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An Experimental Protocol to Support Cognitive Impairment Diagnosis by using Handwriting Analysis

Nicole Dalia Cilia[a], Claudio De Stefano[a], Francesco Fontanella[a,*], Alessandra Scotto Di Freca[a]

[a]*Dipartimento di Ingegneria Elettrica e dell'Informazione (DIEI)*
Università di Cassino e del Lazio meridionale – Italy

Abstract

Nowadays diseases involving cognitive impairments affect millions of people worldwide, with Alzheimer's and Parkinson's diseases being the most common ones. Because of the worldwide average lifespan increment, it is expected that their incidence will increase in the next few decades. Among the daily activities, handwriting is one of the first affected by cognitive impairments. For this reasons, researchers have also been investigating the analysis of handwriting alterations as diagnostic signs for this kind of diseases. In this paper we present an experimental protocol that we developed for the analysis of the handwriting dynamics of patients affected by cognitive impairments. The aim of this protocol is to build a large database that would allow to effectively train different classifier systems. We also detail the most common and effective features previously used in the literature to represent handwriting dynamics of the subjects affected by cognitive impairments.

Keywords: Alzheimer's Disease; Cognitive impairments; Handwriting analysis.

1. Introduction

Cognitive impairments represent a large group of neurological disorders with heterogeneous clinical and pathological expressions, affecting specific subsets of neurons in specific functional anatomic systems; they arise for unknown reasons and progress in a relentless manner [30]. Although treatments may help relieve some of the physical or mental symptoms associated with these diseases, there is currently no cure for them. However, an early diagnosis strongly improves the effectiveness of the available treatments, but it is still a challenging task. To date, clinical diagnoses of such diseases are performed by physicians and may be supported by tools such as imaging (e.g. magnetic resonance imaging), blood tests and lumbar puncture (spinal tap).

* Corresponding author. Tel.: +39-0776-299-3882; fax: +39-0776-299-4358.
E-mail address: fontanella@unicas.it

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A cognitive impairment may evolve into a Dementia Disease (DDs)/Neurodegenerative Disease (NDs), such as, the most commons, Alzheimer's and Parkinson's diseases [12]. Since the risk of being affected by these diseases increases strongly with age [29] and because improvements in the medical field have lengthened lifespan, in most developed and developing countries, it is expected that in the next decades the incidence of DDs/NDs will dramatically increase. This creates a strong need for the improvement of the approaches currently being used for diagnosis of these diseases. Among the motor activities compromised by the cognitive impairments there is certainly the handwriting, which is the result of a complex network of cognitive, kinesthetic and perceptive-motor skills [35]. With the onset of the disease, neurons can not properly control the muscles that allow some movements. On the other hand, neuro-muscular diseases often lead to progressive cognitive, functional and behavioral changes. Deterioration in writing skills had already emerged in the first diagnosis of Alzheimer's disease (AD) in 1907 [22]. In recent decades, however, researchers have more accurately discovered that the handwriting of Alzheimer's patients shows alterations in spatial organization and poor control of movement [27]. Several studies have also been published to study the effectiveness of handwriting analysis as a tool for diagnosis and monitoring of the Parkinson's disease (PD) [34]. Recently, it has been also observed that, when considering the perspective of signal and image processing, there are some aspects of the writing process that are more vulnerable than others and may present diagnostic signs. For example, during the clinical course of AD, dysgraphia occurs both during the initial phase and in the subsequent phase of the progression of the disorder. However, most of the studies which analyze the effects of NDs/DDs on handwriting kinematics published so far have been conducted in the medical and psychology fields, where typically statistical tools are used to investigate the relationship between the disease and each of the variables taken into account to describe patient handwriting. On the contrary, very few studies have been published that use classification algorithms [3, 4, 5, 6, 7, 8] for detecting people affected by NDs/DDs from their handwriting. In the following, the approaches belonging to the first group will be referred as *statistical*, whereas those belonging to the second one will be referred as *classifier-based*.

In a previous work [9], we presented a brief review of the literature of handwriting analysis used to support the diagnosis of NDs. From the literature reviewed, we found that although encouraging results were observed, there are still several open issues that need to be addressed. First of all, there is a lack of a well designed data set [37]. In fact, even though several standard handwriting databases have been created so far, none have been specifically designed for ND research. This database would make it possible a fair comparison of the various proposed approaches. However, designing a database specifically dedicated to NDs/DDs involves many different aspects. The first aspect concerns the cardinality of the set: most of the studies reviewed make use of data sets composed of very few subjects. More recently, some efforts have been made to achieve an acceptable size (55 individuals). However, this reduced data availability severely limits the effectiveness of the classifier-based approaches, that use classification algorithms such as neural networks, SVMs, and decision trees. Another important aspect for the development of the database is the definition of an experimental protocol, namely the set of handwriting tasks the subjects should perform. This because it is fundamental to understand which tasks allow the subjects affected by NDs/DDs to be better discriminated against. Moreover, also the features to be extracted play an important role. In fact, not all the features are affected in the same way by these diseases. For example, from the literature it emerges that features such as pressure and time-in-air seems to be particularly effective in discriminating the handwriting of patients affected by AD, as well as MCI.

In this paper, we present an experimental protocol that has the objective to try to answer the above mentioned issues. In particular, we aim to build a database consisting of hundreds of samples, related to both subjects affected by NDs/DDs and healthy controls. This database will make it possible to improve the performances of the classifier-based approaches, allowing a more effective training of the classification algorithms they are based on. The main advantage of these approaches is that they allow the features to be considered as a whole. On the contrary, statistical approaches evaluate the features singularly, without taking into account the complex interactions that may occur among the features: a feature, which is weakly relevant to the target concept by itself, could significantly improve the classification accuracy if it is used together with some complementary features.

2. The Protocol

As concerns the recruiting criteria they have to take into account the severity of the illness of the patients in accordance with standard clinical tests, such as the Mini-Mental State Examination (MMSE), the Frontal Assessment Battery (FAB), the Montreal Cognitive Assessment (MoCA). In these tests, the cognitive abilities of the examined subject is assessed by using questionnaires including questions and problems in many areas, which range range from orientation to time and place to registration recall. As for the healthy controls, in order to have a fair comparison, demographic as well as educational characteristics must be considered. Finally, both for patients and healthy controls, it must be checked whether they are under medication or not, excluding those using psychotropic drugs, or any other drugs that may influence their cognitive abilities.

As for the proposed experimental protocol, it consists of 25 handwriting tasks, to be written on A4 white sheets, which are stapled and placed on a graphic tablet which records the movements of the pen used by the examined subject. In order to standardize the data collection procedure and to help the experimenter who guide the patient during the execution of the tasks, we also developed a PC application, written in C#. The developed application also automatically save on the PC drive the data (text files) produced by the tablet. As graphic tablet we used a WACOM Bamboo Folio. The aim of the protocol is to record the dynamic of the handwriting of subjects affected by the above mentioned diseases, in order to investigate if the there are some specific features that allow the handwriting of these subjects to be recognized. The white sheets to write on contain the instructions of the tasks and letters/words/phrases/digits to be copied. The choice is motivated by the fact that the patient in this way does not notice the digitized recording mode and does not change his natural writing movements. As explained below, each task aims to identify different features of the patient handwriting gestures. Patients will be asked to follow the instructions printed on the sheets and the indications provided by the experimenter. Moreover, as concerns the experimenter, for each task, he must: (i) read carefully the instructions to the patient; (ii) make sure that the patient has understood the instructions of the task to be performed; (iii) make sure that the subject's handwriting data has been properly recorded and stored on the PC drive. At the same time, the experimenter must pay attention to not influence the patient's performance and keep the experimental settings as unaltered as possible.

The developed application displays to the user a series of screens, one for each task, with the first devoted to the patient data collection. The subsequent screens display to the experimenter: (i) the instructions to read to the subject under exam; (ii) some additional suggestions. As for the tablet, for each task it records the x and y coordinates of the pen, as well as the pressure. The tablet also records the in-air movements.

The tasks of the protocol are arranged in increasing order of difficulty, in terms of the cognitive functions needed to carry out the task. Taking into account their objectives, we have grouped the tasks as follows:

- *Graphic* tasks, whose objective is to test the patient's ability in: (i) writing elementary traits; (ii) joining some points; (iii) drawing figures (simple or complex and scaled in various dimensions).
- *Copy* and *Reverse Copy* tasks, whose objective is to test the patient's abilities in repeating complex graphic gestures, which have a semantic meaning, such as letters, words and numbers (of different lengths and with different spatial organizations).
- *Memory* tasks, whose objective is to test the variation of the graphic section, keeping in memory a word, a letter, a graphic gesture or a motor planning.
- *Dictation*, whose purpose is to investigate how the writing in the task varies (with phrases or numbers) in which the use of the working memory is necessary.

In the following, the tasks making up the experimental protocol are described:

- The first task consists of a signature. This task is very popular in the literature [18].
- In the second and third task the subject have to join two points with a horizontal (task 2) or vertical (task 3) line continuously for four times [39]. The left-right horizontal movements that primarily require the wrist joint movements, whereas the up-down vertical movements require the finger joint movements.
- In the fourth and fifth task subjects is asked to trace a circle continuously for four times. The circle diameter is 6 cm for the task 4 and 3 cm for the task 5. This task allows testing the automaticity of movements and the regularity and coordination of the sequence of movements [33].
- As in [38], in the sixth task the subjects must copy three letters. The letters ('l', 'm', 'p') were chosen so that they had different graphic composition and presented ascender and descender in the stroke.
- The seventh task consists in copying four letters ('n', 'l', 'o' and 'g') on adjacent rows. The aim of the cues is to test the spatial organization abilities of the subject [28].
- The tasks 8 and 9 require the participants to write continuously for four times, in cursive, the letter 'l' and the bigram 'le', respectively [17]. These letters allow testing the motion control alternation.

– The tasks 10, 11, 12 and 13 implies word copying, which is the most explored activity in the analysis of handwriting for individuals with cognitive impairment [17, 28, 38]. Moreover, to observe the variation of the spatial organization, we have introduced the copy of the same word without or with a cue.
– The fourteenth task tests the short-memory and is made of two steps. In the first step the patient is required to memorize three words. In the second step the patient has to write the just memorized words, on a white sheet. This task is aimed at testing the short-term memory, that is one of the cognitive functions affected by AD [26].
– The tasks 15 and 16 requires copying in reverse order two simple words: ”bottiglia” (bottle in English, task 15) and ”casa” (house, task 16). These tasks have been inspired by the MMSE test, where one of the task requires subjects spelling a word backward [14].
– The task 17 requires to copy six words in the appropriate box. The words chosen, as suggested in the literature, [23] are: two regular words of the Italian language (”pane” and ”mela”, bread and apple), two irregular words (”prosciutto” and ”ciliegia”, ham and cherry) and two non-words (”taganaccio” and ”lonfo”), i.e. non-sense words. This task aims to compare the handwriting movements of these different types of words.
– In the eighteenth task participants is asked to write the name of the object shown in a picture (a chair). The task is designed in such a way that a semantic articulation of meaning attribution takes place [31].
– As in [38], in the task 19 the patients is asked to copy the details of a postal order into the appropriate places. This is a complex functional task related to the performance of a daily activity.
– In the twentieth task, subjects is asked to write, above a line (the cue), a simple phrase, dictated them by the experimenter. As in [15], the hypothesis is that the movements can be modified because of the lack of visualization of the stimulus (the copy).
– The task 21 requires retracing a complex form, which is made of a continuous line presenting different radius of curvature. The aim of this task is to test both fine and long motor control abilities of the subject [24, 25].
– In the tasks 22 and 23 a telephone number (10 digits) have to be copied (task 22) or written under dictation (task 23). The hypothesis underlying the introduction of this task is that motor planning in writing a telephone number is different from that for writing a word [38].
– The twenty-fourth task is the Clock Drawing Test (CDT). In [36] the authors found that CDT shows a high sensitivity for mild AD.
– The twenty-fifth and last task consists in copying a paragraph. As suggested by [38] the paragraph was made up of 110 characters and consisted of a part of the story of the FAB test.

3. Feature extraction and selection

As regards the features extraction process, two types of features can be considered: function features and parameter features. The first characterize handwriting movements in terms of time functions, whereas the second are computed by means of a transformation upon the function features.
The most common function features are: (x, y) coordinates, pressure, azimuth, altitude, displacement, velocity and acceleration. Some of these features are directly recorded by the acquisition device, whereas others are numerically derived. Typically, the most used function features are velocity and acceleration: the former contains information related to the slowness of movements, whereas acceleration changes allows tremor to be revealed. As for the features related to the in-air movements, it has been recently demonstrated that they convey very useful information for discriminating the movements of subject affected by AD [32].

As for the parameter features, they have been specifically inspected and/or designed with the aim of performing NDs/DDs analysis [38]. Amongst others two interesting parameters are the total time of the pen movement in-air and on-the-paper while performing a task. In fact, it has been observed that these values increase, as task length and difficulty increase while other values (e.g. pressure) remain constant. Moreover, when a copy task is considered, the in-air time reflects the hesitations of the patients.

The above-mentioned features can be evaluated at global (task level) or local level, which implies an analysis at stroke level. A stroke is generally defined as a single component of the handwritten trait which is connected and continuous, and it is represented by the sequence of points between two consecutive pen-downs and pen-ups on the paper. The number of strokes per second can be considered to be representative of the handwriting frequency: in AD patients a significantly low writing frequency has been observed [20]. As for the jerk, which typically characterizes the handwriting of PD patients, it can be measured in terms of changes in acceleration over time and it is often taken into account with the changes in velocity. These features are also typically normalized on a per-feature basis. In order to obtain complete statistical representation of the available function features, max, min, means, standard deviation, range and median have been considered.

Tremor and irregular muscle contractions introduce randomness to the movements: entropy and energy have the potential to describe handwriting ”noise”. For this reason, Entropy- and energy-based features have also been taken into account [19]. In [21], instead, the authors introduced a metric based on the velocity variability; this metric is based on the observations that low-level control of the muscular systems occurs in terms of milliseconds, while the control of conscious movements cannot be at the same frequency. Similarly, in [10], the authors decomposed the handwriting signal into a finite and small number of components, able to reveal information regarding the most oscillating parts. However, to date, most of the well-known frequency analysis techniques (e.g. Fourier, Wavelet, etc.), have not been still investigated within this field.
Features based on the Plamondon's kinematic theory of rapid human movement have also been used to represent the information related to the timing and motor commands in handwriting movements. The model has also been adopted to study childrens movement [11] and to differentiate between children of different school levels [13], as well as for synthetic handwritten gesture generation [1].

As regards the analysis of the features, as mentioned in the Introduction, most of the presented studies did not consider the complex interactions that may occur among multiple features. In fact, in the pattern recognition field it is well known that a single feature that is weakly correlated to the target class could significantly improve the classification accuracy if it is used together with some complementary features. In contrast, an individually relevant feature may become redundant when used together with other features. For this reason, to best exploit the information contained in the considered features, feature analyses should be conducted using state-of-the-art feature selection tools [2]. These approaches use effective search techniques to find the optimal feature subset, according to an evaluation function which evaluate feature subsets as a whole.

4. Future Work

Once a minimum number (around one hundred) of patient data will be available, we will start a first set of experiments. In this first set we will first evaluate the effectiveness of the features singularly, so as to confirm the results of the works previously presented. Then, we will use state-of-the-art feature selection algorithms to find the feature subsets that best discriminate the handwriting of the patients affected by NDs/DDs from that of the healthy subjects. The feature subsets found will be used to train different classification algorithms, in order to find that achieving the best performance.

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