D1 and D2	Postural movement variables selected in D1 and D2
In patients with PD in the white task	46.98%	18.15%	65.13%	3/12 ($SD_{UD}F$, $SD_{UD,}$ V_{UD})	31/32 variables (but COP V_{AP})
In patients with PD in the structured task	48.24%	17.51%	65.75%	2/12 ($R_{UD}F$ and $SD_{UD}F$)	31/32 variables (but COP V_{ML})
In controls in the white task	48.46%	18.00%	66.46%	5/12 (SD_{LR}, R_{UD}, path lengh, V_{LR}, R_{LR})	32/32 variables (all selected)
In controls in the structured task	62.37%	13.19%	75.16%	8/12 ($R_{UD}F$, $SD_{UD}F$, ellipse, R_{UD}, SD_{UD}, $R_{LR}F$, R_{LR}, SD_{LR})	32/32 variables (all selected)

Table 2. Significant Pearson correlations between eye and postural (i.e. head, neck, lower back and center of pressure (COP) movements) in the white and structured tasks (p<0.01) for the patients with PD and for the healthy controls.

A.

	In the white task	In the structured task
Correlations between eye and postural movements in PD patients	Eye $SD_{UD}F$ & head R_{AP} (r(20)=0.59) Eye $SD_{UD}F$ & head SD_{AP} (r(20)=0.60) Eye SD_{UD} & Head R_{AP} (r(18)=0.70) Eye SD_{UD} & Head SD_{AP} (r(18)=0.65) Eye V_{UD} & Head R_{AP} (r(18)=0.76) Eye V_{UD} & Head SD_{AP} (r(18)=0.76) Eye V_{UD} & Head V_{AP} (r(18)=0.61) Eye V_{UD} & Neck R_{AP} (r(18)=0.66) Eye V_{UD} & Neck SD_{AP} (r(18)=0.64)	Eye $R_{UD}F$ & Head R_{AP} (r(20)=0.57) Eye $R_{UD}F$ & Neck V_{AP} (r(20)=0.58) Eye $SD_{UD}F$ & Neck R_{AP} (r(20)=0.60) Eye $SD_{UD}F$ & Lower back R_{AP} (r(20)=0.62) Eye $SD_{UD}F$ & Lower back SD_{AP} (r(20)=0.61)
Correlations between eye and postural movements in healthy controls	Eye SD_{LR} & COP R_{ML} (r(20)=0.61) Eye SD_{LR} & COP SD_{ML} (r(20)=0.61)	Eye $R_{UD}F$ & COP R_{AP} (r(20)=0.68) Eye $R_{UD}F$ & COP SD_{AP} (r(20)=0.59) Eye $SD_{UD}F$ & COP R_{AP} (r(20)=0.82) Eye $SD_{UD}F$ & COP SD_{AP} (r(20)=0.78)

	Eye R_{UD} & COP V_{AP} (r(19)=0.76)
	Eye R_{LR}F & COP R_{ML} (r(20)=0.57)
	Eye SD_{LR} & COP V_{ML} (r(19)=0.62)
	Eye ellipse area & COP path length (r(19)=0.71)

Note. The significant findings were found in the up-down (UD)/anteroposterior (AP) directions and in the left-right (LR)/mediolateral (ML) directions separately. In these tables, the first variable is always a visual variable and the second one is always a postural one. The lines of results are presented in such a way that significant findings with the characteristics of fixation (name of the visual variable finishing by "F") are presented first and with the time-series (name of the visual variable not finishing by f) are presented second. The variables are the range (R), the standard deviation (SD), the mean velocity (V), the ellipse area and the path length. For example, the first result (top left of the Table, i.e. In the up-down/AP directions: R_{UD}F & Head R_{AP} (r(20)=0.57)) means that the correlation between the range of up-down fixation and the range of head AP displacement was significant. Sometimes, one general variable (path length or ellipse area) was significantly correlated with a variable in the AP and/or ML directions. In this case, the direction of the relation (up-down/AP or left-right /ML) depends on the sign of this last variable.

FIGURE CAPTIONS

Figure 1. Representation of the general hypotheses for patients with Parkinson's disease (PD patients) and controls in both white and structured fixation tasks. In the white fixation task (looking at a cross surrounded by a white background), we expected no PD-related difference in the amount of significant correlations between eye and center of pressure (COP)/body movements. In the structured fixation task (looking at a cross surrounded by larges images showing rooms of houses), we expected to find a lower amount of significant correlations between eye and COP/body movements in PD patients than in controls.

Figure 2. A. Figure showing the position of the participants with respect to the semi-circular panoramic display. The twelve images were projected onto that panoramic display (2.04 m radius, 2 m high). The participants stood 1.71 m behind the center of the semi-circular panoramic display and therefore could see the images subtended by a visual angle of maximum 100°; B. One image of the white fixation task and two images shown during the study in the structured fixation task.

Figure 3. A. Significant Pearson correlations between eye (V_{UD}) and head (R_{AP}) movements in the white task for the patients with Parkinson's disease (PD). Eye V_{UD} corresponds to the mean velocity of eye movements in the up-down direction (in degrees, °) during the task. Head R_{AP} (cm) corresponds to the range of head movements on the anteroposterior axis. B. Significant Pearson correlations between eye (SD_{UD}) and lower back (R_{AP}) movements in the structured task for the PD patients. SD_{UD} corresponds to the standard deviation of eye movements in the up-down direction. C. Significant Pearson correlations between eye (SD_{LR}) and center of pressure (COP) movements in the white task for healthy controls. Eye SD_{LR} corresponds to the standard deviation of eye movements in the left-right direction. COP R_{ML} corresponds to COP movement on the mediolateral direction. D. Significant Pearson correlations between eye (SD_{UD}) and center of pressure (COP R_{AP}) movements in the structured task for healthy controls. $p < 0.01$.

Figure 4. Representation of the results for patients with Parkinson's disease (PD patients) and controls in both white and structured fixation tasks. In the white fixation task, the participants were instructed to look at a cross surrounded by a white background. In the structured fixation task, they were instructed to look at the cross surrounded by larges images showing rooms of houses. The results are the number of significant positive Pearson correlations between eye and COP/body movements.

Figure 1.

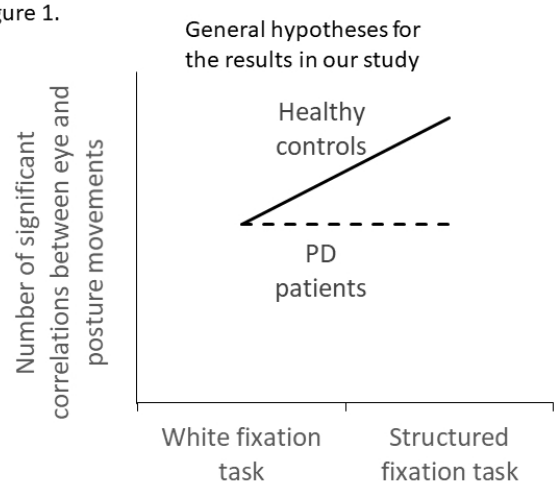

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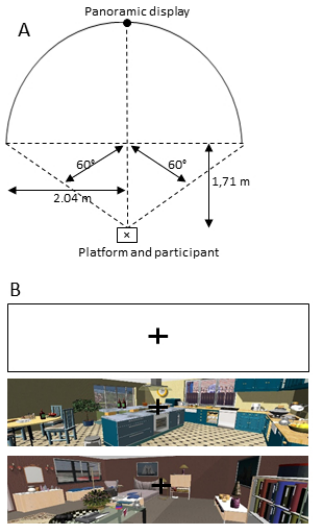
Figure 2.



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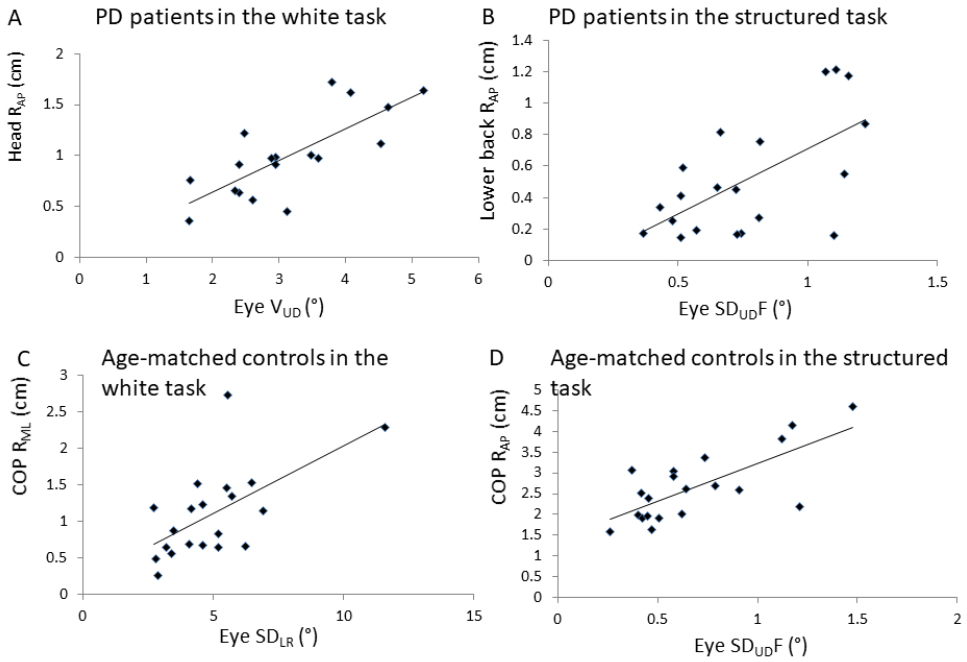

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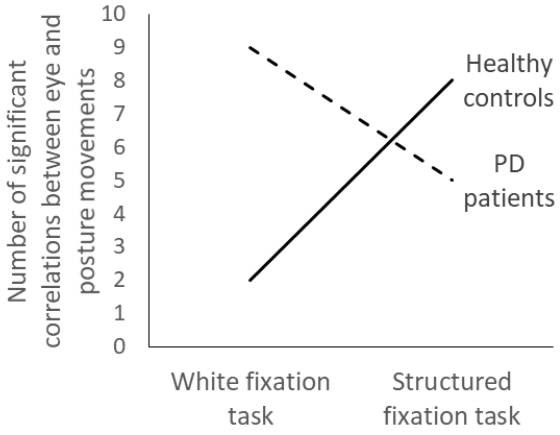
Figure 4.



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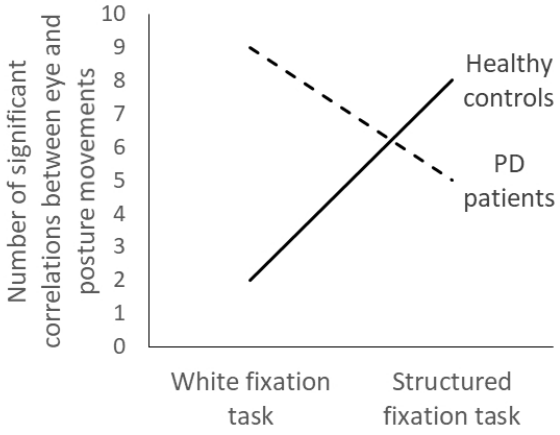
GRAPHICAL ABSTRACTS: The text file should consist of 2-3 sentences (max 500 characters with space) highlighting the major findings. Please upload the text as a Word document file with the file designation "Graphical Abstract Text". For the figure, please upload a figure file with the file designation "Graphical Abstract Figure." The figure should be representative of your manuscript and should contain no caption, heading or outline

PD patients were able to automatically control their posture in quiet stance when they fixated a stationary target surrounded by a white background (white fixation). They did so better than healthy controls. However, they were less able to automatically control their posture when the stationary target was surrounded by an image (structured fixation). Instead of being helped by additional visual information, as healthy subjects were, PD patients were distracted and less efficient.



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