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Closed-Loop VR-Based Interaction to Improve Walking in Parkinson's Disease

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Abstract

Visual cueing have been reported to help improve walking in people with Parkinson's disease. However, many of these studies incorporate instructions and familiarization/practice, making it unclear whether the visual cues themselves were really effective or what parameters of walking are mutable. Here we used a closed-loop virtual visual cueing system to probe the automatic locomotor structures in subjects with idiopathic Parkinson's disease and no freezing episodes. The cues moved in synchrony to the velocity of each subject's walking but in the opposite direction, thereby giving rise to the perception of walking across a stationary landscape. In the absence of explicit instructions and practice, the virtual visual cues induced spontaneous changes among various walking kinematics in moderate-severe but not early-stage subjects. The largest effect was seen in the decrease in time to execute the first step (step initiation). Subjects completed the first step faster in the presence of the visual cues. Step length and walking speed on the other hand, decreased with exposure to the cues, i.e. subjects started out fast but then slowed down in the remainder of the walk. We conclude that the novel effects of the closed-loop visual cues produce mixed outcomes in walking performance. While step initiation improved spontaneously, the normalization of speed and step length would require cognitive strategies and practice as indicated in previous studies.

Keywords: Bradykinesia; Freezing; GaitAid; Gait; Visual cues; Virtual reality; Visual dysfunction

Introduction

The basal ganglia-supplementary motor area (BG-SMA) loop is thought to be involved in a number of stereotypical and spontaneous behaviors including walking by inducing the circuitries of pattern generators in the brainstem and spinal cord [1-5]. In Parkinson's disease (PD), anticipatory postural adjustments (APA) during voluntary stepping were found to be reduced after the area over the SMA underwent 1-Hz repetitive transcranial magnetic stimulations. The severity of PD symptoms was negatively correlated with APA duration. Stepping performance was not affected with stimulation of the dorsolateral premotor cortex [6].

As the disruption of the BG-SMA system increases with the progression of PD, patients become more reliant on the use of vision to move around. The reasons are still unclear but several hypotheses have emerged lately. For example, one possible benefit of visual cues is that it may help PD individuals to focus on their walking [7-12] possibly by aiding the ability to switch cognitive sets and holding short-term memory [13,14] or via greater cortical involvement [11,15-19].

The effect of visual cues in improving walking may occur spontaneously by circumventing the endogenous preparatory or set-related stage of motor control [20-22] which is abnormal in PD [13,23]. The spontaneity is also somewhat validated by clinical observations in individuals with PD. Providing horizontal but not vertical or diagonal lines on the floor serves as a visual aid which helps overcome the phenomenon of shuffling gait or freezing when the individual attempts to walk [24]. It is not clear however, why transverse but not parallel lines are effective in triggering the walking [25,26]. Cadence increased more than controls when PD subjects walked while looking down at transverse lines. The increased cadence was accompanied by enhanced activation of the right lateral premotor region [27]. The beneficial effects of visual cues are confusing because they sometimes produce the opposite effect. PD patients are known to involuntarily slow down or stop walking when nearing a doorway [28,29]. Handwriting is larger when it is carried out with eyes closed [30].

Other studies suggest that the beneficial effect of visual cues on walking may be derived from the use of different neural pathways such as the cerebellar-premotor circuitry [27,31-34] including inputs from the superior parietal region [35] which is thought to enable visually-guided control of lower-body movements [36] when the basal-ganglia-supplementary connections are circumvented in PD [37-39]. Besides proprioceptive signals from the spinocerebellar tract [40], the cerebellum cortex also receives extensive visual signals from the superior colliculi, pretectal areas and lateral geniculate body. These neurons project to the cerebellar cortex via the purkinje and mossy fibres which convey slow- and fast-moving visual stimuli respectively [41].

The phenomenon of freezing in PD is thought to be related to irregularities of the frontal [42,43], brainstem [44-46] visual systems [47,48], and engrained synchronization of the basal ganglia system [49-51]. Bradykinetic gait including reduced step length is therefore thought to be a harbinger of things to come [52]. However, since not every patient goes on to develop dementia or freezing, the mechanism of visually-incited walking remains mysterious.

A number of studies have attempted to determine the effects

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of visual cues on improving walking performance in PD. These experiments included verbal prompting and practice trials, making it unclear how the visual cues themselves might have helped improve their walking. Clinicians often have to strike a delicate balance between allowing patients to explore the interactions between a walking aid and the surrounding workspace versus providing intense practice with detailed instructions and verbal cues. The former can lead to bad habits setting in while the latter can result in frustration and noncompliance. A better understanding of how visual aids can improve walking performance spontaneously would thus provide the needed scientific evidence of their beneficial effects which can then be augmented with practice and instructions.

In the current study, subjects viewed virtual contrasting tiles while walking a linear trajectory without overt instructions or practice in order to determine the exclusive effect of the visual cues, as opposed to goal-oriented walking based on explicit instructions or practice [16,53-61]. The virtual visual cues in the current study are based on a closed-loop (feedback) model of stimulating the visual system [62,63]. The cues are synchronized to the speed of each subject's forward advances but in the reverse direction. This imparts to the subject the perception of walking across stationary tiles (Figure 1). This mode of control keeps in check of any unwanted perception of central or peripheral visual flow from the cues as in the case of an open-loop system. In such a system, the cues move independently of the subject's motion with the objective of augmenting or inducing the visual system and locomotor pattern generators [64]. The potential benefits of open-loop systems however, are offset by their obvious drawback. Open-loop schemes must dabble with the tricky challenge of enhancing walking while simultaneously creating conflicting sensory inputs to the central integrative mechanisms. Resolution of sensory discord is known to be inefficient in PD [65-71].

We hypothesized that the closed-loop visual cues will produce an improvement in walking performance in PD subjects in non-freezing moderate to more severe stages of the disease without incorporating a significant practice or learning component into the activity [72]. In particular, we expect the first step (step initiation) to occur faster. It is possible however, that the visual cues may also be distracting [73] and cause subjects to slow down. Subjects in the early stages of the disease who did not have significant walking impairments were also studied to determine the effects of the visual cues as a function of disease severity.

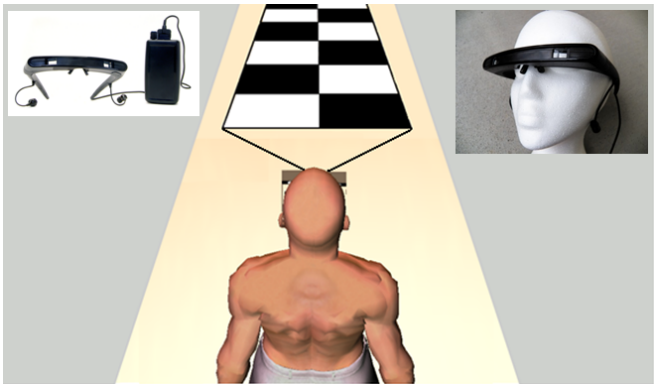

Figure 1: Close-loop virtual tile projection. Images from the GaitAid Virtual Walker™ visual cueing device (insert [75]) superimposed onto the visual scene. The virtual system employs the close-loop mode of control. As the subject walks forward, the tiles move backwards in direct proportion to the subject's speed. The tiles are enlarged for illustration. In reality, they occupy a narrow strip of the subject's nasal field of vision. Left insert figure included with permission of MediGait Ltd [119].

Materials and Methods

Subjects

47 subjects diagnosed with idiopathic Parkinson's disease (PD) in their usual anti-PD drug regimen participated in the study. The study was approved by the institutional review board. 26 were classified as early-stage Hoehn & Yahr (H&Y) 1-2 (17 men and 9 women) while 21 subjects were classified as moderately-severe H&Y 2.5-4 (13 men and 8 women) [74]. Subjects averaged 68.8 +/- 7.9 years old with 8.1+/- 5.4 years disease duration. Freezing was not indicated in any of the subjects, nor was it observed during testing. Details of subjects' characteristics are summarized in Table 1.

Materials

The visual device used in this study is the GaitAid Virtual Walker™ closed-loop system [75]. It has an eyeglass goggle component, dual earphones, and battery source. Earphones which provide auditory clicks also come as part of the device and can be used in conjunction with the visual cues if desired. The battery source is worn on the mid-lateral aspect of the subject's hip and contains a tri-axial accelerometer system. When the device is turned on, virtual visual cues in the form of tiled flooring can be seen through the lenses along the nasal visual field. The device operates in the closed-loop mode in which the accelerometers detect the subject's vertical motions and move the tiled flooring accordingly. The virtual tiles are displayed as black and white squares arranged in two strips of alternating color. They are designed to mimic the real thing in that they not only gradually decrease in size as they lay further away from the subject but the vertical edges are also angled accordingly (Figure 1). As the subject walks, the nearest and largest pair of tiles disappears and is replaced by the next pair ahead while expanding to the same size as the disappearing pair. Adjacent pairs of tiles go through the same replacement algorithm. The overall visual effect is that the speed of the tile movements feels proportional to the subject's movements. The tiles appear to be stationary and the subject perceives walking over them [62,63].

Procedures

All instructions about what to do during the experiments were explained to the subjects while they were seated. Subjects were then familiarized to the goggle still sitting in the chair. They moved their head around while viewing the device that was alternately turned On and Off several times. Subjects were told that during testing, they were to walk at their comfortable pace looking ahead (i.e. not to stare down at their feet) and to keep walking until asked to stop. Subjects then stood up and the first trial was administered immediately. Practice trials were not allowed, i.e. the first trial of each visual condition was the first time subjects experienced them walking. Each visual condition (On versus Off) was dispensed thrice in alternating order with the starting condition counterbalanced among the subjects. Subjects wore the goggle the entire time during the experiment. In each trial, subjects' walking performance over 9.14 meters (30 feet) of level and unobstructed surface was videotaped for blinded analyses afterwards. The primary tester walked with the subject but slightly behind in order to avoid providing any visual feedback or interference to the subject. A gait belt was applied around the subject's waist to ensure safety.

	Age (years)	UPD RS total	Brady	H&Y	Duration (y ears)	RAPID-1	RAPID-2	RAPID-3	MM	PDQ8	PDQ8-1	PDQ8-2	PDQ8-3	PDQ8-4	PDQ8-5	PDQ8-6	PDQ8-7	PDQ8-8
Mean	69/68	16.7/29.9*	2.4/6*	1.7/3*	7.1/9.3	2.7/4.9*	4.3/4.2	2.2/26.9*	27.1/27.6	9.5/13.5*	1.1/1.9*	1.6/2	1.1/1.5	0.7/1	1.5/1.8	1/1.6	1.2/2*	1.3/1.8
Standard Deviation	8/8	7.8/10.6	2/3.5	0.4/0.5	5.2/5.5	2.7/3.9	2.4/2.5	3.8/63.8	3.3/2.8	5.7/5.5	1.2/0.9	1.5/1.2	1.1/1.2	0.8/0.8	1/1.1	1.1/1.3	1.2/1	1.3/0.9
Standard Error	2/2	1.5/2.4	0.4/0.8	0.1/0.1	1/1.2	0.5/0.9	0.5/0.6	0.7/13.9	0.6/0.6	1.1/1.2	0.2/0.2	0.3/0.3	0.2/0.3	0.2/0.2	0.2/0.3	0.2/0.3	0.2/0.2	0.3/0.2
Minimum	55/50	4/13	0/0	1/2.5	0/1.2	0/0	1/1	0/0	20/18	0/5	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
25% Percentile	64/63	10.5/22.6	0.9/3.6	1.5/2.5	3.1/4.8	0/1	2/2	0/0	25.8/26.5	5/9.5	0/1	0/1	0/0.5	0/0	1/1	0/0	0/1	0/1
Median	68/68	16.3/29.5	2.5/5	2/3	6.4/9	1.5/5	5/5	0/2	28/28	9/13	1/2	1.5/2	1/1	0/1	1.5/2	0.5/2	1/2	1/2
75% Percentile	76/75	22.3/36.1	4/8.1	2/3	8.5/11.5	5/9	6/6.5	3/15	30/29.5	14/17	2/3	3/3	2/2.5	1.3/2	2/3	2/3	2/3	2/2
Maximum	84/84	34/52	6/13	2/4	24/25	9/12	8/8	12/270	30/30	21/24	4/3	4/4	4/4	2/2	3/4	3/4	4/3	4/4
Lower 95% CI of Mean	66/65	13.5/24.9	1.6/4.3	1.6/2.7	5/6.8	1.6/3.1	3.4/3.0	0.7/-2	25.8/26.3	7.1/11	0.6/1.5	1/1.5	0.6/0.9	0.4/0.6	1.1/1.3	0.5/0	0.7/1.5	0.8/1.4
Upper 95% CI of Mean	72/72	19.8/34.9	3.3/7.6	1.9/3.2	9.2/11.8	3.8/6.7	5.3/5.4	3.7/55.9	28.4/28.9	11.8/16	1.6/2.3	2.1/2.5	1.5/2	1/0.4	2/2.3	1.4/2.2	1.7/2.4	1.8/2.2
Coefficient of Variation	11.1/12.3	46.7/35.6	82.8/59	23.6/16.9	72.5/59.2	103.3/80.2	55.2/60.2	171.7/237.1	12.1/10.3	60.7/40.2	105.6/49.5	93.5/59.2	101.5/81.9	121/83.7	64.3/64.5	115.7/79.3	103.5/52.4	98.6/48.2

Table 1: Subject characteristics grouped by disease severity. (H&Y 1-2/H&Y 2.5-4). UPDRS, Section 3 of the Unified Parkinson's Disease Rating Scale [76]; Total, total score; Brady, sum of items 40-44; H&Y, Hoehn and Yahr disease rating scale [74]; Duration, disease duration; RAPID-1, 2 and 3, postural instability questionnaire [77]; MMSE, mini-mental status examination [80]; PDQ, quality of life questionnaire [78,79]; PDQ8, total score; PDQ8-1 through 8, individual scores. * $p < .05$.

		Cues Off	Cues On	% Change	Effect size	95% CI
Step Initiation (s)	**T1**	1.23 (.35)	1.21 (.52)	-1.6	.05	-14.8 to 11.7
	Avg	1.17 (.32)	1.10 (.35)	-6.2*	.21	-11.5 to -.9
Step Length (m)	**T1**	.48 (.16)	.47 (.17)	-4.1*	.10	-8.1 to -.1
	Avg	.50 (.16)	.49 (.17)	-2.8*	.10	-5.1 to -.5
Walking Speed (m/s)	**T1**	.83 (.29)	.80 (.30)	-5.2*	.10	-10.3 to -.1
	Avg	.87 (.29)	.88 (.32)	-0.8	.03	-6.4 to 4.8
Cadence (steps/min)	**T1**	102.01 (15.22)	100.72 (19.16)	-1.6	.08	-5.6 to 2.3
	Avg	104.80 (16.31)	103.03 (17.94)	-1.8	.10	-5.4 to 1.9

Table 2: Effect of closed-loop visual cues on the change in walking kinematics in the Hoehn & Yahr 2.5-4 group. % change is expressed as a ratio of visual cues turned On minus Off and divided by Off. T1, first trial; Avg, mean of three trials. Effect size is based on Cohen's *d* [106]. *$p < .05$ compared to the statistical null hypothesis.

		Step Length (m)		Walking Speed (m/s)		Cadence (steps/min)	
		T1	**Avg**	**T1**	**Avg**	**T1**	**Avg**
Step Initiation (s)	T1	0.016	-0.057	-0.356	-0.429	-0.511*	0.061
	Avg	0.126	0.004	-0.159	-0.451*	-0.358	0.214
Step Length (m)	T1	-	-	0.711*	0.392	-0.074	-0.148
	Avg	-	-	0.454*	0.414	-0.181	-0.127
Walking Speed (m/s)	T1	-	-	-	-	0.646*	-0.064
	Avg	-	-	-	-	0.427	0.510*

Table 3: Association among the changes in walking performance as a function of the visual cues in the H&Y 2.5-4 group. T1, first trial; Avg, mean of three trials. * indicates a significant association, $p < .05$.

Data analyses

The primary outcome measures were the change in walking kinematics: duration of first step (step initiation), duration of walking over 9.14 meters, step length, walking speed and cadence. They were calculated based on the distance walked, the number of steps taken and the duration of walking. Changes were quantified as percent-change values by calculating the difference between walking performance with the visual cues On versus Off divided by visual cues Off. The group mean of the first trial and average of three trials in each kinematic measure was then subjected to a one-sample two-tailed t-test to test the effect of the visual cues against the null hypothesis (i.e. zero percent change in performance between visual cues Off and On).

Secondary outcome measures included the use of Pearson simple linear correlation analyses to determine the associations among the walking kinematic variables and disease profiles: disease severity [76], disease duration, postural instability [77], quality of life [78,79] and cognitive state [80]. Additional secondary analyses included comparing the two groups of subjects using independent t-tests. In order to increase the power of detecting group differences, no corrections to were made to minimize the inflated Type I error. The alpha level for the test of significance was set at $p < .05$ in all cases. All analyses were carried out with the GraphPad Prism software (GraphPad Prism v5.04, GraphPad Software Inc., CA).

		UPDRS		H&Y	Postural Instability			MMSE	Quality of Life								
		Total	Brady		RAP-ID-1	RAP-ID-2	RAP-ID-3		PDQ8	PDQ8-1	PDQ8-2	PDQ8-3	PDQ8-4	PDQ8-5	PDQ8-6	PDQ8-7	PDQ8-8
Step Initiation (s)	**T1**	0.11	-0.06	0.08	-0.15	0.16	0.04	0.17	0.23	0.02	0.09	0.34	-0.13	0.18	0.20	-0.27	0.41
	Avg	0.02	0.06	0.04	0.29	0.14	0.21	0.21	0.34	0.31	0.50*	0.59*	0.04	0.21	0.02	-0.50*	0.23
Step Length (m)	**T1**	0.12	-0.39	-0.16	-0.10	0.07	-0.05	0.13	-0.04	-0.26	0.06	-0.18	-0.18	-0.13	0.13	-0.29	0.01
	Avg	-0.17	-0.72*	-0.41*	-0.31	-0.11	-0.10	0.06	-0.26	-0.36	0.10	-0.38	-0.07	-0.22	0.11	-0.26	-0.11
Walking Speed (m/s)	**T1**	0.09	0.01	0.09	0.10	0.21	0.11	-0.09	-0.04	0.00	-0.03	-0.12	-0.03	-0.20	-0.17	-0.09	0.08
	Avg	-0.34	-0.15	-0.11	-0.12	0.05	-0.06	-0.10	-0.38	-0.31	-0.28	-0.38	-0.23	-0.28	-0.33	-0.09	0.03
Cadence (steps/min)	**T1**	-0.02	0.431*	0.16	0.14	0.13	0.17	-0.32	-0.16	0.20	-0.17	-0.14	0.24	-0.30	-0.45*	0.13	-0.09
	Avg	0.235	0.05	-0.09	0.173	-0.12	0.13	0.08	0.18	0.30	0.36	0.12	0.40	-0.05	0.07	-0.01	-0.12

Table 4: Association between subjects' characteristics and change in walking performance in the H&Y 2.5-4 group. T1, first trial; Avg, mean of three trials. * indicates a significant association, $p < .05$. Abbreviations are the same as in Table 1.

Results

In the H&Y stages 2.5-4 group, with the visual cues turned On, subjects' first step initiation was faster, they took shorter steps and walked slower ($p < .05$) without changing their cadence. The visual cues produced the strongest effect in speeding up step initiation (Table 2). The correlations among the walking kinematics ranged between -.511 and .711. Changes in step length covaried positively with walking speed ($p < .05$, Table 3). In addition, faster step initiation was associated with a higher feelings of depression and incidence of muscle cramps ($p < .05$) while a larger decrease in step length was associated with a higher degree of bradykinesia and disease severity ($p < .05$). Faster cadence was associated with a higher degree of body bradykinesia and communication problems ($p < .05$, Table 4).

The H&Y stages 1-2 group did not show a change in any of the walking kinematics as a function of the visual cues. Compared to the H&Y stages 2.5-4 group, average step initiation (1.13 ± .25 s versus 1.17 ± .32 s), walking speed (.91 ± .21 m/s versus .83 ± .29 m/s) and cadence (99.73 ± 9.66 steps/min versus 104.80 ± 15.31 steps/min) were similar when walking without the visual cues whereas step length was shorter (.5 ± .16 m versus .57 ± .09 m, p =.034, 1-tailed).

Discussion

The results of the study demonstrate that close-loop virtual visual cues can spontaneously change the walking kinematics in individuals with moderately severe PD. These changes occurred in the absence of explicit instructions and practice [81,82]. They did not however, translate into what one would typically consider to be better performance in terms of normalizing step length and walking speed.

Walking and other over-learned movements no longer become instinctive in PD but require effort [83-87] especially in tasks that require changing set [13,57,66,68,72,88-91]. The faster step initiation could therefore arise from the visual cues substituting the defective basal ganglia system in changing set from standing to taking the first step. Cadence is generally higher in PD [92,93] though it did not change as a function of the visual cues in the current study. Steps are typically shortened in PD, possibly because maintaining a normal step necessitates higher muscular effort and coordination [13,94]. In terms of the decreased walking speed, it did not relate with any of the disease profiles. Walking speed is a complex gait parameter that is not associated with components of motor skills such as force control, agility, or weight transfer [95].

The step length and walking speed are similar to those reported in the literature for moderate to severe PD [96,97] and higher than PD subjects who withheld their anti-PD medications [98]. The ability to modulate step initiation holds promise for improving walking in PD [99] as cognitive strategies could then be incorporated into the practice by intentionally increasing step length and speed [61,100-105].

Although the magnitudes of change were small by statistical standards [106], they are remarkable considering that subjects were completely naïve to the visual cueing device and the short distance that subjects walked during the tests. The significant decreases in walking speed and step length likely reflects a combination of the distracting visual cues and an apparent effort to walk more carefully since the cues do reduce the central visual passage. The novelty of wearing the goggle likely caused the PD subjects to engage in dual-tasking. It is known that many of them have trouble with such encounters [107-112]. The potential interference is especially illuminating considering that the visuospatio-perceptual system must process both the visual cues and the surrounding concurrently [73,113,114]. Even the instruction manual recommends walking slowly in the beginning and to stop if unsure [115].

The findings of the association among the walking gait changes and disease profiles are consistent with the cognitive mechanisms underlying the beneficial effects of visual cues. The associations between the magnitude of decrease in step length and the higher level of postural bradykinesia and severity of disease could be a reflection of the increasing difficulty in modulating muscle forces as a result of disease progression. As the disease worsens, mental states such as depression and physical impairments such as muscle fatigue, cramps or difficulty getting dressed have accumulating effects on PD patients' overall quality of life including fear of falling [77,116-118]. These factors may hamper efforts to provide meaningful rehabilitation techniques to retain the ability to walk in these people [59].

The failure to find any effect of the visual cues in the H&Y 1-2 group was expected as hypothesized. These subjects have not yet developed overt problems with their walking. The null outcome was therefore not surprising.

In conclusion, the current study demonstrates that in the absence of instructions and practice, closed-loop virtual visual cues can spontaneously increase step initiation speed but decreased walking speed and step length in patients with moderately severe PD. The

increased step length and walking speed reported in previous studies from using visual cues is probably due to cognitive strategies and practice.

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