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Listenmee® and Listenmee® smartphone application: Synchronizing walking to rhythmic auditory cues to improve gait in Parkinson's disease

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ABSTRACT

Evidence supports the use of rhythmic external auditory signals to improve gait in PD patients (Arias & Cudeiro, 2008; Kenyon & Thaut, 2000; McIntosh, Rice & Thaut, 1994; McIntosh et al., 1997; Morris, Iansek, & Matyas, 1994; Thaut, McIntosh, & Rice, 1997; Suteerawattananon, Morris, Etnyre, Jankovic, & Protas , 2004; Willems, Nieuwboer, Chavert, & Desloovere, 2006). However, few prototypes are available for daily use, and to our knowledge, none utilize a smartphone application allowing individualized sounds and cadence. Therefore, we analyzed the effects on gait of Listenmee®, an intelligent glasses system with a portable auditory device, and present its smartphone application, the Listenmee app®, offering over 100 different sounds and an adjustable metronome to individualize the cueing rate as well as its smartwatch with accelerometer to detect magnitude and direction of the proper acceleration, track calorie count, sleep patterns, steps count and daily distances. The present study included patients with

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idiopathic PD presented gait disturbances including freezing. Auditory rhythmic cues were delivered through Listenmee®. Performance was analyzed in a motion and gait analysis laboratory. The results revealed significant improvements in gait performance over three major dependent variables: walking speed in 38.1%, cadence in 28.1% and stride length in 44.5%. Our findings suggest that auditory cueing through Listenmee® may significantly enhance gait performance. Further studies are needed to elucidate the potential role and maximize the benefits of these portable devices.

1. Introduction

One of the most debilitating motor symptoms of Parkinson's disease (PD) is gait dysfunction (Jankovic, Nutt, & Sudarsky, 2001). However, despite the benefits of current pharmacological and surgical therapies for patients with PD, treatment effectiveness and options for gait difficulties remain limited. Evidence supports the use of rhythmic external auditory signals to improve PD patients' gait (Cottam & Sutton, 1986; McIntosh et al., 1994; McIntosh et al., 1997; Quintyn & Cross, 1986; Suteerawattananon et al., 2004; Thaut et al., 1997) suggesting that the use of auditory cues may increase gait stride length and regulate gait cadence. Based on such approach, devices that synchronize over-ground walking to rhythmic auditory cues have been created achieving limited long-term success, mostly due to impractical, uncomfortable, and not portable models (Baram, Aharon-Peretz, Simionovici, & Ron, 2002; Ferrarin et al., 2008). One issue with traditional auditory cueing devices is that they employ open-loop strategies; that is, they impose a sensory signal on the patient, which is generated by an external fixed source that is not affected or directed related to the patient's own movement and velocity. Examples are fixed-velocity visual cues (Arias & Cudeiro, 2008) or environmental rhythmic auditory cues (Willems et al., 2006). In contrast, of the few portable prototypes commercially available for the patient's daily use, none allow for individual programming options to select the sound itself, its intensity, or cadence.

We analyzed the effects on gait of an original device, Listenmee® a portable pair of glasses with a 64 GB SD card able to produce 100 different sounds (Fig. 1). Listenmee® generates auditory rhythmic cues matching the patient's step frequency to improve walking in PD patients. Listenmee® allows the patient the possibility to select sounds manually, including the desired cueing rate (number of sounds delivered in a period of time; beats/min) using the Listenmee app® (Brainmee™, Madrid-Spain [www.brainmee.com]) that was developed to allow users to choose an individualized auditory cues. The employed technology is simple and easy to use. Users can access it through a direct touch screen control system with commands such as "PLAY" and "PAUSE" through a circle type interface on the screen. The user is able to use the mobile touch screen to increase (clockwise) or decrease (counterclockwise) the cueing rate (Fig. 2). The application has different cueing rates as follows: very slow (0–50%), slow (51–100%), fast (101–150%), or very fast (151–200%). The applied tones can vary between 60 and 480 Hz. Together, patient and physician can choose the sound set and cueing rate that is best suited for the patient.

Listenmee® and Listenmee app® come with an online store where users are able to download sounds. It has 4 special categories identified as: "environmental", "drums", "electronics", and "voices". Furthermore each category has 25 different sounds, for a total of 100. In addition, the application allows the possibility to use Bluetooth (with the glasses or any wireless headphones) to provide comfort by keeping the phone in a pocket. It also has a statistical analyses software that shows walking improvement in distances and times. The user's outside walking route performances can be recorded

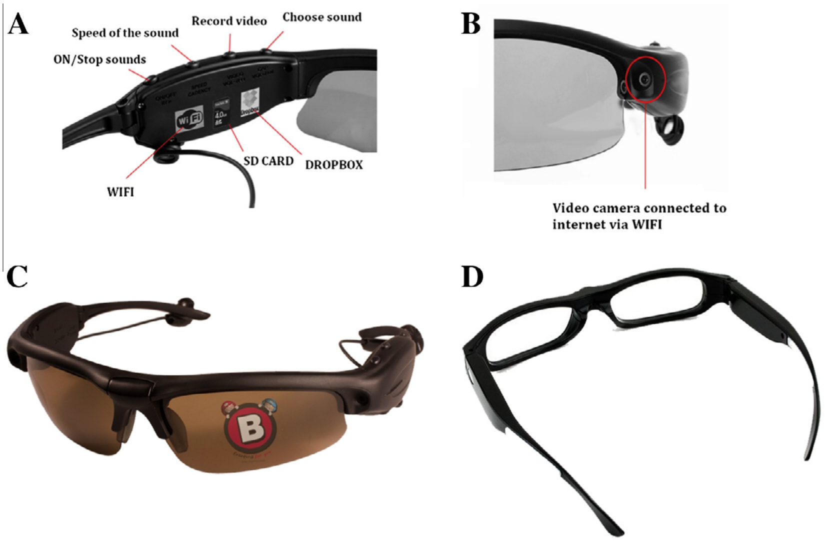

Fig. 1. Listenmee® (A) Lateral view of the prototype; the device consists of a pair of glasses with a SD card of 64 GB able to reproduce 100 different sounds. The prototype allows the possibility to select them manually as well as the cueing hearing rate; it also allows recording the patient's spatial movements and sending them via internet to physician. (B) Video camera on the upper left of the prototype and laser for visual cueing. (C). Auditory feedback device with headphones used in test. (D) New Listenmee lite® version. Both prototypes come with a manual portable wireless remote control to run on or off the sounds.

daily, monthly, and annually by integrating the application with Google monitor maps (GPS). Furthermore the physician can access the patient scores data through Internet at all times.

2. Patients and methods

Idiopathic PD patients diagnosed according to the clinical diagnostic criteria of the United Kingdom Parkinson's Disease Society Brain Bank were recruited from local PD support groups and the Movement Disorders Clinic within the Centro Integral de Movimientos Anormales y Dolor (CIMAD) in Bogota, Colombia. Inclusion criteria were: (1) PD patients with gait difficulty, frequent episodes of falling and/or freezing; (2) ability to stand independently and walk without an assistive device; (3) current use of antiparkinsonian medication; (4) no hearing impairment; (5) preserved ability to understand and follow simple orders; (6) medically stable. A total of ten patients that volunteered for the study met the inclusion criteria. All patients read and signed an institutionally approved consent form prior to any data collection. The selection included 3 women and 7 men with Hoehn-Yarh (Rubinstein, Giladi, & Hausdorff, 2002) scores ranging from 2.5 to 3.0 that were between the ages of 45–65 years. All patients presented with gait difficulty compromising daily quality of life with intermittent or frequent episodes of difficulty with gait initiation, gait maintenance, and dysfunctional turning. Out of the ten total patients, five previously received subthalamic nucleus deep brain stimulation (DBS) and presented with frequent freezing and a tendency to fall. Furthermore, these patients had failed to respond to pharmacological adjustments, physical therapy, or changes in the electrical parameters of DBS programming.

2.1. Gait analysis

All patients underwent observation using the Gait Analysis Laboratory (Gait Laboratory MOVISYS); Capture system used: Vicon Motion System, 8 camera Vicon MX T-Series, 2 video cameras and 2 force plates. Capture Software: Vicon Nexus 1.8. Protocol used for placement of markers: Protocol Davis.,

Fig. 2. Listenmee® App (C and D) the interface used is simple employing a circle type up button touch screen ordering system with commands such as "PLAY", "PAUSE". The user is able to increase (clockwise) or decrease (against clockwise) the cueing rate. It has 4 special categories identified as: "environmental", "drums", "electronics", "voices". Furthermore each category has 25 different sounds, for a total of 100 sounds. Listenmee® and Listenmee app® have a statistical analyses software, recording walking improvement in daily traveled distances and time scores (A and B). The user walking route performances can be recorded daily, monthly and annually by integrating the prototype and app and existing monitor maps (GPS). The physician can access the patient scores data through Internet at all times through telemedicine.

which consists of several cameras (video and infrared), placed around a walkway. The patients had markers located at various points of reference of the body (e.g., iliac spines of the pelvis, ankle malleolus, and the condyles of the knee). Adhesive electrodes measured muscle activity and special reflective markers tracked joint movement.

The use of reflective markers (reflective balls) allowed for very accurate measurement of movements using multiple, computer linked cameras simultaneously. The cameras utilized high-powered strobes with matching filters to record the reflection from the markers placed on the body. Based on the angle and time delay between the original and reflected signal, localization of the marker in space via triangulation was possible. Software was used to collect three-dimensional video data and perform kinematic and kinetic calculations.

Auditory rhythmic cues matching step frequency were delivered through a new external portable device: Listenmee® (Brainmee, Madrid, Spain). Listenmee® allowed auditory cueing rate (number of sounds delivered in a period of time; beats/min) such rate could either be increased or decreased from the patient base-line.

Patients were measured on a 7.62-m (25-ft) walkway while being off-dopaminergic therapy. At first patients were asked to walk at their fastest speed twice to establish baseline control data. Next, they completed the same walking task under each of two conditions: walking with Listenmee® without auditory cues, and walking with Listenmee® delivering auditory cues.

The metronome rate (in beats/min) was set at a cadence 25% faster than the uncued cadence for each patient. Performances were analyzed in a motion and gait analysis laboratory using several cameras (Gait Laboratory MOVISYS). A Wilcoxon Signed Rank test for the analysis of matched pairs was performed to assess differences of gait performance among the two conditions (uncued and walking with auditory cues). This was decided due to previous reported observations that increasing and/or reducing the rate of rhythmic auditory cues can elevate the cadence of walking in Parkinsonian patients (McIntosh et al., 1997; Morris et al., 1994).

Measurements were collected during a single session. Participants performed various trials under each condition. They were familiarized with the walkway and each cue modality.

Patients were first asked to walk at their fastest speed along the seven meters walkway wearing Listenmee® powered off and immediately to walk the same distance turning it on and trying to synchronizing each step with the auditory tones. Patients with previously STN DBS kept the DBS pulse generator on at all times.

The systematic study of the patient motion, involved the analysis of the videos by a group of experts on gait who were blinded toward the device being turned on or off.

The results were reported in terms of change in object of temporo-spatial analysis parameters: i.e. single foot support (phase within the gait cycle during which the body mass is carried by a single limb), average values of opposite foot off, walking speed [meters per second], cadence (number of steps per unit of time) [steps/min], and stride length (distance between successive points of initial contact of the same foot; right and left stride lengths are normally equal) in meters.

The time required to complete the 7.62-m walkway was recorded in seconds. Average walking speed was calculated and expressed in meters per second. The number of steps required to complete each trial was counted and used to calculate the average cadence (steps/min). Average stride length was calculated and expressed in meters (distance/number of steps). For each subject, the mean of the two trials (device on and off) for each dependent variable was calculated and used for the statistical analysis.

3. Results

Assessment of gait performance in this study included three major dependent variables: walking speed (meters per second), cadence (steps/min) and stride length (The distance between 2 successive placements of the same foot) in meters. All patients demonstrated a significant improvement difference in gait performance independently of the use of DBS or not and the condition of freezing of gait. When the device was turned on the mean improvement on the three major variables was: walking speed 40.6%, cadence 30.2% and stride length 50.3% in a singular session analyses.

A Wilcoxon matched pairs signed rank test was conducted in order to find out whether there was a difference in the Cadence, Stride Length and Walking Speed between the two measured conditions, namely performance without a cue and performance under an auditory cue. Results from that analysis indicate that there was a significant difference in how subjects performed under both conditions, in that the performance of all subjects improved on all three variables during the condition with an auditory cue: $W = 0$; $z = 2.52$; $p < .05$ ($p = .0117$). For each variable of gait performance this test was calculated. Also for each calculation we eliminated the data of both the youngest (Patient 2) and the oldest (Patient 10) participant (Table 2).

This clearly means that the auditory-cue-condition made all subjects improve on performance and this without one single exception. For all three variables respectively: Cadence, Stride Length and Walking Speed, this improvement turned out to be statistically significant. All analyses were obtained using StatPlus 2009 Professional Software for Statistical Analyses. Results were computed to analyze gait improvement under two different stimulus conditions, namely with and without acoustic cue.

The study also showed mean improvement in other parameters like: stride time 28.7%, step time 30.5%, single support 34.1% and step length 139.5%. All patients improved in the motion analysis. Rhythmical auditory cueing induced speed changes in all subjects. Freezers and non-freezers showed the same positive response to rhythmical auditory cues (Table 1).

During the course and by the end of the training period, marked improvement was observed in step length, cadence, stride length, and walking speed (Fig. 3).

Table 1
Data from all participating patients on walking with auditory cueing and without auditory cueing, showing improvement in the three major relevant dependent variables.

N	No cue	Aud. cue	Delta abs.	Delta%
CADENCE (Steps per minute)				
1	77.8	98.1	21.7	28%
2	80.3	111.8	31.5	39%
3	84.8	116.0	31.2	37%
4	100.7	114.2	13.5	13%
5	76.4	98.7	21.7	28%
6	77.4	98.1	20.7	27%
7	82.7	109.6	27.0	33%
8	75.1	99.3	21.7	28%
9	74.4	97.1	22.7	31%
10	70.4	97.1	26.7	38%
Std. dev.	8.4	7.8	5.4	6.8%
Average	80.0	104.0	23.8	30.2%
Stride length (meters)				
1	0.44	0.91	0.47	109%
2	0.81	1.21	0.41	50%
3	1.15	1.52	0.37	32%
4	0.87	1.29	0.42	49%
5	0.63	0.91	0.28	44%
6	0.97	1.36	0.39	40%
7	1.25	1.33	0.08	6%
8	1.07	1.34	0.27	25%
9	0.61	0.91	0.31	50%
10	0.60	1.17	0.58	97%
Std. Dev.	0.27	0.22	0.13	16.0%
Average	0.84	1.19	0.36	50.3%
Walking speed (meters per second)				
1	0.35	0.58	0.23	64%
2	0.77	1.12	0.35	46%
3	1.08	1.35	0.27	25%
4	0.78	1.23	0.46	59%
5	0.56	0.81	0.25	44%
6	0.96	1.24	0.29	30%
7	1.17	1.42	0.25	21%
8	1.11	1.22	0.11	10%
9	0.54	0.82	0.28	52%
10	0.57	0.89	0.32	56%
Std. Dev.	0.28	0.28	0.09	11.3%
Average	0.79	1.07	0.28	40.6%

Table 2
The table resumes improvements in the three major relevant dependent variables when removing Subject 2 and 10 from final statistical analyses due to extreme outlier ages, tendency is still maintained.

Parameters	Average (no cue)	SD	Average (aud cue)	SD	Mean improvement	SD
Cadence (steps/minute)	81.2	8.7	103.9	8.0	**22.5 (28.2%)**	5.1
Stride length (meters)	0.87	0.29	1.19	0.24	**0.32 (44.5%)**	0.12
Walking speed (meters/second)	0.82	0.31	1.08	0.31	**0.27 (38,1%)**	0.09

4. Discussion

Gait disturbance is one of the cardinal symptoms in patients with PD. Generally, PD patients walk slowly with dragging steps and decreased arm swing while maintaining a flexed posture. Such gait disturbance and postural instability limits the patient daily living. The aim of this study was to explore

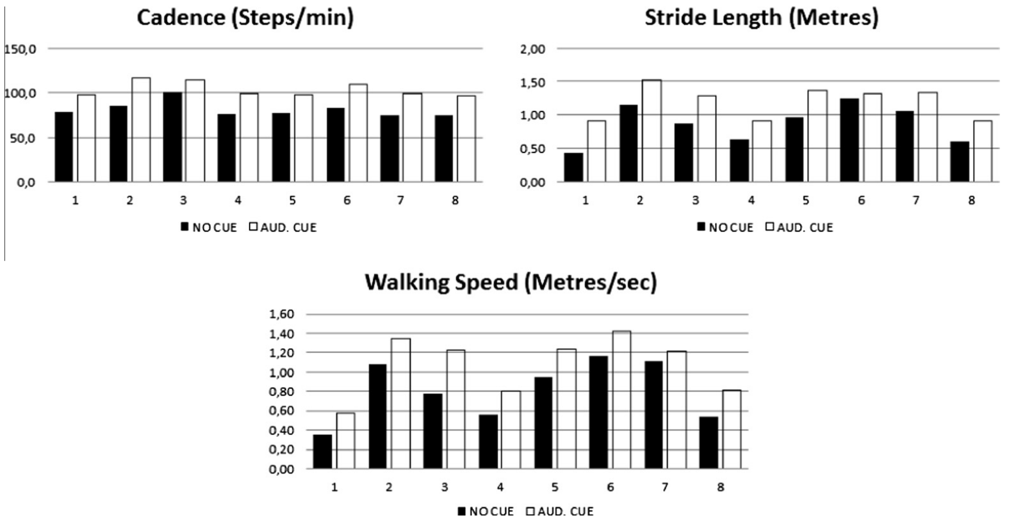

Fig. 3. Graphical representation of the performances of participating patients under two differing conditions over three dependent variables.

the role of giving an external stimulus through a portable device to improve the quality of gait of people with Parkinson's disease.

It is well documented that patients with PD can improve their walking ability when being provided with external visual or auditory cues (Marchese, Diverio, Zucchi, Lentino, & Abbruzzese, 2000; Morris et al., 1994; Nieuwboer, Baker, & Willems, 2009; Rochester, Baker, & Hetherington, 2010; Rubinstein et al., 2002). In Accordance with previous studies, our results evidenced that individuals with PD had a better performance on gait with cues. However, auditory feedback often employs verbal cueing or a metronome (McIntosh et al., 1997; Thaut et al., 1996; Willems et al., 2006); neither is practical for everyday use. As such, neither auditory nor verbal cueing techniques are particularly practical for everyday use. This study is the first, to our knowledge, that investigate a smartphone application which allows individual sounds frequencies. Our findings show that all patients demonstrated a significant improvement difference in gait performance independently of the use of DBS or not and the condition of freezing of gait. This fact may be partially explained by the use of spatial and rhythmic external cues to increase stride length and regulate cadence in PD patients (Arias & Cudeiro, 2008; Willems et al., 2006). In addition, auditory stimulus may activate attention, and a network that includes primary auditory cortex, insula, anterior cingulate and prefrontal cortex. Visual cues will stimulate areas associated with visual stimulus.

In this study step frequency was carefully monitored because at faster step frequency there is an increased risk of falls. Furthermore, as Parkinson' disease patients tend to walk at shorter stride lengths, increasing step frequency could reinforce the present gait disorder.

As a result of this conceptual line, both baseline step frequency and length were measured and the aim was to match frequency cuing and the desired cadence, so that a more normal overall gait performance could be individually reached.

A neuroanatomical explanation for the efficacy of auditory cueing is that the device recruits motor related areas by activating the premotor cortex (PMC), cerebellum, pre-supplementary motor area (pre-SMA) and supplementary motor area (SMA) (Alexander & Crutcher, 1990; Quintyn & Cross, 1986). This corresponds to the hypothesis that the hypokinesia phenomenon of PD is due to overactivation of basal ganglia inhibitory projections to the thalamus causing decreased activity of thalamo-cortical projections areas including the SMA, cingulate motor areas, and primary motor areas (Morris et al., 1994). However more detailed neurological analysis would be necessary to see if this theory properly describes the neurological mechanisms underlying the positive effects auditory cueing.

Morris et al. hypothesize that patients with PD are still able to generate a normal gait pattern but have difficulties in activating the locomotor control system (Morris, Ianesk, Matyas, & Summers, 1996). In this context, visual cues may provide the missing information on appropriate stride length and thus help to compensate for the deficiency in motor set by focusing attention on the criterion stride length. Although the use of visual laser cue has not been analyzed of this study our device provides a combined strategy for patients with PD providing visual cues (laser) projected in synchrony with auditory cues from smartphone application which allows individual adjustments of the cueing rate (beats/min). It has 4 special categories identified as: "environmental", "drums", "electronics", "voices". Furthermore each category has 25 different sounds, for a total of 100 sounds. The use of music elucidating emotion investigations is growing (Juslin & Västfjäll, 2008; Park, Hennig-Fast, & Gutyrchik, 2013). Music generates strong and immediate responses through a neural process. Happiness in music is related to activation of different structures including the striatum, anterior cingulate, parahippocampal gyrus and auditory association areas (Levitin & Tirovolas, 2009; Park et al., 2013). Auditory cues by practical means of cueing are the generation of auditory rhythmic cues using a metronome with instruction to match step frequency to the auditory rhythm. The ideal frequency of such cues has yet to be fully elucidated and is the subject of ongoing studies.

Our study showed improvements in all patients in initiation of walking, cadence, stride time, step length and walking speed on the gait analysis laboratory (video 1).

Consistent with earlier studies, gait speed, cadence and stride length of subjects were improved with auditory cueing (Marchese et al., 2000; McIntosh et al., 1997; Nieuwboer et al., 2009; Rochester et al., 2010; Suteerawattananon et al., 2004; Thaut et al., 1996). When comparing our results with other published studies, regarding during a single session auditory cueing; Listenmee® achieved comparable and in some cases greater rate success in gait performance. In the study by Suteerawattananon et al. (2004) the improvement on walking speed of was 16%. Nevertheless, in the current study was 40.6%, (meters per second). The oneself study, reported improved in gait cadence 12% while the gait cadence improved 30.2% (steps/min) in our study using Listenmee®. Stride length improved majorly using auditory cueing with Listenmee ® achieving 50.3% (in meters) when compared to performance during medication-off period in uncued conditions. Suteerawattananon study reported no significant effect with auditory cueing. Richards et al. also found no difference in stride length during auditory cueing (Richards, Malouin, Bedard, & Cioni, 1992). Specific comparison of the present study with others studies that examined sensory cues during gait reveals that the effects of sensory cues from Listenmee® were better than previous studies, which may be due to the kind of sounds we employed which are not merely orders but have a rhythmic background sound with a continuous infinite music flow.

Evidence suggests that rhythmic sounds patterns through the reticulospinal pathway which is mainly involved in locomotion and postural control are able to increase the excitability of spinal motor neurons, increasing the speed of the muscle respond to a motor command (Suteerawattananon et al., 2004).

Our results their results seem in general supportive of the cuing paradigm developed for RAS training, called SLICE (stepwise limit cycle entrainment) which starts at baseline and increases step cues in percentage steps to bring the overall velocity and strid/cadence system into more normal ranges. Frequencies are only increased when at any given cue frequency a limit cycle (stable performance) has been reached (Kenyon & Thaut, 2000; McIntosh et al., 1997; Thaut et al., 1997).

The promising results of Listenmee® achieved in this first study, allows us to hypothesize those are due to the special kind of sounds created available in Listenmee® which are also available in Listenmee® app. We had select carefully sounds that were able to produce a rhythm frequency (external brain pacing) which are choose for the patient and at the same time they get to choose between 4 commands, we encourage them to use the one that makes them to have a well-being positive sensation.

Listenmee® also emits light through a process of optical amplification based on the stimulated emission of electromagnetic radiation (laser), derived from the lenses; such option has not been analyzed in this study, but comes in every device; such addition its present based on the fact that visual cues have been previously reported to improve stride length in some PD patients (Suteerawattananon et al., 2004). Furthermore smartphone App: Listenmee® App was also developed using the same principles and sounds of Listenmee®.

4.1. Device smartphone application

The application-Listenmee app® (BrainmeeTM, Madrid-Spain [www.brainmee.com]) was developed on a mathematical basis allowing users to choose individual auditory cueing rate (beats/min). The employed technology is simple and easy to use. Users can access it through a direct touch screen ordering system with commands such as "PLAY", "PAUSE" and a circle type interface on the screen. The user is able to use the mobile touch screen to increase (clockwise) or decrease (against clockwise) the cueing rate (Fig. 2). The application has different cueing rates as follows: very slow [0–50%], slow [51–100%], fast [101–150%] or very fast [151–200%]. The applied frequencies can vary between 60 and 480 Hz. Patient and physician together can choose the sound set and cueing rate that is best suited for the patient.

Listenmee® and Listenmee app® come with online store where users are able to download sounds. It has 4 special categories identified as: "environmental", "drums", "electronics", "voices". Furthermore each category has 25 different sounds, for a total of 100 sounds. In addition the application allows the possibility to use Bluetooth (with the glasses or any wireless headphones) to provide comfort, keeping the phone in a pocket. It also has a statistical analyses software, showing walking improvement in distances and times. The user outside walking route performances can be recorded daily, monthly and annually by integrating the application with Google monitor maps (GPS). The physician can access the patient scores data through Internet at all times. A wrist smart watch with accelerometer helps also to track calorie count, sleep patterns, step count and daily distances. The accelerometer allows cueing rating changes according to patient's position and velocities as well to detect magnitude and direction of the proper patient acceleration.

4.2. Study limitations

The small number of included subjects limits the extent that this study can be generalized to the broader population of PD patients with freezing of gait or a DBS. Also, it is possible that a greater number of practice trials under different conditions would result a better performance in locomotion outside the laboratory setting, including environmental situations such as crossing the street at a traffic light. We propose that future studies following a group of patients treated with Listenmee® over a suitable period would be advised to assess the long-term effects of this rehabilitation protocol.

4.3. Concluding remarks

From the results of this first study we conclude that Listenmee© is a safe and effective adjunct for symptomatic improvement of gait in patients with PD including freezing of gait. It appears that clinical application of auditory cues may be another model in the armamentarium of therapies for patients with PD. Further analysis also should involve chronic responses to the cues in PD patients and in other neurodegenerative diseases.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.humov.2014.08.001.

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