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Review

Biomechanical aspects that precede freezing episode during gait in individuals with Parkinson's disease: A systematic review

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ABSTRACT

Background: The freezing episode (FE) management during gait in Parkinson's disease is inefficient with current medications, neurosurgery, and physical interventions. Knowing the biomechanical change patients suffer preceding FE would be the ultimate goal to measure, predict, and prevent these events.
Objective: We performed a systematic review to summarize the kinematic, kinetic, electromyographic, and spatiotemporal characteristics of the events that precede the FE during gait in Parkinson's disease.
Literature Survey: Databases searched included PubMed, Embase, and Cochrane and between 2001 to August 2021.
Methodology: The present study was a systematic review registered in the PROSPERO database (CRD42021255082). Three reviewers searched and selected studies with methodologies involving biomechanical changes and kinetic, kinematic, electromyography, and spatiotemporal changes before FE in a patient with Parkinson's disease. The relevant articles that show the events preceding FE in patients with PD were identified. We excluded studies that describe or compare methods or algorithms to detect FE. Studies may include participants with all PD severity, time of disease, and age.
Synthesis: We selected ten articles for final evaluation. The most consistent results indicate a dramatic reduction of movement excursions with (1) decrease in stride length; (2) decreased gait speed; (3) postural instability with the increased double support phase; (4) incoordination of anterior tibial and gastrocnemius; (5) larger amplitude in the EMG of biceps femoris; (6) decreased range of motion in the sagittal plane at the ankle and hip joints; and (7) anterior pelvic tilt.
Conclusion: FE is characterized by complex motor patterns than normal gait and mismatched gains in the perception and execution of the ongoing movement.

1. Introduction

One of the most debilitating symptoms in patients with Parkinson's disease (PD) is the freezing of gait (FoG), defined as a "brief, episodic absence or marked reduction of forwarding progression of the feet despite the intention to walk" [1]. A recent cohort study found a prevalence of 63% and an incidence of 12.4% of FoG in patients with PD [2]. FoG is expected in the more advanced stages of PD [3], and generally leads to falls, injuries related to the fall, and loss of independence [4].

During freezing episodes (FE), PD patients may have three characteristics [5,6]. First, a patient suddenly cannot start walking or stops moving forward (a condition referred to as "akinesia"). Such a complete absence of movement is perhaps a better-known clinical presentation but is not the most common presentation. Second, FoG is often associated with an effort to overcome the blockage, causing the legs to "trembling in place" [7]. This is the most prevalent FE subtype [8,9]. The third type of presentation is to move forward - with small steps.

The management of the FoG is not efficient with the currently

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available medications, neurosurgery, and physical interventions, given the lack of pathophysiology knowledge of this complex phenomenon [10]. Knowing the biomechanical changes, like the cadence, preceding FE would be beneficial in predicting and preventing these events. In addition, early detection of FE could contribute to cues being administered immediately before freeze onset [11,12]. However, there is no unified vision of the biomechanical markers preceding FE. An in-depth investigation of the dynamics of the biomechanical aspects that precede FE in patients with FoG is fundamental to a better understanding and future treatments. This systematic review aims to identify the kinematic, kinetic, electromyographic, and spatio-temporal characteristics of the events that precede the freezing episode (FE) during gait in Parkinson's disease.

2. Methods

2.1. Selection criteria

This review highlights the biomechanical characteristics that precede FE in patients with Parkinson's Disease. The present study is a systematic review, and it was registered in the PROSPERO database (CRD42021255082). This review included studies according to the following criteria: (1) the methodology involved studies that address biomechanical changes and kinetic, kinematic, electromyography, and spatiotemporal changes before FE in a patient with Parkinson's disease; (2) patients can be on all severity, duration of illness and age (3) written in English.

2.2. Search strategy

Three reviewers independently evaluated the search strategy and the inclusion and exclusion criteria of the studies. The following search strategy was used to identify the studies included in the review: the searches were accomplished in the electronic databases PubMed, Embase, and Cochrane. The research period was conducted between 2001 and August 2021. The search terms and operators applied in the databases were: (biomechanics OR kinetic OR kinematic OR electromyography OR "inertial sensor" OR "plantar pressure" OR "motor patterns") AND (preceding OR onset) AND "freezing of gait" AND Parkinson. We excluded studies that describe or compare methods or algorithms to detect FE [13,14]. The relevant articles that show the events preceding FE in patients with PD were identified according to the reading of the titles and abstracts. Reading these articles in detail, we explore the article's references, seeking complementary studies.

2.3. Study selection

According to the titles and abstract, three independent reviewers evaluated studies identified by the search strategy. The reviewers assessed the complete articles and the selected studies according to the inclusion criteria. Studies that did not fulfill the adopted criteria were excluded according to the limits imposed by the search strategy. Disagreements between reviewers were resolved by consensus. Studies may include participants with all PD severity, time of disease, and age.

2.4. Data extraction

The following information was extracted from the articles: publication identifier, participants characteristics, measurement instruments, biomechanical variables analyzed, results and conclusion.

3. Results

The initial search in the PubMed, Embase, and Cochrane databases resulted in 25 potential articles. After reading the titles and abstracts, seven articles were assessed for eligibility. Next, bibliographic references were read, and five articles were included. Twelve articles were thoroughly analyzed, and finally, ten studies were taken up for our study (Fig. 1).

Table 1 Summarizes the ten selected articles, including author/year, participants characteristics, measuring instrument, results, and conclusions.

4. Discussion

This study aimed to emphasize the biomechanical characteristics which precede FE during gait in patients with Parkinson's disease. Before the FE, patients experience postural instability and degradation of the gait pattern, with deficits in temporal and spatial gait characteristics and a dramatic reduction of movement joint excursions.

Start hesitation (akinetic freezing) is one of the most common phenotypes of FoG, being characterized by a delay in the voluntary step during self-initiated gait. During self-initiated gait preceding FE, there are inefficient weight transfers, with an amplitude [15] and timing [16] disorders, and multiple [17] anticipatory postural adjustments (APA) compared to those without FE. Abnormal APA may include abnormal pauses that disrupt the posture-movement coordination and may precipitate FE, resulting in an inability to take a step [18]. Therefore, it has been reported that these episodes present a complex motor pattern.

Before the FE, there is muscle incoordination and premature activity [19,20]. There is a decrease in amplitude of the anterior tibial in the pre, at the moment, and after FE, along with premature activity in the pre-swing phase in walking and shorter activity in the swing phase. The gastrocnemius presents premature initial and final activity in the support phase and less muscle activity before, during, and after FE on the most affected side. Cantu et al. [20] identified that the bilateral anterior tibial and medial gastrocnemius muscles on the less affected side had lower amplitudes before, during, and after FE. In contrast, the bilateral biceps femoris muscle revealed greater amplitude before, during, and after FE. Nieuwboer et al. [19] identified premature activity of the anterior tibialis in the pre-swing phase, highlighting shorter activity in the swing phase. Nevertheless, the gastrocnemius showed premature initial and final activity in the support phase.

One of the FE subtypes is characterized by "shake in place". In this subtype, FE is associated with the high frequency (3–8 Hz) oscillation of the legs [21], followed by a distal to proximal onset pattern, appearing at the feet, shanks, thighs [22], and abnormal rhythmicity in tibialis anterior and gastrocnemius muscle activation [19]. This suggests that high frequency lower limb acceleration at the feet is not an attempt to overcome a motor block but part of a pathologic gait pattern that precedes a FE.

There is evidence of axial movement in the etiology of FE [23–25]. For example, Palmerini et al. [23] analyzed patients performing turns of 180º and 360º and identified more significant variability in the lumbar region in the pre-FE. These axial impairments may have led to delayed counter-rotation of the head and pelvis during turning.

There is a highlight about the cadence, indicating an increase during the festination and a decrease during the FE. Nieuwboer et al. [26], when analyzing patients performing comfortable walking, comfortable walking with immediate stop, and obstacle walking, identified the cadence increased during festination than regular walking. Mitchell et al. [27] analyzed the kinematics of the trunk during walking in a straight line and turning in found that freezers had lower cadence, variability in gait speed, stride length, and average lateral displacement of the trunk when compared to non-freezers. The decrease in cadence during FE can be explained by attempting to direct the body forward and continue to walk, decreasing the number of steps, suggesting that the inability to generate a higher cadence leads to a collapse of locomotion. FE can be caused by an increasing inability to generate stride length superimposed on a dyscontrol of the cadence. Furthermore, postural instability before FE, which they compensate for by increasing the double support phase [26]. The reduced step length and a successive

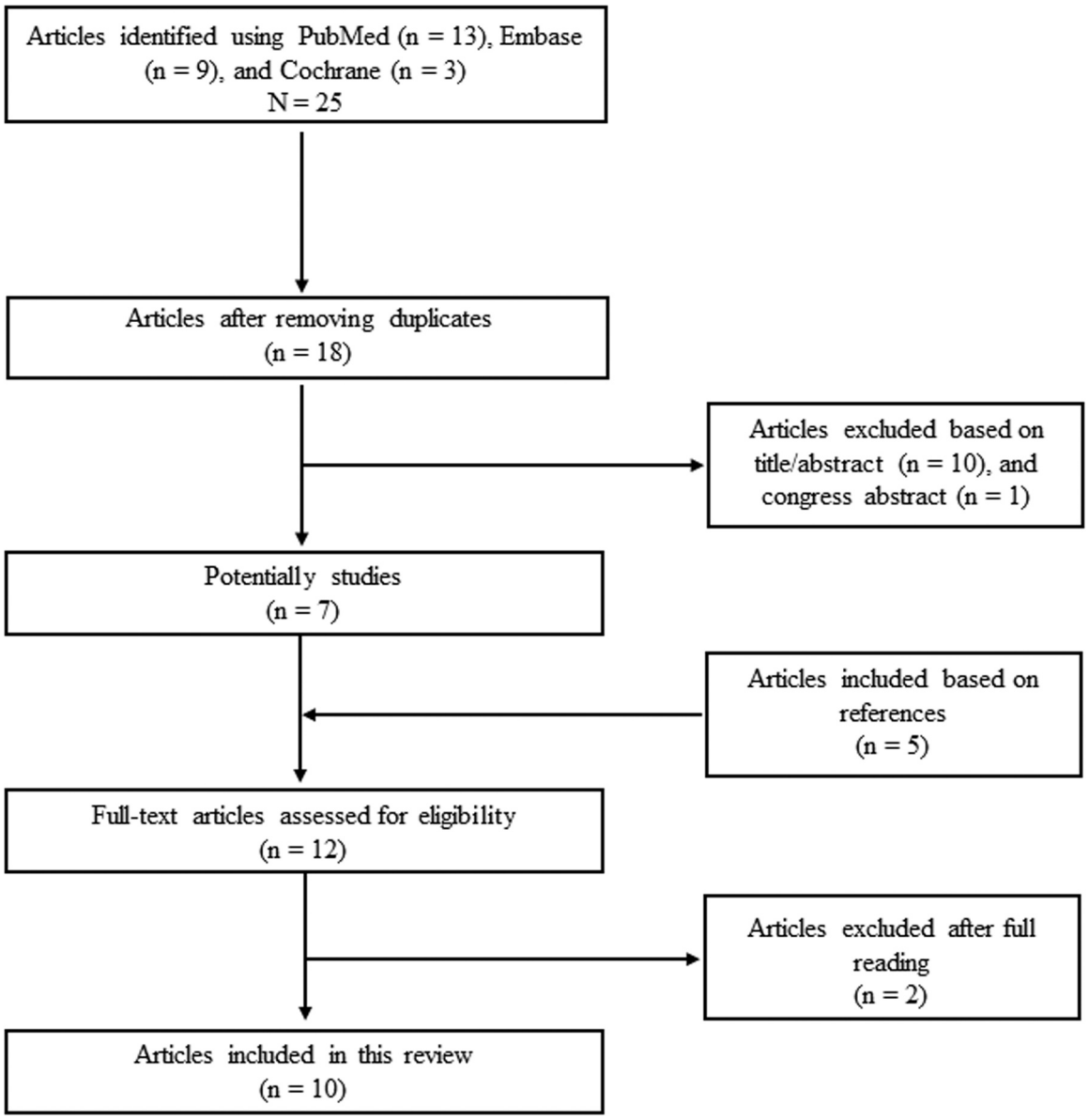

Fig. 1. Diagram of the search strategy.

step-to-step amplitude reduction can lead to FE.

A limitation of the studies is the characterization of FE and its differentiation from festination, for example. A consensus on how to identify FE is presently lacking. Both festination and FOG are highly variable in people with PD, but in general, festination is characterized by rapid and short steps, while FE is characterized by akinesia or trembling of the legs. An open question is whether FE is related to the process of moving forward or cyclical movement. Studies analyzing stepping in place suggest that FE can be a breakdown of coordination of the limbs during cyclical movement, disrupting a repetitive alternating stepping motor program [20,28]. This evidence is supported by studies showing that (1) bimanual drawing tasks have been shown to correlate with FOG-Q [29], and (2) a stationary bike pedaling task, on what the asymmetry of the limbs' pedaling was correlated with FE [30].

The studies show that FE causes a deterioration in gait, distinct from the normal deceleration of gait in that the reduction of propulsive movement is much more significant [24].

Biomechanically, FE is characterized by a complex motor pattern with higher frequency components than normal gait [9,17,22], mismatched gains in the perception and execution of the ongoing movement [28], and a delayed preparation for the change in walking direction [25]. In conclusion, before the FE, there is a dramatic reduction of movement excursions with (1) decrease in stride length; (2) decreased gait speed; (3) postural instability with the increased double support phase; (4) incoordination of anterior tibial and gastrocnemius; (5) larger amplitude in the EMG of biceps femoris; (6) decreased range of motion in the sagittal plane at the ankle and hip joints; and (7) anterior pelvic tilt. As a potential application in rehabilitation, by knowing the patterns of biomechanical events that precede the Freezing of Gait, these events could be predicted. By identifying FE before they happen, cues could be provided for improving gait of PD patients. Further work is needed to improve the modalities of cueing strategy to be applied before the FE.

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Table 1 –
Characteristic of the studies included in the review.

Article	Participants	Task	Instruments/ Methods	Variable	Results	Conclusion
Nieuwboer et al. [26]	14 FoG+ , OFF medication. H&Y ON medication between 2 and 3. H&Y OFF medication between 3 and 4.	Three tasks: 1. Gait at a comfortable self-selected speed.2. Gait at a comfortable self-selected speed with immediate stop after the researcher's oral clue. 3. Gait with obstacles or passing doors with or without a double cognitive task.	Three-dimensional gait analysis. Trials were identified with freezing episode (FE): abrupt episodes of interruption of gait when approaching or crossing obstacles; and festination: abrupt episodes of voluntary increase in cadence during approaching or crossing obstacles. The instrument of the video identified FE and festination.	Spatio-temporal parameters during normal gait festination, voluntary stop, and episodes that precede FE.	Increased cadence (68%) and decreased stride length (69%) during festination* compared to normal gait. No significant difference between stride length in the festination or the pre-freezing. Analysis of the three steps before freezing shows a progressive decrease in stride length (48%) and gait speed (38%), without change in cadence and an increase in the double support phase (66%) compared to gait with a voluntary stop. An exponential increase in cadence and decrease in stride length during festination and FE	FE is caused by an increased inability to generate compatible stride lengths and a lack of cadence. Before FE, there is a postural instability compensated by an increase in the double support phase. The increase in the double support phase might reflect an inability to transfer weight properly in preparation for the step. Festination and FE are deeply related phenomena.
Nieuwboer et al. [19]	11 FoG+ , OFF medication. H&Y ON medication between 2 and 3. H&Y OFF medication between 3 and 4.	Three tasks: 1. Gait at a comfortable self-select speed 2. Gait at a comfortable self-select speed with immediate stop after the researcher's oral clue 3. Gait with obstacles or passing doors with or without a double cognitive task.	Three-dimensional gait analysis. Electromyography in the anterior tibial and lateral gastrocnemius. Trials with FE (abrupt gait interruption episodes when approaching or crossing obstacles) have been identified. The instrument of video identified episodes of FE.	The muscle magnitude was calculated using the integral of the electromyographic signal. The magnitude of each muscle within the gait cycle. Activity duration of each muscle in the support and balance phases. Beginning and end of muscle activities within the support phase. Comparison between trials at normal gait voluntary stop and FE.	Gait cycles before FE: - Anterior Tibial activity in the balance phase initiated prematurely during the pre-balance (M = 72.6%; SD = −3.8) and it was significantly shorter during the balance phase (M = 38.7%; SD = 8.1). - Lateral Gastrocnemius had a premature initial and final activity during the support phase (M = 65.8%; SD = 7.7). - Anterior Tibial (9.9%) total activities were significantly reduced.	Abnormal coordination of the anterior tibial and lateral gastrocnemius before FE. It is suggested a central deficit in the gait cycle coordination.
Nieuwboer et al. [24]	10 FoG+ , OFF medication. H&Y ON medication between 2 and 3. H&Y OFF medication between 3 and 4.	Three tasks:1. Gait at a comfortable self-selected speed. 2. Gait at a comfortable self-selected speed with immediate stop after the researcher's oral clue. 3. Gait with obstacles or passing doors with or without a double cognitive task.	Three-dimensional gait analysis. Trials with FE (abrupt gait interruption episodes when approaching or crossing obstacles) have been identified. The instrument of video identified episodes of FE.	Coordination between the lower limbs. Articular angles in the pelvis, hips, knee, and ankle sagittal plane. Comparison between trials at normal gait voluntary stop posture and FE.	Compared to the stop, pre-freezing stride lengths shortened dramatically (58.4%); cadence increased (42.4%); and speed reduced (41%). Reduction of global pre-FE joint movement. Before FE, it decreased the range of motion in the sagittal plane, mainly in the ankle (57.8% in swing phase and 61.5% during the push-off phase of stance), knee (34.9%), hip (53.3%) and anterior pelvic tilt (31%) joints. Knee and hip flexion during the swing were lower on the FE side.	The anterior pelvic tilt observed before FE possibly indicates a lack of anticipatory postural adaptation, consequently increasing the risk of falling forward. There is no coordination before FE, merely abnormalities in movements related to acceleration and increased flexion and postural adaptation.
Chee et al. [31]	16 FoG+ , H&Y 3.88 (0.81) 10 FOG-, H&Y 2.10 (0.61) 10 healthy	Gait at 100%, 75%, 50%, and 25% of the participant's standard stride length.	Pressure sensor to measure the spatio-temporal parameters of the gait. Observational analysis to identify FE. The FE was defined as an unintended and temporary phenomenon in which the feet fail to move. The end of FE was defined when the step length returned to its standard value.	FE numbers. Spatio-temporal parameters of gait.	Increase in FE in PD+FOG in 50% (M= 32.7; SD=8.02) and 25% (M=14.17; SD=4.81) conditions. Predominant FE occurred in the 25% condition.	Reduced step length and successive step length reductions might cause FE.
Jacobs et al. [17]	10 FoG+ 10 healthy	Voluntary steps from a somatosensory clue. Voluntary and	Force plate and EMG in bilateral medial gastrocnemius, anterior	Number, time, and APAs amplitude. Delay at the beginning of the APA.	PD produces multiples APAs. Multiple APAs cause knee tremors.	Multiple APAs and knee tremors that cause FE can be caused by a worse

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Table 1 – (*continued*)

Article	Participants	Task	Instruments/ Methods	Variable	Results	Conclusion
		protective steps in response to a previous translation of the support base.	tibial and tensor fascia lata.			coupling between normal APA and voluntary steps.
Nantel et al. [28]	14 FoG+ 14 FoG- 10 healthy	Stepping in Place (SIP) task, raising the legs alternately at a self-selected pace.	Force plate. A FE was defined when the patient was unable to lift the foot from the force plate completely; i.e., when the vertical forces did not reach 100% (foot instance) and 0% (lifting phase)	Stepping cycle symmetry and rhythmicity of SIP. Correlation between Freezing of Gait Questionnaire (FoG-Q) and SIP. FE: Peaks reaching values below 15% and above 85%and separated by more than 400 ms were detected	FoG+ had more significant SIP asymmetry (M = 10.2%; SD = 5.4) and arrhythmicity (M = 5.0; SD = 1.6) compared to controls (asymmetry: M = 5.7%, SD = 1.6; arrhythmicity: M = 3.3, SD = 0.7) and FoG- (asymmetry: M = 6.5%, SD = 3.8; arrhythmicity: M = 3.2, SD = 0.8).	SIP cycle asymmetry and stride time variability were worse in FoG+ .
Yungher et al. [22]	14 FoG+ , OFF medication. H&Y 2.7 (0.6).	Timed up and Go task.	Inertial sensors are positioned in the lumbar region and bilaterally thigh, ankle, and midfoot region — FE identified by two experienced professionals and over the spectral analysis of inertial sensors frequency.	Differences at the beginning of the freezing frequency band between the thigh, ankle, and foot regions. The time between the last heel strike (left or right) and freezing.	Start of the frequency band from distal to proximal freezing (feet left: M = 232 ms, SE = 43; feet right: 259 ms, SE = 45; shank left: M = 226 ms, SE = 41; shank right: M = 194 ms; SE = 45; thigh left: M = 66 ms, SE = 43; thigh right: M = 16 ms, SE = 43). Peak spectral analysis has a leaning to decrease distal to proximal.	FE is characterized by high-frequency oscillation in the feet, which progresses proximally.
Palmerini et al. [23]	11 FoG+ , ON medication. H&Y between 2 and 4.	Activities that induce FoG as 360° turns, 180° turns, the figure of 8 shapes, dual cognitive task.	Inertial sensors in the lower back and bilaterally ankle region.	Turns quality, gait symmetry, gait amplitude, and freezing frequency bands analyze episodes before freezing (2 s before freezing). FE onset was defined as the disturbance of the alternation between the right and left steps.	There was a significant difference between gait and pre- FE in the variables: turn quality, a cross-correlation between right and left, mean of right/left variability, lumbar region variability, and frequency spectral analysis.	There is a degradation of gait which occurs before FE.
Cantu et al. [20]	12 FoG+ , OFF medication H&Y ON medication: 2.7 (0.9). H&Y OFF medication: 3.1 (1.0).14 FoG-, OFF medication. H&Y ON medication: 1.9 (0.7). H&Y OFF medication: 2.3 (0.7).	SIP	Surface EMGs were collected bilaterally from the proximal muscles (rectus femoris - RF; and biceps femoris - BF) and distal muscles (tibialis anterior - TA; and medial gastrocnemius - MG).	Amplitude (RMS), variability (CoV), and inter-muscle functional connectivity were analyzed in four periods: baseline, 2 s before FE, during the FE, and 2 s after FE.	Bilateral TA and GM amplitude on the less affected side was lower before (TA: M = 0.102 mV, SD = 0.10; GM: M = 0.035 mV, SD = 0,02), during (TA: M = 0.103 mV, SD = 0.10; GM: M = 0.033 mV, SD = 0.02) and after (TA: M = 0.103 mV, SD = 0.10; GM: M = 0.036, SD = 0.02) FE than the baseline. Bilateral BF amplitude was greater before (most affected: M = 0.060 mV, SD = 0.,02; least affected: M = 0.067 mV, SD = 0.03) during (most affected: M = 0.057 mV, SD = 0.02; least affected: M = 0.053 mV, SD = 0.02), and after (most affected: M = 0.067 mV, SD = 0.03; least affected: M = 0.057 mV, SD = 0.02) FE when compared to baseline. Altered variability in all muscles during FE. Variability returns to the baseline value, except for bilateral TA. Increased functional connectivity between the distal muscles on the less affected side before FE (M = 0.192; SD = 0.01). Reduced variability in MG on the least affected side during FE.	There were changes in the electromyographic characteristic of the proximal and distal muscles of the lower limb in FE. Injury and adaptive strategies of the proximal muscles of the lower limb in FE.
	9 FoG+ 9 FoG-	Compare the gait and trunk	Inertial sensors in the region of sternum,	Spatio-temporal parameters of gait.	While turning: FE lower cadence (M = 98.8 steps/min;	FE deficits in adjusting the spatio-temporal and

(*continued on next page*)

Table 1 – (*continued*)

Article	Participants	Task	Instruments/ Methods	Variable	Results	Conclusion
Mitchell et al. [27]	OFF medication H&Y between 2 and 3	kinematics when walking in a straight line and continuous turning.	sacrum, right and left wrist, and right and left ankle.		SD = 4.1), variability in gait speed (M = 0.116 m/s; SD = 0.010) and stride length (M = 7.28% leg length; SD = 0.51), and mediolateral trunk Spatio-temporal parameters were different between walking and turning tasks.	kinematic parameters of the trunk while turning. FE reduced variability of spatial and temporal gait parameters while turning, which is probably related to reducing amplitude and fear of falling.

FoG+: freezers. FoG-: non-freezers. FE: freezing episode. SIP: stepping in place. FoG-Q: Freezing of Gait Questionnaire. APA: anticipatory postural adjustment. * festination: "rapid, small steps, done in an attempt to keep the center of gravity in between the feet while the trunk leans forward involuntarily and shift the center of gravity forward" [32]

Conflict of interest statement

Authors declare to have no actual or potential conflict of interest including financial, personal or other relationships which might influence results and their interpretation.

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