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The Association between Prefrontal Cortex Activity and Turning Behavior in People with and without Freezing of Gait

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Abstract—Turning elicits Freezing of Gait (FoG) episodes in people with Parkinson's disease (PD) and is thought to require higher cortical control compared to straight ahead gait. Functional near infrared spectroscopy (fNIRS) has been used to examine prefrontal cortex (PFC) activity while walking, but the relationship between PFC activity and turn performance remains unclear. The aim of this pilot study was to examine PFC activity during turning in PD and healthy controls, and to investigate the association between PFC activity and turning. Thirty-two subjects, 15 freezers (PD + FoG) and 17 non-freezers (PD − FoG), and 8 controls were asked to perform a 2-min turning-in-place test under single-task (ST) and dual-task (DT) conditions. Each participant wore an fNIRS system to measure changes in oxyhemoglobin, as measure of PFC activity, and inertial sensors to quantify turning. Our results show a significant group ($p = .050$), task ($p = .039$), and interaction ($p = .047$) for the PFC activity during turning. Specifically, PD + FoG show higher PFC during turning compared to the other groups; PFC activity during DT is overall different compared to ST with an opposite trend in PD + FoG compared to controls and PD − FoG. In addition, higher PFC is associated with worse FoG in PD + FoG ($r = 0.57$, $p = .048$) and with lower number of turns in PD − FoG ($r = -0.70$, $p = .002$). The increased PFC activity in PD and the association between higher PFC activity and poorer turning performance may be a sign of poor movement automaticity in PD. Although further investigations are required, these pilot findings may guide development of personalized treatments to improve motor automaticity in PD. © 2019 Published by Elsevier Ltd on behalf of IBRO.

Key words: Turning; Freezing of Gait; Wearable Sensors; fNIRS.

INTRODUCTION

The ability to change direction while walking is an important component of functional mobility that requires the central nervous system to coordinate body re-orientation to a new travel direction maintaining stability (Courtine, 2004; Herman et al., 2011; Mellone et al., 2016). In addition, turning is thought to require increased neural resources compared to straight ahead gait (Herman et al., 2011) as postural transitions place greater load on integration regions (Crenna et al., 2007) and executive functions (Herman et al., 2011; King et al., 2012). People with Parkinson's disease (PD) show turning deficits compared to healthy peers. Specifically, turns are slower and more steps are required to complete a turn in PD. Turning impairments occur early in the disease, even before straight-ahead gait deficits transpire (King et al., 2012).

Turning is also known to elicit Freezing of Gait (FoG) episodes in those patients with self-reported FoG (Stack and Ashburn, 2008; Spildooren et al., 2010; Mancini et al., 2017). FoG has been defined as "a brief, episodic absence or marked reduction of forward progression of the feet despite the intention to walk" (Nutt et al., 2011), and FoG episodes are perceived as a feeling of having "their feet glued to the floor". Among all common clinical symptoms of PD, FoG is one of the most debilitating, directly affecting the overall quality of life and balance perception (Moore et al., 2007). These episodes are associated with falls and injuries and most likely happen when initiating walking, turning or passing through narrow passages (Nutt et al., 2011). In general, PD impacts subcortical pathways leading to a disrupted automatic control of movement accompanied by a compensatory shift to a more voluntary cortical control (Wu et al., 2015), hallmark of mobility disability in PD. Moreover, PD is often accompanied by cognitive dysfunction, and specifically alteration in executive function domains, including response inhibition and set-shifting, has been reported in people with PD with FoG compared to without FoG (Vandenbossche et al., 2011; Peterson et al., 2015; Peterson et al., 2016). Furthermore, several studies reported associations between gait and cognitive function: in fact, attention

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demanding tasks have been seen to change walking patterns in people with cognitive impairments and alterations in executive functions have been associated with gait disturbances (Yogev-Seligmann et al., 2008).

Difficulty in multitasking can therefore be a debilitating problem in PD, and even more in those who experience FoG (PD + FoG) (Peterson et al., 2015), who show decreased cadency and increased dysrythmicity (Spildooren et al., 2010) when turning performing a secondary cognitively demanding task, namely dual-task (DT), compared to those without FoG (PD − FoG). The addition of a DT while walking or turning can also increase occurrence of FoG episodes (Nutt et al., 2011).

The ability to walk while carrying out a cognitive task relies on executive functions (Maidan et al., 2016) with projections stemming from the prefrontal cortex (PFC) (Ridderinkhof et al., 2004; Maidan et al., 2016; Nieuwhof et al., 2016). An emerging body of literature has examined PFC activity during walking and balance tasks in both healthy young (Miyai et al., 2001; Mirelman et al., 2014) and old individuals while performing a DT (Holtzer et al., 2011), and in people with Parkinson's disease (Maidan et al., 2015) using functional near infrared spectroscopy (fNIRS) techniques (Stuart et al., 2018; Stuart et al., 2019a). With fNIRS, relative concentration of oxygenated (HbO2) and deoxygenated hemoglobin (HHb) can be recorded non-invasively during dynamic movements. Specifically, increased HbO_2 accompanied by decreased HHb is related to increased blood flow, which reflects increased cortical activity (Vitorio et al., 2017).

To date, few studies have investigated PFC activity during turning in people with PD: one study has found an increase in PFC activity during FoG episodes when turning 180° while walking (Maidan et al., 2015). The authors attributed this increased cortical activation to compensatory mechanisms for underlying PD-related deficits in automatic movement control. However, the relationship between PFC activity and turning performance in PD remains unclear, particularly during highly demanding tasks, such as continuous 360° turns-in-place. These have been found to elicit more FOG episodes than 180° during walking, which may be further impacted under dual-task conditions, and therefore understanding PFC activity during 360° turns could inform mechanisms underlying FoG. However, to the author's knowledge, no studies investigated the role of the PFC while performing 360° turning-in-place.

In addition, some evidences showed that PD + FOG present more pronounced cognitive and executive dysfunctions compared to PD − FoG and healthy controls, suggesting that these deficits may be related to motor dysfunction (Peterson et al., 2016).

Therefore, based on these evidences, this pilot study aimed to examine PFC activity in PD and older adult controls during continuous 360° turns-in-place. We hypothesized that; i) PD + FoG would have increased PFC activation while turning than PD − FoG and old adult controls, particularly during a DT; and ii) increased PFC activation would be associated with poor turning performance.

METHODS

Participants

Thirty-four participants with idiopathic PD, confirmed by a neurologist, were recruited through the Parkinson's Center of Oregon Clinic at Oregon Health & Science University. Eight healthy control subjects (CTR) of similar age were recruited from the community. Exclusion criteria for both groups were: inability to stand or walk for 2 min at a time, factors affecting gait such as hip replacement, musculoskeletal disorders, uncorrected vision or vestibular problems, and inability to follow instructions. Inclusion criteria for subjects with PD were: between 50 and 90 years old and met criteria for idiopathic PD according to the Brain Bank Criteria for PD. All PD participants were tested in their "OFF" medication state, at least 12 h after the last administration of their usual anti-parkinsonian medications.

All participants gave their written informed consent to a protocol approved by the Institutional Review Board of Oregon Health and Science University.

Experimental Procedures

Clinical assessment. Participants with PD were clinically rated by a trained examiner on the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III (Goetz et al., 2008), which covers the motor evaluation of disability and includes ratings for tremor, bradykinesia, rigidity, and balance. In addition, perceived Freezing of Gait status was evaluated with the New Freezing of Gait Questionnaire (NFoGQ) (Nieuwboer et al., 2009). Based on the results of this clinical scale, PD participants were defined as freezers, PD + FoG, if they obtained a score > 0, and non-freezers, PD − FoG, based on a NFoGQ score = 0.

Then, cognitive function was assessed with the following tests: Frontal Assessment Battery (FAB) (Dubois et al., 2000), Montreal Cognitive Assessment test (MoCA) (Rossetti et al., 2011), the Royall clock drawing tasks (CLOX 1 and 2) (Royall et al., 1998), and the Trail Making Test (TMT, both versions A and B), which provide information about speed of processing, mental flexibility, and executive functions (Tombaugh, 2004). MoCA scale was also administered to the control group.

Turning assessment. Participants performed a 2-min turning-in-place task at self-selected pace. The test involved 20 s of quiet standing at the beginning and at the end of the task, in which participants were asked to stand still and look forward, intermediated with 80 s of turning-in-place. Instructions about beginning and ending of the trial (i.e. "starting now" or "stop and relax") as well as those about the 80-s turning-in-place (i.e. start turning, stop turning and stand still), were given by the experimenter. The turning-in-place portion consisted of alternating 360° turns to the right and left under a single-task (ST) or DT conditions. The DT condition consisted of executing the turning task while

performing a concurrent cognitive task, in this case an auditory Modified AX-Continuous Performance Task (Riccio et al., 2002). In the DT condition, participants were required to push a handheld button after a two-paired letters sequence: the sequence consisted of a cue letter ‘‘A” and a probe letter ‘‘I” presented sequentially so that the target trail was ‘‘AI” and participants were asked to respond as fast as possible after the probe letter. This happened in both the quiet standing and the turning phases. No information about task priority was assigned to participants not to influence the task execution. ST and DT conditions were randomized, and a gait instructor stood beside the participant for the entire duration of the testing session to ensure safety and avoid eventually falls due to dizziness or postural instability.

Equipment

While performing all the turning tasks, subjects were equipped with a wireless continuous wave fNIRS system (OctaMon, Artinis Medical Systems, Elst, The Netherlands), designed to image the PFC of adult humans. The fNIRS device consisted of a headband with two light detectors and eight light emitters (wavelengths 760 and 850 nm) positioned over the forehead of the participants. The system used a diode laser, which emitted near-infrared light to reach the cerebral cortex. In the cortex, near-infrared light is absorbed in a different wavelength by HbO_2 and HHb, while another portion was scattered back to the surface, where it was measured.

The headband was placed in the standard 10–20 EEG placement to measure prefrontal activity (i.e. a height of 15% of the distance from nasion to inion and at 7% of the head circumference from left and right) (Ayaz et al., 2006). For the first eight participants, the detector–emitter separation was of 3.5 cm, which has been shown to allow light to penetrate about 1.75 cm into the skull (Maidan et al., 2015) and the sampling frequency was set to 10 Hz. For the subsequent participants, due to an update in the system, the fNIRS system was modified in order to remove the components of superficial interference (peripheral blood flow changes in extra-cerebral layers of the head), so the emitters distance was reduced to 1.5 cm for two out of the eight channels (Gagnon, 2012) (one channel on the right and one on the left). Also, the sampling frequency was set to 50 Hz. Potential differences due to the modification in the system were checked during the statistical analysis, as explained in the statistical analysis section and, since there were no differences, the two groups of participants were merged and included in the study. In addition, we assessed the spatial locations of all fNIRS channels in all of the tested participants using the Polhemus Patriot 3D digitizer. 3D co-ordinates included fNIRS channels and reference points of the Naision, Inion, left and right auricular regions to account for individual head size/shape variance. Data were then processed using NIRS-SPM in Matlab to allow for registration of the channel data onto Montreal Neurological Institute (MNI) standard brain space, which reported that the fNIRS recorded cortical activity over Brodmann areas 9 and 10 for all participants.

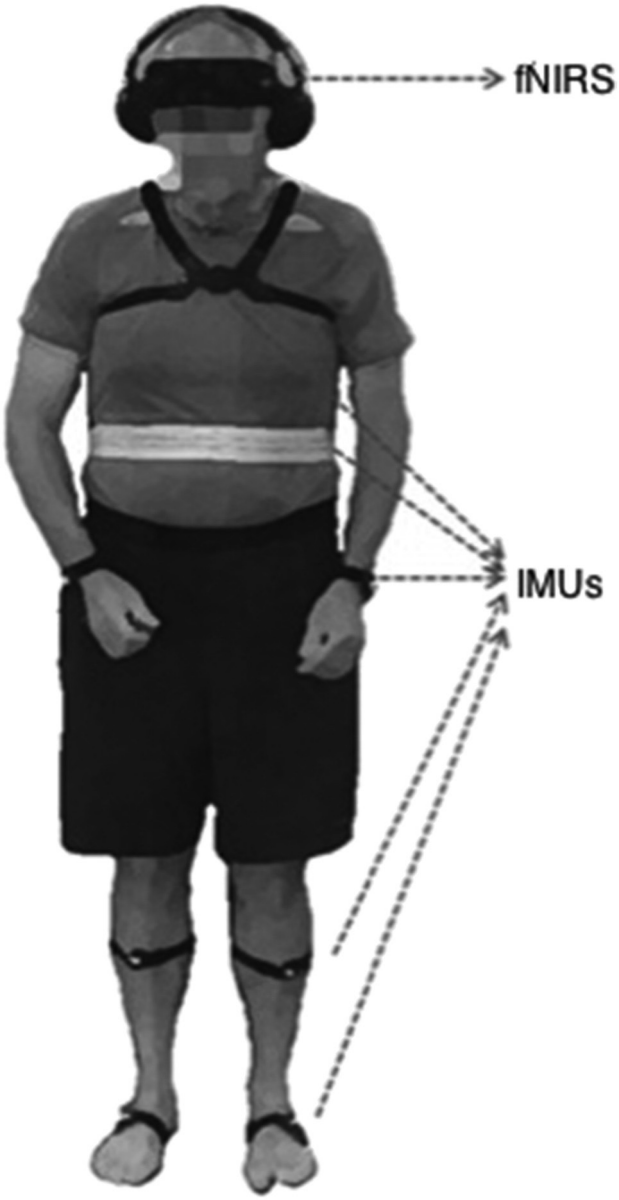


Fig. 1. Set-up example with the fNIRS headband on the forehead (a) and location of IMUs (b) on a participant’s body.

Turning execution was quantified with eight synchronized inertial measurement units (IMUs) (128 Hz, Opal, APDM, Portland, Oregon, USA) located at the sternum and pelvis levels, on the wrists, shanks and both feet of participants. Fig. 1a shows the fNIRS and IMUs placement. Each IMU consisted of tri-axial accelerometers, gyroscopes, and magnetometers, and were securely fixed to the participant’s body with Velcro straps. The fNIRS and the IMU system were synchronized through the Artinis PortaSync. The turning trials were also video recorded and reviewed to check for freezing episodes.

Data analysis

The primary outcome measure was the change (Δ) in HbO_2 while turning relative to standing. ΔHbO_2 was

chosen due to its sensitivity to walking-related changes in cortical activity (Miyai et al., 2001; Harada et al., 2009). Secondary outcome measures included ΔHHb and turning characteristics of velocity, duration, jerk and FoG ratio (Mancini et al., 2017).

fNIRS analysis. Data processing for fNIRS signals was conducted following current recommendations (Herold et al., 2017; Vitorio et al., 2017; Stuart et al., 2018). Using modified Beer–Lambert law, raw intensity measurements were converted to HbO_2 and HHb signals for each of the eight channels that cover the entire forehead. All channels were considered for analysis, apart from the participants with short-separation reference channels, for whom reference channel correction of the fNIRS signal was performed. This step corrected signal distortions due to artifacts caused by breathing, cardiac cycle, vasomotor or in general superficial interference (Tak and Ye, 2014; Herold et al., 2017). First, a scaling factor was determined by detecting the peaks (positive and negative) of the heart rate within the long and short-separation channel signals, then dividing them to produce the scaling factor. This was then used to remove the potential artifacts due to superficial interference detected within the short-separation reference channels within the long-separation channels. The following formulas describe the reference channel correction:

$$\textit{Scaling factor} = \frac{\textit{Peak to peak difference in heart rate in long seperation channel}}{\textit{Peak to peak difference in heart rate in short separation channel}}$$

$$\textit{fNIRS signal} = \textit{long separation channel signal} - (\textit{short separation channel signal} \times \textit{Scaling factor})$$

Then, a low-pass filter with a cut-off frequency of 0.14 Hz (Huppert et al., 2009) based on canonical hemodynamic response function, removed high-frequency noise (Friston et al., 2000) in all the channels. Subsequently, data were then zeroed to the initial baseline (first 20 s before starting to turn), and average across all six (in case of reference channel present) or eight channels (Maidan et al., 2018). Finally, the grand average of the HbO_2 and HHb traces during the trials was visually inspected to ensure divergence between HbO_2 and HHb traces, as a lack of divergence may indicate noise interference. Finally, the median value of the grand averaged HbO_2 signals was calculated during turning. Representative HbO_2 and HHb traces during standing and turning are shown in Fig. 2.

IMUs analysis. The following objective turning measures were estimated from the inertial sensors: the FoG Ratio (AD), an indicator of FoG severity, as proposed by Mancini et al. (2017), calculated from the antero-posterior shank acceleration signals; the average jerkiness (m^2/s^5), defined as the derivative of the acceleration measured along the unit medio-lateral axis, used to quantify fluidity of turning; the number of turns, computed by the participants during the trial, from yaw angular velocity of the sensor on the posterior trunk; the average duration (s) of every turn; the average turn peak angular velocity (degree/s) from the yaw angular velocity of the sensor on the posterior trunk. Turns were detected using the angular rotational rate of the sensor placed at the pelvis, measured by the gyroscope about the vertical axis, as proposed by El-Gohary et al. (2014). Fig. 2 also shows representative raw data of the angular velocity sensed at the lumbar level during turning.

Statistical analysis

The values ΔHbO_2 and ΔHHb, clinical assessment scores, and behavioral measures obtained by IMUs were examined for normality (Shapiro–Wilk Normality Test) and the resulting not normally distributed parameters were log-transformed. Z-score analysis was conducted so that the participants which presented a value that exceeded 3 standard deviations from the mean were considered as outliers and excluded. Then, the Levene's test was used to examine homogeneity of variance across the sample. Subsequently, data were analyzed as follows: i) paired or independent t-test was used to investigate whether there were differences between left and right hemisphere among participants, and whether there were differences in the clinical scores between PD + FoG and PD − FoG, ii) general linear models were fit, using the Restricted Maximum Likelihood Estimation (REML) to investigate whether outcomes differed between groups. We used the REML estimation over the ML to avoid bias due to our small sample size (McNeish and Stapleton, 2016). Each model was adjusted for group, task (ST versus DT), and the group*task interaction (to test whether groups had different linear trend between task conditions). Each model included a random intercept for each subject to account for the repeated measurements within each subject. To limit the comparisons and focus on overall group differences, only when a significant group effects was found, post-hoc analyses were performed (two-sample t-test, $p < .01$, Bonferroni correction). Lastly, Pearson correlations analyzed the associations between PFC activity and turning performance indices in PD + FoG and PD − FoG groups. The statistical analysis was performed using Matlab R2016b (The Mathworks Inc., Natick, MA, USA) and SPSS v24 (IBM Inc., IBM Corp., Armonk, NY, U.S.A.). A significance level of 0.05 was used for the linear mixed model analysis.

RESULTS

Participant characteristics and clinical scales scores

After the statistical analysis, two out of 34 participants initially involved in the study were excluded as considered outliers. Therefore, 32 PD (15 PD + FoG and 17 PD − FoG) participants were included in the subsequent analysis. All demographic characteristics and clinical scale scores are reported in Table 1. There were no differences in age or disease duration among groups. PD + FoG had worse disease severity (MDS-UPDRS Part III, $p \leq .05$) and poorer executive function (Trail Making Test Part B, $p \leq .01$) than PD − FoG. On

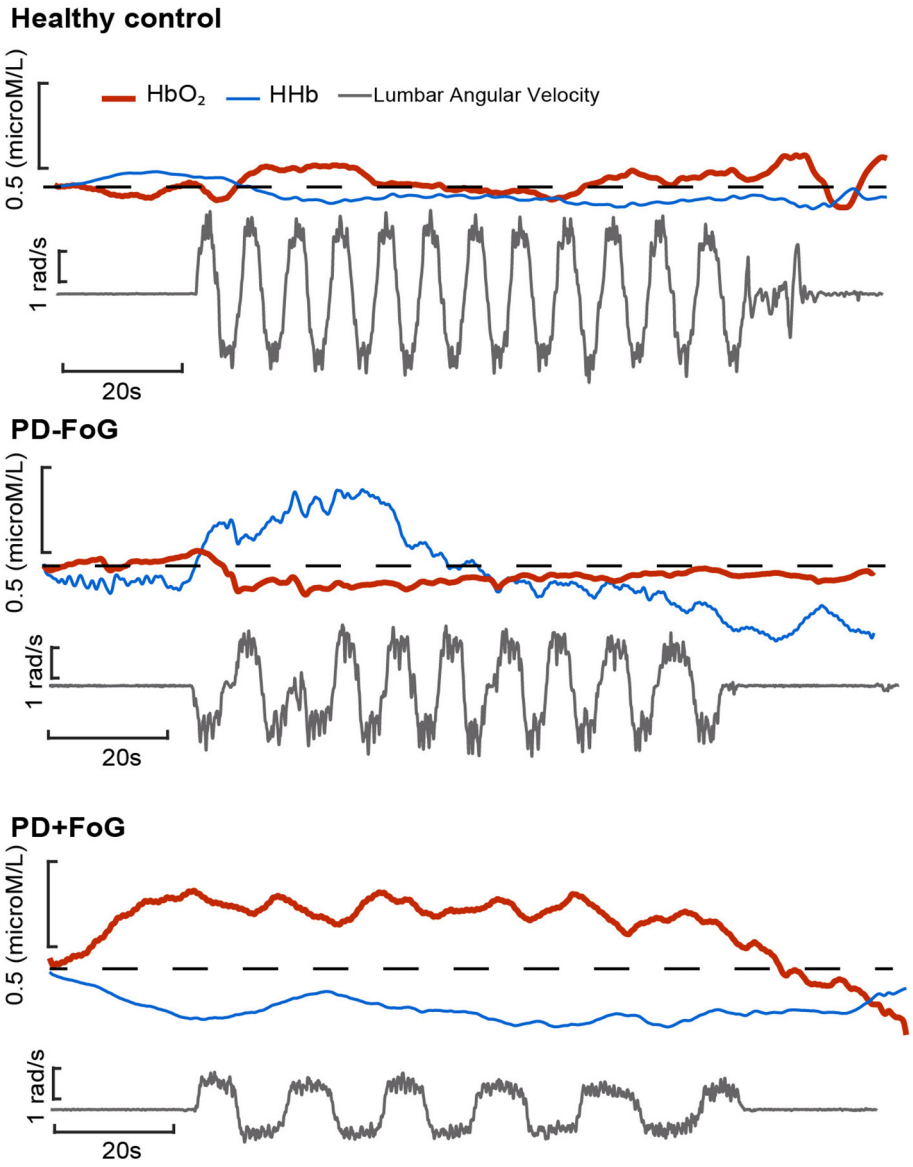


Fig. 2. Representative signals (HbO_2, HHb, and angular velocity of the lumbar sensor) during turning in a healthy control, PD − FoG, and PD + FoG. fNIRS was pre-processing as described in the method and this was the visual inspection step.

the other hand, PD − FoG had lower scores in the MoCA than PD + FoG ($p \leq .05$).

Video analysis results showed that in the PD + FoG group, 9 out 15 participants experienced from 1 to 3 FoG episodes while performing the ST turning. During the DT condition, 10 out 15 PD + FoG experienced from 2 up to 10 FoG episodes. Specifically, the total number of episodes during DT was higher compared to ST ($p = .001$).

HbO_2 concentration while turning is higher in PD compared to healthy controls

Our primary outcome measure, HbO_2 concentration while turning nearly reached significance in showing a group*task interaction effect ($F(1,75) = 4.05$, $p = .04$) and a group effect ($F(1,75) = 3.96$, $p = .05$), while it shows a significant task effect ($F(1,75) = 4.40$, $p = .03$). Overall, PFC may be higher in PD + FOG compared to the other groups, in the ST condition with an opposite trend for the DT condition, see Fig. 3. No group ($F(1,73) = 1.102$, $p = .33$), task ($F(1,73) = 0.017$, $p = .896$) or group*task interaction ($F(1,73) = 0.064$, $p = .93$) effect was significant for the HHb concentration.

Increased PFC activity during turning is associated with poorer turning performance and visuo-spatial abilities

Radar plots in Fig. 4 represent results of ΔHbO_2 correlation analysis between turning performance and clinical scale scores. In PD + FoG, a higher PFC activation while turning was associated with: a higher FoG Ratio (FoG Ratio, $r = 0.567$, $p = .048$), and worse visuo-spatial ability (CLOX2, $r = -0.669$, $p = .034$), in

Table 1. Participant demographic characteristics and clinical scores (Mean ± SEM) are reported.

	CTR	PD – FoG	PD + FoG	p value
Age	66.5 ± 5.5	69.9 ± 4.3	66.9 ± 5.0	0.205
Total of participants	8	17	15	0.076
No. of Participants (males)	5	13	11	0.065
Disease Duration (years)		9.35 ± 6.7	13.5 ± 6.0	0.083
MDS-UPDRS_Part III[a]		33.5 ± 11.2	46.9 ± 11.8	**0.006**
MoCA[a]	26.6 ± 1.9	25.4 ± 3.8	28.7 ± 1.3	**0.023**
FAB		13.7 ± 3.1	15.4 ± 2.4	0.277
Clock 1		12.1 ± 1.5	11.7 ± 0.8	0.610
Clock 2		13.7 ± 1.5	13.1 ± 5.5	0.299
TMT-A		45.4 ± 16.2	78.5 ± 71.2	0.167
TMT-B[a]		68.4 ± 24.5	129.9 ± 57.4	**0.010**
NFOGQ		0	14.2 ± 7.3	

[a] Significant differences ($p < .05$) between PD + FoG and PD – FoG.

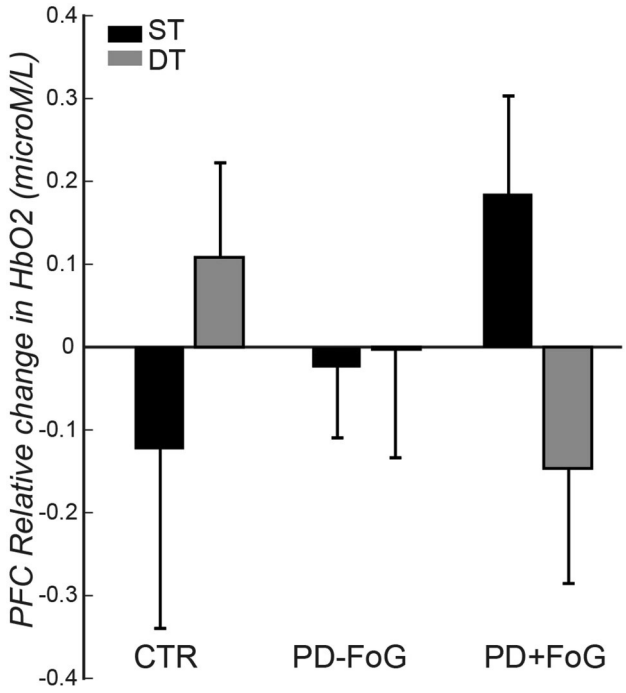


Fig. 3. PFC relative change in HbO_2 in CTR, PD – FoG, and PD + FoG, in both ST and DT conditions. Mean and standard error are displayed for each group.

the ST condition, whereas in PD – FoG, a higher PFC activity was associated with a lower number of turns completed ($r = -0.700$, $p = .002$) in the dual-task condition. For what concerns ΔHHb, correlation analysis results show that in PD + FOG a higher HHb is associated with a worse turning velocity ($r = -0.573$, $p = .040$) in the ST condition.

Accuracy of the cognitive task performed while seating does not show differences compared to the task performed while turning among groups

Due to technical issues with the Bluetooth synchronization, the DT accuracy was not evaluated in all participants: cognitive performance results have been reported, while seated, for 6 healthy controls (Accuracy, mean ± SEM = 1.00 ± 0.00), 14 PD – FoG (0.85 ± 0.16), and 8 PD + FoG (0.72 ± 0.22), and while turning (CTRs = 0.94 ± 0.03, PD – FoG = 0.91 ± 0.14, and PD + FoG = 0.75 ± 0.34). The performance measured during the concurrent cognitive task shows no group ($F(1,49) = 1.28$, $p = .2$), condition ($F(1,49) = 0.09$, $p = .9$) or group*condition ($F(1,49) = 0.34$, $p = .6$) effect.

People with PD show specific impairments in turning quality compared to controls

The turning behavioral measures are reported in Table 2. Overall, only group effects were significant across all measures ($F(1,72) > 4$, and $p < .04$). PD (both PD + FoG and PD – FoG) completed less numbers of turns during the tasks, turned slower, and took a longer time to turn compared to CTRs ($p < .001$). Changes in turning jerkiness were no longer significant across groups when considering a $p < .01$. Among all the objective measures of turning quality, only the FoG Ratio differed between PD + FoG and PD – FoG ($p = .009$). No task or group*task interaction effect was significant.

DISCUSSION

To our knowledge, this pilot study is the first to examine PFC activity, measured with fNIRS, during 360° turning-in-place in people with PD and in CTRs. Here we investigated the association between PFC activity and quality of turning measured with inertial sensors. Our findings showed that: i) PFC activity when turning during ST was greater in PD + FoG compared to PD – FoG and CTRs; ii) PFC activity when turning was associated with turn performance in PD (FoG Ratio and number of turns).

As expected, PD + FoG had worse disease severity and poorer executive function than PD – FoG, which support previous research (Amboni et al., 2008). Also in keeping with previous literature, video analysis results show that PD + FoG experienced FoG episode both during ST and DT, and the number of episodes in DT was higher than in ST (Nutt et al., 2011). In addition, similarly to previous work (Mancini et al., 2018), people with PD

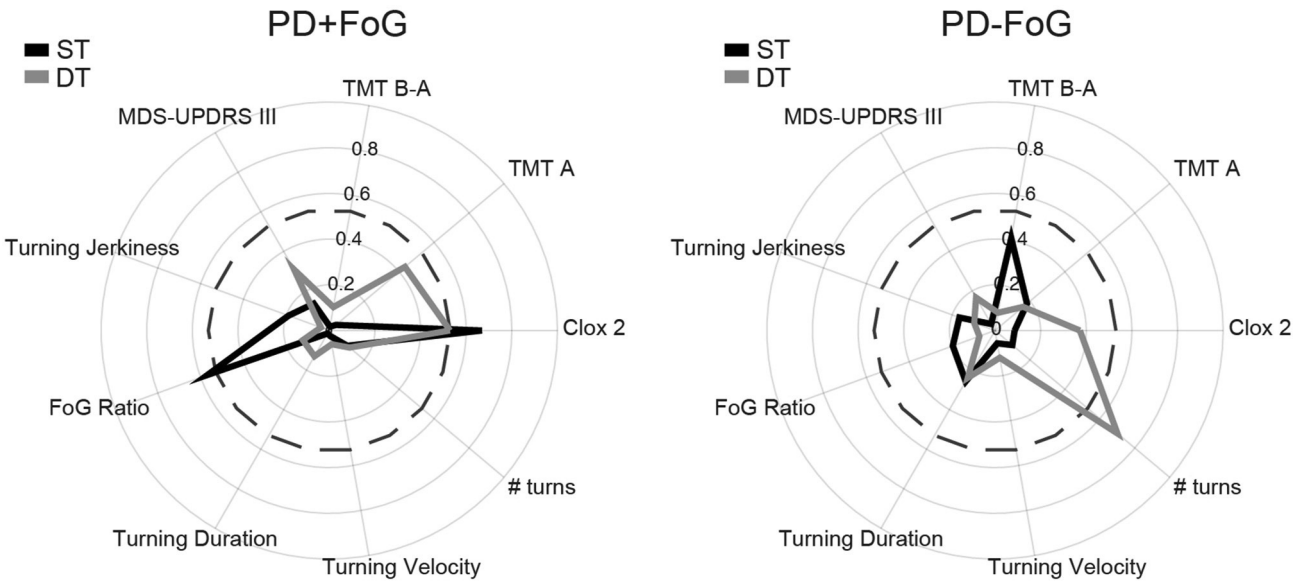


Fig. 4. Correlation analysis results between PFC relative changes, turning parameters, and clinical scale scores in PD + FoG and PD – FoG.

Table 2. Results of turning performance (Mean ± SEM) are reported. Linear mixed model results to investigate the group, task and group*task interaction are reported on the right side of the table.

		CTR	PD – FoG	PD + FoG	Group		Task		Interaction	
					F	p	F	p	F	p
Jerkiness	ST	0.27 ± 0.08	0.29 ± 0.01	0.33 ± 0.01	4.16	0.04	0.43	0.51	0.39	0.67
[m^2/s^5]	DT	0.25 ± 0.04	0.3 ± 0.01	0.35 ± 0.02						
FoG Ratio	ST	0.18 ± 0.06	0.26 ± 0.02	0.41 ± 0.04	8.55	0.01	3.43	0.07	2.25	0.12
[AD]	DT	0.21 ± 0.08	0.24 ± 0.02	0.52 ± 0.06						
Turn Duration	ST	3.7 ± 0.69	5.4 ± 1.1	7.2 ± 4.4	9.29	0.01	0.63	0.43	0.37	0.69
[s]	DT	3.6 ± 0.46	6 ± 2.0	7.3 ± 4.3						
Turn Peak Velocity	ST	158.9 ± 22.2	110.2 ± 26.9	99.9 ± 31.1	14.29	≤0.01	0.002	0.96	0.18	0.83
[degrees/s]	DT	160.9 ± 14.8	102.7 ± 26.1	100.7 ± 30.6						
# of Turns	ST	22.5 ± 2.6	15.3 ± 2.8	15.5 ± 3.2	29.23	≤0.01	1.08	0.30	1.11	0.34
	DT	24 ± 2.7	14 ± 3.6	15 ± 4.9						
Hhb	ST	−0.14 ± 0.48	−0.04 ± 0.29	−0.11 ± 0.19	1.10	0.33	0.017	0.89	0.06	0.93
[microML]	DT	−0.20 ± 0.51	−0.02 ± 0.32	−0.11 ± 0.24						
HbO_2	ST	−0.02 ± 0.46	−0.02 ± 0.35	0.18 ± 0.44	3.96	0.05	4.40	0.03	4.05	0.04
[microML]	DT	0.10 ± 0.34	−0.002 ± 0.5	−0.06 ± 0.41						

generally performed the 360° turning-in-place task worse than CTRs, as they were slower. The novel objective of this study was to observe PFC activity during a 360° turning-in-place task. Our results show a tendency towards a higher activation of the PFC in PD compared to CTRs, particularly for the PD + FOG group, confirming previous findings (Maidan et al., 2015) in which authors found a significant increase in PFC activity during a single 180° turn only in people with PD when a FoG episode occurred.

In the present study, two different PFC activity trends were observed; 1) within the ST condition, we found decreased activation of the PFC in CTRs, while PD + FoG had increased activation of the PFC; and 2) within the DT condition, an opposite trend was observed with respect to the ST condition. Executive projections stem from the PFC (Ridderinkhof et al., 2004); therefore, increased PFC activation when turning under ST in PD may indicate a greater requirement for executive control due to a loss of movement automaticity (Wu et al., 2015). Indeed, PD participants have difficulties in performing automatic as well as complex tasks, such as turning, likely due to an increased demand on the PFC in order to execute basic motor operations via executive–attentional processes (Wu et al., 2015). However, when considering the DT condition trends, while CTRs appeared to recruit the PFC to perform the cognitive DT, PD participants tended to have reduced PFC activation, which may indicate involvement of other cortical networks to execute a DT while turning.

Another interesting result was the significant association between increased PFC activity and poorer turning performance in both PD + FoG and PD – FoG. Specifically, while turning, higher PFC activity was related to higher FoG Ratio (PD + FoG, in ST) and a lower number of turns (PD – FoG, in DT). Such

association may indicate a marker of poor automaticity in PD, as higher PFC activation corresponds to worse motor performance, suggesting the involvement of executive function in performing the task. The need of increased PFC activation to perform the task may suggest a switch from automatic to voluntary cortical control, as already observed in previous research (Maidan et al., 2015).

Lastly, in keeping with previous studies (Mancini et al., 2017; Mancini et al., 2018), we showed no differences between healthy controls and people with PD in the accuracy of the cognitive dual-task, for both the seated and turning test. These results suggest that, even in situations that require keeping two tasks active in parallel, people with PD can accomplish the concurrent DT with a similar accuracy compared to healthy controls; in addition, the behavioral performance was similar between ST and DT with the exception of the FoG Ratio and number of FoG episodes (higher in DT compared to ST). In addition, the post-hoc tests carried out for the behavioral measures of turning showed that the FoG Ratio, an indicator of FoG severity, was the only parameter which discriminated between PD + FoG and PD − FoG, in line with our previous findings (Mancini et al., 2017). The absence of differences between PD + FoG and PD − FoG for the other behavioral turning parameters shows that disease severity, rather than episodes of freezing, might influence turn performance. In fact, in the present study, disease duration was similar across PD + FoG and PD − FoG.

Several study limitations should be acknowledged. First, the sample size of this study is relatively small, limiting the power of the analysis. Secondly, the used fNIRS system did not allow assessment of activation in other regions of the brain than the PFC or the involvement of neural networks, which future studies could examine. Furthermore, few technical issues with the Bluetooth synchronization did not allow to calculate accuracy of the DT in the entire group of participants: further improvements on the system will hopefully confirm the current accuracy assessment. In addition, the choice of the distance for short-separation fNIRS channels to control for superficial hemodynamics or systemic changes has been controversial; specifically, some papers showed 1.5 cm or less as optimal distance (Gagnon, 2012), while other recommended 0.8 cm for prefrontal regions in adults (Brigadoi and Cooper, 2015). Due to structure of our hardware, we physically could not place the channels at a smaller distance than 1.5 cm from the source. Therefore, with a distance of 1.5 cm instead of 0.8 cm or similar we might have lost some sensitivity; however, it should not be drastic. In fact, if we were to see a signal changing as much in the reference channel as in the deep channel, then most likely we would be seeing a global, systemic effect causing (part of) the change (Tachtsidis and Scholkmann, 2016). Our present study is examining, with synchronized equipment, both cortical activity and the behavioral performance, and the reliability of the present fNIRS preprocessing has been found to be good in turning and walking motor task in healthy young adults (Stuart et al., 2019b).

In summary, this preliminary study suggests the involvement of the PFC in people with PD while performing a challenging task such as a continuous 360° turning-in-place task. The increased activation of the PFC in people with PD compared to CTRs and the association between that increased PFC activity and poorer turning performance highlight the loss of automaticity in people with PD, with a switch to voluntary control. Although further investigations in a larger cohort are required to confirm these findings, the pilot findings could ultimately guide the development of personalized treatments to improve motor automaticity in PD.

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