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 Key words: Parkinson's Disease, gait initiation, freezing of gait, cueing devices, assistive devices.

<u>Abstract</u>

Background: Freezing of gait (FOG) remains one of the most common debilitating aspects of Parkinson's disease and has been linked to injuries, falls and reduced quality of life. Although commercially available portable cueing devices exist claiming to assist with overcoming freezing; their immediate effectiveness in overcoming gait initiation failure currently unknown. This study investigated the effects of three different types of cueing device in people with Parkinson's disease who experience freezing.

Methods: Twenty participants with idiopathic Parkinson's disease who experienced freezing during gait but who were able to walk short distances indoors independently were recruited. At least three attempts at gait initiation were recorded using a ten camera Qualisys motion analysis system and four force platforms. Test conditions were: laser cane, sound metronome, vibrating metronome, walking stick and no intervention. Results: During testing 12 of the 20 participants had freezing episodes, from these participants 100 freezing and 91 non-freezing trials were recorded. Clear differences in the movement patterns were seen between freezing and non-freezing episodes. The laser cane was most effective cueing device at improving the forwards/backwards and side to side movement and had the least number of freezing episodes. The walking stick also showed significant improvements compared to the other conditions. The vibration metronome appeared to disrupt movement compared to the sound metronome at the same beat frequency.

Conclusion: This study identified differences in the movement patterns between freezing episodes and non-freezing episodes, and identified immediate improvements during gait initiation when using the laser cane over the other interventions.

Introduction

Freezing of gait (FOG) remains one of the most common debilitating aspects of Parkinson's disease. It has been linked to injuries and falls and is a main contributory factor in reducing quality of life [1-4]. FOG causes temporary cessation of effective stepping and a sensation of "feet being glued to the floor" [1,5,6] and occurs when people turn (63%), initiate walking (23%), walk through narrow spaces (12%) and reach destinations (9%) [7].

There are multiple factors that can induce and overcome components of FOG [8, 9] with pharmacological and surgical intervention often unable to ameliorate symptoms [10]. The European guidelines for Parkinson's Disease strongly recommend using cues for the improvement of walking speed, however they weakly recommend against cueing of gait for improvement of freezing of gait [11]. This can be due to the limited literature that is available on this topic and the variety of cues used to improve freezing of gait. Transverse lines (TL) on the floor have been shown to improve gait in people with Parkinson's disease [12-15], including an increase in stride length [12,14,15] and improvement in gait initiation [12,15]. Other external cues, such as somato-sensory, visual and auditory stimuli, have also been used with mixed results, however these studies focussed mainly on steady state gait and not on overcoming gait initiation failure [16,17].

Gait initiation failure or "start hesitation" is a component of FOG which is described as a difficulty in initiating gait in the Unified Parkinson's Disease Rating Scale (UPDRS) [18]. Gait initiation is normally a stereotypical and unconsidered transition from stance

into walking [19,20]. Giladi et al explored the presence of motor blocks in a sample of 990 people with Parkinson's disease; 318 were found to have FOG, 86% of these had blocks in initiation of gait [5].

Studies on gait initiation failure are few. Jiang and Norman investigated the effects of visual and auditory cues on gait initiation in people with Parkinson's disease [12]. They found differences in maximum horizontal force between people with Parkinson's disease who freeze and do not freeze and between the different cues. The auditory cues used were rhythmic sounds matched to the participant's average step time and the visual cues were high-contrast transverse lines on the floor adjusted for the participant's height and first step length, which although beneficial has a limited practical value outside of the laboratory setting [21]. Moreover, the auditory cues in this study did not produce a significant difference when compared to the no cue condition. Unfortunately, the authors grouped the individuals with and without gait initiation difficulty together when studying the effect of the different cues, therefore diluting the effect and the potential clinical relevance of the findings.

Van Wegen et al investigated the use of a rhythmic somato-sensory cueing device attached to the wrist on gait initiation in people with Parkinson's disease. This showed that participants were able to modify their stepping pattern. The authors suggested that such cues draw attention to the act of walking [22]. Dibble et al [23] considered the effects of different sensory cueing methods on gait initiation in people Parkinson's disease. The cueing methods were a single and repetitive auditory signal from an electronic metronome and an electrical stimulus from a neuromuscular stimulator. Dibble and coworkers found that both these sensory cueing modalities had a negative effect on displacement of the body and swing limb [23]. Cubo et al examined the effects of a metronome in 12 patients with freezing when in their 'on' state and reached similar conclusions: walking time increased when using the metronome [24].

To date no study has compared three types of cueing device (somato-sensory, visual and auditory cues) and their immediate effects on gait initiation in individuals who suffer from FOG episodes. The aim of this study was to explore which of three cueing modalities was most effective in reducing the FOG frequency and to determine how these cueing modalities facilitate gait initiation performance.

Method

Twenty participants were recruited from local Parkinson's Disease Society groups (14 males and 6 females), mean age 68 years (range 49-84 years) and 11.5 years (range 1-23 years) since diagnosis. Inclusion criteria were; idiopathic PD diagnosed by a neurologist, ability to walk indoors without physical assistance, a score of 2 (occasional freezing when walking) or 3 (frequent freezing when walking, occasionally falls from freezing) on item 14 (freezing when walking) of the Unified Parkinson's Disease Rating Scale (UPDRS) [18], adequate hearing and vision to perceive sound and visual cues and no acute condition likely to cause gait impairment. For participants with motor fluctuations, timing of their data collection was based on their response to UPDRS item 14. Where participants met the freezing criteria only during an "off" period they voluntarily delayed their medication and were tested during an expected 'off' phase. Ethical approval was

gained from Cumbria and Lancashire NHS Research Ethics Committee ref: 08/H1015/76. All participants gave written informed consent according to the declaration of Helsinki [25] before entering the study.

Gait initiation data were collected at 100 Hz using a ten camera Oqus motion analysis system (Qualisys medical AB, Gothenburg, Sweden). The calibrated anatomical system technique (CAST) was used to place and determine the movement of segments [26]. Anatomical markers were placed on the lateral and medial malleoli, epicondyles of femur and humerus, the greater trochanter, anterior and posterior superior iliac spines, head of acromium, ulnar styloid process and medial head of radius. Tracking markers were placed on the head of 1st and 5th metatarsals, calcaneus, anterior aspect of talus, clusters of four markers were placed on the shanks, thighs, arms and forearms. Force data were collected using a two 400mm by 600mm AMTI force plates (BP400600 Advanced Mechanical Technology, Inc. USA) at 200 Hz. The raw data were then exported to Visual 3D (C-Motion. Inc. USA) for processing. The movement and force data were filtered using a fourth order low pass Butterworth filter with a cut off frequency of 6Hz and 25Hz respectively. An area of 10m by 3m was covered in a plain blue coloured carpet matching the laboratory floor which covered the force plates and surrounding area. No wires or camera tripods were immediately in front to limit visual sensory information.

Participants were tested under 5 randomly assigned conditions; no cue, walking stick, a visual cue which was a laser line projected on the floor from a walking stick (LaserCane, U-Step), an auditory cue provided by a metronome (Peterson BodyBeat Pulsing Metronome), and a somato-sensory cue using the same metronome set to vibration mode. Participants chose which hand to use for the walking stick and LaserCane. The metronome was clipped to a belt at the back of the participant, while in vibration mode the vibration device was placed anteriorly over the right side of the pelvis so it could be felt easily. The auditory and somato-sensory cues were set at 70 beats/minute and participants were asked if they felt comfortable with this setting; two chose to reduce the speed of repetition, to 60 and 50 beats/minute.

Participants were asked to rise from a chair, stand briefly with one foot on each force plate, and then begin walking in their own time. This was to ensure that the instructions themselves did not act as a cue. The start of the initiation was defined by the initial movement of the centre of mass (COM) and the centre of pressure (COP) i.e. when the participants started or tried to start moving. The termination of the episode was defined as the swing foot leaving one of the force plates with the threshold of force plates set to 10N. Two experienced neuro-physiotherapists independently determined if a freezing trial occurred. A freezing episode was determined when a consensus was reached. Before the cued trials the participants were asked to use the cue at the start of the initiation and in whatever way they felt would be most helpful. Data collection began while the participant was sitting and continued until they had walked a distance of up to 3 metres, or as far as they were able. Participants wore their usual footwear. No instructions were given with regard to which foot to step off with. Participants rested as required in between each trial. A physiotherapist followed the participants monitoring for loss of balance and to prevent falls.

Outcome measures collected were: percentage of freezing episodes, first step length, second step length, forward COM velocity, sideways COM velocity, number of forward/backward sways, and the number of sideways sways, Forward COP velocity

(m/s) side to side COP velocity. The total body COM was found from a weighted sum of the COM of every segment of the body modelled, this included: feet, shanks, thighs, pelvis, trunk, head, arms and forearms.

Statistical analysis of the data was performed using SPSS version 21. The statistical analysis of the biomechanical outcomes measures was conducted using an independent t-test to determine the differences between all episodes of freezing and non-freezing as all episodes were included, this precluded the use of a paired t-test. A two way repeated measures analysis of variance with post-hoc pairwise comparisons were used to test for differences between the five conditions for all the individuals who had episodes of freezing during testing.

Results

During testing 12 of the 20 participants had freezing episodes, from these twelve participants 100 freezing and 91 non-freezing trials were recorded. All but one participant completed a minimum of 3 trials for each condition due to fatigue. None of the participants had previously used any of the devices apart from the stick. Significant differences between the freezing and non-freezing trails were seen in first step length, second step length, forward center of mass (COM) velocity, sideways COM velocity, number of forward/backward sways, and the number of sideways sways, (table 1). Significant differences were also seen between the different conditions with the laser cane having the fewest number of freezing episodes, and showed the greatest improvement in the first step length, second step length, forward COM velocity, number of forward/backward sways and the number of COM sideways sways compared to no intervention. The walking stick also showed significant improvements in the first step length, forward COM velocity, number of COM sideways sways, and side to side centre of pressure velocity compared to no intervention. However the laser cane showed significant benefits over the walking stick in first step length and number of sideways sways. Sound also showed significant improvements in forward COM velocity, sideways COM velocity, number of forward/backward sways, and the number of sideways sways. However the vibrating metronome appeared to disrupt movement compared to the sound metronome at the same beat frequency with significant changes in first step length, forward COM velocity, sideways COM velocity, number of forward/backward sways and the number of sideways sways, table 2.

Discussion

This current study identified immediate functional benefits of the laser cane and the walking stick over the other interventions. Participants had a greater first step length with a greater forward COM velocity and experienced a fewer number of sideway sways when using either the laser cane or the stick when compared with no cue. Second step length and the number of forward sways also improved in using the laser cane over the other devices. Hass et al also explored balance in individuals with PD with the use of COP-COM and found that individuals with impaired postural control produced shorter COP-COM distances than individuals without clinically detectable balance impairment [27], however the authors are unaware of anyone previously considering the COM velocity during gait initiation. Historically an inverted stick had a beneficial effect on overcoming freezing [28,29] even though in this study the stick was not included as a cueing device

as such, but rather as a control condition for the laser cane, it also showed a benefit over other devices except the laser cane. The effect of the laser cane supports Donovan et al [21] who demonstrated a modest but significant reduction of FOG as first outcome measure (FOG Questionnaire) in 26 patients using the U-Step cane or walker equipped with a laser light beam. Donovan also found modest effect of a laser-light visual cue in overcoming freezing of gait in a community environment but this was not specific to addressing start hesitation nor tested participants in the "off state". Therefore the effectiveness and acceptability of such devices in day to day use in the home and outdoor environments has yet to be fully determined. Interestingly in this current study vibration appeared to disrupt movement compared to the sound metronome at the same beat frequency for the majority of participants, although one individual reported a positive effect during testing. However caution is advised about using vibration until more is known about optimum frequency and location [17,23].

During testing 12 of the 20 participants had freezing episodes, from these participants 100 freezing and 91 non-freezing trials were recorded. Previous studies have had difficulty in obtaining freezing data in the laboratory environment [10,30]. Nieuwboer et al. recorded eight participants who "froze" out of sixty reported freezers investigated whilst exploring different cue effects on turning speed [30]. One explanation for this difference in the current study could be a reduced amount of visual-sensory information which was achieved by using a plain blue coloured carpet which matched the laboratory floor and walls, generating a worst case scenario for gait initiation in people with PD. Such environmental factors have been shown to increase FOG episodes such as lower lighting levels and large open spaces [31]. Although light levels were not lowered for this current study the movement analysis laboratory used is a large open space 30m x 20m x 10m. In addition care was taken not to prompt gait initiation with a verbal instruction as participants were required to start walking at their own pace (self-initiated pace) representing an everyday situation. Bunting-Perry et al [32] recorded a greater percentage of individuals with PD experiencing FOG during walking with 17 out of 22 males. However no significant differences were seen when using a rolling walker with and without a laser beam visual cue.

This study identified clear measurable differences in the mechanisms and control between freezing episodes and non-freezing episodes and the effect of commercially available portable cueing devices which showed improvements in step length and COM velocity. This provides important information about the immediate effect of cues on GI for people with PD who are affected by freezing, which could be used to inform practice, but future research is need to determine possible effects of cue training and the longer term effect of using cueing devices [23]. Clinicians also may be reluctant to provide Parkinson's patients with sticks as it is perceived as detrimental due to possible effects on an already flexed posture, however they need to balance the possible adverse effects against the possible beneficial effect as a cue.

Conclusion

This study identified clear measurable differences in the mechanisms and control between freezing episodes and non-freezing episodes in people with Parkinson's disease and immediate functional benefits of the laser cane and the walking stick over the other interventions tested. Both the laser cane and the walking stick could benefit people with Parkinson's disease with gait initiation difficulties.

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Non-freezing trials	Freezing trials	Nothing	Laser	Sound	Vibration	Stick
-	-	81.58	27.50	44.44	68.29	40.00
		(7.53)	(7.34)	(7.74)	(7.25)	(7.85)
0.241*	0.143	0.163	0.271	0.167	0.126	0.204
(0.017)	(0.012)	(0.013)	(0.012)	(0.012)	(0.013)	(0.013)
0.481*	0.272	0.314	0.535	0.353	0.242	.422
(0.030)	(0.025)	(0.046)0	(0.042)	(0.043)	(0.042)	(0.045)
0.513*	0.311	0.335	0.455	0.392	0.324	0.460
(0.021)	(0.018)	(0.017)	(0.016)	(0.016)	(0.017)	(0.016)
-0.168*	-0.149	-0.147	-0.161	-0.182	-0.147	-0.148
(0.005)	(0.007)	(0.007)	(0.006)	(0.007)	(0.007)	(0.006)
2.89*	15.52	12.46	7.54	7.92	14.50	9.18
(0.30)	(1.39)	(1.25)	(1.19)	(1.24)	(1.45)	(1.16)
6.99*	22.41	20.50	10.94	13.64	21.18	15.18
(0.51)	(1.51)	(1.29)	(1.22)	(1.28)	(1.49)	(1.20)
0.144	0.176	0.146	0.139	0.154	0.216	0.138
(0.011)	(0.016)	(0.024)	(0.022)	(0.023)	(0.022)	(0.022)
0.473	0.484	0.504	0.435	0.439	0.603	0.358
	(0.036)	(0.049)	(0.047)			(0.047)
	0.241* (0.017) 0.481* (0.030) 0.513* (0.021) -0.168* (0.005) 2.89* (0.30) 6.99* (0.51) 0.144 (0.011)	0.241* 0.143 (0.017) (0.012) $0.481*$ 0.272 (0.030) (0.025) $0.513*$ 0.311 (0.021) (0.018) $-0.168*$ -0.149 (0.005) (0.007) $2.89*$ 15.52 (0.30) (1.39) $6.99*$ 22.41 (0.51) (1.51) 0.144 0.176 (0.011) (0.016) 0.473 0.484	$ 81.58$ (7.53) (7.53) 0.241^* 0.143 0.163 (0.017) (0.012) (0.013) 0.481^* 0.272 0.314 (0.030) (0.025) $(0.046)0$ 0.513^* 0.311 0.335 (0.021) (0.018) (0.017) -0.168^* -0.149 -0.147 (0.005) (0.007) (0.007) 2.89^* 15.52 12.46 (0.30) (1.39) (1.25) 6.99^* 22.41 20.50 (0.51) (1.51) (1.29) 0.144 0.176 0.146 (0.011) (0.016) (0.024)	- $ 81.58$ 27.50 (7.53) (7.34) $0.241*$ 0.143 0.163 0.271 (0.017) (0.012) (0.013) (0.012) $0.481*$ 0.272 0.314 0.535 (0.030) (0.025) $(0.046)0$ (0.042) $0.513*$ 0.311 0.335 0.455 (0.021) (0.018) (0.017) (0.016) $-0.168*$ -0.149 -0.147 -0.161 (0.005) (0.007) (0.007) (0.006) $2.89*$ 15.52 12.46 7.54 (0.30) (1.39) (1.25) (1.19) $6.99*$ 22.41 20.50 10.94 (0.51) (1.51) (1.29) (1.22) 0.144 0.176 0.146 0.139 (0.011) (0.016) (0.024) (0.022) 0.473 0.484 0.504 0.435	- $ 81.58$ 27.50 44.44 (7.53) (7.34) (7.74) $0.241*$ 0.143 0.163 0.271 0.167 (0.017) (0.012) (0.013) (0.012) (0.012) $0.481*$ 0.272 0.314 0.535 0.353 (0.030) (0.025) $(0.046)0$ (0.042) (0.043) $0.513*$ 0.311 0.335 0.455 0.392 (0.021) (0.018) (0.017) (0.016) (0.016) $-0.168*$ -0.149 -0.147 -0.161 -0.182 (0.005) (0.007) (0.007) (0.006) (0.007) $2.89*$ 15.52 12.46 7.54 7.92 (0.30) (1.39) (1.25) (1.19) (1.24) $6.99*$ 22.41 20.50 10.94 13.64 (0.51) (1.51) (1.29) (1.22) (1.28) 0.144 0.176 0.146 0.139 0.154 (0.011) (0.016) (0.024) (0.022) (0.023) 0.473 0.484 0.504 0.435 0.439	81.5827.5044.44 68.29 .7.53.7.34.7.74.7.250.241*0.1430.1630.2710.1670.126(0.017)(0.012)(0.013)(0.012)(0.013)(0.012)0.481*0.2720.3140.5350.3530.242(0.030)(0.025)(0.046)0(0.042)(0.043)(0.042)0.513*0.3110.3350.4550.3920.324(0.021)(0.018)(0.017)(0.016)(0.016)(0.017)-0.168*-0.149-0.147-0.161-0.182-0.147(0.005)(0.007)(0.007)(0.006)(0.007)(0.007)2.89*15.5212.467.547.9214.50(0.30)(1.39)(1.25)(1.19)(1.24)(1.45)6.99*22.4120.5010.9413.6421.18(0.51)(1.51)(1.29)(1.22)(1.28)(1.49)0.1440.1760.1460.1390.1540.216(0.011)(0.016)(0.024)(0.022)(0.023)(0.022)0.4730.4840.5040.4350.4390.603

Table 1: Mean (SD) values for parameters under the different conditions and comparison between freezing and non-freezing episodes

*Significant differences p<0.05 between Non-Freezing vs. Freezing episodes using an Independent t-test

Table 2: Pairwise comparisons b	between conditions
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Parameter		Nothing vs. Laser	Nothing vs. Sound	Nothing vs. vibration	Nothing vs. Stick	Laser vs. Sound	Laser vs. Vibration	Laser vs. Stick	Sound vs. Vibration	Sound vs. Stick	Vibration vs Stick
First Step	Mean Difference	-0.108*	-0.004	0.037*	-0.041*	0.104*	0.146*	0.067*	0.042*	-0.036*	-0.078*
Length (m)	(SE)	(0.018)	(0.018)	(0.019)	(0.019)	(0.017)	(0.018)	(0.018)	(0.018)	(0.018)	(0.018)
	p-value	0.000	0.810	0.047	0.032	0.000	0.000	0.000	0.019	0.042	0.000
Second Step	Mean Difference	-0.221*	-0.040	0.072	-0.108	0.181*	0.293*	0.113	0.112	-0.068	-0.180*
Length (m)	(SE)	(0.062)	(0.063)	(0.063)	(0.064)	(0.059)	(0.059)	(0.061)	(0.060)	(0.062)	(0.062)
	p-value	0.000	0.531	0.252	0.097	0.003	0.000	0.066	0.065	0.274	0.004
Forward COM	Mean Difference	-0.121*	-0.057*	0.011	-0.126*	0.064*	0.132*	-0.005	0.068*	-0.069*	-0.137*
velocity (m/s)	(SE)	(0.023)	(0.023)	(0.023)	(0.023)	(0.022)	(0.023)	(0.022)	(0.023)	(0.022)	(0.023)
	p-value	0.000	0.016	0.637	0.000	0.005	0.000	0.821	0.004	0.003	0.000
Sideways COM	Mean Difference	0.013	0.034*	0.000	0.001	0.021*	-0.013	-0.013	-0.034*	-0.034*	0.000
velocity (m/s)	(SE)	(0.009)	(0.010)	(0.010)	(0.009)	(0.009)	(0.009)	(0.009)	(0.009)	(0.009)	(0.009)
	p-value	0.151	0.000	0.987	0.949	0.024	0.154	0.154	0.000	0.000	0.962
Number of COM	Mean Difference	4.92*	4.54*	-2.03	3.28	-0.38	-6.96*	-1.64	-6.58*	-1.26	5.32*
forward/backward sways	(SE)	(1.73)	(1.76)	(1.91)	(1.71)	(1.72)	(1.87)	(1.66)	(1.91)	(1.70)	(1.86)
	p-value	0.005	0.011	0.291	0.058	0.826	0.000	0.328	0.001	0.462	0.005
Number of COM	Mean Difference	9.56*	6.86*	-0.68	5.32*	-2.70	-10.24*	-4.24*	-7.54*	-1.54	6.00*
sideways sways	(SE)	(1.78)	(1.81)	(1.97)	(1.76)	(1.77)	(1.93)	(1.71)	(1.96)	(1.75)	(1.91)
	p-value	0.000	0.000	0.729	0.003	0.131	0.000	0.015	0.000	0.379	0.002
Forward centre of	Mean Difference	0.007	-0.008	-0.070*	0.008	-0.015	-0.077*	0.000	-0.062	0.016	0.078*
pressure velocity (m/s)	(SE)	(0.032)	(0.033)	(0.032)	(0.032)	(0.032)	(0.032)	(0.031)	(0.032)	(0.032)	(0.032)
	p-value	0.820	0.812	0.034	0.800	0.64	0.016	0.978	0.055	0.617	0.015

Side to side centre of pressure velocity (m/s)	Mean Difference (SE)	0.068 (0.068)	0.065 (0.069)	-0.100 (0.068)	0.146* (0.068)	-0.003 (0.067)	-0.168* (0.066)	0.078 (0.066)	-0.165* (0.067)	0.081 (0.067)	0.246* (0.066)
	p-value	0.316	0.346	0.146	0.034	0.959	0.013	0.243	0.016	0.229	0.000