FREEZING IN PARKINSON'S DISEASE: IMPROVING QUALITY OF LIFE WITH AN AUTOMATIC CONTROL SYSTEM

Àngels Bayés Rusiñol
Centro Médico Teknon-Grupo Quirón Salud
Andreu Català Mallofré
Universitat Politècnica de Catalunya
Rui Sarmento e Castro
Associaçao Fraunhofer Portugal Research

1. Project Summary

Gait disorders (GD) are one of the most common symptoms in Parkinson's disease (PD). They cause significant reduction in the capacity for self-care, leading to deterioration in the quality of life (QoL) of those affected and their families. Visual and auditory stimulation are known to be effective for the improvement of a PD patient's gait, improving speed, cadence and stride length variability and reducing freezing of gait (FoG). Despite their potential effectiveness, the use of cues is limited by practical constraints such as a lack of portability and administration difficulties in daily life. Novel technological devices offer interesting opportunities in cueing methods. The use of wearable sensors that can detect bradykinetic gait as well as FoG episodes connected to portable devices for the cue administration can help to implement the cues into the daily life of the patient. In this way, an automatic (on-demand) solution can be available when a patient requires it, increasing its effectiveness, and maximizing comfort.

The goal of the project is to evaluate the effectiveness of a Mobility Assistance System (MAS) for PD in terms of gait parameters and quality of life (QoL) in a real environment.

Specific Objectives

- To obtain a reliable FoG detector through an unobtrusive sensor device. Movement sensors combined with signal processing and machine learning approaches are needed to accomplish this goal.
- To determine the degree of improvement in both frequency and duration of freezing episodes with the use of the MAS.
- To determine the degree of improvement in speed, cadence, and the number of steps with the use of the MAS.
- To Improve the usability of the system in the PD population
- To study the association between cognitive performance and benefits of the MAS in PD.
- To demonstrate that the MAS, with automatic triggering of external cues, improves these patients' QoL.

Methodology:

Standard protocol approvals, registrations, and patient consents

All study procedures were conducted in accordance with the 1964 Declaration of Helsinki (2008 Revision) and Good Clinical Practice guidelines. The study was approved by the Research Ethics Committee of Centro Médico Teknon, Quirónsalud group (code 201404.31.32, MASPARK) and by Spanish Agency for Medicines and Health Products (565/16/EC). All patients gave their informed consent before enrolment. All subjects provided written informed consent.

Study participants

Patients with a clinical diagnosis of idiopathic PD according to the UK Parkinson's Disease Society Brain Bank in moderate phase (Hoehn and Yahr scores between 2 and 3 in ON phases), with motor fluctuations, GD and/or FOG motor fluctuations, able to walk unassisted in the OFF phase; between 50 and 80 years of age and the ability to understand the potential risks and benefits of the study were recruited at the Movement Disorder's Unit of the Centro Médico Teknon (UParkinson) from April 2016 to September 2017. Subjects were excluded if they had other health problems that hampered physical activity and gait, met criteria for dementia (Mini Mental State Examination<24), being treated carrying deep brain stimulator or continuous dopaminergic drugs by pumps, or were unwilling to cooperate with study procedures, or were participating in other clinical trials.

Design procedures

This was a randomized crossover study trial divided into 5 principal stages: The first stage was based on the recruitment of the subjects for the study. Sociodemographic data, neurological data, and written informed consent were collected from all subjects enrolled in the study. In the second phase, algorithms for detecting gait disorders were customized. For this purpose, all participants were instructed to wear a waist sensor for 4 days. In the third phase, the participants were cognitively assessed using a neuropsychological battery. In the fourth phase, patients and their families were instructed to carry a mobile phone, a sensor and an auditory cues system in their home. All the patients underwent the following conditions in random order with a rest of 30 days in between. Condition 1: The auditory cues system was not activated when the sensor detected gait alterations. Condition 2: The auditory cues system was activated automatically and provided auditory cues when the sensor detected gait

disturbances. During this phase, the researchers visited the participants once a day and they will help the patients with any incidental problems which may have occurred. The last phase was voluntary and consisted in carrying out the activated system (condition 2) at home for 4 weeks.

Evaluation

All the participants underwent a clinical and neuropsychological evaluation. Likewise, QoL and assistive technology was assessed.

Equipment

Mobility assistance system (MAS) comprises the following elements:

1) The MOVEMENT SENSOR is a commercial product certified as medical device in the EU and consists of a small wearable device that is worn on the waist. Within this device there are algorithms based on artificial intelligence that detect several motor symptoms: bradykinesia, dyskinesia, and freezing of gait and ON-OFF fluctuations. Moreover, the sensor detects falls, gait parameters, energy expenditure, activities and postures.

2) The SMARTPHONE is the interface through which study participants connect to the system. The user interfaces of the smartphone were designed following an iterative user-centred design process, and were heavily based on a previously existing version designed for the project REMPARK1. Standard smartphone applications, such as contacts, calls, and messages, were integrated in the system and disease-specific applications were also developed: Appointments, to record the dates/times of medical appointments; Medication, to keep a medication schedule, remind about medication, and keep a record of one's intakes; My Day, to register, visualize and edit events for current and past days, relative to medication intake, eating hours, feeling well and feeling bad periods; Auditory Cueing System (ACS) controller, to trigger and stop the ACS, change its volume, and change the cueing characteristics.

3) AUDITORY CUEING SYSTEM: The actuator consists of a headset connected wirelessly to the system and which will manage the cues. The sensor is in charge of controlling the headset based on the current patient's detected symptoms.

2. Results

Study participant characteristics

A total of 27 participants were included. Five (18%) dropped out of the study. The reasons were: voluntary abandonment alleging family problems (n=1), sensor difficulties to recognize their walking pattern due to the shape of the iliac crest (n=1), and health problems not related to the study (n=3, fracture of the tarsus of the right foot, dysautonomia, and spine operation).

A total of 22 participants completed the study. 68% (n = 15) were men. Their mean age was 62 ± 9 years, 78% (n = 17) had secondary or university studies. All presented a Hoehn and Yahr of 2.5, and mean duration of the disease was 8 ± 4 years. Half, 50% (n = 11) presented FoG. All patients were evaluated cognitively except one whose mother language was different from Spanish or Catalan. A total of 7 participants (33%) presented mild cognitive impairment according to current criteria.

Effects of the Auditory Cueing System on gait parameters

The gait parameters were compared when the auditory cueing system was used (ACS) and when it was not (n-ACS). No significant differences were found (see **Table 1**).

Parameter	Condition	$\bar{x} \pm \sigma$	Statistic value	*p*-value
Cadence (strides/sec)	With cueing	42.97 ± 3.02	t = -0.4	p = 0.69
	Without cueing	43.15 ± 2.82		
Stride Length (m)	With cueing	0.99 ± 0.22	t = -0.33	p = 0.74
	Without cueing	1.00 ± 0.24		
Speed (m/s)	With cueing	0.71 ± 0.17	t = -0.48	p = 0.63
	Without cueing	0.72 ± 0.18		
No. of FOG / min of walking (number / min)	With cueing	0.31 ± 0.56	t = 0.64	p = 0.52
	Without cueing	0.25 ± 0.52		
Average duration of FOG (s)	With cueing	2.52 ± 1.35	t = 1.55	p = 0.12
	Without cueing	2.23 ± 0.91		

Table 1. Comparison of gait parameters with activated and non-activated MAS.

Several publications have found a relationship between gait parameters and cognitive performance in Parkinson's disease. We assessed cognitive variables by administering widely used neuropsychological tests for the assessment Parkinson's cognitive disorders. With this exploration we were able to classify the participants into people

with mild cognitive impairment (MCI) and without cognitive impairment according to the current criteria of the Movement Disorders Society and we studied whether people with and without MCI benefited differently from MAS. In our sample we observed that people with MCI benefited from MAS in relation to the number of FoG, however, those without MCI worsened the number of FoG with MAS. These results indicate that cognitive performance is an important variable in gait and therefore should be controlled in future studies that study the benefit of a mobility support system. Likewise, in the subgroup of voluntary patients who were given the system for one month for their free use there was a tendency to improve the mobility subscale of the Parkinson's QoL questionnaire.

3. Relevance of the results and possible future implications

The purpose of the MASPARK project was to evaluate the effectiveness of a mobility assistance system through auditory tracks automatically activated by an artificial intelligence system to improve gait disorders in PD and the QoL of people with Parkinson's. Although the use of the mobility assistance system was not associated with gait improvements when it was applied in daily life, the study has helped to test the system in real conditions and to improve it. The results obtained show that the system is safe: its use has not worsened the parameters of the gait nor have incidents caused by the system been observed. In addition, the data obtained show that patient cognition is an important variable to consider since people with PD could benefit differently depending on their cognitive status.

It is also important to note that the accessibility to use the system in real life showed a tendency to improve an aspect of the QoL of people with PD (the mobility dimension), although this could not be considered statistically significant. It should be noted that the results have been obtained in a pilot study, with a small sample of patients, and should be taken as preliminary. It is necessary to expand the sample to test the portable mobility support systems based on the latest technology that could improve the autonomy and QoL of people with Parkinson's.

The development and use of these devices with the described characteristics would allow the doctors to accurately personalize the intake of medicines and, therefore, to

improve the response of the patient to the treatment. These new approaches are aimed at significantly improving the QoL of patients and will allow a deeper understanding of the personalized evolution of the disease. In addition, the use of highly technology-based systems, such as the one in question, could contribute to clinical and epidemiological research. Such tools would provide the unique opportunity to objectively monitor and control the effectiveness of treatment of any given therapy individually, which would sustainably change traditional methods of medical care.

4. Publications and Communications

Rodríguez-Martín D, Samà A, Pérez-López C, Català A, Moreno Arostegui JM, Cabestany J, Bayés À, Alcaine S, Mestre B, Prats A, Crespo MC, Counihan TJ, Browne P, Quinlan LR, ÓLaighin G, Sweeney D, Lewy H, Azuri J, Vainstein G, Annicchiarico R, Costa A, Rodríguez-Molinero A. Home detection of freezing of gait using support vector machines through a single waist-worn triaxial accelerometer PLOS ONE 12(2): e0171764. doi: 10.1371/journal.pone.0171764 (IF=3.057)

Rodríguez-Martín D, Samà A, Pérez-López C, Català A, Mestre B, Alcaine S, Bayes A. Freezing of Gait in Patients with Parkinson's Disease through a Waist-Worn Accelerometer. 19th International Conference of the Catalan Association for Artificial Intelligence, CCIA 2016. Barcelona; 2016. p. 10.

Rodríguez-Martín D, Samà A, Pérez-López C, Català A, Mestre B, Alcaine S, Bayes A. Comparison of features, window sizes and classifiers in detecting Freezing of Gait in patients with Parkinson's Disease through a waist-worn accelerometer. 19th International Conference of the Catalan Association for Artificial Intelligence, CCIA 2016. Barcelona; 2016. p. 10.

Camps J, Samà A, Martín M, Rodiguez-Martín D, Pérez-López C, Alcaine S, Mestre B, Prats A, Crespo-Maraver MC, Cabestany J, Bayes A, Català A. Deep learning for detecting freezing of gait episodes in Parkinson's disease based on accelerometers. In Adv. Comput. Intell; 2017; pp. 344–355, doi: 10.1007/978-3-319-59147-6_30.

Camps J, Samà A, Martín M, Rodiguez-Martín D, Pérez-López C, Moreno JM, Cabestany J, Català A, Alcaine S, Mestre B, Prats A, Crespo-Maraver MC, Counihan TJ, Browne P, Quinland LR, ÓLaighin G, Sweeney D, Lewy H, Vainstein G, Costa A, Annicchiarico R, Bayés A, Rodríguez-Molinero A. A Deep learning for freezing of gait detection in Parkinson's disease patients in their homes using a waist-worn inertial measurement unit. Knowledge-Based Syst. 2017, doi:10.1016/j.knosys.2017.10.017.

Samà A, Rodríguez-Martín D, Pérez-López C, Català A, Alcaine S, Mestre B, Prats A, Crespo MC, Bayes A, et al. Determining the optimal features in freezing of gait detection through a single waist accelerometer in home environments Pattern Recognit. Lett. 2017, 1–9, doi:10.1016/j.patrec.2017.05.009.

Rodríguez-Martín D, Pérez-López C, Samà A, Català A, Moreno Arostegui JM, Cabestany J, Mestre B, Alcaine S, Prats A, Cruz Crespo M, Bayés À. A Waist-Worn Inertial Measurement Unit for Long-Term Monitoring of Parkinson's Disease Patients. Sensors (Basel). 2017 Apr 11;17(4). pii: E827. doi: 10.3390/s17040827.

Rodríguez-Martín D, Samà A, Pérez-López C, Català A. Posture transitions identification based on a triaxial accelerometer and a barometer sensor Adv. Comput. Intell. 2017, 333–343, doi:10.1007/978-3-319-59147-6_29.

Crespo MC, Prats A, Mestre B, Alcaine S, Pérez-López C, Rodriguez-Martín D, Catala A, Bayes A & MASKPARK Group. Automatic auditory cues system for Parkinson's disease. Freezing of Gait Congress. 6-8 June 2018, Leuven (Belgium).

Guimarães V, Nunes F. A Wearable, Customizable, and Automated Auditory Cueing System to Stimulate Gait in Parkinson's. Proceedings of the 12th EAI International Conference on Pervasive Computing Technologies for Healthcare. 2018 http://dx.doi.org/10.4108/eai.20-4-2018.2276278

Prats A, Mestre B, Bayés A. Projecte MASPARK "Project: [436/C/2014 - FREEZING IN PARKINSON'S DISEASE: IMPROVING QUALITY OF LIFE]. FUNDACIÓ DE LA MARATÓ DE TV3". Reunió Interhospitalària del Grup d'Estudis de Trastorns del Moviment de la Societat Catalana de Neurologia. 14 June 2018. Barcelona.

Rodríguez-Martín D, Samà A, Pérez-López C, Català A, Cabestany J. Posture transition analysis with barometers: contribution to accelerometer-based algorithms. Neural Comput Appl. 2018.