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Original Article

Rhythmic laser cue is beneficial for improving gait performance and reducing freezing of turning in Parkinson's disease patients with freezing of gait

Liang Tang[1*], Chao Gao[2*], Dong Wang[1], Anmin Liu[3], Shengdi Chen[2], Dongyun Gu[1,4,5]

[1]Shanghai Key Laboratory of Orthopaedic Implants, Department of Orthopaedic Surgery, Shanghai Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China; [2]Department of Neurology, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China; [3]School of Health Sciences, University of Salford, Manchester, United Kingdom; [4]School of Biomedical Engineering & Med-X Research Institute, Shanghai Jiao Tong University, Shanghai, China; [5]Engineering Research Center of Digital Medicine and Clinical Translation, Ministry of Education of P. R. China, Shanghai, China. [*]Equal contributors.

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Abstract: Background and aim: Gait time components in Parkinson's disease (PD) patients such as step time, gait rhythmicity, symmetry, and coordination are exacerbated during turning. Freezing of gait (FOG) can be triggered off when such gait-timing deficiency exceeds a certain threshold. Whether laser visual cue could improve the impairments of gait time components and reduce freezing episodes in turning remains unclear. Different from continuous laser (CL), rhythmic laser (RL) cue could provide rhythmic temporal information. The aim of this study was to investigate the effect of RL and CL cue to identify which one was better at modulating gait time components and improving gait performance in turning. Methods: Twenty-three patients on dopaminergic medication performed the "8-shaped" turning task. Test conditions included no laser (NL), CL and RL cues. Gait parameters such as numbers of freezing episodes, the turning time, step time, gait arrhythmicity, asymmetry, and discoordination were assessed. Results: The numbers of freezing episodes, the turning time, step time and the gait arrhythmicity were significantly improved in RL cue compared with both CL and NL conditions, whereas no significant difference was found between CL and NL conditions. Gait asymmetry and discoordination did not show significant difference between the three conditions. Conclusion: Compared with CL cue, it seems that synchronization in RL cue might be beneficial in improving the background gait performance and reducing freezing in turning. For PD patients with FOG, RL cue might be promising when applied as an optional technique in gait rehabilitation.

Keywords: Parkinson's disease, freezing of gait, gait analysis, visual cue, laser

Introduction

Gait impairment is a common symptom in patients with Parkinson's disease (PD), of which freezing of gait (FOG) is a very serious type. Freezing of gait is characterized by inability to produce an effective gait initiation and tremor in lower limbs. Generally, FOG often occurs at gait initiation, turning, crossing narrow doorway as well as crowded environments. Moreover, turning occurs frequently in almost all daily activities with five turns being needed in every 10 meter at home [1] and easily induces freezing. Schaafsma *et al.* showed that FOG occurred when turning (63%), initiating walking (23%), walking through narrow spaces (12%) and reaching destinations (9%) [2]. Giladi *et al.* found that 45% of 318 PD patients reported that freezing occurred while turning [1]. FOG often leads to falls and complications such as hip fracture, which seriously affects the quality of life [3].

However, anti-parkinson medication did not improve the gait arrhythmicity and asymmetry in step in place (SIP) gait task [4] and showed negative effect on freezing in some cases [5]. To date, although laser visual cue is widely applied to reduce FOG [6, 7], the effect of laser visual cue is not consistent. Bunting-Perry *et al.* reported that laser visual cue in patients with PD did not improve number of FOG episodes, step length or velocity [8]. Kompoliti *et al*. also demonstrated that no consistent effect has been found when visual cues (including laser visual cue) aid the completion of gait tasks and overcoming FOG [9]. It has been suggested that modulating the gait time components at a steady level in PD patient with FOG could prevent the occurrence of freezing [10]. To our knowledge, studies of laser visual cue mostly focused on the effect on straight-line walking. Few studies have showed the effects of laser cue in turning gait task. Whether laser visual cue could improve the impairments of gait time components and reduce freezing episodes in turning remains unclear.

Compared with the symmetric straight-line walking, turning is a asymmetric task and more vulnerable to impairment since turning requires more coordination, more coupling between posture and gait [11, 12]. Due to the difference of motor nature and temporal component between inner and outer lower-limb [13], asymmetric turning task could exacerbate inter-limb synchronization difficulties [14], which could induce the impairments of gait time components such as shorter step time, asymmetry, arrhythmicity, or bilateral discoordination. It has been reported that freezing is correlated with these impairments and could be triggered off when such impairments exceed a certain threshold [15, 16]. At present, the modality of laser cue is continuous laser (CL) cue, which continuously project laser line on the ground. Obviously, the continuous laser cue cannot provide rhythmic temporal information. It seems that the CL cue might show less effect on the impairments of gait time components and freezing episodes. By contrast, rhythmic laser (RL) visual cue, which rhythmically projects laser line on the ground, contains rhythmic temporal component. Therefore, we speculated that the rhythmic laser cue might compensate for the deficiency of CL cue and contribute to modulate the impairments of gait time components in turning. We adopted the RL cue as a method to improve the gait performance in turning. The CL cue was used as a control in this study. Patients were instructed to perform "8-shaped" turning task under no laser (NL), CL and RL conditions. The purpose of this study was to compare the RL and CL cue, which one was better at improving impairments of gait time components and reducing FOG in "8-shaped" turning task.

Materials and methods

Patients

Subjects were recruited from the Department of Neurology Clinic at Ruijin Hospital, the School of Medicine, Shanghai Jiao Tong University. Thirty patients were enrolled and only twenty-three patients completed the test. Among the seven subjects who withdrew from the test, three were due to the suffered from fracture, the two were due to apoplexy and another two were due to the exposure to laser cue prior to the test. All patients were diagnosed as PD with FOG by a neurologist at the clinic and tested during the "On" state. To achieve a relative "On" state, the patient was asked to complete the task during 1 to 2 hours after the intake of the dopaminergic medication. Inclusion criteria were the following: 1) H&Y (Hoehn-Yahr) stage I-III; 2) the patient could walk independently without any auxiliary orthosis; 3) the patient had a history of FOG could be triggered off using "8-shaped" turning in the clinic. Exclusion criteria were the following: 1) central neurological system disease or musculoskeletal system disease affecting walking ability or postural stability; 2) cardiothoracic disorders that severely influenced walking in daily life; 3) mental or visual disorders.

The experimental protocol was approved by the Ethics Committee of the Ninth People's Hospital of Shanghai affiliated to Shanghai Jiao Tong University, School of Medicine. All subjects provided written informed consent in accordance with the tenets of the Declaration of Helsinki before participating in the experiment.

Procedure

Patients were tested in the gait laboratory, Shanghai Jiao Tong University. Trials were performed along a 10×5 meter walkway surrounded by an eight-camera optical motion capture system operated by Vicon Nexus 1.8.5. The motion data was captured with a sampling rate of 100 Hz, (VICON, Oxford Metrics Ltd., UK). The patients were tested with their own preferable shoes. The retroreflective markers were placed on the corresponding position to the proximal end of the calcaneus (the heel), the first metatarsal head, the second metatarsal head, the fifth metatarsal head, lateral malleolus and medial malleolus, respectively. The laser generator contained two models-rhythmical and continuous projects. The laser generator was attached over chest correspond to the sternum with an elastic bandage. Frequency of the rhythmic projection could be adjusted in accordance with the patient's own stride cadence. Duty cycle was set at 0.5. Laser beam was projected on the ground one step length in front of the patient's feet.

Given the difficulties of inducing freezing episodes in the laboratory environment, we designed an "8-shaped" route gait task including clockwise and anti-clockwise turning so as to continually change the walking trajectory and easily evoke FOG. When the "go" signal was given by the researcher, the patient was instructed to start to walk straight-line several steps, then enter the "8-shaped" turning route, which was 5 m×3 m walking area with the diameter of the turning circle designed as 1.5 meter, to complete the turning task. Each patient was tested in three conditions: no laser (NL), CL and RL. All subjects were tested in baseline condition (NL) first, while the order of the two laser conditions (CL, RL) was randomized between subjects. Prior to trials, the patient was asked to practice a few walks to familiarize test course and the way to synchronize the step-to-step with the rhythm in RL condition. In NL and CL conditions, the patient subject was instructed to turn at self-selected step cadence. While in RL condition, the frequency of RL was set 10% less than the patient's own preferable stride cadence, and the patient was instructed to step matching the rhythm provided by RL. To avoid cross effects, each condition was tested at an interval of 2 days. A research assistant would accompany the patient at his/her behind to ensure an immediate protection in case of the patient's losing balance and falling. After completion of a few trials, the patients were asked to rest for about ten minutes to minimize the effects of fatigue.

Data processing

The gait time components for each gait cycle (including stride time, swing time, step time) were calculated using a self-developed computer program in MATLAB based on the vertical coordinates of the heel and second metatarsal head markers. A freezing episode was expressed as the inability to completely lift the foot from the ground and hesitation until the next step was accomplished independently. The number of freezes and the turning time were calculated by other blinded observers.

During the "8-shaped" turning, step time was expressed as the time interval from the heel strike to the next heel strike of another foot. Discoordination between bilateral lower-limbs was expressed as phase coordination index (PCI) [17], which combined the variability with the inaccuracy of stepping generation. The asymmetry was defined by the equation: 100× ln (SSWT/LSWT) [14]. SSWT is the shortest swing time and LSWT is the longest swing time. For each subject, the SSWT and LSWT were represented as the foot that had the shorter and longer mean swing times in a trial. The step arrhythmicity was defined as the coefficient of variation of step time (CV = SD/mean ×100%) [18].

Statistical analysis

The temporal parameters such as step time, arrhythmicity (step time variability), asymmetry and discoordination were shown as mean ± standard deviation (SD) and submitted to one-way analysis of variance (ANOVA) to see if there were differences between conditions. When a main effect was found in the ANOVA, post-hoc analysis was performed to assess the difference between pairs of conditions. Both median time to complete the "8-shaped" turning and median number of freezing episodes were submitted to Friedman's test to compare the difference between the three laser conditions. Compared to the mean, the medians are not influenced by extreme values. All statistical analyses were performed using SPSS 19.0 with *P*-value set at 0.05.

Results

Clinical profiles

Table 1 shows the clinical characteristics of subjects who completed the study. Of the 23 subjects, 10 were male and 13 were female. Mean age was 70.8±8.4 years ranged from 57 to 83; mean years of freezing periods was 6.7±4.7 years range from 1 to 16; mean motor UPDRS subscore on medications was 26.1± 2.4. Mean H&Y score was 2.17±0.9 (SD).

Fifteen subjects reported that they could synchronize step-to-step with the rhythm of RL cue

Table 1. Clinical features of the patients

Clinical features	PD+FOG (n = 23)
Age (years)	70.8±8.4
Sex (M/F)	10/13
Height (meter)	1.67±0.07
Weight (kg)	65.9±8.5
History of FOG (year)	6.7±4.7
UPDRS part III	26.1±2.4
H&Y stage	2.17±0.9

Notes: The data was expressed in mean ± SD. PD+FOG = Parkinson's disease Patient with freezing of gait, H&Y = Hoehn-Yahr.

and facilitate to turn in "8-shaped" route, five subjects felt they could easily perform turning in CL cue, three subjects didn't have any difference during walking in the three test conditions.

Gait time components

Step time in RL and CL cue were prolonged as compared with NL. Post-hoc analysis found that RL significantly prolonged step time in comparison with both CL and NL conditions. However, step time in CL cue did not show significant difference compared with NL. The step time variability significantly differed among the conditions (F = 7.545, *P* = 0.001). Post-hoc analysis found that RL cue (5.9±1.9%) significantly reduced the step time variability compared with both CL (7.4±2.1%, *P* = 0.029) and NL (8.0±2.3%, *P* = 0.001) conditions. Although the step time variability was improved in CL cue, no significant difference was found between CL and NL condition (*P* = 0.792) (**Table 2**).

The gait time asymmetry and gait discoordination were also improved in RL compared with both CL and NL; however, the improvement did not show statistically significance between three conditions (**Table 2**).

Turning performance

The total numbers of freezing episodes in NL, CL and RL was 63, 44 and 23, respectively. Friedman analysis showed that RL cue could significantly reduce episodes of freezing compared with both CL and NL (Friedman's *P* = 0.001). In contrast, CL cue did not significantly reduce episodes of freezing in comparison with NL (Friedman's *P* = 0.742). The turning time significantly differed in the three conditions (Friedman's *P* = 0.001). Friedman analysis revealed that RL cue could significantly reduce the turning time compared with CL and NL condition. Although the turning time was also reduced in CL cue condition, the difference in comparison with NL condition was not statistically significant (Friedman's *P* = 0.662) (**Table 2**).

Discussion

The results from the study can be summarized in the following three aspects. Firstly, RL cue could significantly improve step time and gait arrhythmicity in "8-shaped" turning. Secondly, the gait asymmetry and discoordination showed no significant difference among the three conditions. Thirdly, RL cue could significantly reduce freezing episodes and turning time in comparison with both CL cue and NL.

In this study, both RL and CL cues are external laser visual cues, which share the common characters. However, they showed significantly different effects on "8-shaped" turning in this study. The results are in agreement with the opinion that the specific information that the cue provides (cue parameter) may play an important role on its effectiveness [19, 20]. The difference between the CL and RL cue is that RL cue could provide rhythmic information, whereas CL could not. As is known that the fundamental deficit in parkinsonian gait is central regulation in step time. In this study, RL cue significantly improved the step time compared to both CL cue and NL conditions. In contrast, step time did not show significant difference between CL cue and NL condition. It seems that RL cue mighty act as a timekeeper to induce a longer step time. In addition, gait arrhythmicity was also improved by RL cue but not by CL cue. Azulay demonstrated that external rhythmic information could compensate for defective internal rhythm of the basal ganglia [21]. Different from CL cue, RL cue might help to compensate for the motor set deficiency via providing appropriate step time, and then maintain the step time at a relative steady level. The beneficial effects of RL cue but not of CL cue on the step time and step arrhythmicity suggested that the RL might synchronize step-to-step with the rhythm provided by RL cue.

Table 2. The gait performance parameters and statistical results

"8-shaped" turning	RL	CL	NL	*P* value	*P* value (post-hoc)		
					RL *vs.* CL	RL *vs.* NL	CL *vs.* NL
Step time (s)	0.54±0.042	0.51±0.038	0.49±0.046	0.001*	0.046*	0.001*	0.276
Arrhythmicity (%)	5.9±1.9	7.4±2.1	8.0±2.3	0.001*	0.029*	0.001*	0.792
Asymmetry	5.9±2.2	6.6±2.3	7.4±2.5	0.071			
Discoordination	10.6±2.0	11.8±3.7	13.0±4.2	0.058			
Turning time (s)	9.8	10.8	11.3	0.001*	0.043*	0.001*	0.662
FOG (sum)	23	44	63	0.001*	0.029*	0.001*	0.742

Notes: Gait time component parameters including step time, arrhythmicity, asymmetry and discoordination in the RL, CL, NL conditions are expressed in mean ± SD. Number of freezing of episodes and turning time are measured as sum. One-way ANOVA analysis compares the parameters of gait time component (step time, arrhythmicity, asymmetry, and discoordination) between NL, CL and RL conditions. Friedman's test was used to compare the median number of freezing episodes and turning time between conditions. *P* value was set at 0.05. *showed significant difference. CL = continuous laser cue, RL = rhythmic laser cue, NL = no laser, FOG = freezing of gait.

In contrast, auditory cue also contains rhythmic information. McIntosh demonstrated that auditory cue could keep the step-to-step entrained, but without synchronized step cadence [22]. Freeman indicated that PD patients with FOG had difficulty in synchronizing step-to-step with auditory cue [23]. Compared with auditory cue, laser visual cue may compensate for a proprioceptive processing deficiency [24, 25], which play an important role in step-to-step synchronization in PD patients with FOG. It seems that RL cue combines the advantage of auditory cue and CL cue.

The effects of RL cue in this study might be explained by the following aspects. First, RL cue can present temporal sequence of gait task to the motor system and help to switch from one movement component in a movement sequence to the next instead of needing internally prepare and plan. Second, In "8-shaped" turning, the walking trajectory was constantly changing. It was a higher challenge gait task for PD patients with FOG. A increased step time means that step cadence becomes slower, which results in a longer time to plan each step-to-step. Third, RL might connect from the visual system project via the lateral geniculate nucleus of the thalamus to the visual cortex and lateral premotorcortex, which receives sensory information for externally guided movements [26, 27].

Contrary to the hypothesis, both RL and CL cues had no effect on improving gait asymmetry. The result also suggested that the components which the cue contains (such as rhythmic temporal component) might modulate the corresponding gait components (such as gait time component). Theoretically, the basic information provided by RL cue were step time and stride time. In this study, gait asymmetry between bilateral lower-limbs was calculated by swing time. Unlike step time or stride time, swing time did not correlate to the rhythmic information produced by RL cue. Therefore, both CL and RL could not modulate swing time.

Gait discoordination also showed no significant difference between the three conditions. "8-shaped" turning is a complicated task and requires a higher level of bilateral coordination. Turning requires the trunk flexibly rotate in a cranial to caudal sequence. Moreover, the impairment of coordination in turning not only exists in bilateral lower limbs, but also shows as an axial rigidity and loss of intersegmental flexibility ("en block"). The "en block" trunk might also adversely influence the lower limbs coordination in "8-shaped" turning task. In contrast to straight-walking, gait coordination in "8-shaped" turning should take the role of trunk into account. In the current study, the gait discoordination was calculated by PCI according to the step time and stride time between the bilateral lower-limbs without consideration the roles of trunk. Perhaps, due to the negative influence of trunk, gait discoordination did not significantly improve between the three conditions.

The most obvious results in this study was that a significant reduction in the numbers of FOG in RL condition. Multiple deficits in gait time components result in FOG. It is demonstrated that improving baseline gait performance associated with FOG would result in a significant reduction in freezing [10, 28]. In this study, multiple gait performance such as step time and arrhythmicity were significantly improved. This would suggest that RL cue might improve the background gait performance and keep the gait performance within the "secure gait zone" to prevent the occurrence of freezing. Additionally, the turning time was correlated with the numbers of freezing episodes. External rhythmic cue provided by RL could also make complex gait task (such as "8-shaped" turning) easier and faster, and give an impetus to speed up gait task [29].

Limitation

Several limitations exist in this study. Firstly, the "8-shaped" turning task applied in this study is to induce freezing episodes in laboratory environment. Although positive results were showed in RL cue condition, whether the similar effects could also be obtained in daily life environments is unknown. Secondly, as it was discussed above, the influence of trunk on gait coordination between bilateral lower-limbs should be taken into account. It is still unknown whether the RL or CL cues could improve the "en block" feature in trunk. Thirdly, the number of subjects was few, which also limits the generalizability of the results. Further studies are needed to resolve these issues.

Conclusion

Compared with CL cue, it seems that synchronization in RL cue might be beneficial in improving the impairments of gait time components such as step time and gait arrhythmicity and reducing freezing in "8-shaped" turning task. Trigger factors of FOG such as turning frequently occur in daily life. To prevent the occurrence of freezing episodes in such circumstance, it is important to improve the background gait performance so as to keep the baseline gait performance away from the threshold of FOG. RL cue might be promising when applied as an optional technique in the rehabilitation training in PD patients with FOG.

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Disclosure of conflict of interest

None.

Address correspondence to: Dongyun Gu, Shanghai Key Laboratory of Orthopaedic Implants, Department of Orthopaedic Surgery, Shanghai Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine, Room 701, No. 3 Building, 639 Zhizaoju Road, Shanghai 200011, China. Tel: +86-21-63139920; Fax: +86-21-63139920; E-mail: dongyungu@sjtu.edu.cn; Shengdi Chen, Department of Neurology, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China. E-mail: Chen_sd@medmail.com.cn

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