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Classification-Based Screening of Parkinson's Disease Patients through Graph and Handwriting Signal †

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Abstract: Parkinson's disease (PD) is one of the most common neurodegenerative diseases, affecting millions of people worldwide, especially the elderly population. It has been demonstrated that handwriting impairment can be an important early marker for the detection of this disease. The aim of this study is to propose a simple and quick way to discriminate PD patients from controls through handwriting tasks using machine learning techniques. We developed a telemonitoring system based on a user-friendly application for drawing tablets that enabled us to collect real-time information about position, pressure, and inclination of the digital pen during the experiment and, simultaneously, to supply visual feedback on the screen to the subject.

Keywords: graph signal; handwriting signal; Parkinson's disease; machine learning; telemonitoring

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1. Introduction

Parkinson's disease (PD) is one of the most common neurodegenerative disorders in the world, second only to Alzheimer's disease [1]. The differential diagnosis of PD is still an open challenge for the scientific community: to this day, a confirmation of the disease is available only postmortem, and the rate of misdiagnosis is high: it has been estimated that 25% of the diagnoses are incorrect [2]. The main cause of PD is the lack of dopamine production, and its main motor symptoms are bradykinesia, tremor, and rigidity [3]: neurologists rely on imaging techniques, such as MRI (Magnetic Resonance Imaging), CT (Computed Tomography) or PET (Positron Emission Tomography), and patient's clinical evaluation [3]. Machine learning techniques have been studied to help the diagnosis of PD and have shown promising results. Pereira et al. presented a review on recent studies concerning computer-assisted methods to aid PD recognition [4], that include speech, gait and handwriting analysis.

In this study, we focused on handwriting of PD's subjects: handwriting requires a complex coordination of consecutive movements, and the motor symptoms of PD can provoke handwriting impairments on the size of letters, that is referred to as micrographia, and on the pressure and kinematics of the pen [5,6], together with a general difficulty of writing which involves different graphological patterns. Since "graphology is a discipline that deals with the dynamic study of the graphic gesture" [7], we based our analysis on computational graphology. Several studies have investigated the most relevant writing features and tasks to be executed for the diagnosis of PD. In [8] is presented the state of the art of these studies. It is possible to collect relevant information from drawings (Archimedean spiral [9–14], circles [15], meanders [12,13], etc.) and from handwritten words and graphemes. The drawing of an Archimedean spiral (spirography) is a common task for tremor and other movement disorder analysis [9]. Thanks to the development of digitizing tablet technologies, it is possible to analyze not only the offline image, but also the kinematic characteristics of the graphic signal and the pressure applied on the tablet [16,17]. "Online" data are those collected while the user writes, while "offline" data are those available after the writing is completed [18]. In the last decade, important databases have been presented in order to study handwriting impairments in PD: the PaHaW database [10], that includes real-time data (pen-position, pen-pressure, pen-inclination) collected from 38 PD patients and 37 control subjects and the HandPD [12] and NewHandPD [13] databases, that include offline images collected by Pereira et al.

Dròtar et al., analyzing the PaHaW database, obtained an accuracy of 85.61% [19]: they demonstrated the relevance not only of the on-tablet movements, but also of the in-air movements, i.e., variation of the pen position while the pen is not touching the table. Considering only the spiral task, they obtained an accuracy of 62.8% [11].

The aim of this work is to analyse handwriting signals from both PD's patients and control subjects and to propose a way to automatically distinguish these two classes. In order to collect the necessary data, we developed a telemonitoring system based on a user-friendly application for drawing tablets that enabled us to collect real-time information about the digital pen during the experiment and, simultaneously, to supply visual feedback on the screen to the subject. Through this system, data can be collected remotely, in order to allow patients to execute tasks in the comfort and safety of their home, reducing the demand on hospital services.

2. Methods and Materials

In this study, we collected data from 22 healthy subjects. All participants are right-handed, with an age in the range (55 ± 15y). Information about subjects' age, gender, dimension of the hand and level of education are collected in Table 1. The educational level was classified according to the UNESCO's ISCED 2011 (International Standard Classification of Education) [20]. This classification distinguishes nine levels of education, from early child education (level 0) to doctoral or equivalent level (level 8). These levels can be aggregated in three categories: low (0–2), medium (3–4), high (5–8) [21]. The hand's dimension has been quantified measuring the distance between the wrist and the top of the distal phalanx of the dominant hand's middle finger.

A commercial drawing tablet with screen "Wacom One" was used for this test, in order to be able to extract both "online" and "offline" features. Wacom tablets are widely used in handwriting movement analysis, as they offer high spatial and temporal resolution [8].

Table 1. Subjects' data.

Age (Mean ± sd)	Number Male/Female	Middle Finger–Wrist Distance (cm) (Mean ± sd)	Level of Education (ISCED 2011) (Mean ± sd)
55.8 ± 6.5	8/14	19.6 ± 1.8	5.1 ± 2.1

An application has been developed by our team using Unity, a development platform, which allowed us to collect information about pen position (x, y), pressure and inclination with a frequency of 133 Hz and, simultaneously, to supply visual feedback on the tablet's screen to the subjects. The application has a start page, where it can be inserted participant's ID and that includes a menu, where the user can choose which task to take.

In order to analyse the data, we used the software MATLAB.

The protocol was divided in four parts: drawing an Archimedean spiral, writing the bigram “le” six times and two Italian sentences, drawing ten concentric circles and writing seven lines of free text. For each part of the protocol a different screen was shown to the subject: firstly, an image of an Archimedean spiral was shown, and the subject was asked to trace it at a comfortable speed; secondly, a blank screen was shown, and the subject was asked to write in cursive 6 times the bigram “le”, and two Italian phrases: “I fiori sono sul prato” and “Nel cielo ci sono le stelle”. On the third screen, a circle was shown, and the subject was asked to draw ten concentric circles inside it. Lastly, a blank screen was shown, and the subject was asked to write in cursive seven lines of free text. The overall duration of the test varied between 10 and 15 min from subject to subject. The subjects have been given the opportunity of trying the tablet before the test. During the execution of the tasks, the subjects were sit in a comfortable position on a chair without armrests, and the tablet was positioned on a table in front of them.

Features were extracted from each task separately.

Data were separated into components, i.e., lines that are traced without lifting the pen from the tablet. In order to do that automatically, indices of the samples where pressure goes from positive to zero and vice versa were saved in a vector of markers. Both in-air and on-tablet features were extracted.

Figure 1 shows an example of the task “bigram le”, where the different components, automatically detected, are represented in different colours and the “in-air” points of the pen-position are represented as blue points. For each component, the velocity was calculated as

$$v = \sqrt{{v_x}^2 + {v_y}^2}, \quad (1)$$

where $v_x = \frac{x_{i+1} - x_i}{t_{i+1} - t_i}$ and $v_y = \frac{y_{i+1} - y_i}{t_{i+1} - t_i}$.

Acceleration and jerk of the components also were calculated. To analyse the spiral, the angular and radial velocity were calculated. Furthermore, the distance of the drawn spiral from the spiral guide was calculated with the following algorithm:

1. For each point of the drawn spiral (x_i, y_i), we found the spiral guide’s closest point to it, (sx_i, sy_i).
2. We calculated the distance of each couple of points (x_i, y_i), (sx_i, sy_i), as

$$d_i = \sqrt{({x_i}^2 - {sx_i}^2) + ({y_i}^2 - {sy_i}^2)} \quad (2)$$

3. We found the parameter

$$p = \sum_i {d_i}^2, \quad (3)$$

that describes how much the drawn spiral is distant from the spiral guide. Smaller p means a higher precision.

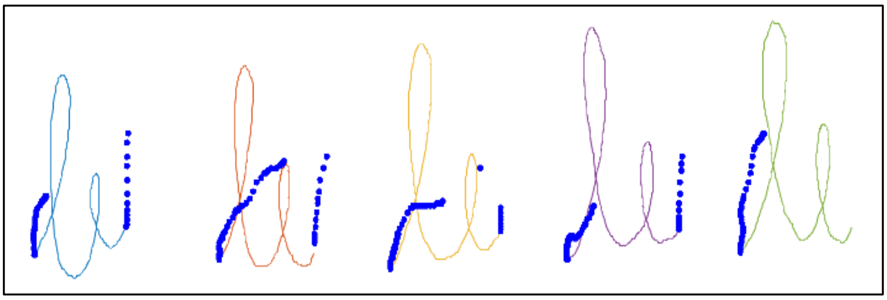

Figure 1. Image of the “bigram le” task wrote by an healthy control subject from our dataset: the points “in-air” of the pen-position are represented in blue. Different components of the “on-tablet” pen-position are represented in different colours.

In order to develop a model for automatic classification of PD, we used data from 36 PD's subjects and 35 healthy control subjects from the PaHaW dataset and data from the 20 healthy control subjects that we collected in our database. Two tasks that the two database have in common have been analysed: the guided spiral and the bigram "le". The features that have been considered are reported in Table 2.

Table 2. Features extracted: *1* if the feature was extracted from the spiral task analysis, *2* if the feature was extracted from the "bigram le" task analysis.

Features	**Task**
Velocity: absolute, vertical, and horizontal	*1,2*
Acceleration: absolute, vertical, and horizontal	*1,2*
Jerk: absolute, vertical, and horizontal	*1,2*
Radial velocity	*1*
Angular velocity	*1*
Variation of velocity, acceleration, and stroke between components	*2*
Number of changes of direction in velocity	*1,2*
Number of changes of direction in acceleration	*1,2*
Number of changes of direction in jerk	*1,2*
Normalized in-air time (time in air over total time)	*1,2*
Velocity on-air: absolute, vertical, and horizontal	*2*
Acceleration on-air: absolute, vertical, and horizontal	*2*
Jerk on-air: absolute, vertical, and horizontal	*2*

3. Results and Discussion

In order to discriminate between PD patients and healthy control subjects, three models have been constructed: one using only data from the spiral task, one using only data from the "bigram le" task, and one using data from both of them. A 10-fold cross-validation was conducted. Results are reported in Table 3. Accuracy, specificity, and sensitivity was calculated in terms of TP (true positive), FP (false positive), TN (true negative) and FN (false negative), as:

$$Accuracy = \frac{TP + TN}{TP + TN + FP + FN} \tag{4}$$

$$Specificity = \frac{TN}{FP + TN} \tag{5}$$

$$Sensitivity = \frac{TP}{FN + TP} \tag{6}$$

Table 3. Model used and classification accuracy, specificity, sensitivity of the two tasks.

	Model	**Accuracy**	**Specificity**	**Sensitivity**
Spiral	Linear SVM	74.2 %	82.4%	62.1%
le	Fine KNN	80.6 %	82.4%	77.8%
Spiral and le	Linear SVM	84.9 %	87.8 %	80.5 %

Considering the two tasks separately, we obtained a higher accuracy for the "bigram le" tasks than for the spiral tasks. Moreover, considering the spiral and the "bigram le" task separately, accuracy that we obtained for the spiral (74.2%) is higher than the accuracy obtained for the spiral by Dròtar et al. (62.8%) and, similarly, considering only the "le bigram" task, the accuracy that we obtained (80.6%) is higher than the accuracy obtained by Dròtar et al. for this task (71%). The highest accuracy (84.9%), specificity (87.8%) and sensitivity (80.5%) are obtained combining the two tasks. The machine learning algorithms that have been employed were the support vector machines (SVM) for the spiral task and the combined tasks, and the fine k-nearest neighbors (Fine KNN) for the "bigram le" task.

4. Conclusions

In this study, an application that allowed us to register data from tablets with a frequency of 133 Hz was presented, to aid the recognition of PD through handwriting impairments. The tool that is proposed is simple and easy-to-use, allowing subjects to make the test in the comfort of their home. Data from 22 healthy subjects were collected and added to the PaHaW database [10,19], a pre-existing dataset that includes data from PD's patients and healthy control subjects. Using only two of the eight tasks that the PaHaW database includes, an accuracy of 84.9%, was obtained, close to the 85.61% accuracy that Dròtar et al. obtained considering all the eight tasks together [19]. We couldn't compare the other tasks because the first language declared from our subjects (Italian) was different from the first language of the PaHaW database's subjects (Czech). However, the protocol that we developed can be used in future studies to collect data from Italian PD's subjects. This work is part of a home-monitoring project, that aims to aid the PD's detection through a combined analysis of the graphological and vocal signal [22].

Institutional Review Board Statement:

Informed Consent Statement:

Data Availability Statement:

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