An automated methodology for levodopa-induced dyskinesia: Assessment based on gyroscope and accelerometer signals

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ABSTRACT

Objective: In this study, a methodology is presented for an automated levodopa-induced dyskinesia (LID) assessment in patients suffering from Parkinson's disease (PD) under real-life conditions.
Methods and Material: The methodology is based on the analysis of signals recorded from several accelerometers and gyroscopes, which are placed on the subjects' body while they were performing a series of standardised motor tasks as well as voluntary movements. Sixteen subjects were enrolled in the study. The recordings were analysed in order to extract several features and, based on these features, a classification technique was used for LID assessment, i.e. detection of LID symptoms and classification of their severity.
Results: The results were compared with the clinical annotation of the signals, provided by two expert neurologists. The analysis was performed related to the number and topology of sensors used; several different experimental settings were evaluated while a 10-fold stratified cross validation technique was employed in all cases. Moreover, several different classification techniques were examined. The ability of the methodology to be generalised was also evaluated using leave-one-patient-out cross validation. The sensitivity and positive predictive values (average for all LID severities) were 80.35% and 76.84%, respectively.
Conclusions: The proposed methodology can be applied in real-life conditions since it can perform LID assessment in recordings which include various PD symptoms (such as tremor, dyskinesia and freezing of gait) of several motor tasks and random voluntary movements.

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1. Introduction

Parkinson's disease (PD) is a neurodegenerative disorder of the central nervous system that is manifested clinically by tremors, bradykinesia, rigidity, flexed posture, postural instability and freezing of gait [1]. The number of persons with PD over 50 years old in western Europe's five most populous nations rose to 4.6 million in 2005, and this figure is expected to reach 9.3 million by 2030 [2]. The identification of the main cause of PD, i.e. the loss of brain cells that produce dopamine which helps coordinate and control muscular activity, led to the introduction of levodopa as a treatment. Levodopa is highly effective in reducing the symptoms of the disease and remains the standard drug for patients suffering from PD [3]. However, long-term PD treatment using levodopa is often complicated by significantly disabling fluctuations and dyskinesias, referred to as levodopa-induced dyskinesia (LID). LID is manifested as jerky, dance-like movements of body parts such as limbs (arms, legs), torso and head [4]. LIDs appear gradually and their severity increases progressively, and once established LIDs are difficult to treat. Therefore, efforts must be made in the direction of preventive strategies, which mainly focus on the optimal adjustment of the levodopa dosage. Prolonging the establishment of LID and minimising its symptoms through optimal adjustment of levodopa dosage can only be achieved through long-term assessment of LID and its severity in PD patients. In addition, effective characterisation and quantification of LID improves the understanding of its pathophysiological mechanisms, and helps towards treatment evaluation.

Clinical methods currently used for LID assessment lack objectivity and cannot be used for long-term monitoring [5]. To overcome the limitations of the short-term and subjective assessments of LID, and to gain insight into the pathophysiology of LID episodes, several computer-based methods have been presented in the literature [6–16]. These methods are based on the analysis of signals obtained using quantitative instrumental

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Table 1
Recordings of the dataset and clinical symptoms duration (s).

Subject number	Category	Record number	Duration	State	Tremor	Bradykinesia	FoG	LID
1	PD	1	17:21	OFF	0:00	1:29	0:00	0:00
		2	16:18	OFF	8:02	1:11	0:19	0:00
		3	17:14	ON	0:00	0:00	0:25	0:00
		4	14:36	ON	2:57	0:00	0:00	0:00
2	PD	1	9:09	ON	0:00	0:00	1:31	0:00
3	PD	1	14:08	ON	0:00	0:00	0:00	0:00
4	LID	1	21:17	OFF	9:32	2:47	2:49	0:00
		2	13:29	ON	0:00	0:00	0:00	4:45
		3	8:55	ON	0:00	0:00	0:00	5:22
5	PD	1	14:08	OFF	0:00	0:00	0:00	0:00
		2	14:42	ON	0:00	0:00	0:00	0:00
6	LID	1	12:57	OFF	0:00	0:00	0:00	0:00
		2	16:15	ON	0:00	0:00	0:00	16:08
7	LID	1	15:06	ON	0:00	0:00	0:11	14:16
		2	14:57	ON	0:00	0:00	0:00	11:15
8	PD	1	11:43	OFF	0:00	4:09	1:44	0:00
9	LID	1	15:25	ON	0:00	0:00	0:00	10:38
10	LID	1	10:17	ON	0:00	0:00	0:00	6:39
11	LID	1	13:51	ON	0:00	0:00	0:00	7:56
12	Control	1	16:01	–	0:00	0:00	0:00	0:00
13	Control	1	15:50	–	0:00	0:00	0:00	0:00
14	Control	1	14:30	–	0:00	0:00	0:00	0:00
15	Control	1	14:17	–	0:00	0:00	0:00	0:00
16	Control	1	13:53	–	0:00	0:00	0:00	0:00
Total		24	5:46:19		20:31	9:36	6:59	1:15:59

techniques, such as surface electromyography [6], Doppler ultrasound [7], gyroscopes [8], accelerometers [9–12], magnetic motion trackers [13–15] and digital drawings [16]. Most of the studies focused on the frequency domain of the signals coming from the movement sensors, while time-domain features have also been employed. The severity of LID has mainly been determined using statistical measures [8,10,13–16] while artificial neural networks and support vector machines (SVM) have also employed [9,11,12,15]. Methods based on sensors which are placed on the subject's body [8–15] greatly differ in the positioning of the sensors, while recordings from a limited number of body locations are used in some cases [6]. Also, in most cases, a limited number of tasks are included in the recording protocol [8,13–16] and/or short-time recordings are used [8–10,12–15]. In most of the aforementioned studies, the datasets used are composed from recordings only including LID symptoms, while recordings with other PD symptoms (such as tremor, bradykinesia, freezing of gait) are not included. All the above limitations, i.e. limited recording positions, small number of involved tasks, short time scale and task specific recordings, pose significant drawbacks in the aforementioned studies since the LID symptoms can vary significantly during the day in relation to their topography (affected body regions), duration and severity. In addition, in most of the aforementioned studies the subjects were instructed to refrain from making voluntary movements. A major challenge for an automated method for LID assessment is to be able to distinguish LID symptoms from any other clinical symptoms that a PD patient may present, during any kind of movement (voluntary or not).

In this study, an automated methodology for LID assessment under real life conditions is presented. The methodology is based on the analysis of the signals recorded from six accelerometers and two gyroscopes, which are placed on certain positions on the subject's body. The signals obtained were analysed and several features were extracted. Based on these features a classification technique was used for LID detection and the classification of its severity. The method has been evaluated using a group of 16 subjects (a total of 24 recordings), including normal subjects, PD patients not presenting LIDs and PD patients suffering from LID of a varying degree of severity. The recordings were made so as to reflect real life conditions, thus several motor tasks and random movements as well as

all common PD symptoms (such as tremors of a variety of severity, bradykinesia and freezing of gait) were included. Extensive evaluation has been performed, and the results are presented for each individual sensor as well as for various sensor combinations. In addition, two cross validation techniques have been employed (10-fold stratified cross validation and leave-one-patient-out cross validation). The results obtained indicate high classification ability. Compared to other approaches the proposed methodology is advantageous since it is fully automated, it can be used for combinations of signals obtained from various sensor configurations, and it can accurately distinguish LIDs from other PD symptoms, under real life conditions.

2. Materials and methods

2.1. Population

In this study we employed patients from the neurology clinic of the University Hospital of Ioannina that were diagnosed with idiopathic PD, as well as normal subjects. The medical ethical committee of the hospital approved the study. 16 subjects were enrolled, with a total number of 24 recordings. The subjects were distributed into three groups: (1) control group (healthy subjects), (2) PD patients not presenting LID symptoms, (3) PD patients with LID symptoms of varying severity. The recordings of PD patients (groups 2 and 3) were performed while the patients were either in the ON or OFF state. Since LID only appears during the ON state, all patients belonging to the third group had at least one recording whilst in the ON state. The recordings from the PD patients included several other PD symptoms, such as tremor (mild and moderate severity), bradykinesia and freezing of gait. PD patients not presenting LID symptoms are aged 60–68 years old, 62.6 ± 3.2 years, with 4–35 years since diagnosis, 2–33 years of levodopa intake and at 1–4 Hoehn & Yahr stage. PD patients with LID symptoms are aged 57–64 years old, 60.1 ± 3.5 years, with 10–35 years since diagnosis, 10–34 years of levodopa intake, 2–4 Hoehn & Yahr stage, and presenting mild to severe LIDs. The patients in the dataset were selected from expert neurologists to reflect real-life conditions related to LID status, i.e. including patients diagnosed with