Dynamic Handwriting Analysis for the Assessment of Neurodegenerative Diseases: A Pattern Recognition Perspective

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(Methodological Review)

***Abstract*—Neurodegenerative diseases, for instance Alzheimer's disease (AD) and Parkinson's disease (PD), affect the peripheral nervous system, where nerve cells send messages that control muscles in order to allow movements. Sick neurons cannot control muscles properly. Handwriting involves cognitive planning, coordination, and execution abilities. Significant changes in handwriting performance are a prominent feature of AD and PD. This paper addresses the most relevant results obtained in the field of online (dynamic) analysis of handwritten trials by AD and PD patients. The survey is made from a pattern recognition point of view, so that different phases are described. Data acquisition deals not only with the device, but also with the handwriting task. Feature extraction can deal with function and parameter features. The classification problem is also discussed along with results already obtained. This paper also highlights the most profitable research directions.**

***Index Terms*—Alzheimer's disease (AD) assessment, kinematics, motor control, online handwriting analysis, Parkinson's disease (PD) assessment, task analysis.**

I. Introduction

NEURODEGENERATIVE disorders, such as Parkinson's disease (PD) and Alzheimer's disease (AD), affect the structure and functions of certain brain regions, resulting in a progressive cognitive, functional, and behavioral decline. Changes in the brain result in degradation of the performance of motor skills.

A special role in the context of neurodegenerative disease assessment can be covered by handwriting. Cerebral cortex, basal ganglia, and cerebellum are involved in learning and performing handwriting [92]—complex activity entailing cognitive, kinaesthetic, and perceptual-motor components. Handwriting problems can be related to the disease as well as to its severity, so changes in writing can be considered a prominent biomarker.

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Fig. 1. Dynamic handwriting ("♦": pen-down; "•": pen-up)

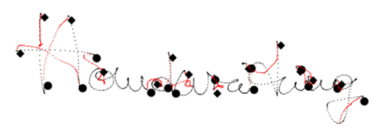

Fig. 2. Dynamic acquisition ("♦": pen-down; "•": pen-up; black dots: on pad samples; red dots: on air movement samples)

For example, it is well known that micrographia (an abnormal reduction in writing size) is typically associated with PD and it can be easily detected by conventional pen-and-paper tasks [40]. Dysgraphia (a progressive disorganization and degeneration of the various components of handwriting) has been observed in patients presenting mild to moderate AD levels [21], [27], [51].

Several advances have already been made in the offline (static) domain [96] but, nowadays, online (dynamic) systems can be adopted. In this case, the trait is represented as a sequence $\{S(n)\}_{n=0,1,\ldots,N}$, where S(n) is the signal value sampled at time $n\Delta t$ of the writing process ($0 \leq n \leq N$), Δt being the sampling period. The online case concerns the treatment of a spatio-temporal representation (see Fig. 1).

The main advantage of online acquisition devices is their ability to acquire kinematics (dynamics) of the writing process which are lost in offline systems. More specifically, dynamic features are: position (x,y), pressure over the writing surface (pad in the following), azimuth (i.e., angle of the pen in the horizontal plane), and altitude (i.e., angle of the pen with respect to the vertical axis). The movement of the pen can be recorded not only while the pen is on the writing surface (on-pad movements), but also when the pen is in the proximity of the surface, i.e., in-air movements (see Fig. 2). The maximum height at which the pen tip is detected is typically in the range of 0.6–1.0 cm depending upon the specific device adopted.

Studies on fine motor control in healthy and unhealthy people have been available so far, so that a growing research interest has arisen toward the possibility to automatically discriminate between impaired subjects and healthy controls (HC), based on

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the kinematic features [69]. The aim is to develop research in the direction of a computer aided diagnosis (CAD) system. It must be stressed that these systems are not intended to replace doctors or to perform a self-diagnosis, but rather to provide additional evidence to the medical staff to support the diagnosis.

This paper points out the most relevant research results related to the application of online handwriting analysis to the assessment of PD and AD disorders. The review is principally organized from a pattern recognition perspective, typically based on data acquisition, feature extraction, and data analysis and classification. Therefore, the paper intends to

1) provide details about data acquisition, feature extraction, and recognition applied to AD as well to PD;
2) point out and discuss the main findings from the two different diseases; and
3) discuss open issues.

The paper is organized as follows. Section II presents the main aspects related to the online data acquisition and Section III discusses the preprocessing and feature extraction phase. Section IV describes research activities concerning the data analysis and the classification phase and presents the main results. Promising research directions are reported in Section V, and the summary of the paper in is provided Section VI.

II. Data Acquisition

Different issues must be taken into account: participant recruiting, choice of the acquisition device, and identification of the most appropriate handwriting tasks. Once all these steps have been completed samples can be collected within a dataset (currently available databases are described at the end of this section).

A. Participant Recruiting

Three aspects can be typically addressed:

1) *Patients:* Severity of the illness in accordance with standard clinical test scores must be taken into account. The Unified PD Rating Scale (UPDRS) is the most commonly used scale in case of PD. It is based on interview and clinical observations most concerning motor evaluation [47]. Standard assessments of AD include cognitive and functional tests such as the Mini-Mental State Examination (MMSE). It consists in a 30-point questionnaire including questions and problems in many areas ranging from orientation to time and place to registration recall [22].
2) *Patients:* Whether the patient is on/off medication must be considered. For example, studies involving PD have shown handwriting changes based on the level of treatment [20], [84].
3) *HCs:* A set of healthy people (controls) must be enrolled. In general, elderly controls (EC) and young controls (YC) can be taken into account; however, a fair comparison should consider demographic as well as educational characteristics.

B. Acquisition Device

A wide set of devices for data acquisition is available. In some situations the use of an electronic pen on a digital screen could be unusual or unfamiliar to patients, so writing with an ink pen on paper fixed to the tablet may be an option [69], [92]. A "training" task to let the user become familiar with the tool can be also considered [88]. The main attributes acquired depend on the specific tool, however, typically acquired parameters are: (x-y) coordinates of the pen position, time stamps, pen orientation (azimuth and altitude), and pressure. In-air movements can be also considered, taking into account the so-called button status, which is a binary variable (0) for pen-up state (in-air movement) and (1) for pen-down state (on-surface movement).

Electronic (smart) pens have been adopted as an alternative to tablets. In this case, active sensors are within the pen and are able to capture position, acceleration and tilt angle of the pen, as well as pressure and vibration (generated in the refill during writing or drawing on a pad) and the pressure of the fingers holding the pen [55], [86].

TABLE I
SIMPLE WRITING TASKS

Pattern	Reference
"eeee"	Cobbah et al. [10]; Contreras-Vidal et al. [11]; Poluha et al. [64]
"elel"	Gangadhar et al. [24]; Smits et al. [77]
"ellhell"	Teulings et al. [83]
"hello hello"	Caligiuri et al. [9]
"l" "le" "les"	Drotár et al. [13]; [14], [15], [16], [17], [18]
"lilili"	Van Gemmert et al. [87]
"lll"	Bidet-Ildei et al. [5]
"llll"	Cobbah et al. [10]; Contreras-Vidal et al., [11]; Oliveira et al. [50]; Poluha et al. [64]; Slavin et al. [75]; Teulings et al. [82]; Ünlü et al. [86]; Van Gemmert et al. [87], Senatore et al. [73];
"lln"	Bidet-Ildei et al. [5]; Van Gemmer et al. [89]
"Die Wellen schlagen hoch"	Siebner et al. [74]
"Ein helles grelles Licht"	Lange et al. [41]; Tucha et al. [84]
"en liesje leerde loesje lopen"	Ponsen et al. [65]
"lektorka" "nepopadnout" "porovnat"	Drotár et al. [13], [14], [15], [16], [17], [18]
"mamma"	Impedovo et al. [31]
"The leveler leveled all levels"	Van Gemmert et al. [88]
"Tramvaj dnes už nepo-jede"	Drotár et al. [13], [14], [15], [16], [17], [18]
writing own name	Rosenblum et al. [69]
Handwritten Signature	Pirlo et al. [59], Zhi et al. [95]

C. Writing Tasks

The writing process involves a complex feedback system and implicates the participation of several cognitive and motor processes. Acquisition tasks can be classified as follow.

1) *Simple drawing tasks:* Straight lines, spirals, meanders, and circles have been frequently used for the evaluation of the motor performance in both PD and AD [12], [20], [56], [72]. In general, all simple drawings have been used for trajectory, tremor, dimension (size), velocity, and acceleration evaluations.
2) *Simple writing tasks:* Nonsense words containing one or more character repetitions have been used (see Table I

for details). Such characters are easy to write in a recursive and continuous way. Moreover, to better address the motor processes, their use minimizes the linguistic-comprehension processes. The "*e*" and "*l*" characters both contain an up- and a down-velocity stroke. According to the Delta-Lognormal Kinematic Theory [62] of the handwriting process which "describes a stroke velocity profile as the output of a system made up of two neuromuscular systems, one agonist (acting in the direction of the movement) and the other antagonist (acting in the opposite direction)," the "*e*" as well the "*l*" characters are constituted by just two velocity strokes. Moreover, the use of "*l*" and "*e*" involves the handwriting of the same character scaled in amplitude. In addition, simple words and short sentences have been also widely adopted (see Table I). Typically, words/sentences used in these tasks are chosen based on their simple orthography and easy syntax. In some situations, the sentence contains words having a common "core" (e.g., "The leveler leveled all levels" [88]) in order to verify how a common pattern is modified with or without a prefix or a suffix. Sentences have been built by including words with ascendant and descendent traits (e.g., "*g*" and "*l*"). A sentence requires a high degree of simultaneous processing and may have a higher neuromotor programming load than a sequence of identical cuttings. It also offers the possibility to better evaluate the motor-planning activity between a character and the following one (in general a hesitation or pause between two characters or words could point out the necessity to replan the writing activity, while fluid writing can reveal the presence of an anticipated motor planning). A sentence allows the capturing of a large number of in-air movements between words [18], conversely a word could also be written without lifting the pen tip from the pad. It has been observed that AD patients, in order to proceed with the writing of a part of the word or of a new word, need to come back on the previously written one and to "rewrite" it, to some extent, in the air again. This aspect is important to evaluate patients with both the sequential programming engine and the competing processes altered [35]. Moreover, a sentence composed of more than one word allows the recording of the effect of fatigue during writing [16], [17]. Handwritten signatures have been taken into account [3], [59] since a signature conveys a lot of information about the signer, related not only to the representation of the name and surname of the signer, but also to the writing system [29], [58]. Variations have been observed on global parameters (e.g., signature size) and on local ones related to longitudinal compression [95].

3) *Complex tasks:* In this case, the handwriting task is part of a more complex task involving motor, cognitive, and functional issues (see Table II). Van Gemmert *et al.* [88] were among the first to verify that PD patients are more vulnerable to a secondary task load than elderly or young controls. The handwriting task has been coupled with a simultaneous hearing and tone counting [8]. When a functional writing task, such as copying the details of a bank check into the appropriate places, is considered, the patient should be able to read the source field, locate the target field to be filled in and write the correct content there. These tasks are typically applied for the analysis of AD more than PD, since AD is primarily characterized by cognitive deficits. Very recently the Clock Drawing Test (CDT) has also been used [6], [25], [48]. CDT is able to reveal visual-spatial deficits: In some cases of dementia, the deficit is evident from the early stages. CDT, as well as many other complex tasks, involves various neuropsychological functions: auditory perception, auditory memory, abstraction capacity, visual memory, visual perception, visual-space functions, programming, and execution capacity. Similarly, constraints on time (duration) and stroke dimension have been investigated [87], [89], as well as the use of visual feedback, in order to reach specific targets while writing [23], [83]. Verbal feedback (reminders to write bigger) have also been investigated [50].

TABLE II
COMPLEX TASKS

Task	Reference
"*The leveler leveled all levels*" written under four different conditions	Van Gemmert et al. [88]
Adapt the size of a drawing to a given (displayed) input	Fucetola et al. [23]; Teulings et al. [83]
Constraints on time (duration) and stroke dimension	Van Gemmert et al. [89]; Van Gemmert et al. [87]
Loop drawing while tone-counting	Broeder et al. [8]
Bank-check field copying	Rosenblum et al. [69]; Werner et al. [92]
Address, phone number, grocery list, details of a check, the alphabet sequence and paragraph copying	Rosenblum et al. [69]; Werner et al. [92]; Garre-Olmo et al. [25]
Clock Drawing	Garre-Olmo et al. [25]; Müller et al. [49]

D. Datasets

Most research has been conducted on reduced sets of patients and HC. A brief description of the most consistent ones is here reported (see Table III).

The Parkinson's Disease Handwriting Database (PaHaW) consists of multiple handwriting samples from 37 Parkinsonian patients and 38 age- and gender-matched controls [14]. Tasks include words written in Czech (the native language of the participants). The main characteristic of the selected words is that they can be written without lifting the pen above the surface. A tablet was overlaid with a white template paper and a conventional ink pen was used.

The original HandPD dataset is comprised of handwritten/drawn trials from healthy and PD people and was primarily designed for static analysis. The dataset was further extended for dynamic analysis and it contains data from 66 individuals (35 healthy controls and 31 PD patients). The new extended version is simply called NewHandPD [55]. Handwritten dynamics were captured by means of a biosensor smart pen (BiSP).

The ParkinsonHW [32] consists of 62 PD patients and 15 HCs. Three types of handwriting tasks were considered: the

TABLE III
DATASETS

Dataset Name	Size	Acq. Device	Tasks	Reference
PaHaW	37 PD 38 ED	Wacom Intuos 4M	Spiral drawing, repetition of *"l", "le", "les", "lektorka", "porovnat", "nepopadnout", "Tramvaj dnes už nepo-jede"*	Drotár et al. 2013 [14]
NewHandPD	31 PD 35 ED	BiSP	Spiral and meander drawing	Pereira et al. 2016 [55]
ParkinsonHW	62 PD 15 ED	Wacom Cintiq 12WX	Spiral drawing and stability test	Isenkul et al. 2014 [32]
ISUNIBA	29 AD 12 ED	Wacom Intuos Touch 5	Repetition of *"Mamma"*	Impedovo et al. 2013 [31]
EMOTHAW	129 HP	Wacom Intuos 4	Copying of: pentagons, house drawing; writing four words; loop drawing; CDT; writing of a sentence	Likforman-Sulem et al. 2017 [43]

Static Spiral Test (SST), the Dynamic Spiral Test (DST), and the Stability Test on a Certain Point (STCP). In addition, the images of the spirals drawn by the PD patients are included. In the SST test, three wound Archimedean spirals are displayed on the tablet screen and patients are asked to retrace the same spiral. In the DST test, the Archimedean spiral appears and disappears at certain time intervals. In the STCP, a red point is displayed in the middle of the screen and subjects are asked to hold the pen on the point without touching the screen.

The ISUNIBA [59] dataset contains handwritten trials collected from 41 people: 12 HC and 29 AD patients. Each participant was requested to write the word *"mamma"* (i.e., Italian of "mom") over different recording sessions. The choice of the word mom, identical to all the authors, is related to the importance of this word, and to the figure associated with it. This word, in addition to being often one of the first words spoken by individuals, is also repeated with high frequency by subjects in an advanced state of AD.

EMOTHAW (EMOtion recognition from HAndWriting and draWing) has been recently developed to investigate emotional states. It does not involve PD and/or AD patients, but tasks adopted are typically used in studies devoted to PD and AD [43]. The dataset could be useful for comparison aims.

III. PREPROCESSING AND FEATURE EXTRACTION

Raw data acquired by the device are generally enhanced by means of standard signal processing algorithms: filtering, noise reduction, and smoothing. Well-known techniques could be applied, however, their use must be circumstantial. In fact they could result in the loss of important information. For example, the normalization of the duration of the signal (in order to have

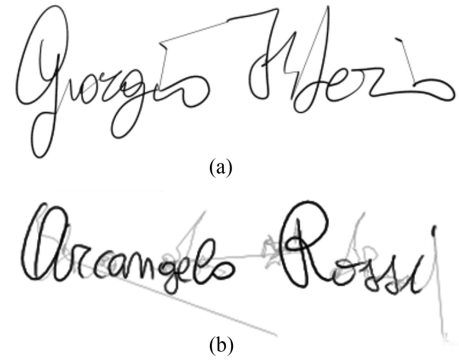

Fig. 3. On-pad (black) and in-air (gray) movements. (a) Belongs to a HC. (b) Belongs to a suspected case. Both users were required to write an invented signature.

all S(n) sequences of the same length) is sometimes applied for signature verification [28]. However, in this domain, it would lead to the loss of information related to the time spent by each participant in performing a specific task (that is a discriminative feature). Given this consideration, it is quite usual to not adopt preprocessing steps (e.g., [92]).

Two types of features can be considered: function features and parameter features. When function features are used the handwritten trials are characterized in terms of a time function whose values constitute the feature set. When parameter features are used the trial is characterized as a vector of elements, each one representative of the value of a feature. In the latter case, the indexes of vector are not referred to a time sequence.

A. Function Features

The most common function features are: position in terms of (x,y) coordinates, time stamp, button status, pressure, azimuth, altitude, displacement, velocity, and acceleration. Some of these features are directly conveyed by the acquisition device, whereas others are numerically derived (see Table IV for details). It is not surprising to note that the most used are velocity (speed) and acceleration: The former conveys information related to the slowness of PD and AD movements, while changes on the acceleration profile are able to reveal tremor. Displacement, velocity, and acceleration can be computed as reported in Table IV, as well as they can be computed along the x or y direction. In order to evaluate in-air-based features, coordinates, azimuth, altitude, velocity, acceleration, azimuth, and altitude can be considered for timestamps having the button status $b(t) = 0$. It has been recently demonstrated that in-air features conveys very useful information [48], [49]. In fact it has been showed that the in-air time in writing is related to functional decline, as well as to difficulties in planning an activity [68]. In order to have an idea of the potentialities of in-air movements, see Fig. 3, in which handwriting fluidity is much more evident in in-air movements than on-the-pad movements.

B. Parameter Features

In this case, the trait is characterized as a vector of elements, each one representative of the value of a feature. Parameter features are obtained by means of transformations on the function

TABLE IV
FUNCTION FEATURES

Feature Name	Source	Description	Disease	Reference
Position	Device	Position in terms of s(x,y)	AD, PD	Drotár et al. [13], [14], [15], [16], [17], [18]; Pereira et al. [55]; Rosenblum et al. [69]; Werner et al. [92]
Button Status	Device	Movement in the air: b(t)=0 Movement on the pad: b(t)=1	AD, PD	Drotár et al. [13], [14], [15], [16], [17], [18]; Rosenblum et al. [69]; Werner et al. [92]
Pressure	Device	Pressure of the pen on the pad (levels of pressure depend upon the acquisition device and are generally normalized [0,1])	AD, PD	Drotár et al. [13], [14], [15], [16], [17], [18]; Garre-Olmo et al. [25]; Ünlü et al. [86]; Rosenblum et al. [69],
Azimuth	Device	Angle between the pen and the vertical plane on the pad	AD, PD	Drotár et al. [13], [14], [15], [16], [17], [18]; Rosenblum et al. [69]; Ünlü et al. [86]; Werner et al. [92]
Altitude	Device	Angle between the pen and the pad plane	AD, PD	Drotár et al. [13], [14], [15], [16], [17], [18]; Rosenblum et al. [69]; Ünlü et al. [86]; Werner et al. [92]
Displacement	Calculated	It can be computed as $d_i = \begin{cases} \sqrt[2]{(x_{i+1}-x_i)^2+(y_{i+1}-y_i)^2}, & 1 \le i \le n-1 \\ d_n - d_{n-1}, & i = n \end{cases}$	PD	Lange et al. [41]
Velocity	Calculated	It can be computed as $v_i = \begin{cases} \frac{d_i}{t_{i+1}-t_i}, & 1 \le i \le n-1 \\ v_n - v_{n-1}, & i = n \end{cases}$	PD, AD	Broderick et al. [7]; Broeder et al. [8]; Caligiuri et al. [9]; Cobbah et al. [10]; Eichhorn et al. [20]; Fucetola et al. [23]; Garre-Olmo et al. [25]; Impedovo et al. [31]; Kotsavasiloglou et al. [38]; Oliveira et al. [50]; Pirlo et al. [59]; Ponsen et al. [65]; San Luciano et al. [70]; Schröter et al. [72]; Slavin et al. [75]; Smits et al. [77]; Tucha et al. [84]; Werner et al. [92]; Yu et al. [94]
Acceleration	Calculated	It can be computed as $a_i = \begin{cases} \frac{v_i}{t_{i+1}-t_i}, & 1 \le i \le n-1 \\ a_n - a_{n-1}, & i = n \end{cases}$	PD, AD	Broderick et al. [7]; Cobbah et al. [10]; Eichhorn et al. [20]; Fucetola et al. [23]; Garre-Olmo et al. [25]; Oliveira et al. [50]; Tucha et al. [84]; Van Gemmer et al. [89]

features (see Table V for details). To some extent also features used in the offline domain could be used [54].

Some parameters have been specifically inspected and/or designed with the aim of performing AD and PD analysis. Among others, two interesting parameters are the total time of the pen movement in-air and on-the-pad 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. When a copy task is considered, the in-air time reflects the hesitations of AD patients.

Parameters can be evaluated at global (task level) or even at local level (typically at stroke level). Although a formal definition of the velocity stroke has been reported in the above, in AD and PD works, stroke is generally considered as a single component of the handwritten trait which is connected and continuous: A stroke is the sequence of samples between two consecutive pen-downs and pen-ups on the pad (see Fig. 4). 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 [35].

Jerk (which characterizes PD) can be measured in terms of number of changes in acceleration (NCA) over time per stroke and it is often taken into account with the number of changes in velocity (NCV). These features are also typically normalized on a perfeature basis. In order to obtain complete statistical representation of the available function features, max, min, means, standard deviation, range, and median have been considered (e.g., v_{max}, p_{range}, etc.).

Tremor and irregular muscle contractions introduce randomness to the movements: Entropy and energy have the potential to describe “noise” in the handwriting process. Entropy- and energy-based features have been calculated starting from the (x,y) coordinates, adopting well-known Shannon and Rény operators. Recently, a metric named normalized velocity variability has been introduced [38], Low-level control of opposing muscular systems occurs in terms of milliseconds, while conscious control of movement cannot be at the same frequency. Similarly, empirical mode decomposition decomposes a signal within finite and a small number of components able to reveal information regarding the most oscillating (high-frequency) part of the signal [16]. It is quite evident that, although there are many other frequency analysis techniques (e.g., Fourier and all the related discrete transforms, etc.), these do not seem to have been investigated within this field.

Features based on the kinematic theory of rapid human movement have also been considered by adopting the Sigma-Lognormal model to represent the information of both the motor commands and timing properties [59]. This model has also been adopted to study and model children’s movement [19] and to differentiate between children of different school levels [21], as well as for synthetic handwritten gesture generation [2].

Many of the above-reported parameters have been normalized, based on the total time duration of the task or stroke.

Finally, in order to reduce data dimensionality and to select the most discriminating features, well-known feature selection schema have been adopted, such as the Mann-Whitney U-test [16] and the Relief algorithm [16], [95].

IV. DATA ANALYSIS AND CLASSIFICATION

The aim of this section is to point out relations between the tasks, features, and main findings observed in the literature. For the sake of simplicity and clarity, the results are discussed separately for PD and AD.

TABLE V
PARAMETER FEATURES

Feature Name	Description	Disease	Reference
Task duration	Total time duration of the performed task	AD	Schröter et al. [72]; Werner et al. [92]; Yan et al. [93]
		PD	Cobbah et al. [10]; Drotàr et al. [13]; Smits et al. [78], Teuligngs [81]
Dimension	Length and/or height of the trait in terms of samples or pixels both at task and at stroke level	AD	Werner et al. [92]
		PD	Drotàr et al. [13], [16], [17];Smits et al. [78] Rosenblum et al. [69]
in-air time	Total time of the pen in-air movements while performing a task	AD	Schröter et al. [72]; Werner et al. [92]; Yan et al. [93]
		PD	Drotár et al. [15]; Rosenblum et al. [69]
Normalized Time in-air	Time in-air normalized on the total task duration	PD	Drotár et al. [18]
On-the-pad time	Total time of the pen on-pad	AD	Schröter et al. [72]; Yan et al. [93], Werner et al. [92]
		PD	Drotár et al. [15], [17], [18]
Normalized Time on-the-pad	Time on-the-pad normalized over the total task duration	PD	Drotár et al. [15], [18]
In-air/on-the-pad ratio	Ratio of the total time of the pen in-air movements over the on-the-pad movements	AD	Yan et al. [93]
		PD	Drotár et al. [15], [17]
Stroke Number	Number of strokes within a task	AD	Schröter et al. [72];
NCV	Number of changes of velocity. (NCV has also been normalized on the duration of the task/stroke)	AD	Yan et al. [93]
		PD	Cobbah et al. [10]; Drotár et al. [13], [15], [16], [17], [18]
NCA	Number of changes of acceleration. (NCA has been also normalized on the duration of the task/stroke)	AD	Yan et al. [93]
		PD	Cobbah et al. [10]; Drotár et al. [13], [15], [16], [17], [18]
NCP	Number of changes of pressure. (NCP has been also normalized on the duration of the task/stroke)	PD	Drotár et al. [17], [18]
Entropy	Shannon or Rény operators applied on (x,y)	PD	Drotár et al. [16], [17]; López et al [45]
Energy	Teager-Kaiser energy or conventional energy	PD	Drotár et al. [16], [17];
NLOGnorm	Number of log-normal components	AD	Impedovo et al. [31], Pirlo et al. [59], Van Gemmert et al. [91];
EMD	Empirical mode decomposition	PD	Drotár et al. [16]

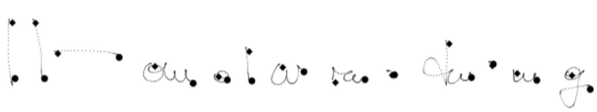

Fig. 4. On-pad strokes of the word in Fig. 2.

A. Parkinson's Disease

1) Handwriting and PD: Insight: PD is usually diagnosed by the first motor symptoms. In particular, slowness [7], [9], [57], [65], [77], [83], [88], reduction in amplitude of repeated actions (bradykinesia) and micrografia [8], [23], [44], [46], [56], [65], [77], [87], [89], [90], tremor, and rigidity are observed [7], [12], [38], [42], [56], [79], [88]. PD patients, if compared to controls, write smaller letters, apply less pressure, and require more performance time.

Phillips *et al*. [56] adopted a simple zig–zag drawing. Results revealed that patients had more difficulties in producing smooth movements rather than in controlling stroke length or duration. This result is confirmed by the one obtained in [83], where users were asked to produce handwriting modifying speed and dimension. Similar results (reduced length, velocity, and height) have been mostly observed also in other different tasks [5], [10], [65], [77]. However, it must be underlined that not all the mentioned characteristics (micrographia, slowness, longer time duration, etc.) have been simultaneously observed during any task; for instance, Bidet-Ildei *et al.* [5] did not observe micrographia or reduction in letter size. However, in the latter case, the result could be related to the reduced length of the adopted pattern (*"lll"* and *"lln"*), in fact micrographia have been generally observed over longer words or within signatures or sentences [89]. In this direction, a unique result has been obtained on non-Western languages (that can be written horizontally as well as vertically from top to bottom): A decrease in size was observed only in the horizontal direction [46]. Regarding micrographia, two recent studies [5], [46], seem to confirm that it may be tied to the control of the extension of the wrist. Moreover, the "Λ" drawing task was considered [7]. The drawing of the shape was requested to be performed from left to right and vice versa. This specific task requires movements in four directions: PD patients showed significantly lower mean velocity, lower acceleration, and higher jerk scores than controls.

Handwriting in PD patients seems to be mainly impaired in force amplitude [80], [83]. Constrains on time (duration) and stroke dimension have been investigated by imposing different dimension targets while writing [87], [89]; a matching to the imposed targets has been observed only to a certain extent, inadequate matching to the required target (in time and dimension) has been related to acceleration inefficiencies.

Visual feedback has been taken into account [23], [83] in order to inspect the capability of adjusting the size of a drawing given as input. In PD patients, the effect was particularly pronounced when they were requested to draw smaller than normal, even if, with practice, improvements were observed. Overall, these findings support the opinion that PD patients may have specific difficulty adjusting to a change in gain (or discrepancy) between visual and kinaesthetic feedback. Visual (target points or examples) and verbal feedback (reminders) have been used to verify whether micrographia could migrate to normal amplitude [50], as well as to study perception and its usage [82]. It has been shown [50] that the stroke dimension can be improved and that improvements persist also shortly afterward in free handwriting (without feedback), however, the increase in the amplitude obtained is due more to an increase in movement time rather than in peak velocity. Practice can help PD patients to partly overcome bradykinesia and to improve the control of repetitive forces [80].

Anticipation can be referred to the ability of the handwriting motor system to plan forthcoming strokes of the writing sequence while the movement of the current stroke is being executed [34]. The anticipation capability has been investigated observing that patients are able to write the pattern without pauses between characters [5], [41]. On the other hand, in different and more complex tasks (involving not only handwriting), difficulties in anticipating the upcoming component of the movement have been observed [76].

The effects of medication (levodopa, dopamimetic, and/or neurostimulation) on handwriting have also been investigated. The evidence is that kinematic handwriting analysis is useful for monitoring the effect of medication [20] in terms of parameter changes as well as tremor reduction. It has been observed [11], [64] that handwriting changes across the medication cycle [10], [41], [84]. The velocity measure was able to distinguish drug-induced PD patients from HC with a high level of accuracy [10]. High-frequency neurostimulation of the subthalamic nucleus has been considered: during stimulation, handwriting movements became faster and smoother, moreover a reduction in micrographia has been observed [67], [74].

Even if PD mainly affects the motor system, also cognition, planning, and execution impairments can be observed in the early stages and, in some situations, prior to diagnosis [33]. So far, it has been positively tested the hypothesis that PD patients are more vulnerable to a moderate level of secondary task load than elderly or young controls [88]. Different conditions were considered: PD patients had increased movement duration, increased total pause duration, and increased jerk. More recently similar results have been observed by combining the writing task with (simultaneous) tone counting [8].

The use of an electronic biosensor pen named BiSP [86] highlighted that, among other features the most discriminating is based on the difference between the controlled writing pressure in *x-y* direction and the tilt tremor of the pen.

2) Handwriting and PD: The Challenge of a CAD: Although studies on the correlation of handwriting and PD have been available for a while, only in the last 5–6 years this evidence has been applied to obtain a CAD system. These studies have also highlighted new findings. Comparing results obtained by different researchers is quite difficult due to the different datasets used and the different experimental set ups adopted.

The first result to be pointed out deals with a task to be used for assessment. It has been verified that, on the PaHaW dataset, the use of all tasks gives better classification performance (PD versus healthy) in terms of accuracy, if compared to the use of a single writing task [13]. The use of only some specific tasks has also been investigated. In particular, the Archimedean spiral drawing seems to be useful for discrimination purposes due to tremor evaluation. Similarly, on another dataset, the use of just this task was able to achieve a sensitivity of 0.86 [70]. Very recently also the use of a simple horizontal line drawn at a constant velocity has been inspected: accuracy of 88.63% was achieved [38]. An excellent accuracy (97.50%) has been obtained in the following two tasks: writing one's own name and copying an address [69].

Although an in-air feature set seems, under certain conditions, to outperform an on-surface one [14], better results can be achieved by combining both according to a feature selection scheme [15], [69].

Among the other on-surface features, pressure has been demonstrated to be very useful [18], [70]. It has been shown that pressure-based features outperform other kinematic features [18]. However, it must be underlined that there is not a specific feature set able to clearly outperform the other independently of the considered writing task.

In addition to conventional kinematic handwriting measures, entropy, signal energy, and EMC gave the best accuracy in the PaHaW dataset [16].

For classification purpose, support vector machine (SVM)—with a Radial Basis Function Kernel [13]–[18], Discriminant Analysis [69], Convolutional Neural Network [55], and Naïve Bayes [38] have been successfully used. Table VI summarizes the results.

Finally, as well as feature selection, it has been observed that a specific task could be better than another for discrimination aim. This has been the case of the guided spiral drawing, which has provided the best classification results if compared to other tasks [95]. This result suggests to combine feature selection along with task selection.

Fig. 5 shows a timeline of the milestones in the PD CAD development.

B. Alzheimer's Disease

1) Handwriting and AD: Insight: AD first results in cognitive rather than motor degradation. In fact, handwriting tasks have generally been coupled with cognitive ones [72], [75], [92], [94]. So far it has been observed that in the mild phase of the disease there are few possible lexico-semantic problems in the speaking process, which worsen with the progression of the disease. A similar trend can be observed in written tasks: AD is associated with deterioration in fine motor control and coordination [63], [93]. This result has been confirmed also in different writing tasks. The popular *"llll"* pattern under different writing conditions (including visual feedback) has been considered: AD patients' strokes had a less consistent length, duration, and peak velocity than the controls [75]. A similar result has also been obtained in the circle drawing task: movements of AD patients have been observed to be significantly less automated, accurate, and regular than the controls [72].

The use of the Delta-Lognormal [62] and the Sigma-Lognormal [52] representation of handwriting generation showed that the maximum speed value is almost regular in healthy persons while it is greatly reduced at the beginning of the disease and completely lost in the advanced stage [31]. A similar result has been achieved taking into account a wide set of tasks dealing with fine movements (straight lines, cursive-connected loops, a single circle, continuous circle drawing, etc.). Results showed that slowness and irregularity of movement of AD patients were not present in all tasks [94]. Impairment was

TABLE VI
PD CAD SYSTEMS ABBREVIATIONS: T = TABLET; ST = SHEET OF PAPER FIXED ON THE TABLET; EP = ELECTRONIC PEN: AUC = AREA UNDER THE ROC; ACC = ACCURACY

Reference	Participants	Device	Tasks	Features	Classifier	Results
Drotár et al. 2013 [13]	Dataset PaHaW			On-surface features	SVM Radial Basis Function	ACC = 79.4%
Drotár et al., 2013 [14]				16 In-air selected features	SVM Radial Basis Function	ACC = 80.09%
Drotár et al. 2014 [15]				On-surface features + in-air features	SVM Radial Basis Function	ACC = 85.61%
Drotár et al., 2015 [16]				Entropy, signal energy, empirical mode decomposition (on-surface) + feature selections	SVM Radial Basis Function	ACC = 88.1%
Drotár et al., 2015 [17]				Stroke height/width, duration, writing length, NCP, Entropy, Energy	SVM Radial Basis Function	AUC = 89,09%
Drotár et al., 2016 [18]				Kinematic and pressure features + feature selection	SVM Radial Basis Function	ACC = 82,5%
Rosenblum et al., 2013 [69]	20 PD 20 EC	ST	Name writing, copying an address	On-surface + in-air features	Discriminant Analysis	ACC = 97.5%
Pereira et al., 2016 [55]	14 PD 21 EC	EP	Spiral and meander drawing	Pressure, grip pressure, refill pressure, tilt and acceleration	Convolutional Neural Networks	ACC = 87.14%
Kotsavasiloglou et al., 2017 [38]	24 PD 20 EC	T	Line drawing	Position, Normalized Velocity Variability, Velocity's Standard Deviation, Mean Velocity, Entropy	Naïve Bayes	ACC = 88.63%
Zham et al. [95]	31 PD 31 EC	T	Sentence and characters writing, Archimedean guided spiral	Displacement, pressure, average speed,, Rate at which pen tip changes position and velocity, max acceleration, + feature selection	Naïve Bayes	AUC = 93,3% Archimedean guided spiral

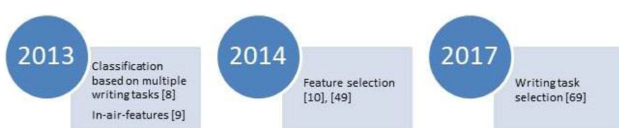

Fig. 5. Timeline of the milestones in the PD CAD development.

not found in the straight lines and cursive-connected loop tasks. AD patients exhibited difficulties in drawing due to a reduced ability in wrist and finger coordination.

In general, AD patients produce slower, less smooth, less coordinated, and less consistent handwriting movements than their healthy counterparts.

2) Handwriting and AD: The Challenge of a CAD: Werner *et al.* [92] adopted a discriminant analysis to determine which feature would be the best predictor of group membership (AD versus EC). Temporal measures (especially in-air time) were higher in the AD patients group, while the mean pressure was lower. Although velocity and pressure remained relatively stable across the different tasks, the temporal and spatial measures increased with the difficulty of the task: the increase was reflected mainly in the in-air measures.

Handwritten signatures have been demonstrated to be useful. Velocity-based features related to the Sigma-Lognormal model of the kinematic theory of rapid human movement have been adopted [59]. In this case, a Bagging CART (classification and regression tree) classifier was able to achieve an equal error rate of 3%.

Garre-Olmo *et al.* [25] were among the first to adopt copying tasks (including two- and three-dimensional (3-D) figures) and the CDT. Several kinematic features were used in order to classify participants (by means of a discriminant analysis). Additionally, energy and complexity were also considered. Classification performance was strictly dependent on the task considered. Moreover, function features were able (in general) to provide better accuracy results. Regarding the CDT, it has been shown that in-air features are the most consistent for discrimination purposes [49].

Müller *et al.* [48] referred to the copying of a 3-D house. A receiver operating characteristic curve (ROC) and logistic regression analyses were used. Once again, in-air time was significantly different between the groups (AD patients versus controls), as well as on-surface time and total time (i.e., in-air plus on-surface time).

Details are reported in Table VII. Fig. 6 shows a timeline of the milestones in the AD CAD development.

V. FUTURE RESEARCH DIRECTIONS

Much evidence linking PD and AD to handwriting/drawing is available. Although some specific open issues have been already pointed out, in the following the most relevant are briefly discussed.

A. Dataset

Many researchers have adopted databases/datasets built by collecting data themselves. These datasets are different in tasks, size (in general very reduced), acquisition devices, etc. The lack of a big dataset involving a statistically significant number of patients, as well as, a set of significant tasks, greatly limits research development. None of the datasets currently available provide meta-data that could be useful to perform a deep analysis and to support CAD development establishing stage of the disease, the medical treatment (if any), educational information as well as many other factors (risk factors, contour conditions, etc.). It must be underlined that there is the lack of research on non-Western languages, on the other hand this would be of great interest since scripts have many pictorial elements could convey useful information [85].

Acquisition sessions should be repeated over time in order to study the evolution of the disease and its effects on the handwriting (the task should be repeated ideally every 6–9 months).

TABLE VII
AD CAD SYSTEMS ABBREVIATIONS: T = TABLET; ST = SHEET OF PAPER FIXED ON THE TABLET

Reference	Participants	Device	Tasks	Main features	Classifier	Results
Werner et al., 2006 [92]	22 AD 41 EC	ST	Copying: a phone number, a grocery list, the details of a check, the alphabet sequence and a paragraph	Size, duration (on-paper time and the in-air), pressure, mean velocity, mean pressure	Discriminant Analysis	ACC = 72%
Pirlo et al., 2015 [59]	29 AD 30 EC	T	Handwritten Signature	Velocity profiles	Bagging CART	EER= 3%
Garre-Olmo et al., 2017 [25]	23 AD 17 EC	ST	Dictated sentence writing, free sentence writing, two and three dimension drawing, clock drawing	Pressure, time, velocity, acceleration, energy, complexity	Discriminant Analysis	ACC = from 63.5% to 100% depending on the task
Müller et al., 2017 [48]	20 AD 20 EC	T	Three-dimensional house copying	in-air time, on-surface time, total time	Logistic Regression	ACC = 0.925
Müller et al., 2017 [49]	20 AD 20 EC	T	Clock drawing test	in-air time, on-surface time, total time	Logistic Regression	ACC = 87.2%

Fig. 6. Timeline of the milestones in the AD CAD development.

Datasets should also include "suspected" patients.

Unfortunately, developing such a benchmark database is a time-consuming and expensive process. It involves not only scientific and technical issues, like those related to acquisition devices and protocols as well as the statistical relevance of the population of the individuals involved, but also legal aspects related to data privacy and intellectual property rights.

B. Multimodalities

Acquisition tasks should include not only handwriting and/or drawing but also finger taps [36], [53]—think of the daily use of smartphones and the connected potentialities. From this point of view, a new research direction could be the investigation of the evolution of keystroke and touch dynamics. The combination of handwriting with other biometrics should be also considered, since it has been shown that diseases can be diagnosed with other traits as well, including speech [39], [71], gait [1], eye movements [4], [66], and gesture. This will reinforce the overall accuracy. In order to include gesture, the use of a camera or a kinect could be considered during the writing phases [27]. This would result in a system in which the two modalities are referred to the same action. The recording of the voice would require the use of a microphone and the assessment of some specific tasks designed for the aim.

The use of multiple modalities would result within a complete CAD framework.

C. Features

Many features have been considered to date. Some of them are directly conveyed from the handwriting recognition task, some others are able to better describe tremor or other characteristics connected to the diseases. Even if a set of more than two hundred features has been evaluated in general, there is a large number of well-known features still not considered: Fourier based and more in general transform based. At the same time some new specifically devoted features could be also designed and based on a specific task, as for instance a distance metrics for the guided spiral drawing task [95].

Feature selection has been considered taking into account different "general purpose" strategies [16], [18], [95], such as the e Mann-Whitney U-test, Relief algorithm, etc. Also, in this case, there is a plethora of other well-known techniques and specifically designed schema that could be considered. It is our opinion that feature selection should be coupled with task selection; in fact many researchers have found, in other application fields, that a set of features is better than another for a specific task [29]. Feature evaluation/selection could also be moved to a per-user or per-class (to be defined) or per-zone perspective. In other words, given a specific task, a set of features could be used in order to distinguish healthy versusnonhealthy, another one to classify stages of the disease. The situation could be completely different if another handwriting task would be considered.

D. Classification

It is worth noting that, to date, the classification problem has been considered as a binary one [14]–[18], [49], [92]; i.e., healthy versus nonhealthy. This is quite restrictive. The classification challenge should consider different stages of the disease. The subsequent steps would be the one in which HC are classified between healthy and those that have a certain probability to be exposed to the disease risk. To this aim, stability/complexity analysis could be considered, in order to reveal the most relevant regions of the patterns [58], [29].

Even if multiple tasks are available, up to date, the classification has been performed on a lumped feature vector containing features belonging to the whole set of tasks. More sophisticated (and probably performing) schema could be investigated and based on multiple classifiers [37] also considering feedback learning [30], [61]. In the case of measurement level fusion, score normalization must be considered [60].

E. Implementation

The main advantage of a CAD system based on dynamic handwriting analysis is that it is noninvasive and cost effective, making it more accessible to the final users. The system could be made available to both doctors at hospitals as well as patients at home. This last scenario makes sense, if we consider handwriting tasks to be performed for "rehabilitation" or exercise purposes. In this case, the system would be able to trace the course of the disease. Finally, if we consider the development of an app able to work with keystroke and touch dynamics more than handwriting, then it could be part of the next generation of our mobile devices.

VI. Summary

Handwriting is a good medium as a biomarker for the assessment of AD and PD. From this point of view, this paper has provided a comprehensive overview of the literature dealing with the application of online handwriting analysis to the assessment of the mentioned diseases from a pattern recognition perspective based on data acquisition, feature extraction, data analysis, and classification. The main findings have been highlighted and discussed.

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References

[1] E. Abdulhay, N. Arunkumar, K. Narasimhan, E. Vellaiappan, and V. Venkatraman, "Gait and tremor investigation using machine learning techniques for the diagnosis of Parkinson disease," *Future Gener. Comput. Syst.*, vol. 83, pp. 366–373, Jun. 2018.

[2] A. Almaksour, E. Anquetil, R. Plamondon, and C. O'Reilly, "Synthetic handwritten gesture generation using Sigma-Logormal model for evolving handwriting classifier," in *Proc. 15th Biennal Conf. Int. Graphonomics Soc.*, 2011, pp. 98–101.

[3] C. E. Anderson and M. P. Fisher, "Signatures of persons with Parkinsonism and hepatic encephalopathy as comparison standards," in *Proc. 9th Biennial Conf. Int. Graphonomics Soc.*, 1999, pp. 15–18.

[4] T.R. Barber *et al.*, "Apathy in rapid eye movement sleep behaviour disorder is common and under-recognized," *Eur. J. Neurol.*, vol. 25, no. 3, pp. 469–e32, 2018.

[5] C. Bidet-Ildei, P. Pollak, S. Kandel, V. Fraix, and J. P. Orliaguet, "Handwriting in patients with Parkinson disease: Effect of L-dopa and stimulation of the sub-thalamic nucleus on motor anticipation," *Human Movement Sci.*, vol. 30, no. 4, pp. 783–791, 2011.

[6] S. Borson, J. Scanlan, M. Brush, P. Vitaliano, and A. Dokmak, "The Mini-Cog: A cognitive 'vital signs' measure for dementia screening in multilingual elderly," *Int. J. Geriatric Psychiatry*, vol. 15, no. 11, pp. 1021–1027, 2000.

[7] M. P. Broderick, A. W. Van Gemmert, H. A. Shill, and G. E. Stelmach, "Hypometria and bradykinesia during drawing movements in individuals with Parkinson's disease." *Experimental Brain Res.*, vol. 197, no. 3, pp. 223–233, 2009.

[8] S. Broeder, E. Nackaerts, A. Nieuwboer, B. C. Smits-Engelsman, S. P. Swinnen, and E. Heremans, "The effects of dual tasking on handwriting in patients with Parkinson's disease," *Neuroscience*, vol. 263, pp. 193–202, 2014.

[9] M. P. Caligiuri, H. L. Teulings, J. V. Filoteo, D. Song, and J. B. Lohr, "Quantitative measurement of handwriting in the assessment of drug-induced Parkinsonism," *Human Movement Sci.*, vol. 25, no. 4, pp. 510–522, 2006.

[10] W. G. K. Cobbah and M. C. Fairhurst, "Computer analysis of handwriting dynamics during dopamimetic tests in Parkinson's disease," in *Proc. 26th Euromicro Conf.*, 2000, pp. 414–418.

[11] J. L. Contreras-Vidal, P. Poluha, H. L. Teulings, and G. E. Stelmach, "Neural dynamics of short and medium-term motor control effects of levodopa therapy in Parkinson's disease," *Artif. Intell. Med.*, vol. 13, no. 1, pp. 57–79, 1998.

[12] F. Costa, S. Marino, and A. Accardo, "Kinematic analysis of handwriting in Parkinson disease," in *Proc. Biennial Conf. Int. Graphonomics Soc.*, 2017, pp. 135–138.

[13] P. Drotár, J. Mekyska, Z. Smékal, I. Rektorová, L. Masarová, and M. Faundez-Zanuy, "Prediction potential of different handwriting tasks for diagnosis of Parkinson's," in *Proc. 4th IEEE Int. Conf. E-Health Bioeng.*, 2013, pp. 1–4.

[14] P. Drotár, J. Mekyska, I. Rektorová, L. Masarová, Z. Smékal, and M. Faundez-Zanuy, "A new modality for quantitative evaluation of Parkinson's disease: In-air movement," in *Proc. 13th Int. Conf. Bioinformatics Bioeng.*, 2013, pp. 1–4.

[15] P. Drotár, J. Mekyska, I. Rektorová, L. Masarová, Z. Smékal, and M. Faundez-Zanuy, "Analysis of in-air movement in handwriting: A novel marker for Parkinson's disease," *Comput. Methods Programs Biomed.*, vol. 117, no. 3, pp. 405–411, 2014.

[16] P. Drotár, J. Mekyska, I. Rektorová, L. Masarová, Z. Smékal, and M. Faundez-Zanuy, "Decision support framework for Parkinson's disease based on novel handwriting markers," *IEEE Trans. Neural Syst. Rehabil. Eng.*, vol. 23, no. 3, pp. 508–516, May 2015.

[17] P. Drotár, J. Mekyska, I. Rektorová, L. Masarová, Z. Smékal, and M. Faundez-Zanuy, "Contribution of different handwriting modalities to differential diagnosis of Parkinson's disease," in *Proc. IEEE Int. Symp. Med. Meas. Appl.*, 2015, pp. 344–348.

[18] P. Drotár, J. Mekyska, I. Rektorová, L. Masarová, Z. Smékal, and M. Faundez-Zanuy, "Evaluation of handwriting kinematics and pressure for differential diagnosis of Parkinson's disease," *Artif. Intell. Med.*, vol. 67, pp. 39–46, 2016.

[19] T. Duval, R. Plamondon, C. O'Reilly, and C. J. Vaillantm, "On the use of the Sigma-Lognormal model to study children handwriting," in *Proc. 16th Biennial Conf. Int. Graphonomics Soc.*, 2013, pp. 26–29.

[20] T.E. Eichhorn *et al.*, "Computational analysis of open loop handwriting movements in Parkinson's disease: A rapid method to detect dopaminergic effects," *Movement Disorders*, vol. 11, no. 3, pp. 289–297, 1996.

[21] M. C. Fairhurst, S. Hoque, and M. Razian, "Improved screening of developmental dyspraxia using on-line image analysis," in *Proc. 8th World Conf. Syst., Cybern. Informat.*, vol. 3, 2005, pp. 160–165.

[22] M. F. Folstein, L. N. Robins, and J. E. Helzer, "The mini-mental state examination," *Archives General Psychiatry*, vol. 40, no. 7, p. 812, 1983.

[23] R. Fucetola and M. C. Smith, "Distorted visual feedback effects on drawing in Parkinson's disease," *Acta Psychologica*, vol. 95, no. 3, pp. 255–266, 1997.

[24] G. Gangadhar *et al.*, "A computational model of Parkinsonian handwriting that highlights the role of the indirect pathway in the basal ganglia," *Human Movement Sci.*, vol. 28, no. 5, pp. 602–618, 2009.

[25] J. Garre-Olmo, M. Faúndez-Zanuy, K. López de Ipiña, L. Calvó-Perxas, and L. O. Turró-Garriga, "Kinematic and pressure features of handwriting and drawing: Preliminary results between patients with mild cognitive impairment, Alzheimer disease and healthy controls," *Current Alzheimer Res.*, vol. 14, pp. 960–968, 2017.

[26] O. Geman and H. Costin, "Nonlinear dynamics, artificial neural networks and neuro-fuzzy classifier for automatic assessing of tremor severity," in *Proc. 2013 E-Health Bioeng. Conf.*, Iasi, Romania, 2013, pp. 1–4.

[27] S. Glénat, L. Heutte, T. Paquet, "Computer-based diagnosis of dyspraxia: The meddraw project," in *Proc. 12th Conf. Int. Graphonomics Soc.*, 2005, pp. 49–53.

[28] D. Impedovo, G. Pirlo, "Automatic signature verification: The state of the art," *IEEE Trans. Syst., Man, Cybern. C*, vol. 38, no. 5, pp. 609–635, Sep. 2008.

[29] D. Impedovo and G. Pirlo, "On the measurement of local stability of handwriting: An application to static signature verification," in *Proc. IEEE Workshop Biometric Meas. Syst. Security Med. Appl.*, Taranto, Italy, 2010, pp. 41–44.

[30] D. Impedovo and G. Pirlo, "Updating knowledge in feedback-based multi-classifier systems," in *Proc. Int. Conf. Document Anal. Recog.*, Beijing, China, 2011, pp. 227–231.

[31] D. Impedovo *et al.*, "Writing generation model for health care neuromuscular system investigation," in *Proc. Int. Meeting Comput. Intell. Methods Bioinformat. Biostatist.*, 2013, pp. 137–148.

[32] M. Isenkul, B. Sakar, and O. Kursun, "Improved spiral test using digitized graphics tablet for monitoring Parkinson's disease," in *Proc. Int. Conf. e-Health Telemed.*, 2014, pp. 171–175.

[33] J. Jankovic, "Parkinson's disease: Clinical features and diagnosis," *J. Neurol., Neurosurgery Psychiatry*, vol. 79, pp. 368–376, 2008.

[34] S. Kandel, J. P. Orliaguet, and L. J. Boe, "Detecting anticipatory events in handwriting movements," *Perception*, vol. 29, pp. 953–964, 2000.

[35] J. Kawa, A. Bednorz, P. Stępień, J. Derejczyk, and M. Bugdol, "Spatial and dynamical handwriting analysis in mild cognitive impairment," *Comput. Biol. Med.*, vol. 82, pp. 21–28, 2017.

[36] T. Khan, D. Nyholm, J. Westin, and M. Dougherty, "A computer vision framework for finger-tapping evaluation in Parkinson's disease," *Artif. Intell. Med.*, vol. 60, no. 1, pp. 27–40, 2014.

[37] J. Kittler, M. Hatef, R. P. W. Duin, and J. Matias, "On combining classifiers," *IEEE Trans. Pattern Anal. Mach. Intell.*, vol. 20, no. 3, pp. 226–239, Mar. 1998.

[38] C. Kotsavasiloglou, N. Kostikis, D. Hristu-Varsakelis, and M. Arnaoutoglou, “Machine learning-based classification of simple drawing movements in Parkinson’s disease,” *Biomed. Signal Process. Control*, vol. 31, pp. 174–180, 2017.

[39] S. Lahmiri, D. A. Dawson, and A. Shmeul, “Performance of machine learning methods in diagnosing Parkinson’s disease based on dysphonia measures,” *Biomed. Eng. Lett.*, vol. 8, no. 1, pp. 29–39, 2018.

[40] A. E. Lang and A. M. Lozano, “Parkinson’s disease. New England,” *J. Med.*, vol. 339, no. 15, pp. 1044–1053, 1998.

[41] K.W. Lange *et al.*, “Brain dopamine and kinematics of graphomotor functions,” *Human Movement Sci.*, vol. 25, no. 4, pp. 492–509, 2006.

[42] K.W. Lange, O. Tucha, A. Reiter, L. Mecklinger, S. Birzer, and G.L. Alders, “Disturbances of handwriting fluency in Parkinson’s disease,” in *Proc. 11th Biennial Conf. Int. Graphonomics Soc.*, 2003, pp. 150–154.

[43] L. Likforman-Sulem, A. Esposito, M. Faundez-Zanuy, S. Clémençon, and G. Cordasco, “EMOTHAW: A novel database for emotional state recognition from handwriting and drawing,” *IEEE Trans. Human-Mach. Syst.*, vol. 47, no. 2, pp. 273–284, Apr. 2017.

[44] M. G. Longstaff, P. R. Mahant, M. A. Stacy, A. W. Van Gemmert, B.C. Leis, and G.E. Stelmach, “Continuously scaling a continuous movement: Parkinsonian patients choose a smaller scaling ratio and produce more variable movements compared to elderly controls,” in *Proc. 10th Biennial Conf. Int. Graphonomics Soc.*, 2001, pp. 84–89.

[45] K. López de Ipiña *et al.*, “Selection of entropy based features for the analysis of the Archimedes’ spiral applied to essential tremor,” in *Proc. 2015 4th Int. Work Conf. Bioinspired Intell. (IWOBI)*, San Sebastian, Spain, 2015, pp. 157–162.

[46] H. I. Ma, W. J. Hwang, S. H. Chang, and T. Y. Wang, “Progressive micrographia shown in horizontal, but not vertical, writing in Parkinson’s disease,” *Behavioural Neurol.*, vol. 27, no. 2, 169–174, 2013.

[47] P. Martínez-Martín, A. Gil-Nagel, L. M. Gracia, J. B. Gómez, J. Martínez-Sarriés, and F. Bermejo, “Unified Parkinson’s disease rating scale characteristics and structure,” *Movement disorders*, vol. 9, no. 1, pp. 76–83, 1994.

[48] S. Müller, O. Preische, P. Heymann, U. Elbing, and C. Laske, “Diagnostic value of a tablet-based drawing task for discrimination of patients in the early course of Alzheimer’s disease from healthy individuals,” *J. Alzheimer’s Disease*, vol. 55, no. 4, pp. 1463–1469, 2017.

[49] S. Müller, O. Preische, P. Heymann, U. Elbing, and C. Laske, “Increased diagnostic accuracy of digital vs. conventional clock drawing test for discrimination of patients in the early course of alzheimer’s disease from cognitively healthy individuals,” *Frontiers Aging Neurosci.*, vol. 9, pp. 1–10, 2017.

[50] R. M. Oliveira, J. M. Gurd, P. Nixon, J. C. Marshall, and R. E. Passingham, “Micrographia in Parkinson’s disease: the effect of providing external cues,” *J. Neurol., Neurosurgery Psychiatry*, vol. 63, no. 4, pp. 429–433, 1997.

[51] E. Onofri *et al.*, “Dysgraphia in relation to cognitive performance in patients with Alzheimer’s disease,” *J. Intellectual Disability-Diagnosis Treatment*, vol. 1, no. 2, pp. 113–124, 2013.

[52] C. O’Reilly and R. Plamondon, “Development of a Sigma–Lognormal representation for on-line signatures,” *Pattern Recog.*, vol. 42, no. 12, pp. 3324–3337, 2009.

[53] M. Pastorino *et al.*, “Assessment of bradykinesia in Parkinson’s disease patients through a multi-parametric system,” in *Proc. Int. Conf. Eng. Med. Biol. Soc.*, 2011, pp. 1810–1813.

[54] C. R. Pereira *et al.*, “A step towards the automated diagnosis of Parkinson’s disease: Analyzing handwriting movements,” in *Proc. 28th Int. Symp. Comput.-Based Med. Syst.*, 2015, pp. 171–176.

[55] C.R. Pereira, S.A. Weber, C. Hook, G. H. Rosa, and J.P. Papa, “Deep learning-aided Parkinson’s disease diagnosis from handwritten dynamics,” in *Proc. 29th SIBGRAPI Conf. Graph., Patterns Images*, 2016, pp. 340–346.

[56] J. G. Phillips, G. E. Stelmach, and N. Teasdale, “What can indices of handwriting quality tell us about Parkinsonian handwriting?,” *Human Movement Sci.*, vol. 10, no. 2, pp. 301–314, 1991.

[57] M. Pier, W. Hulstijn, and B. Sabbe, “Motor slowing in major depression, Parkinson’s disease and normal aging,” in *Proc. 10th Biennial Conf. Int. Graphonomics Soc.*, 2001, pp. 197–202.

[58] G. Pirlo, V. Cuccovillo, M. Diaz-Cabrera, D. Impedovo, and P. Mignone, “Multidomain verification of dynamic signatures using local stability analysis,” *IEEE Trans. Human-Mach. Syst.*, vol. 45, no. 6, pp. 805–810, Dec. 2015.

[59] G. Pirlo, M. M. Diaz-Cabrera, M.A. Ferrer, D. Impedovo, F. Occhionero, and U. Zurlo, “Early diagnosis of neurodegenerative diseases by handwritten signature analysis,” in *Proc. Int. Conf. Image Anal. Process.*, 2015, pp. 290–297.

[60] G. Pirlo and D. Impedovo, “Adaptive score normalization for output integration in multiclassifier systems,” *IEEE Signal Process. Lett.*, vol. 19, no. 12, pp. 837–840, Dec. 2012.

[61] G. Pirlo, C. A. Trullo, and D. Impedovo, “A feedback-based multiclassifier system,” in *Proc. 10th Int. Conf. Document Anal. Recog.*, Barcelona, Spain, 2009, pp. 713–717.

[62] R. Plamondon, “A kinematic theory of rapid human movements. Part I: Movement representation and generation,” *Biol. Cybern.*, vol. 72, pp. 295–307, 1995.

[63] H. Platel *et al.*, “Characteristics and evolution of writing impairment in Alzheimer’s disease,” *Neuropsychologia*, vol. 31, no. 11, pp. 1147–1158, 1993.

[64] P. Poluha, H. L. Teulings, and R. Brookshire, “Handwriting and speech changes across the levodopa cycle in Parkinson’s disease,” *Acta psychologica*, vol. 100, no. 1, pp. 71–84, 1998.

[65] M. M. Ponsen, A. Daffertshofer, E. C. Wolters, P. J. Beek, and H. W. Berendse, “Impairment of complex upper limb motor function in de novo Parkinson’s disease,” *Parkinsonism Related Disorders*, vol. 14, no. 3, pp. 199–204, 2008.

[66] E. Pretegiani and L. M. Optican, “Eye movements in Parkinson’s disease and inherited Parkinsonian syndromes,” *Frontiers Neurol.*, vol. 8, 2017, Art. no. 592.

[67] B.K. Randhawa, B.G. Farley, and L.A. Boyd. “Repetitive transcranial magnetic stimulation improves handwriting in Parkinson’s disease,” *Parkinson’s Disease*, vol. 2013, 2013, Art. no. 751925.

[68] S. Rosenblum, B. Engel-Yeger, and Y. Fogel, “Age-related changes in executive control and their relationships with activity performance in handwriting,” *Human Movement Sci.*, vol. 32, pp. 363–376, 2013.

[69] S. Rosenblum, M. Samuel, S. Zlotnik, I. Erikh, and I. Schlesinger, “Handwriting as an objective tool for Parkinson’s disease diagnosis,” *J. Neurol.*, vol. 260, no. 9, pp. 2357–2361, 2013.

[70] M. San Luciano *et al.*, “Digitized spiral drawing: A possible biomarker for early Parkinson’s disease,” *PloS one*, vol. 11, no. 10, 2016, Art. no. e0162799.

[71] E. Schalling, K. Johansson, and L. Hartelius, “Speech and communication changes reported by people with Parkinson’s Disease,” *Folia Phoniatr Logop.*, vol. 69, no. 3, pp. 131–141, 2017.

[72] A. Schröter, R. Mergl, K. Bürger, H. Hampel, H. J. Möller, and U. Hegerl, “Kinematic analysis of handwriting movements in patients with Alzheimer’s disease, mild cognitive impairment, depression and healthy subjects,” *Dementia Geriatric Cognitive Disorders*, vol. 15, no. 3, pp. 132–142, 2003.

[73] R. Senatore and A. Marcelli, “Do handwriting difficulties of Parkinson’s patients depend on their impaired ability to retain the motor plan? A pilot study,” in *Proc. Biennial Conf. Int. Graphonomics Soc.*, 2017, pp. 139–142

[74] H.R. Siebner, A. Ceballos-Baumann, H. Standhardt, C. Auer, B. Conrad, and F. Alesch, “Changes in handwriting resulting from bilateral high-frequency stimulation of the subthalamic nucleus in Parkinson’s disease,” *Movement disorders*, vol. 14, no. 6, pp. 964–971, 1999.

[75] M. J. Slavin, J. G. Phillips, J. L. Bradshaw, K. A. Hall, and I. Presnell, “Consistency of handwriting movements in dementia of the Alzheimer’s type: A comparison with Huntington’s and Parkinson’s diseases,” *J. Int. Neuropsychological Soc.*, vol. 5, no. 1, pp. 20–25, 1999.

[76] A. L. Smiley-Oyen, K. A. Lowry, and J. P. Kerr, “Planning and control of sequential rapid aiming in adults with Parkinson’s disease,” *J. Motor Behavior*, vol. 39, pp. 103–114, 2007

[77] E. J. Smits *et al.*, “Standardized handwriting to assess bradykinesia, micrographia and tremor in Parkinson’s disease,” *PloS one*, vol. 9, no. 5, 2014, Art. no. e97614.

[78] E. J. Smits *et al.*, “Graphical tasks to measure upper limb function in patients with Parkinson’s disease: Validity and response to dopaminergic medication,” *IEEE J. Biomed. Health Informat.*, vol. 21, no. 1, pp. 283–289, Jan. 2017.

[79] S. Sveinbjornsdottir, “The clinical symptoms of Parkinson’s disease,” *J. Neurochem.*, vol. 139, pp. 318–324, 2017.

[80] S. P. Swinnen, M. Steyvers, L. Van Den Bergh, and G. E. Stelmach, “Motor learning and Parkinson’s disease: Refinement of within-limb and between-limb coordination as a result of practice,” *Behavioural Brain Res.*, vol. 111, no. 1, pp. 45–59, 2000.

[81] H. L. Teulings, “Optimatization of movements duration in accurate handwriting strokes in different directions in young, elderly, and Parkinsonian subjects,” in *Proc.10th Biennial Conf. Int. Graphonomics Soc.*, 2001, pp. 40–45.

[82] H. L. Teulings, J. L. Contreras-Vidal, G. E. Stelmach, and C. H. Adler, “Adaptation of handwriting size under distorted visual feedback in patients with Parkinson’s disease and elderly and young controls,” *J. Neurol., Neurosurgery Psychiatry*, vol. 72, no. 3, pp. 315–324, 2002.

[83] H. L. Teulings and G. E. Stelmach, "Control of stroke size, peak acceleration, and stroke duration in Parkinsonian handwriting," *Human Movement Sci.*, vol. 10, no. 2, pp. 315–334, 1991.

[84] O. Tucha *et al.*, "Kinematic analysis of dopaminergic effects on skilled handwriting movements in Parkinson's disease," *J. Neural Transmiss.*, vol. 113, no. 5, pp. 609–623, 2006.

[85] K. Ubul, G. Tursun, A. Aysa, D. Impedovo, G. Pirlo, and T. Yibulayin, "Script identification of multi-script documents: A survey," *IEEE Access*, vol. 5, pp. 6546–6559, 2017.

[86] A. Ünlü, R. Brause, and K. Krakow, "Handwriting analysis for diagnosis and prognosis of Parkinson's disease," in *Proc. Int. Symp. Biol. Med. Data Anal.*, Berlin, Germany: Springer, 2006, pp. 441–450.

[87] A.W. Van Gemmert, C. H. Adler, and G. E. Stelmach, "Parkinson's disease patients undershoot target size in handwriting and similar tasks," *J. Neurol., Neurosurgery Psychiatry*, vol. 74, no. 11, pp. 1502–1508, 2003.

[88] A.W. Van Gemmert, H. L. Teulings, and G. E. Stelmach, "The influence of mental and motor load on handwriting movements in Parkinsonian patients," *Acta Psychologica*, vol. 100, no. 1, pp. 161–175, 1998.

[89] A.W. Van Gemmert, H. L. Teulings, and G. E. Stelmach, "Parkinsonian patients reduce their stroke size with increased processing demands," *Brain Cognition*, vol. 47, no. 3, pp. 504–512, 2001.

[90] A. W. Van Gemmert, C. H. Adler, and G. E. Stelmach, "The isochronic size range is reduced in handwriting of Parkinsonian patients," in *Proc. 10th Biennial Conf. Int. Graphonomics Soc.*, 2001, pp. 36–39.

[91] A.W. Van Gemmert, R. Plamondon, and C. O.' Reilly, "Using the Sigmalognormal model to investigate handwriting of individuals with Parkinson's disease," in *Proc. 16th Biennial Conf. Int. Graphonomics Soc.*, Nara, Japan, Jun. 2013, pp. 119–122.

[92] P. Werner, S. Rosenblum, G. Bar-On, J. Heinik, and A. Korczyn, "Handwriting process variables discriminating mild Alzheimer's disease and mild cognitive impairment," *J. Gerontology Ser. B, Psychological Sci. Social Sci.*, vol. 61, no. 4, pp. 228–236, 2006.

[93] J.H. Yan, S. Rountree, P. Massman, R. S. Doody, and H. Li, "Alzheimer's disease and mild cognitive impairment deteriorate fine movement control," *J. Psychiatric Res.*, vol. 42, no. 14, pp. 1203–1212, 2008.

[94] N. Y. Yu and S. H. Chang, "Kinematic analyses of graphomotor functions in individuals with Alzheimer's disease and amnestic mild cognitive impairment," *J. Med. Biol. Eng.*, vol. 36, no. 3, pp. 334–343, 2016.

[95] P. Zham, S. Arjunan, S. Raghav, and D. K. Kumar, "Efficacy of guided spiral drawing in the classification of Parkinson's disease," *IEEE J. Biomed. Health Informat.*, to be published, doi: 10.1109/JBHI.2017.2762008.

[96] N. Zhi, B.K. Jaeger, A. Gouldstone, R. Sipahi, and S. Frank, "Toward monitoring Parkinson's though analysis of static handwriting samples: A quantitative analytical framework," *IEEE J. Biomed. Health Informat.*, vol. 21, no. 2, pp. 488–495, Mar. 2017.

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