Visuomotor control of walking in Parkinson's disease: Exploring possible links between conscious movement processing and freezing of gait

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Abstract

INTRODUCTION: Changes in visual attention have been argued to influence freezing of gait (FOG) in people with Parkinson's Disease (PD). However, the specific visual search patterns of people with FOG pathology (PD+FOG) and potential underlying mechanisms are not well understood. The current study explored visual search behavior in PD+FOG while walking on a pathway featuring environmental features known to exacerbate FOG (e.g., narrow doorway and tripping hazards). Potential attentional underpinning mechanisms were also assessed, such as conscious movement processing.

METHODS: Visual search behavior of twelve people with PD+FOG tested in ON-state (M_{age}=74.3) and twelve age-matched healthy controls (M_{age}=72.5) were analysed during a complex walking task. The task required participants to step over an obstacle and navigate through a narrow doorway, surrounded by clutter.

RESULTS: People with PD+FOG more frequently directed visual attention to ongoing and imminent steps compared to healthy controls (*Mdn*=26% vs *Mdn*=14%, respectively; p=0.042). Self-reported conscious movement processing was also significantly higher in people with PD+FOG. The one participant who froze during the walking task fixated the future trip hazard (obstacle, approximately 6 steps ahead) almost exclusively during freezing trials (i.e., 60-100% of the trial). In contrast, during 'non-freeze' trials, this participant increased the duration of fixations towards ongoing and imminent steps.

CONCLUSION: Results suggest that people with PD+FOG strongly monitor/control ongoing and immediately upcoming stepping movements. However, prolonged fixations towards threats to future movements might prevent people with PD+FOG from processing the visual information needed to do this, thereby provoke freezing episodes.

Keywords: Visual search; Gaze behavior; Freezing of gait; Parkinson's disease; Conscious movement processing; Anxiety.

Introduction

1.1 Parkinson's disease and freezing of gait

Parkinson's disease (PD) is a neurodegenerative disease characterised by both motor (e.g. disturbances in the control of posture and gait, bradykinesia, rigidity and tremor) and non-motor symptoms (e.g. cognitive dysfunction, anxiety and depression) [1–3]. Arguably, one of the most disabling motor symptoms of PD is freezing of gait (FOG). FOG is defined as "an episodic inability (lasting seconds) to generate effective stepping" (p. 424) [4], with individuals who experience FOG describing as if their feet are 'glued to the floor'. FOG is experienced by between 25% to 60% of people with PD, and is known to contribute to increased falls, loss of independence, and reduced quality of life [3,5,6].

Various motor and non-motor theories have been proposed to explain the underlying mechanisms of FOG [7–10]. Possible explanations include: the loss of automaticity of movement due to neurodegeneration in the basal ganglia-supplementary motor area loop; frontal executive dysfunction including problems in inhibition, divided attention and visuospatial function; a heightened reliance on online vision to maintain effective stepping, and; the accumulation of various motor impairments, such as impaired gait rhythmicity or impaired coupling of posture with gait [7–13]. However, there is no widely accepted theory that describes a singular pathogenesis of FOG. Consequently, designing effective therapeutic treatments to target this common and debilitating symptom of PD remains a significant challenge. Moreover, while FOG occurs more frequently in the 'OFF state' (i.e., when not taking dopaminergic medication [14]), FOG is often resistant to pharmacological and surgical interventions [8,15]. This emphasizes the need for novel rehabilitation and therapeutic strategies.

1.2 Anxiety and FOG

Although the precise underlying mechanisms are unclear, there is evidence that FOG is strongly influenced by anxiety [16,17]. Frequently reported freeze-inducing situations include those involving time-pressures (e.g., stepping on or off a train before the doors close) or confined spaces (e.g., walking through narrow passages or cluttered spaces), as well as during more complex walking tasks such as turning or dual tasking [18,19]—with these situations often accompanied by heightened stress and anxiety [16,20]. Indeed, when defining FOG, Giladi and Nieuwboer [4] highlight stress (and distraction) as key triggers of FOG episodes.

Direct evidence for a causal relationship between anxiety and FOG was described by Ehgoetz Martens and colleagues [16]. Here, inducing anxiety via a threatening environment in virtual reality led to an increase in the number and duration of freezing episodes. It has been suggested that anxiety may contribute to FOG via interference between the limbic, cognitive and motor circuits within the basal ganglia [16,21]. This may result in preferential attention being allocated towards processing threat-related stimuli, thus distracting attention away from other processes necessary for effective control of gait, such as consciously regulating an ongoing stepping movement [15,17]. Indeed, anxiety-related deficits in shifting attention between different processes is associated with exacerbated FOG [17]. However, little is known about the specific gait-related processes that anxiety may distract attention away from.

1.3 Parkinson's Disease and visuo-motor control during locomotion

Locomotion requires effective visual guidance to safely guide ongoing and future steps, particularly in complex environments [22–26]. In people with PD – and particularly in those with FOG (henceforth referred to as: PD+FOG) – visual guidance appears even more important, possibly to compensate for proprioceptive dysfunction [12,13,27–30]. Specifically, people with PD+FOG seem to rely more strongly on visual information to process ongoing stepping movements [12], a control strategy which likely reflects increased conscious processing of movement [12,31,32]. People with PD generally report an increased use of conscious movement strategies to regulate walking movements [33,34], particularly when walking in complex environments necessitating effective visuomotor control [34]. Such

conscious movement strategy likely reflects a potentially adaptive mechanism employed to overcome the loss of movement automaticity [35].

1.4. Anxiety and visuomotor control during walking

Given the above-described links between attention and visuomotor control of gait in PD (see also: [36]), a potential way through which anxiety may contribute to freezing in PD+FOG is by disrupting the visuomotor and attentional control of walking in this population. Anxiety has been shown to disrupt attentional processing during gait [37,38], and to lead to altered visuomotor control in healthy young and older adults [31,32,39,40]. Specifically, research highlights that anxious individuals will exhibit a visual bias towards (perceived) threatening stimuli [31,39,40], thus distracting attention from processing the visual information required for maintenance of effective locomotion.

In line with the above, while people with PD typically demonstrate an increased susceptibility to visual distraction by task-irrelevant stimuli during locomotion [41], people with PD+FOG may be particularly vulnerable to such distractions, due to deficits in cognitive inhibition coupled to a stronger reliance on visual information to regulate locomotion [12,42]. Beck et al. [12] reported that people with PD+FOG (compared to PD-no-FOG) purposefully kept their gaze fixated on the surface of the upcoming path – a control strategy causally associated with increased conscious movement processing in healthy young adults [31]. People with PD+FOG likely adopted such control strategy in an attempt to "decrease the perceived threat of the upcoming doorway" (p. 17) [12], and to ensure that attention is not distracted from perceiving the visual information required for effective locomotion (also see [11]). Indeed, in their definition of FOG, Giladi and Nieuwboer [4] specifically claim that symptoms can be overcome through "focused attention" (p. 424)—specifically towards aspects of stepping [7]. Based on these collective findings, we therefore hypothesize that failing to inhibit preferential (visual) attention being directed towards threat-related stimuli may be one possible trigger of FOG, due to the 'distraction' of visual attention away from necessary information to guide subsequent/imminent steps.

1.5. The current study

The current study aims to explore how people with PD+FOG use vision to control gait when confronted with environmental features known to exacerbate FOG (e.g., narrow doorway and environmental stepping constraints, such as a raised obstacle). We hypothesize that people with PD+FOG will rely on conscious visual monitoring to regulate gait to a greater extent than healthy age-matched adults. We hypothesize that this will manifest itself in visual search behaviors needed to consciously process both the ongoing and imminent steps, i.e., fixating 1–2 steps ahead [31–33]. We therefore predict that people with PD+FOG, as compared to healthy age-matched controls, will (i) report greater anxiety and conscious movement processing during gait, and (ii) fixate the immediate walkway to a greater degree (i.e., looking 1-2 steps ahead); given that such behavior is associated with heightened conscious processing of ongoing and immediately upcoming stepping movements [31,32]. This visual search behavior is hypothesized to occur at the expense of planning future stepping actions (i.e., previewing future areas of the walking path [31,32]). Finally, to distinguish adaptive from maladaptive (i.e., freezing-specific) visual search behavior, we aimed to compare trials in which participants with PD+FOG do, and do not, freeze. We hypothesized that participants with PD+FOG would freeze when they failed to allocate visual attention to the aspect of the walkway relevant to the planning/execution of imminent steps (e.g., instead fixating the doorway).

2. Material and methods

2.1 Participants

Twenty-four individuals participated in the study: Twelve individuals with idiopathic PD and twelve healthy age-matched controls. All participants in the PD group were classified as PD+FOG, as they answered ‘Yes’ to the first question of the New Freezing of Gait Questionnaire, “did you experience any freezing of gait episodes within the last month?” [43], and/or experienced an episode of freezing during a laboratory assessment [44]. All PD+FOG participants were taking dopamine replacement therapy, and testing occurred in the ON state of medication (approximately 1 h after taking a dose). People with PD+FOG were recruited from local Parkinson’s UK peer-support and exercise groups. Healthy age-matched controls were recruited from the community.

Exclusion criteria for both groups were cardiovascular, musculoskeletal or (for PD+FOG individuals, additional) neurological impairments, and inability to walk 15m without a walking aid. We also assessed participants' general cognitive function (Montreal Cognitive Assessment [45]), to ensure that none had severe cognitive impairment (MoCA<18). Due to the visuomotor control aspect of the research, participants were also excluded if they demonstrated either static visual acuity of less than 20/40 or significant deficits in contrast sensitivity (log contrast sensitivity score of 1). Prior to testing, we also assessed participants' executive function (Trail Making Test [46]), and working memory (WMS-III-digits [47]). Motor assessment involved fall history and Timed-Up-and-Go (TUG [48]). All participants also completed the Gait-Specific Attentional Profile (G-SAP [49]) to determine their gait-related (trait) anxiety and trait propensity to consciously control gait-related movements. The 11-item G-SAP consists of three 3-item subscales (anxiety [e.g., "I feel tense"], conscious movement processing [e.g., "I consciously try to control the way I move"] and fall-related ruminations [e.g., "Worrisome thoughts about falling run through my mind") and one 2-item subscale (processing inefficiency [e.g., "I find it difficult to concentrate on two things at once"). This assessment requires participants to answer how they generally feel when they walk, rating items on a 5-point Likert scale (1 = not at all; 5 = very much so). Subscale scores range from either 3-15 (anxiety, conscious movement processing and fall-related rumination) or 2-10 (processing inefficiency).[1] For the PD+FOG group we also recorded the time since diagnosis, Hoehn-Yahr stage [50], UPDRS-III [51], and item B.1.3. on the Freezing of Gait Questionnaire [52,53]. Please see Table 1 for participant characteristics.

Institutional ethical approval was obtained from the local ethics committee and the research was carried out in accordance with the principles laid down by the Declaration of Helsinki. All participants provided written informed consent prior to participation.

2.2 Procedure

All participants completed six walking trials on an 8-meter pressure-sensitive walkway (GAITRite™; CIR Systems Inc. Clifton, NJ). The walking task required participants to adapt

[1] The G-SAP questionnaire can be accessed through the following repository: https://osf.io/8jbaf/

their gait by negotiating both a 20cm high wooden obstacle (placed halfway along the path) and a narrow doorway at the end of the walkway. The doorway width was adjusted to 105% of the participant's shoulder width, as FOG is known to be more frequent when walking through narrow doorways [27,28]. The walkway was surrounded by 'clutter' (standardized for each participant), which consisted of chairs, bins and stools (see Figure 1a).

Participants were fitted with a Mobile Eye-XG portable eye-tracking system (ASL, Bedford, MA) that records participants' gaze wirelessly at 30Hz. The eye-tracker was calibrated beforehand for each participant. Participants were then instructed to stand still at the beginning of the walkway with their eyes closed (to prevent previewing of the walkway). As soon as they heard a predefined auditory tone, they were asked to open their eyes and start walking at a self-determined pace. They were instructed to step over the obstacle and continue walking through the doorway, before turning left and returning to the starting position.

*** Figure 1 near here***

2.3 Data analysis

2.3.1 Gait analysis. Gait performance was analysed using the GAITRite^{TM} system, recording the following variables: velocity (cm/s), stride velocity (cm/s), stride velocity variability, step length (cm), step length variability, step time (s), step time variability, base of support (cm), and single and double limb support (% of gait cycles).

2.3.2. Freezing analysis. Freezing episodes were analysed through video analysis (recording at 50Hz). FOG was defined as a transient inability to generate effective stepping, often leading to a halt [7]. More specifically, a trial was rated as a freezing trial when the participant failed to make a successful step, i.e., when displaying one or more heel off movement(s) without moving forwards. Two raters (LH & TJE) visually analysed all trials independently. When no consensus was reached, a third independent researcher was adopted (EK). However, initial inter-rater agreement was 100%, so the third rater was not consulted. This procedure has been validated in previous research [54–56].

2.3.3 Gaze behavior. Visual fixations were defined as a gaze that endured on a single location for three frames or longer [57,58]. Fixations were classified as towards either: (1) the

immediate walkway (i.e., the current and immediate stepping areas before the obstacle), (2) the obstacle itself, (3) future areas beyond the obstacle (including towards the doorway), and (4) task-irrelevant areas outside of the walkway (e.g., towards the clutter) (Figure 1). Fixations towards walkway areas beyond the obstacle (i.e., the walkway area behind the obstacle and the doorway) were combined into a single area of interest ("future areas"), as fixations on the pathway after the obstacle were primarily focused on the walkway directly in front of the doorway. Fixation durations were analysed from the occurrence of the first fixation until when participants initiated the step towards the obstacle (i.e., toe-off when stepping over the obstacle), as identified through video analysis (see Section 2.3.2). These systems were synchronised via identifying the frame in which the auditory 'go' tone occurred that indicated the beginning of the trial.

The primary variable of interest for the eye-tracking analysis was the duration of visual fixations on the four separate areas of interest (as a percentage of total fixation duration). Variables were averaged across each participant. Trials in which the crosshair disappeared for five frames or more, and for which it was not possible to analyse the eye-tracking data, were discarded. Participants with a trial-discard rate higher than 50% were excluded from eye-tracking analyses (i.e. participants were only included in analyses if they presented three-or-more usable eye-tracking trials). This procedure resulted in the exclusion of ten trials in total, and no participants excluded from eye-tracking analysis. A total of 63 trials were analysed for the PD+FOG group (M=5.25 trials per participant) and 71 trials for the healthy control group (M=5.92 trials per participant).

2.4 Statistical analysis

Data was analysed using SPSS and significance was set at an alpha level of 0.05. First, potential differences between the PD+FOG and healthy control group in demographic, motor and cognitive function were explored using the appropriate statistical tests (i.e., chi-square for dichotomous variables, Mann-Whitney U tests for all other variables given the non-normal distribution of the data). Next, we used independent t-tests to compare the gait variables between the PD+FOG (during non-freezing trials only) and healthy control group. Our main analyses concerned multiple non-parametric Mann-Whitney U tests to compare G-SAP-scores

and gaze variables (both were non-normally distributed) between the PD+FOG and healthy control group. We used one-sided tests to compare gait-related anxiety and conscious processing (G-SAP-Anxiety & Conscious movement processing), the duration of fixations on the four areas of interest between PD+FOG and healthy control group, in addition to gait outcomes. This procedure was justified given our clear directional hypotheses for these outcome measures [59,60]. For the purpose of consistency, we calculated the same effect size measure (*r)* for all comparisons, using the following formula: $r = \frac{z}{\sqrt{N}}$ [61].

As only one participant with PD+FOG (Participant 6) demonstrated freezing *during* the walking trial, we were unable to run our originally planned within-group analysis of gaze variables between the trials where people with PD+FOG did and did not freeze. As reported in previous research, FOG is notoriously difficult to induce in a laboratory setting [62]. Unfortunately, the current study encountered the same problem. Hence, for Participant 6 we instead adopted a case-study approach (similar to that utilized previously by Schlenstedt et al. [54]) and performed a more in-depth analysis of this participant's gaze behavior (and G-SAP scores). Visual search behavior was assessed on a trial-by-trial basis, specifically contrasting changes in visual search behavior over time, highlighting the 4 freezing and the 2 non-freezing trails.

3. Results

3.1 Participant Characteristics

The characteristics of participants with PD+FOG (N=12) and healthy age-matched controls (N=12) are summarized in Table 1. Group differences were observed in some aspects of motor and cognitive function; PD+FOG had worse scores on the TUG (p<0.001, r=0.937), MoCA (p=0.010, r=0.523), and TMT-A (p=0.044, r=0.511; Table 1). Please note that we also highlighted the characteristics of the one participant who froze (PD+FOG P6) during the experiment (see section 3.3).

*** Table 1 near here***

3.2. Between-group differences (PD+FOG and healthy age-matched controls)

3.2.1 Gait-Specific Attentional Profile (G-SAP). Significant differences in G-SAP scores were found between groups (Figure 2). As expected, the PD+FOG group reported greater (trait) Conscious Movement Processing (*Mdn*=10.5, *IQR*=5.25) during walking compared to healthy age-matched controls (*Mdn*=6, *IQR*=3.5; *Z*=2.811, *p*=0.002, *r*=0.574). The PD+FOG group also reported significantly greater trait-Anxiety (PD+FOG: *Mdn*=8, *IQR*=5.75; Controls: *Mdn*=3, *IQR*=0; *Z*=3.590, *p*<0.001, *r*=0.733), and Processing Inefficiency (PD+FOG: *Mdn*=4.5, IQR=2.5; Controls: *Mdn*=2.5, IQR=1.75; *Z*=2.494, *p*=0.014, *r*=0.509). There were no differences in self-reported Fall-related Ruminations (PD+FOG: *Mdn*=6.5, *IQR*=5.5; Controls: *Mdn*=4.5, *IQR*=3.5; *Z*=0.964; *p*=0.347, *r*=0.197) during gait in daily life.

*** Figure 2 near here***

3.2.2 Gait characteristics. Due to technical issues, GAITRite data for one PD+FOG participant was excluded from GAITRite analysis. Compared to age-matched controls, gait in people with PD+FOG was characterised by significantly lower walking speed ($t(21)=4.229$, $p<0.001$, $r=0.882$), reduced stride velocity ($t(21)=4.209$, $p<0.001$, $r=0.878$), greater step time ($t(21)=1.775$, $p=0.025$, $r=0.370$), in addition to shorter step lengths ($t(21)=4.886$, $p<0.001$, $r=1.019$) and greater step length variability ($t(21)=1.781$, $p=0.025$, $r=0.371$; see Table 2). Further, single limb support duration was reduced in people with PD+FOG ($t(21)= 2.086$, $p=0.025$, $r=0.435$), with double limb support was significantly increased ($t(21)=2.011$, $p=0.029$, $r=0.419$). All other measures were statistically similar between groups (t's$(21)\leq1.423$, p's≥0.085, r's≤0.295).

Table 2 near here

3.2.3 Gaze behavior. Compared to controls (*Mdn*=14.1%, *IQR*=27.7), the PD+FOG group spent a significantly greater proportion of time fixating the immediate walkway

(*Mdn*=26.4%, *IQR*=29.0; *Z*=1.73, *p*=0.042, *r*=0.353; Figure 3). The PD+FOG group spent a somewhat smaller proportion of time fixating future walkway areas (*Mdn*=4.7%, *IQR*=20.7) compared to controls (*Mdn*=15.2%, *IQR*=27.8), but this difference was not significant (*Z*=1.4, *p*=0.083, *r*=0.283). There were no between-group differences in the proportion of time spent fixating either the obstacle (PD+FOG: *Mdn*=59.7%, *IQR*=37.1; Control: *Mdn*=64.6%, *IQR*=10.2; *Z*=0.520, *p*=0.603, *r*=0.106) or areas outside of the walking path (PD+FOG: *Mdn*=0%, *IQR*=0; Control: *Mdn*=0%, *IQR*=0; *Z*=0.603, *p*=0.547, *r*=0.123).

*** Figure 3 near here***

3.3 Within-subject changes in gaze behavior between non-freezing and freezing trials.

In this section, we take a closer look at the gaze behavior[2] of Participant 6; the only PD participant who experienced freezing episodes during the walking trials.[3] As can be seen in Table 1, this participant was relatively old (83 years of age), and had somewhat less favourable scores on item 3 of the FOG-Q questionnaire, in addition to measures of general motor function (TUG) when compared to the rest of the PD+FOG group. However, PD-specific variables (e.g. UPDRS, years since diagnosis) were similar to the rest of the group, while scores on the cognitive tests were relatively high.

Figure 4 depicts participant 6's visual search data over the six walking trials. Freezing episodes occurred in four trials (trials 1-3 and trial 6). This consisted of five total freezes (3 trials = 1 freeze, 1 trial = 2 freezes). In each instance, the freeze occurred directly preceding the obstacle, and the mean duration of freezing episodes was 1.21 seconds (*SD* = 0.50). As gaze tracking data were analysed until the point in which the step over the obstacle was initiated, this within-subject analysis thus contains data both preceding, during, and following the freezing episode.

[2] As freezing trials disrupted GAITRite recordings, we could not compare gait characteristics between freezing and non-freezing trials. However, GAITRite data for the non-freeze trials was included in the main between-group analyses.

[3] It should be pointed out that another participant also experienced a single freeze during the experiment. However, this occurred only once, directly *after* completing the first walking trial, but not during the actual trial itself (i.e., following the completion of the trial itself, and when walking back towards the 'start line'). Consequently, this participant was not included in this section.

3.3.1 Gaze behavior. As Figure 4 illustrates, during the first three freezing trials, this participant largely prioritised fixating the obstacle (fixating this for between 90-100% of the approach towards the obstacle). However, during the following two non-freezing trials, the duration of fixations was spread more evenly across each of the three areas of interest (immediate walkway, obstacle, future walkway areas). Of particular note, fixations towards the immediate walkway (a gaze behavior associated with greater conscious movement processing) increased to approximately 30%. During the final freezing trial, the participant once again directed preferential attention towards the obstacle (fixating this area for approximately 60% of the approach), and did not fixate the immediate walkway a single time (0% fixation duration). It is, however, worth noting that the duration of fixations on future areas during this final freeze trial (approximately 40%) was substantially greater than those observed during the first three freeze trials (0%), and was instead generally comparable to gaze behavior observed during the two non-freeze trials.

***Figure 4 near hear ***

3.3.2 Gait-specific Attentional Profile. As depicted in Figure 2, participant 6 showed the highest score on conscious movement processing (RS = 14) and one of the highest scores (RS = 6) on processing inefficiency compared to the rest of the PD+FOG group on the Gait-specific Attentional Profile. Scores on gait-specific anxiety (trait) and gait-specific fall-related ruminations are in the lower part of the range compared to the rest of the PD+FOG group.

4. Discussion

The aim of the present study was to explore (1) whether people with PD+FOG report greater conscious movement processing during gait, and display visual search behaviors indicative of conscious movement processing of individual/ongoing steps (compared to healthy age-matched controls), and (2) if freezing episodes are associated with the disruption of these processes. Accordingly, we will first discuss and interpret the main findings of the between-group comparison of people with PD+FOG and healthy controls, before discussing the within-

subject changes in visual search that we observed in the participant who showed freezing during the walking trials.

4.1 Between group differences in visual search, gait-specific conscious processing, and gait characteristics

As predicted, people with PD+FOG spent more time fixating the immediate walkway compared to controls, and reciprocally tended to fixate future areas less. These results suggest that people with PD+FOG visually prioritise ongoing stepping actions at the expense of directing attention to future walkway areas. Further, we found that people with PD+FOG exhibited patterns of cautious gait, characterised by – among other behaviors – slower gait, shorter steps, increased double limb support and greater step length variability. Finally, people with PD+FOG reported significantly greater gait-specific conscious movement processing, anxiety and processing inefficiencies during walking in daily life.

Between-group results suggest that people with PD+FOG direct preferential attention towards immediate areas of the walkway (approximately one to four steps ahead) at the expense of planning future steps. These findings are consistent with previously observed [12] and self-reported [11] gaze behavior in people with PD+FOG. Similar gaze patterns have been observed in both anxious healthy older adults reporting greater conscious movement processing [32] and in young adults during experimentally-induced conditions of conscious movement processing [31]. We therefore interpret the prioritization of the immediate walkway in people with PD+FOG to reflect increased conscious movement processing. This interpretation is further corroborated by our PD+FOG sample reporting that they consciously process their walking movements to a greater extent than healthy controls. Further, the gait characteristics observed in the PD+FOG group (lower walking speed, greater step time, shorter and more variable step lengths, and increased double limb support) all suggest a more consciously processed, conservative gait behavior [63,64]. These observed gait patterns are also consistent with earlier studies on gait in people with PD+FOG [27,65,66]. Future large-scale research could look to further explore the association between visual search behavior and patterns of gait indicative of more conscious forms of locomotive control (e.g., increased gait variability [63]) in people with PD+FOG.

An important question relates to whether directing preferential attention to the immediate walkway (and the associated heightened conscious movement processing) is unique to people with PD+FOG, or whether this visual search strategy is characteristic of PD in general (irrespective of freezing). It is important to emphasize that the group differences in visual search discussed above concern the visual search patterns in *non-freezing* trials. In a way, the people with PD+FOG were thus showing *adaptive* visual behavior that may have prevented them from freezing. Indeed, people with PD+FOG often report the need to consciously disengage attention from threatening freeze-related stimuli, such as doorways and narrow apertures [11], and Giladi and Nieuwboer [4] claim that FOG symptoms can be overcome through "focused attention" (p. 424)—specifically towards aspects of stepping [7].

Previous research has shown that PD in general (i.e., not only PD+FOG) is associated with greater conscious processing of walking movements [33,34]. On this basis, the overall group results presented here may well be similar to visual search behavior in people with PD who do not experience freezing in daily life; particularly if these behaviors are indeed a consequence of and/or required to engage in conscious movement processing (as suggested above). However, the absolute level of conscious processing required may well be higher in people with PD+FOG than in people with Parkinson's who do not experience FOG. For instance, advanced PD is associated with both increased FOG prevalence [67–69] and greater self-reported conscious processing [70]. People with PD+FOG specifically report that they need to actively direct their gaze to their feet and the intended walking path to improve gait control during walking in daily-life environments [11]. Moreover, Beck et al. [12] found that people with PD+FOG (compared to people with PD but without FOG) will look more frequently, and for longer durations, at the pathway they are currently walking on. Thus, while we did not include a PD-no-FOG group in the present research, we deem it likely that these individuals would be positioned somewhere between healthy controls and PD+FOG on the continuum of conscious movement processing; fixating ongoing and immediately upcoming steps to a greater degree than healthy controls, but less than PD+FOG. This idea is additionally supported by previous research by Almeida and Lebold [27]. In this study, both PD+FOG and PD-no-FOG exhibited similar patterns of cautious, more variable gait when approaching a

doorway (compared to healthy controls), but the magnitude of these effects was less pronounced for PD-no-FOG.

In people with PD+FOG, conscious movement processing – and associated changes in visuomotor control of gait – may compensate for reduced proprioceptive function reported in this population [71]. Such motor control strategy may thus help ensure accurate foot placement in the absence of reliable proprioceptive feedback [12,29]. Therefore, while PD in general is likely characterised by increased conscious processing of gait (and hence biased visual attention towards ongoing and immediately upcoming steps), we suggest that failing to successfully use this strategy may be especially detrimental to people with PD+FOG – and thereby result in a freeze. The next section describes the within changes in visual search between freezing and non-freezing trials in Participant 6, which appear to support this perspective.

4.2 Within-subject differences in visual search during freezing and non-freezing trials

The within-subject comparison of freezing and non-freezing trials of Participant 6 revealed marked differences in visual search. During freezing trials Participant 6 fixated almost exclusively on the obstacle, but this was at the expense of either regulating ongoing steps (i.e., fixating the immediate walkway) or planning future stepping actions (i.e., fixating future walkway areas beyond the obstacle). This seems to resemble the attentional bias for threatening stimuli that has been observed previously in anxious (healthy) individuals during obstacle stepping tasks [39,40]. Indeed, individuals with PD demonstrate difficulty with obstacle crossing [30,72,73], and often express concerns about their safety during such tasks [11]. Hence, we infer that Participant 6 likely perceived the obstacle as a threat.

By contrast, during non-freezing trials Participant 6 showed markedly reduced duration of fixations towards the obstacle, and instead had increased duration of fixations towards the immediate walkway and future areas. During the final freeze trial, however, the duration of fixations on future areas (approximately 40%) was substantially greater than those observed during the first three freeze trials (0%), and was instead comparable to gaze behavior observed during the two non-freeze trials. In contrast, fixations towards the immediate walkway remained consistently low during all freezing trials (approx. average of 5%). Consequently, we

suggest that it is this specific visual search process – fixations (or lack of) towards immediate walkway areas – that are associated with freezing episodes.

Participant 6 also scored the highest on the Conscious Movement Processing G-SAP-subscale. This suggests that conscious movement processing was crucial for this participant to effectively control locomotion in daily life. Directing attention to the obstacle will likely have distracted the participant and made it difficult to maintain the level of conscious processing required for effective walking – given that directing visual attention to the ongoing/imminent step appears to be a requirement of such form of motor control [31]. Our findings imply that this may have contributed to the observed freezing episodes leading up to the obstacle.

4.3 Anxiety, conscious movement processing and freezing of gait

Combined, the above results suggest that people with PD+FOG increase conscious control to guide stepping, and that disrupting this process may lead to freezing episodes. Results of Participant 6 suggest that an excessive visual bias toward stimuli which threaten locomotion (e.g., in this instance the obstacle, given that this repeatedly triggered FOG) may be an especially powerful distractor. This interpretation would be in line with Attentional Control Theory (ACT [74]). ACT suggests that anxious performers have the tendency to direct attention away from task-relevant cues towards threat-related (task-irrelevant) stimuli, affecting task performance [74,75]. Such task-irrelevant stimuli can be internal, e.g., worrisome thoughts about the task, or external, e.g., in the form of threatening distractor stimuli [76].

Anxiety is a widespread problem in people with PD, particularly in those who experience FOG [20]. This finding was also evident in our sample, as people with PD+FOG scored significantly higher on the anxiety subscale of the G-SAP, compared to healthy aged matched controls. In the context of ACT, individuals with PD will therefore likely be more vulnerable to the distracting effects of threatening stimuli. However, we propose that the effects of distraction may be more detrimental compared to healthy adults, and even result in freezing due to a ‘perfect storm’ of a combination of factors: (i) impaired ability to inhibit threat-related distractors, (ii) reduced ability to divide attention [16], and (iii) the lack of automatic motor

control system to "fall back on" when distracted. This assumption fits with the idea that basal ganglia processing is more easily overloaded by simultaneous limbic/cognitive/motor processing demands in individuals with PD, leading to a freezing episode [16,21]. Such claim is further supported by the results observed in the present study, whereby people with PD+FOG reported increased gait-specific processing inefficiency. Increasing conscious movement processing might help direct attention away from threatening stimuli, and thereby decrease the demand on processing resources necessary to operate stepping and prevent a (potentially freeze-inducing) processing overload [12,15].

4.4 Practical implications

As deficits in automatic processing are at the core of PD, it is expected that conscious top-down processes are necessary to control stepping movements, especially when dopaminergic medication is wearing off [77]. Indeed, our results suggest that people with PD+FOG need to consciously control their stepping to navigate complex walking environments, and that threatening stimuli distract the individual from conscious movement processing, potentially leading to a freeze. Practical implications of the current findings might include the development of interventions targeting maladaptive gaze behavior by encouraging conscious control of movement to guide every step. Improving visual sampling strategies by instructing people with PD+FOG to direct gaze one or two steps ahead while walking (encouraging conscious movement processing [31,32]) and preventing hypervigilance towards threats, might therefore be an effective intervention to target freezing of gait. Similar visuomotor control training paradigms have been tested before in older adult population and proved effective [78]. Analogies, such as "imagining your own footprints in the sand" [79], could form effective implicit strategies that would help people with PD+FOG to maintain focus without potentially overburdening already limited processing resources with a large set of movement rules.

4.5 Limitations and Directions for Future Work

The current study is the first that explicitly compares visual search behavior in trials where a freeze occurs to trials where a freeze does not occur; however, within-trial freezes

were rare and only observed in a single participant. It is likely that our decision to test participants during the ON state of dopaminergic medication contributed to the low number of within-trial freezes observed. However, FOG is known to persist to some degree even following 'full' (i.e., ample dopaminergic dosage) ON state [80]. Furthermore, as every PD+FOG participant in the present research took dopaminergic medication, testing in the ON state allowed for a representative assessment of the visuomotor and attentional processes occurring during everyday (i.e., medicated) freeze-provoking situations. The present findings therefore contribute, to a greater extent, to our representative understanding of triggers of FOG in daily life rather than the pathophysiological underpinnings of FOG. Future work should look to replicate this study during both ON and OFF states—especially considering that individuals who experience FOG during ON state may be distinct from those that only experience FOG when off medication [80].

Due to a small sample size, and high levels of heterogeneity in PD, future work should also look to confirm the present results in a larger sample. A larger sample would also (likely) produce more freezing trials, thus allowing for the case study results from Participant 6 to be extended to a larger cohort. Moreover, as noted previously, the current design does not include a non-freezing PD group which make it difficult to determine whether the observed results are specific to people with PD+FOG or individuals with PD in general. While the current design is common in FOG research (e.g., [28,81]), future research should nonetheless explore whether the findings in our cohort of people with PD+FOG are also applicable to people with PD in general. Further, future research should investigate a potential causal link between visual search patterns and FOG, and the potential mediating role of gait-specific attentional factors (e.g., conscious movement processing).

A final note concerns the operationalization of conscious movement processing and threat-related visual processing. In the present research, we considered gaze directed towards the walkway areas needed to process ongoing movements/plan short-term movements (e.g., the immediate walkway) to be indicative of conscious movement processing (as per [31,32]). While we should be cautious when attempting to infer cognitive processes from visual search behavior alone, when combined with the self-reported conscious movement processing, and the gait performance outcomes (e.g., increased variability), we suggest these visual search

behaviors likely reflect the heightened conscious movement processing reported in our cohort, and the conscious (visual) processing of individual stepping movements reported previously by people with PD [33]. Relatedly, we interpreted the increased fixations towards the obstacle observed in Participant 6 during freezing trials to resemble the attentional bias for threatening stimuli that has been previously reported in anxious individuals during obstacle stepping tasks [39,40]. Indeed, as the obstacle repeatedly triggered FOG in this participant – and, thus, represents a threat to locomotion – the direction of preferential attention towards this walkway area seemingly reflects a gaze bias for threatening stimuli. However, future research could look to confirm such interpretation by assessing physiological threat-responses, such as heart rate variability or skin conductivity outcomes.

5. Conclusion

The present findings suggest that due to the deterioration of automatic movement control, people with PD+FOG need to direct visual attention to their ongoing and immediately upcoming steps to allow for effective conscious movement processing. However, prolonged fixations towards distracting stimuli (in this instance, threats to balance) might prevent people with PD+FOG from consciously controlling their movements effectively, thereby provoking or contributing to freezing episodes. This suggests that strategies that promote conscious processing of ongoing stepping movements and/or those that prevent attention from being distracted by threatening stimuli may be successful in reducing freezing episodes.

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Tables

Table 1. Characteristics of people with PD+FOG and healthy age-matched controls.

	PD+FOG (N=12) Mean±SD (range)[a]	Controls (N=12) Mean±SD (range)[a]	*p*	PD+FOG *PT 6*
General Characteristics				
Age in years	74.3±5.2 (64-83)	72.4±5.2 (64-82)	0.266	83
Sex (m/f; n)	7/5	5/7	0.414	Male
PD-specific information				
Years since diagnosis	9.1±4.1 (3-15)	N/A		4
Hoehn Yahr Stage (1-5)[b]	2±0 (2-4)	N/A		2
UPDRSIII (0-56)	15.3±7.8 (6-31)	N/A		9
FOGQ-item 3b (0-4) [b]	3±0.8 (0[c]-3)			3
Motor function				
Falls in past 6 months[b] (n)	0±4 (0-10)[d]	0±1 (0-5)[d]	1.000	4
TUG (s)	12.9±2.2 (9.1-16.7)	9.3±1.3 (6.7-10.9)	**<0.001**	16.7
Cognitive function				
MoCA (0-30)	26.4±2.0 (22-30)	28.6±1.8 (24-30)	**0.010**	27
WSMIII Digit (0-30)	16.8±4.0 (10-23)	15.5±4.0 (13-27)	0.242	19
TMT-A (s)	47.3±17.1 (27-81)[d]	32.2±9.4 (19-55)	**0.044**	35.0
TMT-B (s)	132.6±72.5 (59-300)[d]	87.3±26.0 (56-150)	0.118	71.0
TMT-B-A (s)	85.3±62.8 (29-233)[d]	55.0±22.5 (30-120)	0.316	36.1

NB: Variables that are significantly different between groups are emphasized. The data for the one participant who froze ('PD+FOG P6') during the experiment is highlighted in the last column.

[a] Unless indicated otherwise; [b] Data expressed as median ± interquartile range (total range); [c] One participant answered '0' because freezing only happened when *initiating* walking from certain positions, not *during* gait; [d] Data missing for one group member; Abbreviations: f = female; FOGQ = Freezing of Gait Questionnaire – item

3; m = male; MoCA = Montreal Cognitive Assessment; n=number; N/A = Not applicable; PD = Parkinson's Disease; TMT = Trail Making Test; TUG = Timed-up-and-Go; UPDRSIII = Unified Parkinson's Disease Rating Scale, section 3; WSM-III = Wechsler Memory Scale III;

Table 2. Gait characteristics of people with PD+FOG and healthy age-matched controls.

	PD+FOG (N=11) Mean±SD	**Controls (N=12) Mean±SD**	***p***	**Effect size (*r*)**
Velocity (cm/s)	87.7±15.6	117.1±17.6	**<0.001**	0.882
Stride velocity (cm/s)	88.8±15.7	118.2±17.7	**<0.001**	0.878
Stride velocity variability	12.0±2.7	12.4±3.1	0.369	0.071
Step length (cm)	52.3±4.7	65.6±7.8	**<0.001**	1.019
Step length variability	7.5±1.4	6.1±2.2	**0.045**	0.371
Step time (s)	0.61±0.07	0.56±0.05	**0.045**	0.370
Step time variability	0.11±0.02	0.10±0.02	0.085	0.297
Base of support (cm)	11.1±4.3	10.3±2.6	0.293	0.116
Single limb support (%)	34.7±1.7	36.4±2.3	**0.025**	0.435
Double limb support (%)	30.3±3.4	26.9±4.7	**0.029**	0.419

Highlights

- Results indicated visual prioritization of ongoing steps in freezing of gait.
- This was associated with greater conscious processing of walking movements.
- Conscious processing might be crucial to guide stepping due to de-automatization.
- Visual search also assessed during freezing episodes using case study approach.
- Threat-related fixations may prevent conscious processing and provoke freezing.

Figure 1

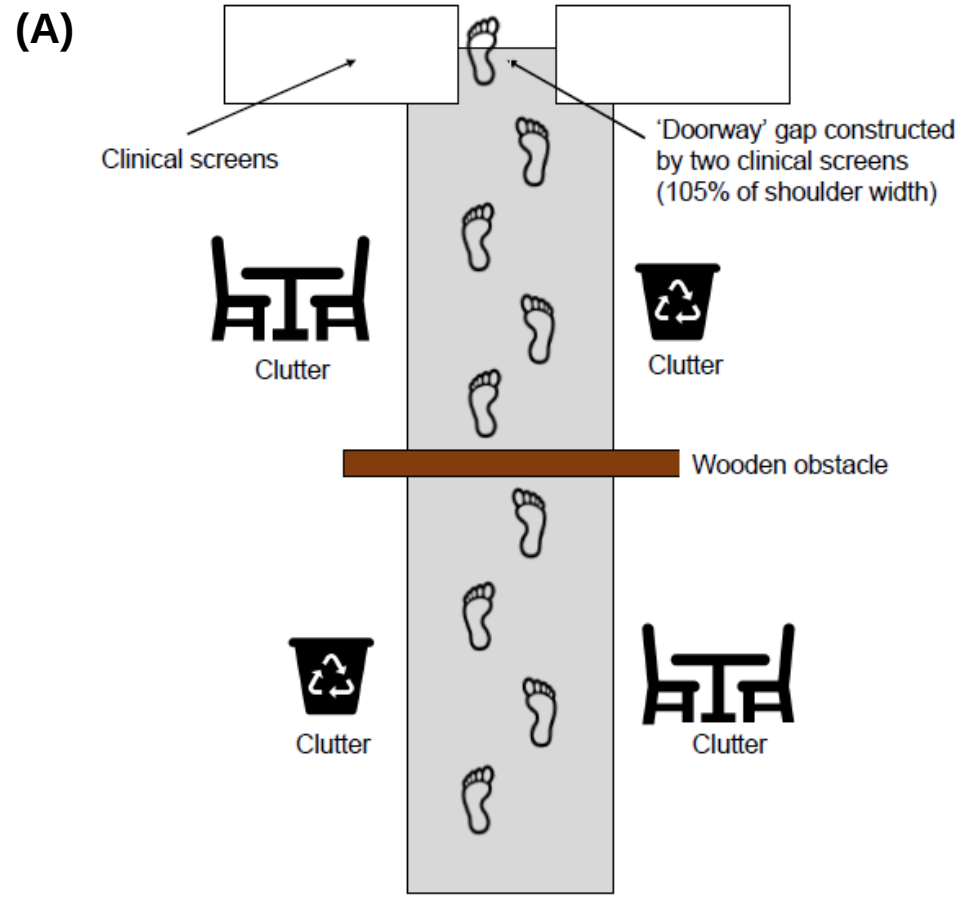

Figure 1. (A) An illustration of the walkway indicating the areas of interest for the eye tracker analysis, these being: 1) immediate walkway, 2) the obstacle, 3) future areas and 4) the outside area. (B) From left to right, fixations on the immediate walkway, the obstacle and the future areas.

Figure 2

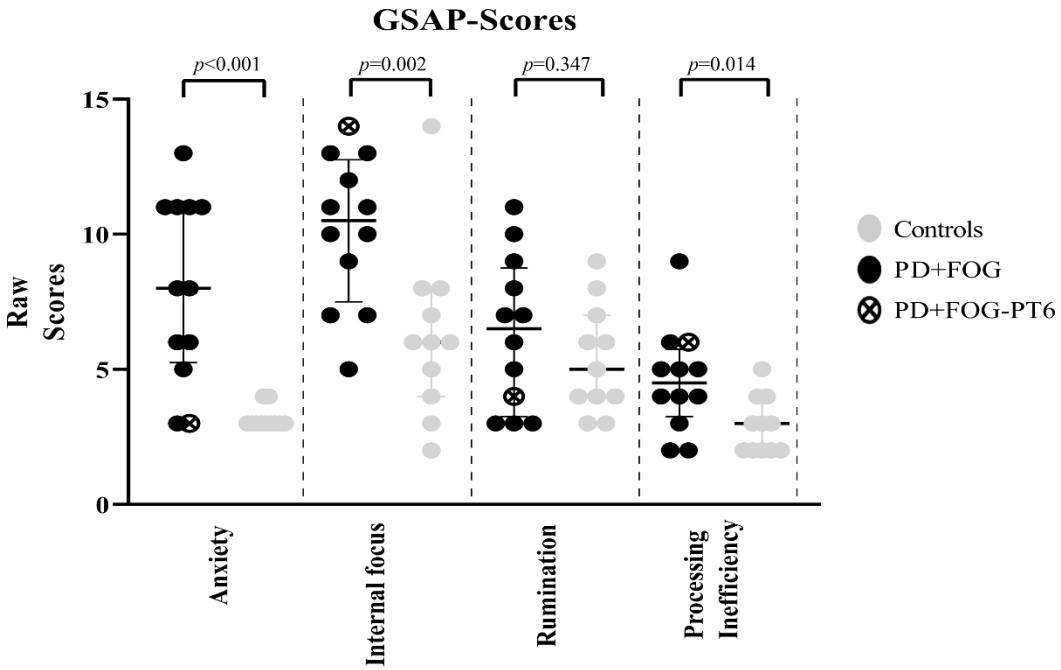

Figure 2. Gait-Specific Attentional Profile (GSAP) scores (median±interquartile range) for the PD+FOG (solid circles) and healthy control group (grey circles). The only participant with PD+FOG who did show freezing during the walking trials is marked with a crossed circle (Participant 6; Pt 6). Please also note that the possible score range for the subscales of gait-specific Anxiety, Conscious Movement Processing, and Fall-related Ruminations is 3-15, whereas the score range for Processing Inefficiency is 2-10.

Figure 3

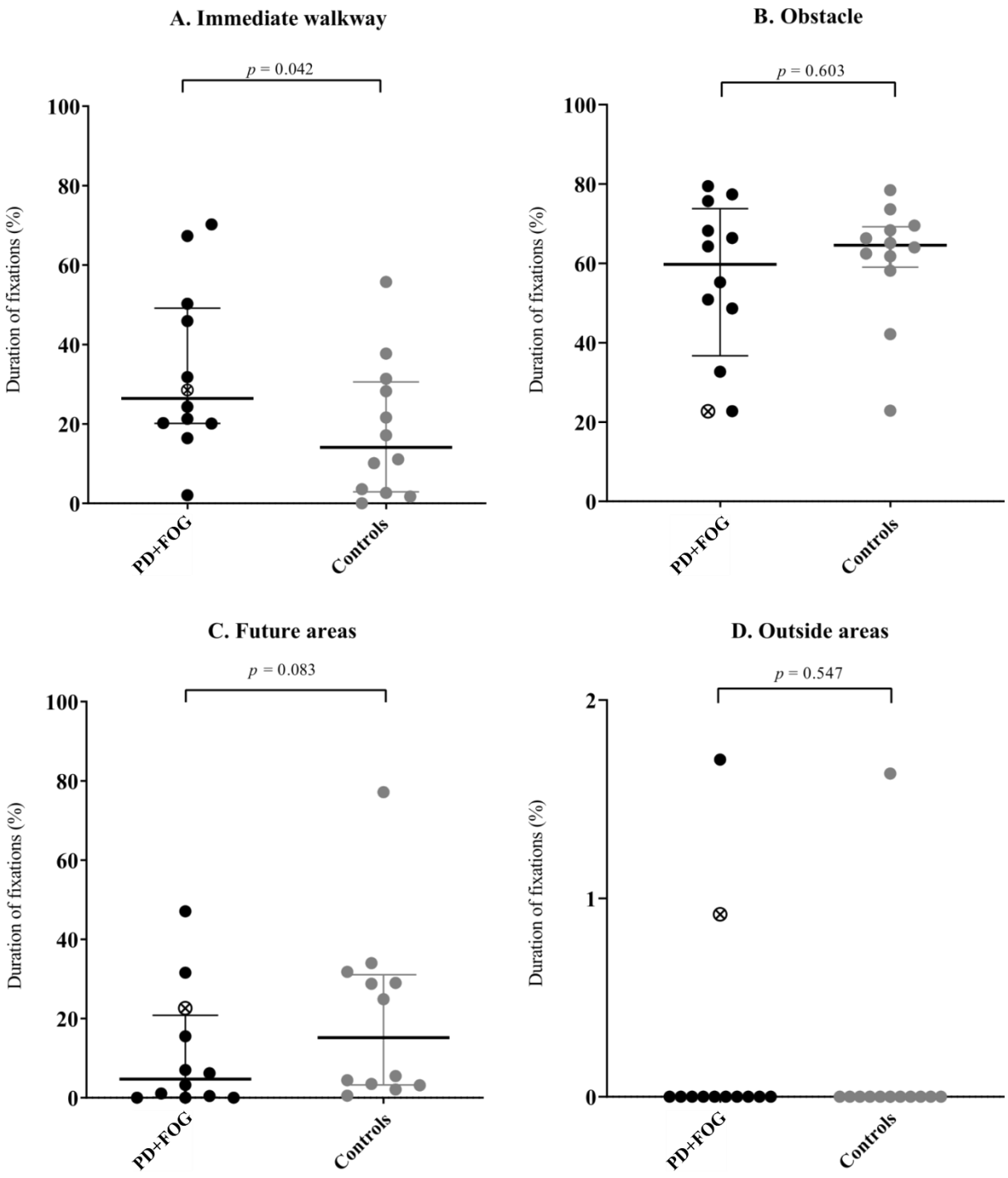

Figure 3. Visual search behaviour of people with PD+FOG and healthy age-matched controls during non-freezing trials. Shown are the median percentage (% plus interquartile range) of the duration of trials that participants fixated: the immediate walkway (A), the obstacle (B), future areas (C), and outside areas (D). The results of the participant who froze (PD+FOG P6) are highlighted as unfilled, crossed circle. Note, however, these data are for trials in which the participant *did not* freeze.

Figure 4

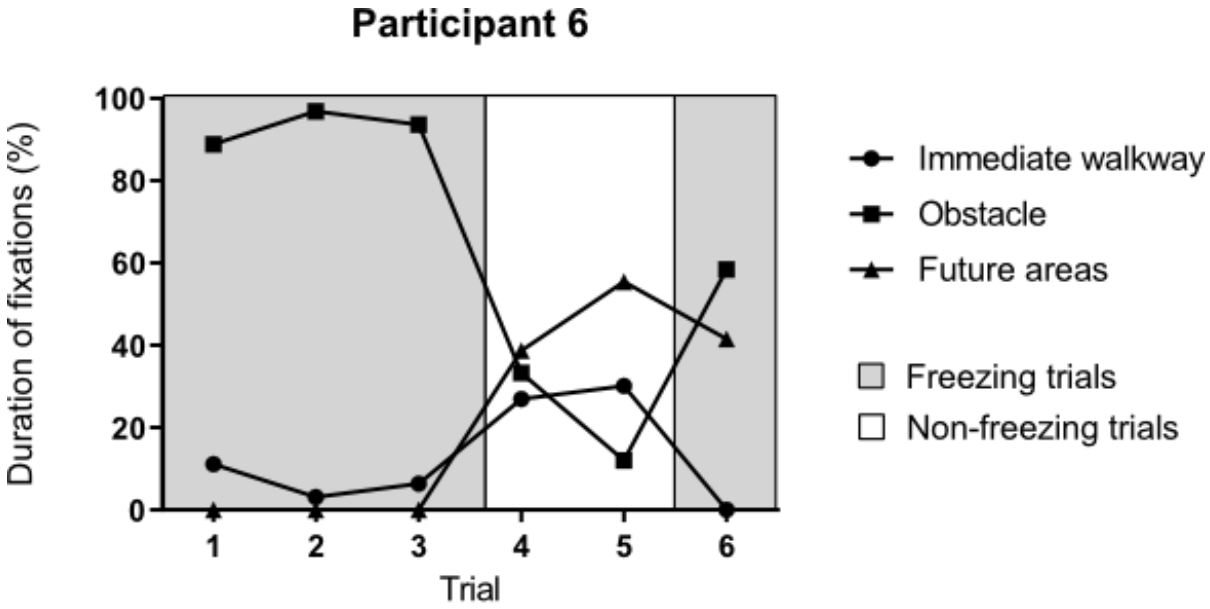

Figure 4. Differences in visual search behaviour (percentage of duration of fixations towards the three task-relevant areas of interest) between freezing- and non-freezing trials for participant 6 in the PD+POG group.