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Multi-parametric system for the continuous assessment and monitoring of motor status in Parkinson's disease: an entropy-based gait comparison

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Abstract— **A "Multi-parametric system for the continuous assessment and monitoring of motor status in Parkinson's disease" (PERFORM), is an FP7 project from the European Commission that aims at providing an innovative and reliable tool, able to evaluate, monitor and manage patients suffering from motor neurodegenerative diseases. The current work is related to a module of the project that is in charge of assessing PD patients during locomotion. These initial analyses of gait are based on analyses of Sample Entropy in the acceleration signals. Four PD patients are compared to four healthy using a set of five wireless sensors located in the limbs and in the trunk. A metric to assess the level of symmetry during locomotion, an important clinical feature, is proposed. Results show considerable differences between the patients and the subjects, both for sample entropy (in 3 of the 5 sensors) and in the gait asymmetry index (left vs. right limbs). Future work is proposed including age-matched subjects and a larger sample.**

I. Introduction

PARKINSON'S disease (PD) is a common neurodegenerative disorder that affects motor skills and speech. It is characterized by muscle rigidity, a slowing of physical movement such as bradykinesia, tremor and other symptoms [1]. Substitution therapy with dopaminergic drugs effectively reverses all the symptoms and signs of the disease at the beginning of treatment. However, after a variable period of time, this initially excellent response is complicated by the appearance of disorders known as Motor Response Complications (MRCs) [2]. PD drastically increases with age, affecting 1% -2% of the population over 65; figures that are expected to double by 2020 [3].

PERFORM is a project partially funded by The European Union Commission under the Seventh Framework Program, aiming at providing an innovative and reliable tool that is able to monitor and evaluate motor neurodegenerative disease patients. Parkinson's disease and Amyotrophic Lateral Sclerosis (ALS) are the model diseases being taken into account for the design and the evaluation of the system.

The PERFORM project is based on the development of an intelligent system that seamlessly integrates a wide range of wearable micro-sensors constantly monitoring several motor and physiological signals of the patients. Data acquired are pre-processed by advanced knowledge processing methods, integrated by fusion algorithms to allow health professionals to remotely monitor the overall status of the patients and adjust medication schedules and personalize treatment. Personalization of treatment will occur through PERFORM's capability to keep track of the timing and doses of the drugs and meals that the patients are taking.

Gait is one of the cardinal affections on patients with PD. Shuffle walking and bradykinesia are two of the most common affections. This affection goes beyond gait itself and severely increases the probability that the patients will fall even when compared with other fall-prone populations. Another possible effect of falls is incapacitating fear of falling again [4].

Gait (and falls) is a part of the Unified Parkinson's Disease Rating Scale (UPDRS), used in most countries to assess patients. Question 29 is usually evaluated by a physician while the patient is visiting the doctor and it addresses the amount of shuffling, festination, and level of disturbance of the gait pattern of the patient. PERFORM, will address this issue through accelerometry, and as described previously, it will allow for the constant monitoring of the gait parameter, attempting to rate the patient with the same reliability of a physician.

The gait module of PERFORM will also produce other metrics that we believe physicians will consider useful at the time of managing a patient through PERFORM.

Symmetry is an important feature in Parkinson's disease, as at the disease's onset, the appearance of the symptoms most usually affects only one side of the body. As the disease progresses, the side of the body initially not affected becomes affected too, thus decreasing the initial asymmetry. This has been taken into account for the design of our gait analysis module.

The current work presents our initial approach to the design of the gait assessment module within PERFORM.

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This work is based in a comparison of PD patients vs. controls through entropy analyses.

We have decided to initiate the assessment of gait based on Entropy Analyses. Entropy of information allows evaluating the complexity of human gait and is useful to assess the level of symmetry of limb movements during walking [5]. Analyzing data collected from PD's patients, it has been proved that the variability of gait parameters like stride length, step frequency, speed of locomotion is higher compared to healthy subjects [6]. In the present work, we look at Sample Entropy [7] and we propose a "Gait symmetry index" as an initial approach to asses gait itself and the symmetry of the movements of the limbs in a sample of PD patients and controls.

II. Methodology

A. Experimental setup

Eight subjects participated in the current study, separated in two groups: four PD patients and four healthy subjects. In the PD patient group, we had 3 males and a female (age 62 +/- 2.9 St Dev). In the healthy subject group, three males and one female (age 27.25 +/- 3.3 St Dev). Patients had taken their medication shortly before the testing sessions. The symptoms were rated by a professional Neurologist with more than 20 years of experience with PD patients. Four accelerometers were placed on the right and left forearms, and on the right and left calves with a fifth accelerometer being placed on the trunk, just at the base of the sternum. The study took place in a control environment, in which subjects walked in three trials. In the first trial, the subject walked in a straight line for 4 meters, turned back towards the left and returned in the same straight line to the starting position. In the second trial, the subject turned back towards the right and in the third trial the subject only walked the initial 4 meters and ended in a standing position. All subjects (patients and controls) complied through a signed form of ethical approval and disclaimer approved by the ethical committee of the "Clinica Universitaria de Navarra" and accepted by the "Universidad Politécnica de Madrid".

Fig. 1 Experiment in Clinic of University of Navarra

B. Measurement System

Motion data was collected using the SHIMMER platform [8]. SHIMMER is a small cordless sensor platform designed by Intel® as a wearable device for health-sensing applications. All sensors provide 3-axis accelerometer signals large storage, and low-power standards based communication capabilities. They also provide a Bluetooth protocol capability that allow SHIMMERs to stream the data to a computer.

Fig 2 Shimmer platform

The sensor size is similar to that of a matchbox. Sensors on the arms and legs were attached on specially designed elastic bands, which allow fixation to any wrist or ankle size. Sampling rate was set to 100Hz by default for each signal. During the experiment, the accelerometry measurements were complemented by a reflective marker and high-speed camera collection system. This complimentary analysis served as a support tool to validate the data used for this work.

C. Sample Entropy Technique

There are many techniques to calculate the function of Entropy of Information of a time series. The techniques most used in gait analysis are "Sample Entropy and Approximation Entropy" [9][7]. Both techniques quantify the regularity of a time series and provide a useful estimation of the pattern symmetry of human gait during walking. In this study we have calculated the SampEn of five signals coming from the accelerometers attached on the limbs and on the trunk of the subjects. The signals were filtered with a LPF the Cut-off frequency of 3Hz and that elaborated with the following algorithm:

Given a time series of N points, {x(1),x(2), …, x(N)}, forms N-m vectors let the following series be:

$$x_m(i) = \{x_i, x_{i+1}, \ldots, x_{i+m-1}\} \quad (1)$$

This series is called "template" for $1 \leq i \leq N+m$. A match occurs if the distance between two $x_m(i), x_m(j)$ vectors

$$d(x_m(i), x_m(j)) = \max\{|x_{i+k} - x_{j+k}|, 0 \leq k \leq m-1\}$$

defined as follows:

(2)

is smaller than a specified tolerance level "*r*". In this study "r=0.2σ" has been chosen.

Let $n_i^m(r)$ be the number of $x_m(i)$ vectors that match $x_m(j)$ at tolerance level "r", then

$$C_i^m(r) = n_i^m/(N-m-1) \quad (3)$$

represents the probability that any vector $x_m(i)$ matches the vector $x_m(j)$

The average of

$$C_i^m(r), C(r) = (N-m)^{-1}\sum_{i=1}^{N-m} C_i^m(r) \quad (4)$$

represents the probability that any two vectors match each other.
SampEn is defined as:

$$SampEn(m,r) = \lim_{N\to\infty}\left[-\ln\frac{C^{m+1}(r)}{C^{m(r)}}\right] \quad (5)$$

which is estimated by the statistic:

$$SampEn(m,r) = -\ln\frac{C^{m+1}(r)}{C^m(r)} \quad (6)$$

So, SampEn(m,r) is the negative of the natural logarithm of the conditional probability that two sequences that are close within a tolerance $r\sigma$ from *m* consecutive points remain close at next point [5].

D. Symmetry Comparison

To assess the progressive decrease in asymmetry as the PD progresses, we propose a Gait Symmetry Index (GSI), to be calculated in the following way:

$$GSI = \frac{min\,(SampEnR, SampEnL)}{max(SampEnR, SamprEnL)} \quad (7)$$

This proposed metric is no more than a ratio that compares the minimum between the entropies obtained from the sensors in the right or left limbs, to those obtained from the limbs from the other side of the body.

III. Results

A. Sample Entropy

The values of SampEn evaluated in real patients and healthy subjects differed significantly. Figures 3-7 show the values of SampEn in function of *r*. The graphs show the values of SampEn calculated for each limb and for the trunk. Fig.2 shows the comparisons between PD's patients and control subjects for each sensor. Though the standard deviation in the cases of left leg and right arm does not allow for a statistical separation the two groups of subjects, in the others cases the values of SampEn are significantly different. As shown, the entropy of the limbs of a person affected by PD evaluated during walking is higher than that of a normal subject. This increase of variability in PD patients is mainly attributable to the effects of the symptom Bradikynesia. The subjects affected by PD progressively lose complexity in their movements and, consequently, their gait parameters increase their irregularity. As a consequence of this increase in variability, the entropy of the time series acquired from the PD patient accelerometers increases substantially.

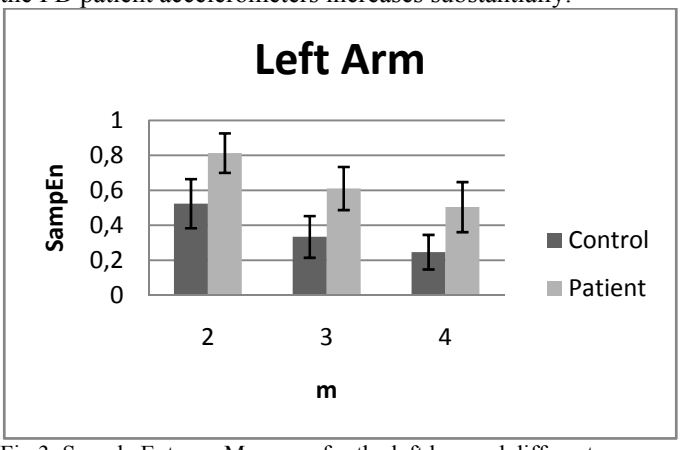

Fig 3. Sample Entropy Measures for the left leg, and different m values.

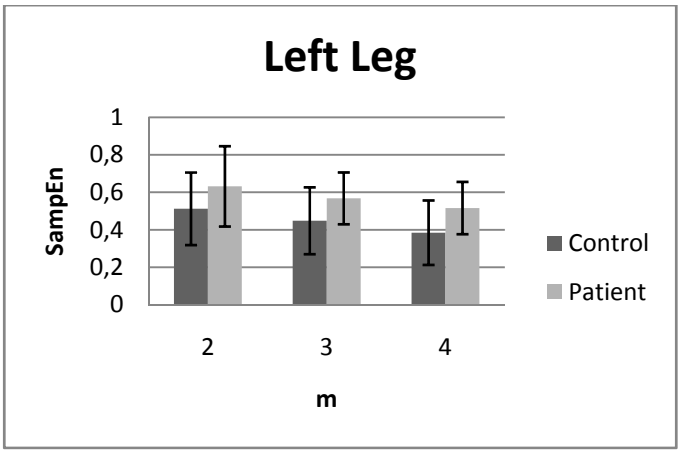

Fig 4 Sample Entropy Measures for the left leg, and different m values.

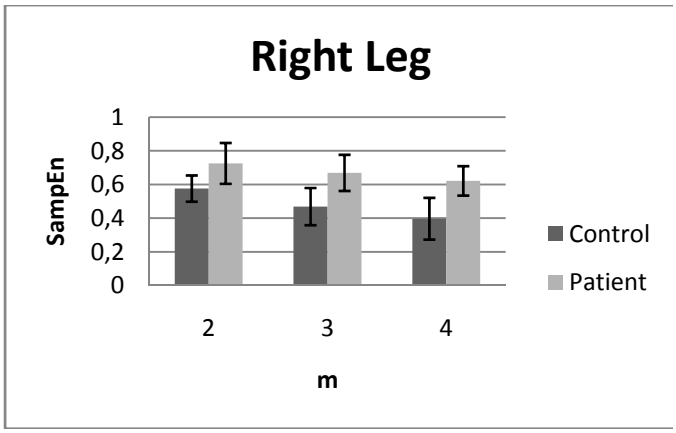

Fig 5. Sample Entropy Measures for the right leg, and different m values.

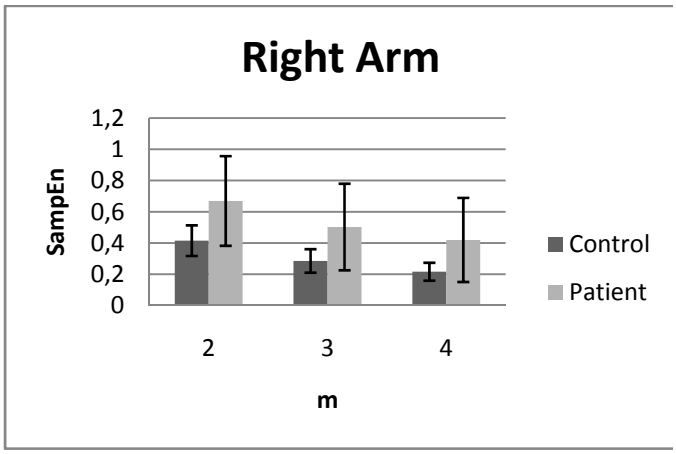

Fig. 6 Sample Entropy Measures for the right arm, and different m values.

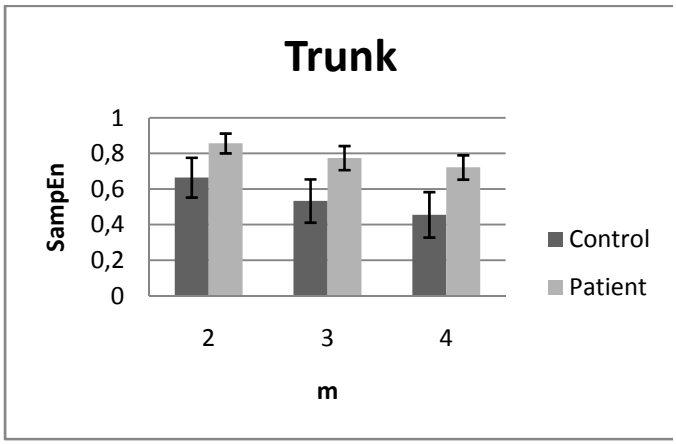

Fig 7 Sample Entropy Measures for the trunk, and different m values.

B. Gait symmetry Index

GSI results show a significant difference between the legs of the controls and the legs of the PD patients for M>2. GSIs were calculated on the average entropies for the group of patients and subjects. The values obtained for the legs differed in 11.6% and 13.4% for M=3 and M=4 respectively, with respect to the control values.

Table 1. GSI comparison for upper and lower limbs.

GSI	M=2	M=3	M=4
Control Legs	0.88	0.95	0.96
Control Arms	0.79	0.85	0.87
PD Legs	0.87	0.84	0.83
PD Arms	0.82	0.82	0.83

IV. CONCLUSION

The proposed metrics seem to provide a useful tool to the analysis of motor disorders. The experiment shows significant sample entropy differences between Parkinson's disease patients and control subjects. Nevertheless, results on right arm and left leg show large standard deviation values which means that more recordings and more subjects are needed to validate the results. To confirm these initial results, we will not only continue the testing on a larger sample, but we will also collect the data on controls paired with PD patients in terms of age. As is, age could very well be a factor affecting the gait pattern and causing the differences in sample Entropy that we found. Regarding the GSI, it looks like a promising metric to compare the extent of the asymmetry of PD patients during gait.

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