The influence of cueing and an attentional strategy on freezing of gait in Parkinson's disease during turning.

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Background and Purpose: Individuals with Parkinson's Disease turn more en-bloc than healthy controls which may contribute to freezing during turning. Therefore, we wanted to understand the influence of auditory cueing and an attentional strategy on en-bloc turning and how this related to FOG. **Methods:** 15 participants with FOG were asked to turn 180° during baseline condition, unilateral cueing and an attentional strategy prompting to start the turn with head rotation first. FOG-occurrence, axial rotation, COM-deviation, knee-flexion amplitude and total turn velocity were measured using 3D motion analysis while OFF-medication. Fourteen age-matched controls were recruited to provide normal reference values. **Results:** Thirty-nine FOG-episodes occurred in 5 participants. FOG occurred in 52.8% of baseline trials compared to 34.6% of trials using the head-first strategy and only in 3.8% of the auditory cueing trials. During the head-first strategy, the initiation of head, trunk and pelvic rotation as well as the head-pelvis separation resembled the normal turning pattern of healthy controls, but the COM shift to the inner side of the turn was exaggerated. By contrast, during cueing, turning became more en-bloc with a decreased head-pelvis separation and knee-flexion amplitude. **Discussion:** Cueing reduced FOG but did not correct the axial movement deficits. The head-first strategy was effective in improving head-pelvis dissociation but had only limited effects on FOG. **Conclusion:** These results suggest that axial and COM-deviation impairments are not directly related to FOG but may rather indicate a compensatory mechanism. Cueing reinforced the en-bloc movement and might as such help to prevent FOG by triggering an alternative neural mechanism for movement generation. A video Abstract is available for more insights from the authors.

KEYWORDS

Parkinson's disease, freezing of gait, attention, movement strategy, turning, walking

INTRODUCTION

Parkinsonian gait is characterized by a decreased step length and walking velocity[1]. Even in de novo patients, gait velocity and leg swing times are already decreased and gait variability and asymmetry increased[2]. When the disease progresses, gait disability worsens and up to 80% of patients with Parkinson's disease (PD) develop freezing of gait (FOG)[3]. FOG is often preceded by hastening, frequently indicated as festination (i.e. small steps at a high frequency)[4] and is described by patients as if their feet are glued to the floor[5]. FOG in PD has been shown to cause falls[6], depression and reduced quality of life[7]. It is experienced by individuals with PD as their most disabling gait problem.

FOG occurs especially during turning[8,9]. Quite apart from FOG, turning is already impaired in the early stages of the disease[10]. Participants with PD need more steps and time to complete a turn in comparison with healthy subjects[10,11,12] and show a decreased axial head-pelvis rotation[10,13]. A recent study focusing on axial behavior during turning in participants with and without FOG and controls found that the reduced axial movement in participants with PD was highly gait speed dependent, explaining some of the group differences. Furthermore, in trials in which FOG occurred, head movements did not precede trunk rotation and turns were characterized by more 'en-bloc' movement of head and pelvis[13]. This raises the question whether en-bloc axial movement actually triggers FOG[13,14]. A second possible trigger for FOG is the lack of center of mass (COM) deviation to the inner side of the turn, which is related to axial movement impairment. During normal turning, the COM is shifted towards the inner side of the turning cycle as a result of the lateral trunk flexion towards the same side[15,16,17]. During 'en-bloc' turning, a lack of medial COM deviation (towards the inner side of the turn) may be associated with an incomplete weight shift, affecting toe-clearance of the outer leg during swing-phase and thus result in FOG[18]. Shifting the base of support more explicitly towards the inner side of the turning cycle is a strategy which is used in the clinic to reduce

FOG[19]. Based on these findings, we hypothesized that if en-bloc movement is a causal factor of FOG, normalization of the impaired head-pelvis dissociation may reduce FOG. Secondly, we expected that COM deviation during turning is impaired in individuals with FOG compared to healthy subjects. Finally, the step length at the inner side of the turning cycle is smaller than that of the outer side and therefore requires modulation of pattern generation. The inherent asymmetry of turning also challenges the maintenance of a stable gait rhythm. These factors together were proposed to lead to a breakdown of pattern generation[20] and may also underlie FOG during a turn.

So far, research into specific physiotherapeutic methods to alleviate FOG during turning has suggested that cueing[18,21,22] can reduce FOG. Cueing is defined as "applying temporal or spatial stimuli associated with the initiation and ongoing facilitation of motor activity"[23]. It temporarily improves step length, cadence, asymmetry and gait velocity in patients with PD (review[24,25]) by externally generating movement patterns to compensate for the impairment of self-initiated movement typically seen in PD[26] and consequently reducing the risk of festination and FOG. However, till now rehabilitation methods such as cueing to reduce FOG were especially designed for normal symmetrical gait.

The present study compared the effects of auditory cueing, designed to correct foot-fall patterns, with a cognitive strategy designed to consciously correct head-pelvis dissociation during turning in individuals with FOG. We expected that, as a result of the cognitive head-first strategy, the axial rotation would improve, resulting in FOG-reduction during turning. We also predicted that FOG improvement as a result of the head-first-strategy might be more pronounced in comparison to cueing. Hence, the aim of this study was to deepen the insight into the role of axial versus appendicular movement correction to alleviate FOG.

METHODS

Participants

Fifteen participants with PD and Freezing Of Gait (First item of New Freezing of Gait Questionnaire (NFOG-Q)=1)[27] and in Hoehn & Yahr[28] stage II or III while on medication, were recruited after signing a written informed consent (for subject characteristics: see Table 1). The diagnosis of PD was assigned by a movement disorders neurologist using the UK Brain Bank criteria[29]. The participants were able to walk 10 meters repeatedly while off of their parkinsonian medication and had no dementia (MMSE>24)[30] or comorbidity that affected gait. Individuals with a neurostimulator for deep brain stimulation were excluded. Fourteen healthy individuals with comparable age were recruited to provide normal reference values on trunk movement and COM deviation data (Table 1). The study was approved by the local ethics committee of KU Leuven – University of Leuven.

Experimental protocol

Participants with PD were tested in off-medication state, 12 to 15 hours after the last medication intake. They were asked to walk 5m and turn 180° to the left and right side around two retroreflective markers placed 0.5 meters apart as previously described[12] (see Figure 1). After a baseline condition, in which participants walked without either cueing or head-first strategies, blocks of two cueing conditions (cueing the right or the left leg) and one condition in which the attention strategy was offered, were tested in random order. The protocol ended with a second baseline condition to assess potential carry-over effects. Every condition consisted of 6 trials (3 trials of turning to the left and 3 to the right). During the cueing conditions, a unilateral auditory cue was provided during the whole trajectory which cued the heel strike of either the leg at the inner or the outer side of the turning cycle at 90% of the preferred stride frequency (determined during straight-line gait). This cueing frequency was imposed to reduce the possible cadence increase during turning, which was found in a previous study to be associated with FOG[12]. Participants were asked to match the initial heel contact of every right or left leg (dependent on the turn direction) with the auditory cue. During the attention strategy, participants were asked to focus on initiating the turn with their head and look at where they had to go to during the turn. Rest periods were included between the different conditions to avoid fatigue and used to debrief participants about whether the strategy had been helpful to perform the turn and easy to use.

<Figure 1>

Equipment

Data were collected using an eight camera VICON 3D capturing system (Vicon Motion Systems, Workstation 612). Thirty-four retroreflective markers (14 mm in diameter) were placed bilaterally on the front and back of the head, shoulder, elbow, wrist, second metacarpal, anterior superior iliac spine, thigh, lateral epicondyle, tibia, lateral malleolus, second metatarsal and the calcaneus, and on C7, T10, clavicle, the xiphoid process of the sternum, the sacrum and in the middle of the left scapula to allow for COM calculations, according to the full body plugInGait marker configuration (VICON, Oxford Metrics, Oxford, UK).

Outcome measures

The turn was analyzed between 10° and 170° of pelvic rotation in relation to the laboratory axes, avoiding possible stretches of normal gait at the start or end of the turn[13]. The following parameters were calculated to characterize turning behavior of interest:

1) Onset of head, trunk and pelvic rotation: defined as the position of the COM in relation to the retroreflective marker on the floor when the head, trunk or pelvis reaches 10° of rotation in relation to the laboratory axes, as used in previous studies[13];

2) Head-pelvis separation: angular difference (°) between head and pelvis, calculated for every 5 degrees of pelvic rotation (from 10 to 170°)[13];
3) FOG-occurrence: FOG was defined as an episode of inability to generate effective stepping often leading to a halt[31], based on visual analysis of the 3D images using Vicon workstation software. Two raters, blinded for turn strategy first detected all FOG-trials. When in doubt, the opinion of a third rater was adopted to resolve.
4) Medial COM deviation during turning (i.e. COM deviation towards the inner side of the turn): This was defined as the distance from the COM position to the line between the centre of pelvis (calculated as the mean position of the LASI, RASI and SACR markers) and the midpoint of the left and right anterior superior iliac spine (LASI and RASI) (see Figure 2). The medial COM deviation was calculated for every 5 degrees of pelvic rotation (from 10 to 170°). A negative value means that the COM was closer to the inside of the turn than the line connecting the pelvis markers.
5) Total turn velocity (°/s): calculated from the total time needed to rotate the pelvis from 10 to 170°;
6) Knee flexion amplitude during the turning: Maximum range of motion of knee flexion-extension at the inner leg of the turning cycle as a derivated measure of step length, i.e. movement amplitude. This outcome measure was analyzed to capture hypokinesia during gait in participants with FOG.

<Figure2>

Data-analysis

Subject characteristics were analyzed with a student T-test. Occurrence of FOG was analyzed using a Pearson's chi-square (X^2) test within the group of freezers who actually froze during the protocol (n=5). FOG-trials were excluded for the COM and movement analyses. After checking for comparability, baseline conditions at the beginning (first baseline) and end (second baseline) of the data collection were pooled to avoid missing data (as a result of FOG-episodes).

All kinematic data were calculated as an average over the six trials (3 trials for each side, left and right side pooled) and analyzed using a 3*3 repeated measures ANOVA with two repeated factors (condition: baseline, unilateral cueing, head-first attention strategy; body part: head, thorax and pelvis) for the turn initiation and a repeated measures ANOVA with one one repeated factor (condition) for head pelvis separation, medio-lateral COM deviation, total turn velocity and knee-flexion amplitude. Post-hoc Newman-Keuls tests (for normal data) and Bonferroni corrections (for curve analyses) were executed when significant differences were found. Turning data from age-matched controls[13] were used as baseline reference data and statistically compared to the different conditions in freezers using T-test for normal data and Bonferroni corrections for curve analyses. All statistical analyses were performed using Statistica (version 9.0) and levels of significance were set at α=0.05.

RESULTS

Table 1 represents the subject characteristics. Healthy controls and participants with freezing of gait were comparable for age and leg length. The MMSE was significantly different between groups.

<Table1>

No differences were seen between cueing the inner or outer side of the turning cycle for the onset of head, trunk and pelvic rotation, head-pelvis separation, total turn velocity, COM-deviation and knee-amplitude. Therefore, both unilateral cueing-strategies were pooled for further analysis.

Effects on Freezing Of Gait

Freezing occurred in 5 participants during the protocol, resulting in a total of 39 FOG-trials. FOG occurred in 52.8% (N=28) of baseline trials compared to 34.6% (N=9) of trials using the attention strategy (X^2=3.5, p>0.05) and only 3.8% (N=2) of trials when a unilateral cue was offered (X^2=48.1, p<0.001). More specifically, 4 participants froze during the first baseline condition. Two of those individuals, did not freeze when using the head-first attention strategy and none of those individuals froze during the cueing condition. However, one additional participant developed some short-lasting FOG-episodes during cueing. This individual reported difficulties to match heel contact with the cue and reported that the cue-frequency was too low. Three other participants initially experienced problems adjusting to the cueing rhythm and reported that this condition required more concentration. On the other hand, 9 participants reported that turning itself was helped by the presence of an auditory cue. Two individuals put forward that they experienced rigidity opposing the head-first rotation strategy and only 3 participants felt that it improved turning. FOG-occurrence was comparable (X^2=0.1, p>0,05) between the first (53.8% of trials) and second baseline (51.9% of trials).

Effects of cueing and attention on turn preparation

The initiation of head, trunk and pelvic rotation in relation to the turning marker is depicted in Figure 3. A significant interaction-effect (p=.002) of condition*body part for turn initiation was found. The turn started at a distance of approximately 200mm before the actual turning marker and this pattern was comparable for baseline, cueing and head-first attention strategy (i.e. 10° pelvic rotation occurs at 207.4 mm, 197.0 mm and 294.1 mm respectively before the turning marker, p-values vary between p=0.09 and p=0.82). This pattern was also similar to that of age-matched healthy controls during normal turning (i.e. 10° pelvis rotation occurs at 244.7 mm before the turning marker, p=0.50, p=0.33 and p=0.43 respectively).

Participants with PD started to rotate their head before the trunk and pelvis in all conditions. However, during baseline and cueing condition, this head initiation occurred significantly closer to the turning marker in comparison to age-matched controls during normal turning (459.1 mm and 427.7 vs. 762.3 mm before the turning marker, p<0.01). During the head-first attention strategy a much more pronounced head movement was found preceding trunk and pelvic rotation. This initiation of head rotation occurred at 752.7 mm before the turning marker, which was significantly different in comparison to the baseline or cueing condition (459.1 mm and 427.7 mm respectively before the turning marker, p<0.001), and strongly resembled the turning pattern of healthy controls during normal turning (p=0.94) (see Figure 3). This indicated that participants with PD were able to adopt the head-first strategy adequately.

In the subgroup of freezers who actually froze during the protocol, comparable results were seen for turn preparation and axial movement during turning. However, due to the small sample size, no statistical analysis was performed on this subgroup.

<Figure 3>

The effects of cueing and attention on axial movement during turning

The maximum head-pelvis separation decreased significantly during the cueing condition and increased during the head-attention strategy compared to baseline (20.3±6.2° during cueing and 40.7±10.0° during head-attention vs. 25.6±5.8° at baseline, p=0.005 and p<0.001) and consequently matched the reference data of age-matched controls (34.5±9.8°) during head-attention strategy (p=0.12 vs. p=0.009 and p<0.001 for baseline and cueing condition respectively).

Participants reached the maximum separation of the head and pelvis at a significant smaller turning angle during the head-attention strategy compared to the baseline or cueing condition (61.1±22.3° vs. 76.5±17.5° and 82.8±22.0° of pelvic rotation, p=0.03 and p=0.009). No significant difference was found for turning angle at maximum separation in comparison to age-matched healthy controls (67.7±18.2° of pelvic rotation, p=0.32 for baseline condition, p=0.12 for cueing condition and p=0.49 for head-attention strategy).

Head-pelvis separation during the head attention strategy was significantly greater than in the baseline condition during the whole turn in participants with FOG (see Figure 4A). This was in contrast to the cueing strategy, in which the head-pelvis separation was significantly smaller from 25° till 105° pelvic rotation compared to the baseline condition (Figure 4A). This resulted in a significant difference in head-pelvis separation during the whole turn in participants with FOG during the cueing strategy in comparison to normal turning of age matched controls and a tendency towards significance for baseline condition. The head-pelvis separation was comparable for participants with FOG and age-matched control data during the head-attention strategy.

<Figure4>

The medio-lateral COM deviation towards the inner side of the turning cycle was significantly larger in participants from the beginning of the turn till 160° pelvic rotation during the head attention strategy compared to the baseline or cueing condition (Figure 4B). Thus, when attention to the head rotation was applied during turning, the medial COM deviation was significantly higher in participants with FOG in comparison to normal turning of healthy controls from 20° till 160° pelvic rotation. No difference was found during baseline and cueing condition in comparison to healthy controls.

Stepping movement

Total turn velocity decreased during the cueing and the head attention strategy (59.8°/s at baseline vs. 50.6°/s during cueing and 51.7°/s during head-attention, $p<0.01$), wich made the turn also slower than that of healthy controls (94.1°/s). Knee flexion amplitude was significantly smaller while cueing, compared to baseline or the attention strategy (46.2±7.3° vs. 49.3±7.7° and 48.9±7.5° respectively, $p<0.01$). Age-matched controls had a knee flexion amplitude of 57.6±4.5°, which was significantly larger than all three conditions in participants with FOG.

DISCUSSION

In the present experiment, we investigated whether en-bloc movement during turning would be corrected by applying either unilateral cueing or a head-first attention strategy and whether this would lead to an alleviation of FOG. Despite the fact that participants with FOG were able to increase head rotation at the start of their turn and improve maximum head-pelvis separation during the head-first strategy, FOG was less reduced using this strategy than during auditory cueing when these movement corrections did not happen. Only three of the fifteen participants reported that the attention strategy was helpful for turning. Two participants indicated that the exaggerated head rotation was hindered by neck rigidity. Higher neck rigidity was found earlier to be related to an increased coupling between head and pelvis during turning in participants with FOG[13]. Furthermore, Macht et al.[3] showed that patients with rigidity as their main symptom had a higher chance of developing FOG.

In contrast, FOG was strongly reduced by unilateral cueing and most participants with FOG reported that cueing positively affected turning. Interestingly, cueing aggravated the “en-bloc” movement (instead of normalizing the impaired head-pelvis dissociation) and decreased the knee flexion amplitude of the participants indicating that they made shorter steps, which is often seen prior to a FOG-episode. Still, this alleviated FOG and suggests that the en-bloc movement in PD is not the primary movement deficit which induces FOG. Instead, it may signify a secondary compensatory mechanism for impaired postural control and imbalance during turning[32], which is especially pronounced in individuals who experience FOG. The results also indicated that the cueing strategy reinforced “en-bloc” movement, making the preparation of the head-pelvis orientation in the new walking direction less demanding and therefore reduces FOG occurrence. The decreased knee amplitude during cueing highlights that “en-bloc” movement is related to reduced velocity[33] and decreased step length[34].

Both during cueing and the head-attention strategy, the total turn velocity decreased in comparison to baseline turning. The decreased velocity during the cueing condition can be explained by the fact that cueing was set at a lower than normal cadence (-10%), induced en-bloc turning[17] and required more effort[35]. Similarly, the slowing effect of the attention-demanding head strategy might have been a result of the additional cognitive load during this condition which may have masked a potential improvement on FOG.

COM deviation towards the inner side of the turning cycle has previously been found to be related to the degree of axial rotation and the turning velocity[17]. Indeed, despite the slowness of turning, COM deviated more during the head-attention strategy compared to baseline, resulting in an amplified medial position. Cueing on the contrary, did not affect the medio-lateral position of the COM. This suggests that the medio-lateral weight shift may not be of critical importance in the etiology of FOG and the cue-induced en-bloc turning might have created a safer turn and as such prevented FOG, in contrast to what was hypothesized previously. On the other hand in the clinic, the conscious facilitation of alternating weight displacement before or during FOG has been adopted as a useful cognitive strategy to restore and resume the gait pattern. Recent study demonstrated that freezers have a specific deficit with directional control of weight-shifting[36]. In a study of Bengevoord et al, no differences were found in participants with FOG in comparison to participants without FOG in COM behavior during turning. However, a reduced COM deviation towards the inner side of the turning cycle was found just before FOG episodes[37]. Therefore, further research on the effect of medio-lateral weight-shift during turning on FOG is necessary.

A second difference between the head-attention strategy and cueing is the mode of generation of movement. During the attentional strategy, turning was driven by internally generated motor control, requiring additional cognitive load. Cueing, on the other hand, evoked an externally generated turning movement. Freezing is alleviated by the provision of external cues, possibly because movement automaticity is even more impaired in individuals with freezing of gait[38]. In addition, recent work showed that during a cued response selection task while OFF-medication, individuals with Parkinson's disease increased connectivity between the lateral premotor cortex and the prefrontal cortex, possibly to compensate for the reduced connectivity between putamen and the supplementary motor area and the premotor cortex[39, 40].

Whether the effects of cueing were related to the information provided by the cue (cueing parameter) or acted through a mechanism of external versus internal movement generation remains unclear. Willems et al. showed that cueing effects were frequency-dependent particularly in individuals without FOG[41], suggesting a corrective role. Different modalities of externally generated movements (auditory, visual and somatosensory) on the other hand, activated the same motor cortical areas in healthy controls[42]. A recent study of Yang et al. showed that an attentional strategy based on visual imagery emphasizing a stable step pattern while turning, improved turning time, step asymmetry and freezing[43]. This suggests that the cueing parameter (i.e. emphasizing a stable gait pattern in comparison to en-bloc reduction) is more important in reducing freezing of gait than the mode of movement generation (i.e. internal versus external generation). Yang et al. however compared two different groups instead of a test-retest paradigm and included a longer training session.

Even though cueing seems the most effective way to reduce FOG, Rahman et al.[44] showed that PD patients with freezing of gait preferred cognitive strategies over cueing. Intelligent cueing devices, only inducing a cue when FOG might occur[45, 46], may therefore be indicated.

To minimize the load on the participants, this study was executed in one day, with only a short training duration and no long-term follow-up. Therefore, the current results might have underestimated the effect of cueing and attentional strategies on FOG as a rehabilitation intervention. Furthermore, a limitation of this study was that provoking FOG during clinical testing is always a challenge as participants are more attentive in a laboratory setting compared to during their daily life activities[47]. This might explain why only five of the fifteen participants with FOG froze during the protocol. However, increasing the turning difficulties to elicit more FOG would have also increased the missing values, illustrating the difficulties of effect studies on this unpredictable phenomenon.

CONCLUSIONS

In conclusion, we found that cueing was effective in reducing FOG, although it emphasized rather than reduced axial movement deficits. Attentional strategies, on the other hand, were effective in improving head-pelvis dissociation and medial COM shifting but this had only a minor alleviating effect on FOG. These results indicate that axial and COM-movement impairment contribute less than expected to FOG but may rather indicate a compensatory mechanism to cope with balance problems inherent to turning. These findings have important implications for clinical practice as they might suggest to reinforce rather than to correct these implicit compensatory patterns. Further research should focus on the influence of weight-shifting during turning to explore the possible impact on freezing of gait.

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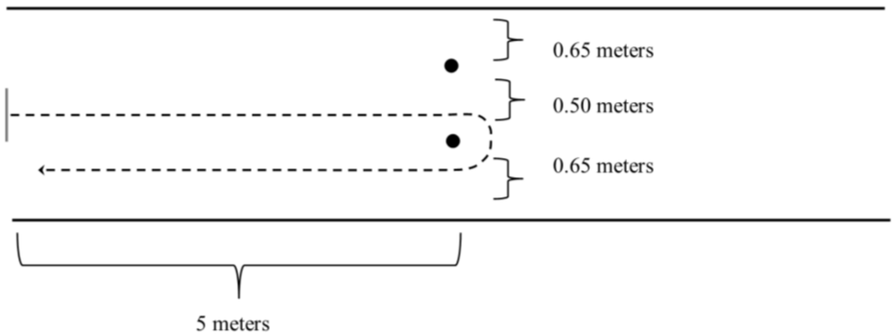


Figure 1: Walkway

Participants were asked to turn 180° around the left or right retroreflective marker (●).

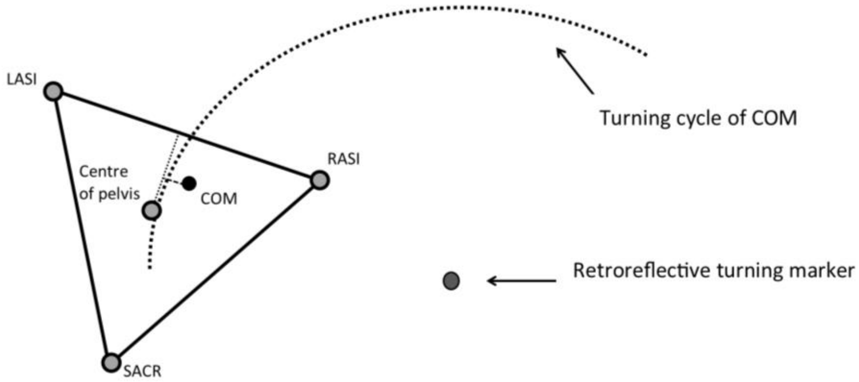


Figure 2: COM deviation to the inner side of the turning cycle when turning 180° to the right.

SACR= sacrum, LASI= left anterior superior iliac spine, RASI= right anterior superior iliac spine.

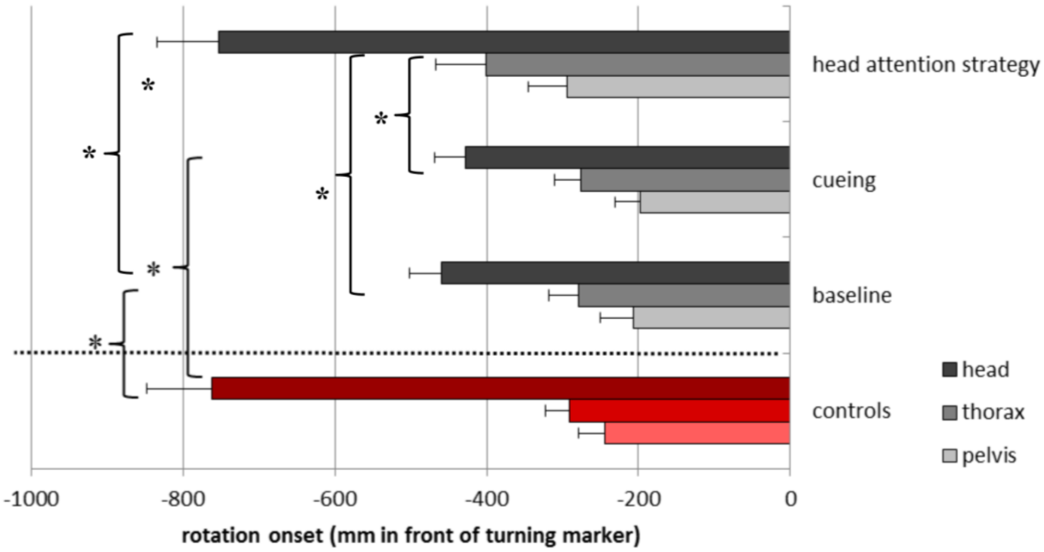
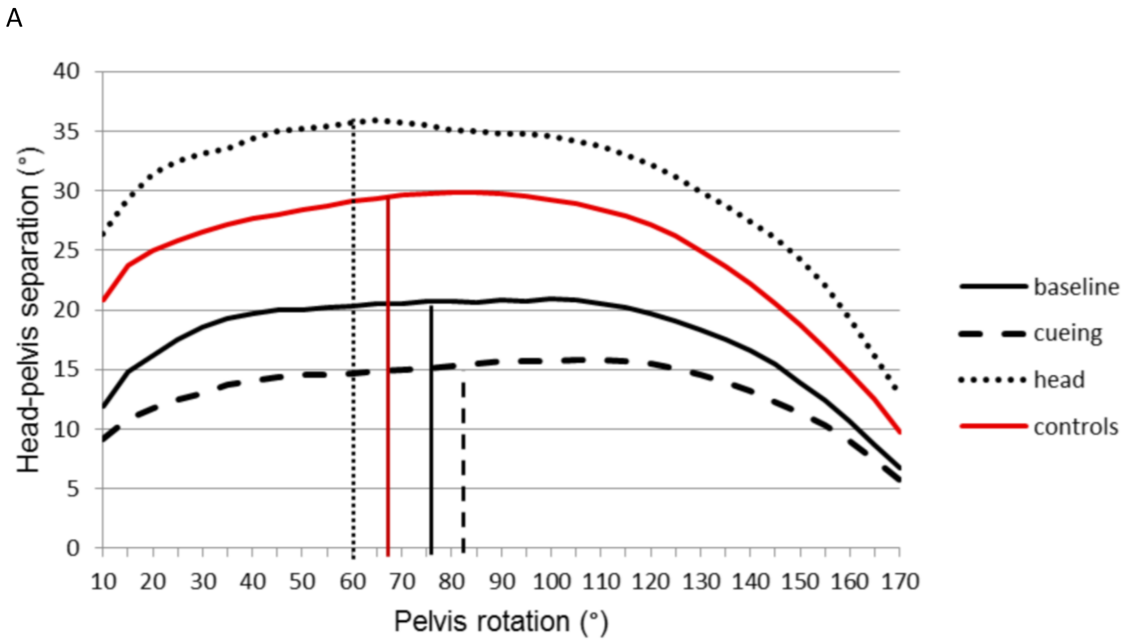


Figure 3: The onset of head, thorax and pelvic rotation expressed in mm distance to the retroreflective turning markers placed on the ground during baseline, cueing condition and head attention strategy. Reference data from normal turning of age-matched controls were statistically compared to freezers. *= $p<0.05$



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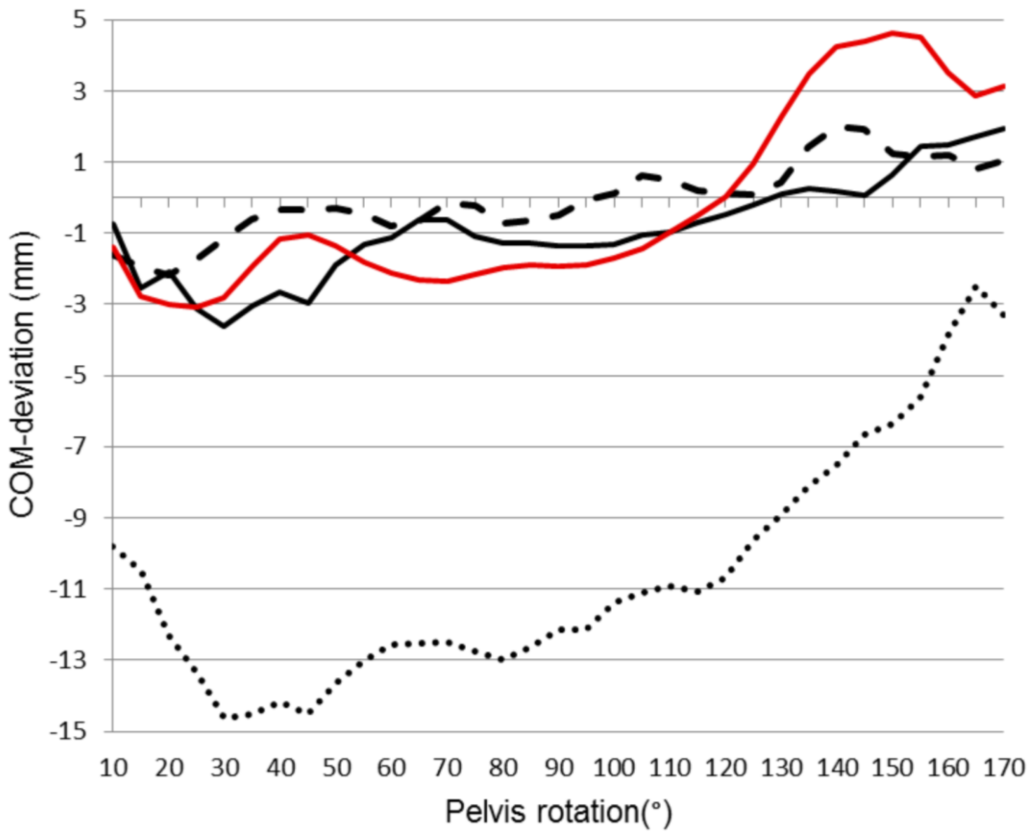

Figure 4: Head-pelvis separation and turning angle at maximum head-pelvis separation (A) and Medial COM-deviation (B) during baseline, cueing condition or head-first attention strategy. A negative value means that the COM deviated more to the inner side of the turning cycle. The red line visualizes reference data from age-matched controls. To aid clarity, no error bars were inserted in the figure. Standard deviation of head-pelvis separation varied between 3.3° and 7.3° during baseline condition, between 3.1° and 6.7° while cueing and between 7.0° and 12.5° during the head attention strategy. SD of COM-deviation varied between 2.7 mm and 6.3 mm during baseline condition, between 2.3 mm and 4.1 mm while cueing and between 5.2 mm and 8.8 mm during the head attention strategy.

Table 1: Participant characteristics: mean (SD) measured when OFF medication.

	Participants with FOG (n=15)	Healthy Controls (n=14)	p-value
Age (years)	67.4 (8.8)	65.2 (6.8)	0.46
Leg length (cm)	88.5 (4.9)	90.1 (4.9)	0.40
MMSE	27.6 (1.5)	29.1 (1.3)	<0.01
Disease duration (years)	9.3 (3.9)		
H&Y	2.4 (0.4)		
UPDRS III	42.9 (9.1)		