A Brief Overview on Handwriting Analysis for Neurodegenerative Disease Diagnosys

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Abstract. Degenerative nerve diseases affect many of your body's activities, such as balance, movement, talking, breathing, and heart function. These disease cannot be cured, nonetheless an early diagnosis can help to better manage the symptoms and the evolution of these diseases.
Since handwriting involves several cognitive abilities, clinicians started to consider handwriting analysis as an effective tool for early diagnoses for this kind of diseases. Moreover, as they show different handwriting impairments as they evolve, handwriting analysis can be also used for monitoring them along the clinical course.
This paper provides a brief overview on the use of handwriting analysis for early diagnosis, monitoring and tracking of neurodegenerative diseases. In particular, we taken into account Alzheimer and Parkinson diseases.

1 Introduction

Neurodegenerative diseases (NGD) affect the peripheral nervous system which includes muscles, the nerve-muscle junction, nerves in the limbs, and motor nerve cells in the spinal cord. Nerve cells send the messages that control these muscles in order to allow movements, including handwriting. Sick/died neurons cannot properly control muscles. These diseases are incurable, but early screening and identification can reduce the "diagnostic odyssey". On the other hand NMD often result in progressive cognitive, functional and behavioural changes. The current clinical diagnostic tools include imaging (e.g. magnetic resonance imaging, or MRI), blood tests, lumbar puncture (spinal tap).

Handwriting results from a complex network composed by cognitive, kinesthetic, and perceptual-motor abilities [28]. Furthermore, visual and kinesthetic perception, motor planning, eye-hand coordination, visual-motor integration, dexterity, and manual skills are involved. Significant changes of the handwriting performances are a prominent feature of Alzheimer Disease (AD) as well as

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Parkinson Disease (PD). Learning and performing handwriting requires the interactions of multiple brain areas, comprising cerebral cortex, basal ganglia and cerebellum [10]. In seeking to understand all the breadth and facets of motor learning, many researchers have used different approaches, such as neuroimaging and intracranial recordings, clinical treatments, and proposed neural schemes aimed at evaluating the viability of theories regarding the way these areas cooperate for motor learning/generation. One of the earliest neural schemes for motor control, which envisages the cooperation among cortex, cerebellum and basal ganglia, was proposed in 1974 [1]. On the other hand, the perspective of signal and image processing must be considered: there are certain aspects of the writing process that are more vulnerable than other and may present diagnostic signs [13]. Dysgraphia has been observed in patients presenting mild to moderate levels AD [14] and PD [16].

The idea of handwriting analysis within this field of application is also encouraged by the fact that the Minnesota Handwriting Assessment (MHA) is used to identify students (6-8 years old) with difficulties related to autism. The test is also used to evaluate treatment effectiveness over time. It inspects the legibility, handwriting speed, legibility, form, alignment, size and spacing. The MHA is a standard in US, it requires 10 minutes to be performed and it costs less than 130$. This last aspect opens for a real possibility of having, in future, a similar NGD assessment.

The paper is organized as follows: Section 2 describes the state of the art for early detection and monitoring of NGD by handwriting analysis; Section 3 illustrates the open issues that still need to be addressed; finally, Section 4 is devoted to the conclusions.

2 State of the Art

As mentioned in the Introduction, handwriting involves several cognitive abilities. For this reason, handwriting analysis can be used as an effective tool for early diagnoses for NGD [14, 23]. Moreover, since this kind of diseases show different handwriting impairments as they evolve, handwriting analysis can be also used for monitoring them along the clinical course [8, 25, 33]. Studies involving neural recordings have provided a large body of knowledge about the neural processes occurring in the brain areas related to motor learning. First studies on the brain areas governing handwriting observed that it implies the learning of motor sequences by two distinct neural systems, comprising cortex-basal ganglia and cortex-cerebellum loop circuits [12, 6]. A neural model of cortico-cerebellar interactions during attentive imitation and predictive learning of sequential handwriting movements, suggests how cortical mechanisms interact with predictive cerebellar learning during movement imitation [5]. Recently a recurrent neural network actor-critic model of the basal ganglia and a feed-forward correlation-based learning model of the cerebellum was proposed suggesting that basal ganglia and cerebellar learning systems work in parallel and interact with each other. However, these works did not provide computational models to test the validity

of the neural schemes or comprised only basal ganglia [6] or cerebellum [5], or were built with a simplified level of biological abstraction [2]. To develop effective and efficient systems for the early detection and monitoring of NGD by Handwriting analysis, defining effective features plays a key role. For this reason, new methodologies of features extraction and classification have been proposed, taking into account both image processing techniques and writing generation model techniques. In particular, it has been observed that the use of Sigma-Lognormal [15] and Delta-Log [18] models can be adopted to generate features representing the strokes [9]. These models have been developed from the kinematics theory of rapid human movements [19, 20] and in[9] the authors presented a system for handwriting analysis to investigate insurgence and monitoring of the Alzheimer's disease.

Significant handwriting difficulties were already reported by Alois Alzheimer when describing the first patient with Alzheimer's Disease (AD) in 1907. He observed that the patient reduplicated the same syllable and forgot some others. The evolution of agraphic impairments in AD was described in [21] and included lexicosemantic disturbances at the beginning of the disease, with impairments becoming more and more phonological as the dementia becomes more severe. More recently, several studies analyzed the dynamic of the handwriting process in order to detect and monitor AD [31, 9, 24, 17, 32]. In [31] the authors performs kinematic measures of the handwriting process of persons with mild cognitive impairment (MCI) compared with those with mild Alzheimers disease and healthy controls; the aim was to assess the importance of measures for the differentiation of the groups and to assess the characteristics of the handwriting process across different functional tasks. Impedovo D et al. [9] use the Delta-Log and Sigma-Log models mentioned above to investigate on the handwriting generation processes and present a computational system to investigate insurgence and monitoring of AD. In [24] the authors analyze handwriting kinematic to quantify differences in fine hand motor function in patients with probable AD and mild cognitive impairment compared to depressed patients and healthy controls. The authors found that both patients with MCI and patients with probable AD exhibited loss of fine motor performance and the movements of AD patients were significantly less regular than those of healthy controls. Recently, also handwritten signatures have been investigated for early diagnosis of NGD [17]. Pirlo et al. used the sigma-lognormal model for the signature representation, then they analyzed the health condition of the signer in terms of Alzheimer disease. The proposed approach has shown to be cheap and effective. In the study presented in [32], the patients performed four types of handwriting movements on a digitizer. Movement time and smoothness were analyzed between the groups of patients take into account (probable AD, MCI and normal controls) and across the movement patterns. Kinematic profiles were also compared among the groups. AD and MCI patients demonstrated slower, less smooth, less coordinated, and less consistent handwriting movements than their healthy counterparts.

Parkinson's disease (PD) is a long-term degenerative disorder of the central nervous system that mainly affects the motor system. Even if, to date, clinical

assessment remains the gold standard in the diagnosis of Parkinsons disease, many studies have been proposed that use handwriting for detecting and monitoring PD, since abnormal handwriting is a well recognized manifestation of PD, with micrographia being characteristic [7]. Handwriting anomalies may appear years at the early stages of the disease and thus may be one of the first signs of impending PD. Previous research has shown that handwriting measures have the potential for identifying various stages of PD, effects of varied interventions [4] and the effect of medication [22]. Moreover, studies focusing on understanding the mechanism underlying micrographia found significant differences between the handwriting of PD patients and healthy subjects[27, 29]. More recently, further studies have been conducted to analyze the handwriting of patients affected by PD [23, 11, 26, 3]. In [23] the authors try to identify simple characteristics of handwriting which could accurately differentiate PD patients from healthy controls. Patients were asked to write their name and to copy an address on a paper affixed to a digitizer. Mean pressure and mean velocity was measured for the entire task and the spatial and temporal characteristics were measured for each stroke. The experimental results confirmed that these routine writing tasks can be used to differentiate PD patients from healthy controls. Letanneux et al. [11] identified several studies that investigated handwriting in PD, either with conventional pencil-and-paper measures or with graphic tablets, and reported their findings on key spatiotemporal and kinematic variables. They found that kinematic variables (velocity, fluency) differentiate better between control participants and PD patients, and between off- and on-treatment PD patients, than the traditional measure of static writing size. Moreover, since handwriting deficit for PD patients is not restricted to micrographia, they propose the term "PD dysgraphia", which encompasses all deficits characteristic of Parkinsonian handwriting. In [26] in order to assess whether standardized handwriting can provide quantitative measures to distinguish PD patients from healthy controls, the authors recorded pen tip trajectories during circle, spiral and line drawing and repeated character 'elelelel' and sentence writing. The experimental results show that these tasks can provide objective measures for bradykinesia, tremor and micrographia to distinguish Parkinson patients from healthy controls. Finally, Drotár et al. in [3], present a novel PD handwriting database consisting of handwriting samples from (PD) patients and healthy controls. Each sample contains kinematic and pressure data of height handwriting tasks. The tasks include drawing an Archimedean spiral, repetitively writing orthographically simple syllables and words, and writing of a sentence. To discriminate between PD patients and healthy subjects, the authors use three well known and widely used classifiers: K-nearest neighbors, ensemble AdaBoost classifier, and support vector machines (SVM), which was the best performing one.

3 Open Issues

Although some research has been already carried out and some encouraging result has been observed, there are still many open issues that must be addressed.

First of all there is the lack of a well designed dataset [30]. This involves many different aspects:

- Cardinality of the set: in fact even considering papers dealing with PD, most of them make use of datasets composed by very few subjects. More recently some effort has been done in order to get an acceptable dimension (55 individual) [16].
- Acquisition tool and protocol: in many cases off-line acquisition has been performed due to the availability of handwritten document, however it must be considered that on-line acquisition is able to provide a wide set of useful dynamics. On the other hand, the choice of the acquisition tool also affect the amount of dynamics that can be taken into account (e.g. pen-based camera, pad, frontal video, etc.).
- Cognitive model: as already mentioned, neurodegenerative diseases do not involve only functional and behavioural changes (can be encountered within the handwriting), but also result in progressive cognitive decay. The acquisition protocol should take into account, to some extent, also this aspect in order to be able to convey as much information as possible.
- Number and periodicity of sessions: in order to be able to identify disease at different stages, a set of different users is needed. At the same time in order to have the possibility to understand the evolution of the disease over time, the same patient must be enrolled into the system in a periodic way, or when some specific event is occurred.

The second issue is that to face the classification problem. Often standard Signal Processing and Pattern Recognition techniques are applied with very few cases of specialization to the field. The main problem is that the medical knowledge of the evolution of the disease cannot be ignored: an automatic system able to distinguish an healthy person and a late-stage sick one has a very reduced usefulness in real word. From this perspective the challenge is to identify patients at different stages, tracking the evolution and to understand/identify signs of worsening. It must be underlined that today there is no cure for AD but it can only be somehow managed, so that an early diagnosis and follow up may have profound implications for carers and doctors. Research on handwriting and neuro-muscular diseases is not expected to replace standard techniques, but to strengthen them by allowing an earlier diagnosis. To this aim Pattern Recognition approaches should be specifically studied and coupled with Cognitive and neuro-muscular generation models.

4 Conclusions

In this paper we propose a brief overview of the handwriting analysis approaches for early diagnosis, monitoring and tracking of neurodegenerative diseases. In particular we taken into account Alzheimer and Parkinson diseases. Furthermore, we also discuss the still open issues in the field that must be addressed.

Handwriting analysis is an effective tool for dealing with the diagnosis and monitoring of the above cited diseases, nonetheless some issues are open, and are mainly related to: (i) because of their cardinalities, most of the datasets currently available does not allow pattern recognition tools to be effective; (ii) since handwriting kinematics has shown to be useful for discriminating between patients and healthy controls, new protocols for the on-line acquisition of handwriting should be defined; (iii) defining pattern recognition tools specifically devised for the automatic diagnosis and monitoring of neurodegenerative diseases.

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