Artificial Intelligence In Medicine xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

Artificial Intelligence In Medicine

journal homepage: www.elsevier.com/locate/artmed

Review

A survey on computer-assisted Parkinson's Disease diagnosis

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ARTICLE INFO

Keywords:
Parkinson's Disease
Parkinsonian
Machine Learning

ABSTRACT

Background and objective: In this work, we present a systematic review concerning the recent enabling technologies as a tool to the diagnosis, treatment and better quality of life of patients diagnosed with Parkinson's Disease (PD), as well as an analysis of future trends on new approaches to this end.
Methods: In this review, we compile a number of works published at some well-established databases, such as Science Direct, IEEEXplore, PubMed, Plos One, Multidisciplinary Digital Publishing Institute (MDPI), Association for Computing Machinery (ACM), Springer and Hindawi Publishing Corporation. Each selected work has been carefully analyzed in order to identify its objective, methodology and results.
Results: The review showed the majority of works make use of signal-based data, which are often acquired by means of sensors. Also, we have observed the increasing number of works that employ virtual reality and e-health monitoring systems to increase the life quality of PD patients. Despite the different approaches found in the literature, almost all of them make use of some sort of machine learning mechanism to aid the automatic PD diagnosis.
Conclusions: The main focus of this survey is to consider computer-assisted diagnosis, and how effective they can be when handling the problem of PD identification. Also, the main contribution of this review is to consider very recent works only, mainly from 2015 and 2016.

1. Introduction

Parkinson's Disease (PD), firstly described by the English and physician James Parkinson [1] in 1817, is a chronic, progressive and neuron-degenerative illness that affects people worldwide. Although there is a number of possible symptoms, PD is often related to progressive bradysinesia, i.e. the slowness of movement, as well as tremors and muscle stiffness, which can worsen over time. The cadence in the gait, fatigue, somnolence, and the so-called freezing-of-gate are very common symptoms of PD. Also, the patients usually feature changes in speech and writing skills [2].

Currently, approximately 60,000 Americans are diagnosed with PD [3]. However, such statistics may be underestimated, since thousands of potential individuals remain uncovered by exams or any sort of clinical diagnosis. As a matter of fact, around 7 to 10 million people might be living with PD nowadays, which turns out to be a problem of public health that deserves a considerable attention [3].

The main cause of Parkinson's Disease is related to the degeneration of a small part of the brain, the so-called *substantia nigra*. As soon as the cells from this region start to die, the brain becomes deprived of a chemical substance known as *dopamine*, which allows the brain cells to get involved in the control of movement. Therefore, the lower the level of dopamine, the higher the probability of being affected by Parkinson's Disease [2]. As such, with the absence of such substance, the brain cells can no longer send messages properly, causing depression, sleep disturbances, memory impairment and disorders related to the autonomic nervous system. Additionally, PD also may be triggered by hereditary causes [2]. A secondary form of PD, known as Idiopathic Parkinson's Syndrome (IPS), has been pointed out by researches as well. The disease has different causes that distinguish it from PD, such as side effects of

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https://doi.org/10.1016/j.artmed.2018.08.007
Received 20 October 2017; Received in revised form 14 June 2018; Accepted 25 August 2018
0933-3657/

Please cite this article as: Pereira, C.R., Artificial Intelligence In Medicine, https://doi.org/10.1016/j.artmed.2018.08.007

medication and vascular pressure encephalopathy. IPS may also produce sequelae of neurodegenerative disorders [4]. Atypical Parkinsonian Syndromes (APS), such as Progressive Supranuclear Palsy (PSP) and Multiple System Atrophy (MSA), differ from PD by a considerably widespread neuronal involvement, thus resulting in additional clinical signs, more rapid disease progression, as well as a poor response to dopamine replacement therapy [5].

Since it has no cure, several chemical methods have been used to treat Parkinson's Disease in its early stages, being the *Levodopa* (L-dopa) one of the most widely used for such purpose. Another treatment that is indeed effective in the treatment of PD concerns the DBS, which consists of a implantation of device similar to a cardiac pacemaker to stimulate electrically some target regions in the brain [6].

In order to better manage such disease and to increase the life quality of PD patients, a bundle of researchers from different areas have worked together. As such, the literature is rich in a number of different works, that range from chemical- and behavioral-driven studies to computer-assisted diagnosis. The main contribution of this work relies on the latter approaches, which make use of computer tools to help researchers when handling the diagnosis of Parkinson's Disease in a faster and more effective way. In this survey, we tried to compile the most prominent works related to computer methods to automatic identify PD, as well as to help its diagnosis.

In order to give a taste of what is going on concerning this research field, most works make use of artificial intelligence (i.e. machine learning) to learn the most important features that can be considered when diagnosing some individual. Spadotto et al. [7], for instance, introduced the Optimum-Path Forest (OPF) [8,9] classifier to aid the automatic identification of Parkinson's Disease, and later on the same group of authors proposed an evolutionary-based approach to select the most discriminative set of features that help improving PD recognition rates [10]. The OPF classifier seemed to be a suitable tool, since it is parameterless and easy-to-manage.

Pan et al. [11] analyzed the performance of Support Vector Machines with Radial Basis Function (SVM-RBF) in order to compare the onset of tremor in patients with Parkinson's disease. Gharehchopogh et al. [12] used Artificial Neural Networks with Multi-Layer Perceptron to diagnose the effects caused by Parkinson's disease. One year later, Hariharan et al. [13] developed a new feature weighting method using Gaussian Mixture Models to enrich the discriminative ability of some dysphonia-based features, thus achieving 100% of classification accuracy. However, one should notice that a machine might be always prune to errors, which means a perfect recognition rate usually cannot be generalized to all kinds of unseen data. Peker et al. [14] used sound-based features and complex-valued neural networks to aid PD diagnosis as well. Braatz and Coleman [15] developed a mathematical model based on biochemical systems theory to examine the changes that occur over the course of PD, as well as to identify what processes would be the most effective targets for treatment. The model predicts that combined tools, initiated as early as possible and targeting a wide range of pathways, are the most effective ones.

As one can observe, most works that address PD automatic recognition cope with voice-based data. Procedures to identify voiced and unvoiced (silent) periods have been actively pursued to analyze continuous speech samples, since most techniques that quantify periodicity and regularity in voice signals are applied in the voiced regions only [16]. Das [17] presented a comparison of multiple classification methods for the diagnosis of PD, among them Neural Networks, and Regression and Decision Trees. Several evaluation methods were employed to calculate the performance of that classifiers, being the experiments conducted in a dataset composed of a range of biomedical voice measurements from 31 people, in which 23 diagnosed with Parkinson's disease. The best results were obtained by Neural Networks (around 92.9% of PD recognition rate). However, other pathologies may generate speech variances as well, such as MDI (Mild Cognitive Impairment), AD (Alzheimer's Disease) and depression. In 2014, Weber et al. [18] used a biometric pen together with SVMs to learn handwritten dynamics from PD patients.

Although they are outnumbered when compared to signal-driven applications, image processing-based approaches have been used to detect Parkinson's Disease either. In 2015, Pereira et al. [19] proposed to extract features from writing exams using visual features learned from drawings the patients were asked to do. The authors also designed and made available a dataset called "HandPD" with all images and features extracted from the handwriting exams.[1] In 2018, Pereira et al. [20] used Convolutional Neural Networks to analyze data related to handwritten dynamics in the context of computer-assisted PD recognition.

In regard to enabling technologies to aid patients with PD, we have compiled eight reviews. Bhande and Raut [21], in 2013, presented a brief analysis to illustrate the merits of a number of available research techniques based on neural networks. More recently, in 2015, Oung et al. [22] carried out a review on technologies for the assessment of motor disorders in PD, considering, for example, wearable, audio, and multimodal sensors. In the same year, Bind et al. [23] presented a comprehensive review concerning the prediction of Parkinson's Disease by means of machine learning techniques.

Pasluosta et al. [24] focused on PD as a representative disease model by evaluating the Internet-of-Things (IoT) platform in the context of healthcare. The authors considered the potential of combining wearable technology with the IoT in the healthcare scenario, as well as the engagement of patients in the assessment of symptoms, diagnosis, and consecutive treatment options. Zhao et al. [25] also analyzed E-health support in PD, but now with smart glasses.

Harris et al. [26] carried out a review about the so-called *exergaming* (i.e. the combination of exercising with games) as a viable therapeutic tool to improve static and dynamic balance. Stamford et al. [27], in 2015, assessed the use of different engineering technologies in the context of PD diagnosis. Ekker et al. [28] conducted a study about visual rehabilitation by means of wearable devices, making use of the telemedicine for neurorehabilitation in PD-affected patients.

As aforementioned, we aim at compiling together a number of works that attempt to handle the problem of automatic PD diagnosis, since the literature lacks on a more recent compilation of related works. We present an extensive comparison about different methodologies to deal with Parkinson's Disease using machine learning techniques. The reminder of this paper is organized as follows. Section 2 presents the methodology employed to conduct this review, as well as the different techniques used in the papers referred in this work. Section 3 presents several datasets employed in some related works, and Section 4 discusses the research that have been conducted to cope with PD. Finally, Section 5 states conclusions and future tendencies.

2. Enabling technologies

In order to select works within the scope addressed in this systematic review, a relevant search in Science Direct, IEEEXplore, PubMed, Plos One, Multidisciplinary Digital Publishing Institute (MDPI), Association for Computing Machinery (ACM), Springer and Hindawi Publishing Corporation databases was carried out. To this end, only two key words were considered for searching purposes: (i) "Parkinson's Disease" and (ii) "Parkinsonian". The main idea is to make the selection of works fairly tiresome, but quite able to cover a total of 84 recent works published in between 2015 (76 works) and early 2016 (8 works). Some works published in 2014 and earlier were briefly discussed in the previous section.

The next sections describe in deeper details the works divided by their main application domain, i.e. web application, sensors, virtual and augmented reality, smart-phone devices, signals analysis, image

[1] http://wwwp.fc.unesp.br/papa/pub/datasets/Handpd/.

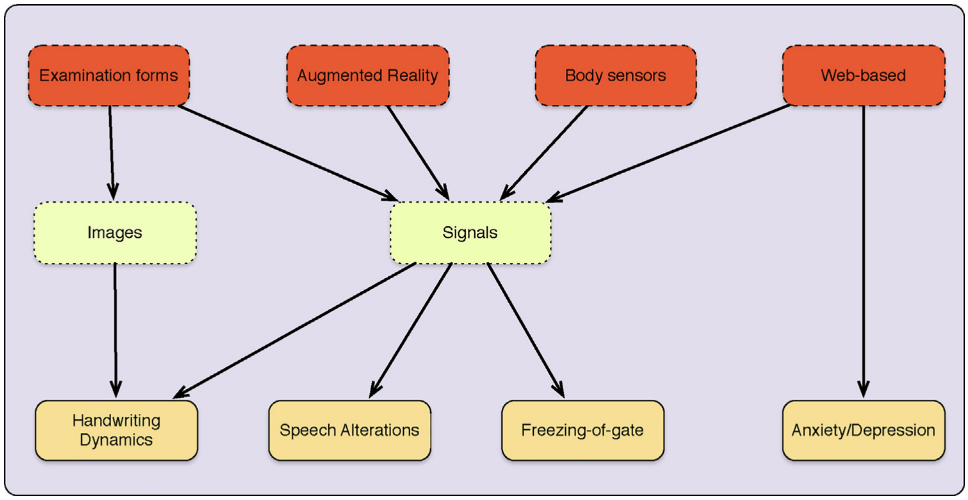

Fig. 1. Taxonomy adopted in this work. The dashed modules stand for the acquisition devices, the dotted ones denote the source of data, and the solid modules correspond to the possible side effects that are aimed to be detected.

processing and machine learning. The main reason for choosing such taxonomy concerns the fact that most computer-assisted PD recognition systems make use of data that usually come from either images or signals. The former source of data is usually in charge of quantifying the amount of tremors when performing some handwriting tasks, such as drawing spirals and meanders. Signals are often extracted from sensors to detect the freezing-of-gate or to recognize subtle alterations in the muscle or speech-oriented tasks.

Apart from those sources, the acquisition devices vary in number, type, and sizes. Speech measurements can be acquired from digital microphones, for instance, while alterations in the gate are usually identified using sensors attached to the body. Muscle stiffness can be also detected by means of sensors, and virtual and augmented reality can help to recognize disturbances in the orientation. Therefore, the methodology adopted in this survey aimed at covering most of the application domain and data sources that are usually employed to cope with computer-assisted PD identification. Fig. 1 depicts the taxonomy adopted in this work.

2.1. Machine learning

Machine Learning is a branch of computational intelligence dedicated to the development of algorithms that enable a computer program to improve its performance based on prior (learned) information. Since the very beginning of “Perceptron”, new mathematical modelings of the working mechanism of the brain have been pursued daily. Such intense research has motivated a number of works that aimed at using machine learning-oriented techniques to aid Parkinson's Disease recognition.

Drotár et al. [29], for instance, proposed to study some features based on entropy, energy and intrinsic measures of the handwriting skills of an individual. The authors also considered applying such measures to in-air movements and pressure to exploit the full potential of the handwriting. An SVM-RBF kernel was used for classification purposes, thus achieving a classification accuracy of around 81.3% of prediction performance. Connolly et al. [30] applied Linear Discriminant AnalysisSupport (LDA), Support Vector Machines and *k*-nearest neighbor (*k*-nn) upon local field potentials sensed from an implanted deep brain stimulation device. For such analysis, 83 montages were recorded from 15 patients suffering from advanced idiopathic PD, thus obtaining an accuracy rate of 91%.

Wahid et al. [31] presented a study with two main contributions: firstly, they used a multiple regression normalization strategy to identify differences in spatial-temporal gait features between PD patients and control (healthy) individuals. Secondly, they evaluated the effectiveness of machine learning strategies in classifying PD gait after multiple regression normalization. The authors argued the study has important implications for the analysis of spatial-temporal gait data concerning the diagnosis of PD, as well as the evaluation of its severity with five machine learning strategies employed to classify PD gait: kernel Fisher Fiscriminant (KFD), Naïve Bayesian Approach (NB), *k*-nn, SVM, and Random Forest (RF).

Smith et al. [32] employed evolutionary algorithms to provide clinically relevant and objective measures to identify PD both in humans and animal models. The human data were collected from commercial sensors via non-invasive procedures, and the animal data were collected using fruit flies with and without PD genetic mutations. Their work used Cartesian Genetic Programming, thus showing such technique can be successfully applied to the assessment of movements in humans when distinguishing PD patients from healthy controls, as well as to classify severity of dyskinesia in patients.

Hirschauer et al. [33] presented a new method for the diagnosis of PD based on continuous phonation samples, which were used as attributes. A technique called minimum Redundancy Maximum Relevance (mRMR) was applied for the identification of the most relevant attributes, and the results were compared to a variety of feature selection algorithms. The dataset used in this study was originally obtained from the University of Oxford in cooperation with the National Voice and Speech Center, Denver, Colorado.[2] After the feature selection process, the data are used to feed to different neural classifiers: a standard Artificial Neural Network (ANN) and a Complex-Valued Neural Network (CVANN). The results were promising: ANN obtained an accuracy of 94.28%, and CVANN achieved an accuracy of 98.12%.

Ahmadlou et al. [34] presented an Enhanced Probabilistic Neural Networks (EPNN), a machine learning technique that make use of local decision circles surrounding training samples to control the spread of the Gaussian kernel. Using the Parkinson's Progression Markers Initiative[3] dataset, the proposed approach obtained an accuracy of 98.6% when classifying healthy people from PD patients, and 92.5% of recognition rate when dealing with data of six clinical exams and functional neuroimaging data for two regions of interest of the brain.

Segovia et al. [35] demonstrated a new method based on SVMs and Bayesian networks to separate IPS from APS that makes use of the ^{18}F-FDG PET dataset, that allows assessing the glucose metabolism of the brain. Their methodology achieved an accuracy rate over 78%, a reasonable result between sensitivity and specificity, suggesting the

[2] https://archive.ics.uci.edu/ml/datasets/Parkinsons.
[3] http://www.ppmi-info.org/access-data-specimens/download-data/.

proposed method is suitable to assist the diagnosis of PD. Cook et al. [36] proposed to employ a combination between smart home and machine learning technologies to observe and quantify the behavioural changes of PD patients. The main focus is to aid the clinical assessment and a better understanding of the differences between healthy older adults (HOA) and older adults with cognitive and physical impairments, also classified by the authors as mild cognitive impairment (MCI). The results indicated that smart homes, wearable devices and ubiquitous computing technologies can be useful for monitoring the activity of PD patients, as well as to pinpoint the differences between HOAs and older adults with PD or MCI. However, the authors described some limitations concerning the devices, such as to operate in settings with multiple residents and interrupted activities.

In 2015, Shamir et al. [37] proposed an approach called Clinical Decision Support Systems (CDSS) to examine the results of the incorporation of patient-specific symptoms and medications into three key functions: (i) information retrieval; (ii) visualization of treatment; and (iii) recommendation on expected effective stimulation and drug dosages. In order to fulfil this purpose, the authors used Naïve Bayes, Support Vector Machines and Random Forest to predict the treatment outcomes. The combined machine learning algorithms were able to accurately predict 86% of the motor improvement scores at one year after surgery.

Tucker et al. [38] proposed a low-cost data mining-driven approach composed of non-wearable multimodal sensors to model and predict a PD patient's adherence to medication protocols based on variations in their gait. Using whole-body movement data readings from the patients, it is possible to discriminate PD patients that are “on” or “off” medication with an accuracy of 97% using an individually customized model, and an accuracy of 78% considering a generalized model containing multiple patient gait data.

Procházka et al. [39] presented a novel method of Bayesian gait recognition using a Kinect sensor (data acquisition and spatial modelling) combined with signal processing techniques and Bayesian classifier for gait feature analysis aiming at recognizing individuals affected by Parkinson's disease Singh and Samavedham [40] proposed an innovative and effective approach for monitoring the disease progression and clinical diagnosis, which is based on the combination of Self-Organizing Maps and Least Squares Support Vector Machines. The proposed approach can achieve an accuracy of up to 97% concerning the differential diagnosis of PD using the PPMI dataset. The same group of authors used unsupervised learning techniques to identify reliable biomarkers to aid the diagnosis of neurodegenerative diseases [41]. Table 1 summarizes the main works concerning machine learning-based solutions for the automatic PD diagnosis.

2.2. Image analysis

Zhang et al. [42] tested the hypothesis that changes in cortical thinning can be detected in PD patients without dementia, as well as these changes are correlated with measured cognitive decline thought its relationships to cognitive impairment using high-resolution T1 weighted magnetic resonance images (MRI) of the brain. An advanced hierarchical multivariate Bayesian model to analyze the cortical thickness measurement and thinning pattern was adopted, with suitable results observed. Szymanski et al. [43] used WEKA [44] and Rough Set Exploration System data mining methods to analyze neurological data of PD patients with the local cerebral blood flow (CBF) measured by the Single-Photon Emission Computed Tomography (SPECT). The results were correlated with the Unified Parkinson's Disease Rating Scale, being possible to demonstrate that CBF changes suggest that a general state of PD is stronger related to the CBF than to only motor symptoms.

Paredes et al. [45] developed the e-Motion Capture System, which is a Kinect-based software to calculate motor (cadence, stride and step length) and spatio-temporal (velocity and acceleration) parameters that affect the quality of life in patients with PD. In order to assess the reliability of the proposed system as a benchmark reference, a multiple-camera 3D motion capture system to track the gait pattern during a walking test was employed. The authors stated the e-Motion Capture System was able to measure the motor and spatial-temporal variables that are sensitive to changes in the timeline of the disease.

Hewavitharanage et al. [46] applied a grey-level dependence matrix in order to segment the *rima glottidis*[4] in 4D laryngeal Computed Tomography (CT) scans in PD patients in order to identify vocal impairments. The SVM-based segmentation algorithm showed to be useful in distinguishing the *rima glottidis* area from the remaining tissues of the larynx. Bhalchandra et al. [47] used image analysis to segment the high-activity regions of the brain using SPECT images. Such regions correspond to the concentration of the striatal dopamine transporter, which is in charge of transmitting the dopamine substance related to the motor control. An accuracy rate of 99.42% was achieved by means of Discriminant Analysis and Support Vector Machines. In the same year, Wu et al. [48] analyzed the application of Auto-Regressive (AR) models to describe the stochastic process underlying stride series of idiopathic PD patients, which are used as features to distinguish the PD stride series from the healthy normal cases. The Linear Discriminant Analysis (LDA) and Support Vector Machines were employed, being SVM better than LDA for the separation of both healthy and idiopathic PD groups, with relatively high sensitivity (0.72), specificity (0.89), and area under the curve (0.83) values, showing the autoregressive model parameters could be useful for the classification of stride series.

Rana et al. [49] used Computer-assisted Diagnostic Techniques to analyze five well documented regions of interest affected by PD using a 3D volumetric T1-weighted magnetic resonance imaging to discriminate PD patients from healthy subjects. The experiments were conducted using Support Vector Machines, which achieved a maximum accuracy of 86.67%. Rocha et al. [50] investigated the impact of a recent version of Kinect (version 2) in the context of PD clinical assessment when compared against the former Kinect (version 1) over 3D body data acquired from normal and PD patients treated with deep brain stimulation. In order to validate the methods, the statistical analysis showed it is possible to highlight the gait parameters are useful to distinguish between non-PD and PD patients with 96% of accuracy concerning the new version of Kinect, as well as 72% considering the former Kinect device.

Li et al. [51] collected data from 10 patients (6 men and 4 women) with Parkinson's Disease acquired by means of sensors implanted with deep brain stimulation devices. Since the literature points the *subthalamic nucleus* (STN) as one of the most important regions of the brain concerning the treatment of PD patients, the authors developed an automated algorithm for MRI data using the Level Set method for image segmentation in order to aid neurosurgeons to better place the electrodes in the brain. In short, this algorithm seeks to facilitate neurosurgeons in the preoperative process and provides clinical guidance for reducing the repeated intraoperative adjustments, as well as the risk of bleeding.

Wabnegger et al. [52] investigated the use of facial emotion recognition in PD to compare brain activation during emotion perception between PD patients and healthy controls. The participants were shown pictures of different facial expressions, while the brain activity was captured by means of functional Magnetic Resonance Imaging (fMRI). The study did not conclude whether PD patients and the control group have enough discrepancies in such context or not. However, other works [53,54] observed the lack of emotion in PD patients considering more than 40 individuals and 8 different emotions (controlling, vindictive/angry, distant, socially avoidant, non-assertive, exploitable/overly accommodating, self-sacrificing, and needy).

Castellanos et al. [55] analyzed an automated method to segment the *substantia nigra* and *locus coeruleus* volumes based on Neuromelanin-

[4] An opening between the true vocal cords and the arytenoid cartilages.

Table 1
Machine learning-related works.

Reference	Dataset	Purpose of the study	Results
Drotár et al. [29]	Parkinson's Disease Handwriting Database.	To study features based on entropy and energy concerning the handwriting skills.	Accuracy of 81.30% using SVM with RBF kernel.
Connolly et al. [30]	Data from 15 patients with a large set of spectral features.	To employ signals sensed from Deep Brain Stimulation.	A leave-one-out cross- validation error of around 7% was obtained with SVM.
Wahid et al. [31]	Data from 23 PD patients and 26 aged-matched controls.	To identify differences in spatial-temporal gait features between PD patients and control (healthy) individuals using multiple regression normalization.	Accuracy of 87.40% using KFD, 82.00% using NB, 84.40% using *k*-nn, 86.00% using SVM, and 80.00% using RF.
Smith et al. [32]	Data from 49 PD patients and 41 age-matched healthy controls.	To apply Evolutionary Algorithms to study motor functions in both humans and animal models.	Accuracy of 78.00%.
Hirschauer et al. [33]	Parkinson's Data Set obtained from UCI Machine Learning Repository.	To present a new feature selection algorithm known as mRMR.	Accuracy of 94.28% using ANN, and 98.12% using CVANN.
Segovia et al. [35]	F-FDG PET dataset.	To distinguish Parkinson's disease from APS using machine learning techniques.	Accuracy of 75.86% using SVM, and accuracy of 78.16% using NB.
Shamir et al. [37]	Clinical data from 10 patients and 89 post-DBS surgery visits were used.	To develop a proof-of-concept implementation of a CDSS that incorporates patient-specific details on both stimulation and medication.	Accuracy of 71.00% using SVM, 64.00% using NB, and 64.00% using RF.
Tucker et al. [38]	Composed of non-wearable multimodal sensors.	To model and predict PD patients' adherence to medication protocols based on variations in their gait.	There are several results due to the number of experiments performed in terms of true positive, false positive, false negative, and true negative measures.
Procházka et al. [39]	Kinect sensor (data acquisition and spatial modelling).	To propose a novel method of Bayesian gait recognition.	Accuracy of 94.1%.
Ahmadlou et al. [34]	Parkinson's Progression Markers Initiative.	To present a new machine learning technique that makes use of local decision circles surrounding training samples to control the width of the Gaussian kernel.	Accuracy of 98.6% when classifying healthy people from PD patients, and an accuracy of 92.5% when dealing with data of six clinical exams and functional neuro-imaging data.

Sensitive MRI (NM-MRI) in patients with idiopathic (when the source of the disease is unknown) and monogenic (genetic inheritance pattern determined by a single gene) PD patients. The authors found evidences that NM-MRI can provide highly accurate diagnosis (sensitivity of around 91% and specificity of 89%). Gilat et al. [56] used a virtual reality paradigm in combination with fMRI to explore the neural correlation in 17 PD patients with freezing of gait (FoG), and 10 PD patients without FoG while off their dopaminergic medication. The results state the PD patients with FoG show alterations in the blood oxygen level responses across regions that implicate the prospective recruitment of a stopping network, which may be manifested pathologically as a freeze when the sensorimotor processing becomes more complex.

Feis et al. [57] introduced a multimodal approach to model symptom sides at disease onset in brain morphology based on different aspects of diffusion MR parameters and multi-kernel support vector classification. They consider these results as a major step in further predictive clinical models of Parkinson's Disease by incorporating the many clinical aspects that determine the progression of the disease.

Illán et al. [58] proposed a computer-assisted system to PD diagnosis based on SPECT imagery. The tool developed in their work aimed at helping physicians in the daily routines and comprises a full pipeline for image processing, i.e. preprocessing, normalization, and classification. The authors reported promising classification rates using the SVM classifier, with an area under the curve of 0.9681. Segovia et al. [59] proposed a method to classify images of the brain into two classes: control or patient. The idea is to assist PD identification using regions from each hemisphere of the brain individually. Support Vector Machines and the Partial Least Squares were employed for classification purposes, with recognition results nearly to 94.7%.

Rojas et al. [60] proposed a new approach for feature extraction of brain SPECT images of the brain. The work aimed at PD identification using Empirical Mode Decomposition and a dataset composed of 80 images from Spain, obtaining an accuracy of around 95%. Martinez-Murcia et al. [61] designed a tool to help physicians in the identification PD patients using data from SPECT images obtained from three distinct datasets: Virgen de la Victoria database – VV, Virgen de las Nieves database – VN, Parkinson's progression markers initiative database – PPMI. 3D-based texture information is extracted from the images, which is further used to feed an SVM classifier. Recognition rates of 97.4% were obtained using a leave-one-out cross-validation approach, thus showing the suitability of the proposed approach.

Martínez-Murcia et al. [62] proposed a tool for PD identification using DaTSCAN images and Independent Component Analysis-based features to train a classifier. The proposed approach was tested on two datasets (VV and PPMI), obtaining results nearly to 94.7% and 91.3% for VV and PPMI datasets, respectively. Brahim et al. [63] presented a comparison of different approaches to handle the problem of intensity normalization in DaTSCAN SPECT imaging. A leave-one-out cross-validation technique over two different methods (one based on Gaussian Mixture Model and the other based on Mean Squared Error optimization) allowed recognition rates of around 92.91%. Table 2 summarizes the main papers presented in this session.

2.3. Signal analysis

Karamintziou et al. [6] presented a novel approach based on closed-loop deep brain stimulation system for PD treatment. The proposed work operates according to an online real-time algorithm that integrates a sensitive biomarker approach together with an improved modification of a stochastic dynamical phase model. The approach is validated as a control parameter, as well as its potential to support on-demand stimulation with enfolds the dynamics of adaptive stimulation and the minimum-energy desynchronizing control of neuronal activity.

Villa-Canãs et al. [64] analyzed the low-frequency components of continuous speech signals uttered by PD patients using four-time-frequency approaches based on Wigner-Ville distribution. The idea is to determine whether the features associated to changes in the spectrum can be used to identify the tremor in speech signals of PD patients. The spectra are characterized based on energy analysis and spectral centroids, and the automatic detection is carried out using Support Vector Machines. The authors achieved around 72% of accuracy when discriminating between PD and healthy speakers.

Restrepo-Agudelo and Roldán-Vasco [65] developed a method to simulate the intracranial signals recorded during a deep brain stimulation surgery of a patient with Parkinson's Disease. The method, called Auto-Regressive Parametric Model, allowed the reconstruction of the signal in time-domain with an accuracy nearly to 95% with respect to the real and simulated signals. Su and Chuang [66] adopted a fuzzy

Table 2
Image analysis-related works.

References	Dataset	Study proposal	Results
Zhang et al. [42]	Data obtained from the Institutional Review Board/Human Subjects Protection Office.	To adopt an advanced hierarchical multivariate Bayesian model to analyze the cortical thickness measurement and thinning pattern.	Cortical anatomical changes and altered functional networks are likely related to PD cognitive symptoms.
Paredes et al. [45]	Data from 15 PD patients with large set of spectral features.	Signals sensed from the Deep Brain Stimulation.	A tool to calculate motor and spatio-temporal parameters that affect the quality of life in patients with PD.
Bhalchandra et al. [47]	NeuroSPECT Imaging.	To segment the high-activity regions of the brain.	Accuracy of 99.42% by means of Discriminant Analysis and SVM.
Wu et al. [48]	NeuroSPECT Imaging.	To analyze Auto-Regressive models to describe the stochastic process underlying stride series of idiopathic patients.	Sensitivity of 0.72, specificity of 0.89, and area under the curve of 0.83 using SVM.
Rana et al. [49]	T1-weighted magnetic resonance imaging.	To discriminate PD patients from healthy subjects.	Accuracy of 86.67% using SVM.
Rocha et al. [50]	3D body data acquired from normal and PD patients.	To asses that statistical analysis are useful to distinguish between non-PD and PD patients	Accuracy of 96% concerning the new version of Kinect, as well as 72% considering its former version.
Li et al. [51]	Data from 10 patients (6 men and 4 women) acquired using sensors implanted with DBS devices.	To develop an MRI image segmentation approach using Level Set.	The authors assessed the proposed method has facilitated neurosurgeons in the preoperative process.
Castellanos et al. [55]	Patients with idiopathic and monogenic diseases.	To present an automated method to segment the *substantia nigra* based on Neuromelanin-Sensitive MRI.	Sensitivity of 91% and specificity of 89%.
Gilat et al. [56]	17 patients with FoG and 10 patients without FoG.	Virtual reality paradigm in combination with fMRI.	The results stated the PD patients with FoG show alterations in the blood oxygen level responses.
Illán et al. [58]	208 DaTSCAN images (100 controls and 108 patients).	To evaluate the impact of design elements for the development of a tool to help physicians.	The results showed promising results with an area under the curve of 0.9681 using SVM.
Segovia et al. [59]	189 images (94 controls and 95 pathological images).	To assist automatic PD identification using *in vivo* images of the brain.	Recognition rate of 94.7% using SVM and Partial Least Squares.
Rojas et al. [60]	A 80-DaTSCAN image database.	To assist automatic PD identification using DaTSCAN SPECT images of the brain.	Recognition rate of 94.7% using SVM and Partial Least Squares.
Martinez-Murcia et al. [61]	Three databases: VV, VN and PPMI.	To assist automatic PD identification.	Recognition rate of 94.7% using SVM.
Martínez-Murcia et. al [62]	Two databases: VV and PPMI.	To assist automatic PD identification.	cellcolor[HTML]EFEFEF Recognition rates of 94.7% and 93.1% for VV and PPMI datasets, respectively.
Brahim et al. [63]	127 DaTSCAN SPECT images (68 control individuals and 59 patients).	To assist automatic PD identification.	Recognition rates of 92.91%.

entropy-based dynamic feature selection approach that showed to be effective to remove insignificant features concerning speech pattern classification of PD patients. The authors used Linear Discriminant Analysis to distinguish voice samples between PD patients and health people, thus obtaining an accuracy rate up to 97.5%.

Handojoseno et al. [67] investigated the brain dynamic changes associated with freezing of gait during turning using electroencephalogram (EEG) signals, which were classified via Levenberg Marquardt and Backpropagation Neural Networks. The authors achieved an accuracy of 71%, showing that gait during turning is associated with significant alterations in the high beta and theta power spectral densities across the occipital and parietal areas, being the visual cortex region an optimal reference location for the detection of a turning freeze. According to the authors, this is the first study that shows cortical dynamic changes associated with freezing of gait during turning.

Ertugrul et al. [68] studied a standard approach to PD detection, and proposed one-dimensional local binary patterns (Shifted 1D-LBP) and methods based on mechanical learning. Signals based on gait with different circumstances were employed in the experiments, thus allowing an accuracy nearly to 88.88%. The author states the technique can be successfully employed not only to PD detection, but to detect patterns that were formed by local changes in signals. Smekal et al. [69] carried out an acoustic analysis of hypokinetic dysarthria in patients with PD using a quantitative analysis of vowels in Czech language, introducing a new speech feature based on empirical mode decomposition that increases global performance when combined with the sequential forward feature selection technique. The authors observed an accuracy rate of 94% concerning different vowels identification in PD patients. Mekyska et al. [70] carried out a complex acoustic analysis of phonation in patients with PD focusing on the estimation of the disease progress, being able to identify vowels whose analysis provides best estimation of particular clinical scores used for assessment. The authors introduced a new concept of PD progress quantification based on acoustic analysis of phonation and Random Forests, achieving a sensitivity of 92.86% and specificity of 85.71%.

Ruonala et al. [71] investigated the effects of a commonly used antiparkinsonian medication (levodopa) on cardiac autonomic regulation. The functioning of autonomic nervous system during levodopa medication was examined in patients with advanced PD. Resting state electrocardiogram measurements were performed over 11 patients with idiopathic PD 30 minutes before the administration of levodopa, where the heart rate variability measurements show that parasympathetic nervous system activity is decreased and the sympatho-vagal balance is shifted towards sympathetic control. Later on, i.e. 60 minutes after the administration of levedopa, the parasympathetic nervous system activates slightly, thus causing a decrease in the heart rate.

Arnulfo et al. [72] characterized and compared the spiking and bursting activity in the dorsolateral and ventral subthalamic nucleus sub-regions using intra operative multi-electrode recordings and highly accurate channel localization techniques in PD patients, suggesting the existing functional difference among subthalamic nucleus regions possibly arises from different network connections rather than intrinsic neuronal properties. Dai et al. [73] proposed a novel method based on the empirical mode decomposition to filtered electromyograms (EMG), which makes use of a flexible number of features for PD detection. The signals were preprocessed in three stages by means of a novel bandpass filtering technique in order to show the features are linearly separable. Later, the proposed algorithm was implemented as a mobile application to be more flexible than the existing methods.

Eftaxias et al. [74] presented a new hybrid-constrained complex singular spectrum analysis method for the assessment of Parkinson's tremor by the separation of real EMG signals, in which the characteristics of tremor within a subspace of the single channel surface were measured during the prescribed hand movement (including flexion and extension), and further decomposed using singular spectrum analysis. The method showed a great potential for biomedical multichannel signal processing. Mohammed et al. [75] proposed the use of patient-specific dynamic feature extraction via Local field potential signal combined with adaptive Support Vector Machines that uses the selected features when detecting PD or non-PD patients by adjusting its decision boundary until a suitable model is obtained. The authors achieved a classification accuracy greater than 98%.

Belalcazar-Bolanos et al. [76] proposed the estimation of the different glottal flow features by means of the Iterative and/or Adaptive Inverse Filtering considering the nonlinear dynamic behavior of the vocal folds (Spanish vowels) to detect PD. The authors obtained accuracy rates of up to 75.3%, sensitivity of 0.79, and specificity of 0.72 when all vowels are considered in the experiments. Iuppariello et al. [77] defined a new kinematic index to evaluate the smoothness of the movements based on the minimum-jerk theory. The work aimed at studying the kinematic quality and the motor composition of visually-guided reaching movements from people with PD by applying a submovement decomposition method based on a mixture of Gaussian pulses.

Alekhya and Chakravarthy [78] developed a 2D spiking network to analyze the cognitive aspects of PD during medication and deep brain stimulation. The authors observed the eletrode's position and current spread independently lead to a critical change in performance levels, as well as the work shows that simulated PD “on” medication performed poorly compared to healthy individuals. Thanawattano et al. [79] developed and analyzed the performance of a novel feature based on the hypothesis that PD patients have more temporal fluctuation of tremor while performing resting tasks than action tasks. The signals were acquired via a gyroscope sensor attached to the subject's finger. The tremor fluctuation was defined as the area of 95% of a confidence ellipse covering the two-dimensional signal considering 32 PD and 20 patients diagnosed with Essential Tremor (ET). The proposed work was able to discriminate PD from ET patients with 100% of accuracy. Camara et al. [80] developed an automatic real-time system for resting tremor episode detection in 10 PD patients using fuzzy models. In regard to the classification step, electrophysiological signals obtained from Local field potential (recorded in the STN) and electromyography were adopted, achieving accuracies of 98.7%.

Recent studies have pointed out that besides the freezing of gait, many people with Parkinson's disease also suffer from freezing in the upper limbs (FoUL). In order to investigate whether upper limb freezing and other abnormalities during writing are provoked by gradual changes in amplitude sustained in patients with and without freezing of gait or not, Heremans et al. [81] collected signs of 34 patients with PD, being 17 with and 17 without FoG. The experiments were conducted on a touch-sensitive writing tablet, which confirms the hypothesis that some patients with FoG also suffer from FoUL.

In another paper, Chomiak et al. [82] analyzed patients with FoG by means of a 4th generation iPod Touch sensor in order to capture data from hip flexion and step height. The work examined whether stepping-in-place with a concurrent mental task (e.g. subtraction) can be used as a simple method for evaluating cognitive-motor deficits in people with PD or not. The results indicated that during concurrent tasks, the step height of PD patients with FoG was significantly worse than PD patients with non-freezing of gate and control individuals.

According to Naranjo et al. [83], vocal involvement may be one of the first indicators of PD. Therefore, their work extracted voice recordings and considers an advanced statistical approach to pattern recognition. Basically, the system discriminates people with PD from healthy controls based on acoustic characteristics extracted from voice recordings using the Bayesian classification approach. The results obtained in the experiments show an accuracy rate of 85% when considering all subjects, but this percentage is reduced to 75.3% when considering cross-validation. The results were better for women (87.6%) than for men (70.6%), thus highlighting a need for a tecnhique that should be applied differently for both man and women.

Defazio et al. [84] analyzed 48 people with Parkinson's Disease and 37 healthy subjects by means of voice/speech measurements using the Robertson Dysarthria Profile (RDP), which is a clinical-perceptual method to explore all components potentially involved in speech difficulties. The approach used in this work observed that patients with early PD would theoretically express less severe voice/speech symptoms. The conclusions suggested that RDP may be a useful tool to detect speech/voice disturbances in early PD patients, even when these disturbances do not carry a significant level of disability.

Lancioni et al. [85] evaluated the use of technology-aided leisure and communication tools (music and videos, verbal statements/requests, reading, text messaging, telephone calls and prayers) on three participants with advanced PD that possessed minimal or unreliable motor responses, being unable to operate conventional interface devices. The obtained results were more promissor and relevant given the limited amount of evidence available on helping persons affected by PD with leisure and communication. Braatz and Coleman [15] proposed a mathematical model based on the biochemical systems theory to examine the changes that occur over the course of the Parkinson's Disease, as well as identify the processes that would be the most effective targets for treatment. The model predicts that combined tools might be the most effective ones. Table 3 summarizes the details of the main papers presented in this session.

2.4. Smartphone devices

Mobile devices use features of personal computers that can be extended to cope with profiles of different users. Also, mobile-oriented applications can make use of a number of sensors available at tablets and cell phones, which can measure hand tremors and other movements. Arora et al. [86] evaluated a system based on smartphones in a home and community setting during 35 days to detect and monitor the symptoms of PD. The system was able to assess voice, posture, gait, finger tapping, and response time with mean sensitivity and specificity of 96.2% and 96.9% for the detection of Parkinson's Disease, respectively.

Recently, Ivkovic et al. [87] presented a study about the movement modulation and motor-cognitive integration effectiveness of smartphone-based tactile cues (TC) from different activities in moderately impaired PD patients and healthy individuals, who performed seated heel tapping and straight line walking tasks with and without a secondary motor task. The smartphone-driven TC showed to be a promissor tool and user-friendly movement modulation aid.

Kostikis et al. [88] proposed a smartphone-based system to accurately assess upper limb tremor in 25 PD patients using a phone's accelerometer and gyroscope information to compute a set of metrics that can be used to quantify a patient's tremor symptoms. The authors used machine learning techniques to correctly classify 82% of the PD patients and 90% of the healthy volunteers, being possible to remotely evaluate the patient's condition. The proposed tool has low cost, is platform independent, noninvasive, and requires no expertise to be used.

Bai et al. [89] developed a friendly mobile system using an open-source platform in smartphones to aid PD patients, which features an interactive interface, a large font, a big button, an intuitive graphical interface, an important feature enhancement and some simplified functions, thus being suitable for the elderly people affected by PD. The proposed application also includes an improved main menu composed of several functions like telephone, SMS, internet, medication calendar, photo gallery, and emergency button, as well as a scrollable full screen containing graphical buttons. The application contains a main menu and a reply message voice button function either.

Table 3
Works related to signal analysis.

References	Dataset	Study proposal	Techniques/results
Villa-Canãs et al. [64]	Four-time-frequency approaches based on Wigner-Ville distribution.	To determine whether the features associated to changes in the spectrum can be used to identify the tremor in speech signals of PD patients	Accuracy of 72% when discriminating between PD and healthy speakers.
Chuang [66]	Deep brain stimulation surgery of a patient with Parkinson's Disease.	Fuzzy entropy-based dynamic feature selection approach that showed to be effective to remove insignificant features	Accuracy rate up to 97.5%.
Handojoseno et al. [67]	Electroencephalogram signals.	To investigate the brain dynamic changes associated with freezing of gait during turning.	Accuracy of 71%, showing that gait during turning is associated with significant alterations.
Ertugrul et al. [68]	Signals based on gait with different circumstances.	To propose an one-dimensional local binary pattern approach, as well as methods based on mechanical learning.	Accuracy rate up to 88.88%
Mekyska et al. [70]	Based on complex acoustic analysis of phonation	To investigate the progress of PD using acoustic data	The authors introduced a new concept of PD progress quantification based on acoustic analysis of phonation and Random Forests, achieving a sensitivity of 0.92% and specificity of 0.85.
Mohammed et al. [75]	Patient-specific dynamic feature extraction.	To select features when detecting PD or non-PD patients by adjusting its decision boundary until a suitable model is obtained.	Accuracy of around 98% using SVM.
Belalcazar-Bolanos et al. [76]	Different glottal flow features.	To propose the estimation of the different glottal flow features.	Accuracy rates of up to 75.3%, sensitivity of 0.79, and specificity of 0.72 using Adaptive Inverse Filtering.
Thanawattano et al. [79]	The signals were acquired via a gyroscope sensor attached to the subject's finger.	To develop and analyze the performance of a novel feature based on the hypothesis that PD patients have more temporal fluctuation of tremor while performing resting tasks than action tasks.	Accuracy of 100%.
Camara et al. [80]	Electrophysiological signals.	To develop an automatic real-time system for resting tremor episode detection in PD patients.	Accuracy of 98.7% using fuzzy models.
Naranjo et al. [83]	Data set with voice recordings.	To discriminate people with PD from healthy controls based on acoustic characteristics extracted from voice recordings using the Bayesian classification approach.	The results were better for women (87.6%) than for men (70.6%) using the Bayesian classification.
Camara et al. [80]	Electrophysiological signals.	To develop an automatic real-time system for resting tremor episode detection in PD patients.	Accuracy of 98.7% using fuzzy models.

Kim et al. [90] proposed a novel smartphone-based system using inertial sensors to detect FoG symptoms in an unconstrained way. Several motions such as ankle, trouser pocket, waist and chest pocket, were evaluate. Data obtained and pre-processed via discriminative features extracted from accelerometer and gyroscope motion signals of the smartphone were used to classify FoG episodes from normal walking using AdaBoost.M1 classifier with sensitivity of 86% at the waist, and 84% and 81% in the trouser pocket and at the ankle, respectively.

Ellis et al. [91] evaluated the performance of smartphone-based gait analysis using the smartphone built-in tri-axial accelerometer and gyroscope to calculate successive step times and step lengths, being validated from heel-mounted foot-switch sensors and an instrumented pressure-driven sensor. The authors stated the proposed method was able to serve as an alternative to conventional gait analysis methods. Table 4 summarizes the main papers presented in this session.

2.5. Virtual and augmented reality

Virtual reality is an advanced interface to computer applications, in which users can navigate and interact with a three-dimensional environment generated by computers from multi-sensory devices. Augmented reality is a mixture of real and virtual worlds at some point of reality/virtuality continuous that connects real and virtual environments, as well as overlay virtual objects.

Yang et al. [92] analyzed a home-based virtual reality environment able to improve balance, walking, and quality of life in 23 patients with idiopathic PD. The study did not find any difference between the effects of the home and the virtual reality-based training, which highlights VR is able to build realistic environments that can help dealing with PD. Waechter et al. [93] submitted 16 PD patients to navigation through a customized virtual reality (VR) corridor by stepping in place on a force plate while EEG data was recorded. The VR environment was combined with a cognitive, visual two-stimulus-oddball response task, which was repeated while seated to allow for comparisons to the stepping-in-place condition. The environment proves to be a very efficient and reliable method to induce FoG-like symptoms in a controlled fashion in PD participants with FoG, providing a platform for further experiments on the pathology of freezing of gait. According to the authors, the study was the first of its kind that investigated event-related potential during locomotion in a clinical population. FoG participants demonstrated decreased behavioral performance for the stepping-in-place condition

Table 4
Works based on smartphone devices.

References	Dataset	Study proposal	Techniques/results
Arora et al. [86]	Data acquired during 35 days to detect and monitor the symptoms of PD.	An in-home system based on smartphones able to assess voice, posture, gait, finger tapping.	Mean sensitivity and specificity of 0.96 and 0.96 for the detection of Parkinson's Disease, respectively.
Kostikis et al. [88]	Data acquired using a phone's accelerometer and gyroscope information.	To propose a smartphone-based system to accurately assess upper limb tremor in PD patients.	The authors used machine learning techniques to correctly classify 82% of the PD patients and 90% of the healthy volunteers.
Kim et al. [90]	Data obtained from accelerometer and gyroscope motion signals of the smartphone.	To propose a novel smartphone-based system using inertial sensors to detect FoG symptoms in an unconstrained way.	Classifier with sensitivity of 0.86 at the waist, and 0.84 and 0.81 in the trouser pocket and at the ankle, respectively.

Table 5
Works based on virtual and augmented reality.

References	Dataset	Study proposal	Techniques/results
Yang et al. [92]	A total of 23 patients with idiopathic PD were recruited and underwent twelve 50-minute training sessions during the 6-week training period.	The study tested if the home-based virtual reality balance training is more effective than the conventional home balance training in improving balance.	The two training options were equally effective in improving balance, walking, and quality of life among community-dwelling patients with PD.
Waechter et al. [93]	A total of 16 PD participants with and without clinically confirmed FoG symptoms were recruited.	The author did make use of a customized virtual reality technique, where the individuals stepping in place on a force plate while electroencephalography data was recorded.	The VR environment appears to be a very efficient and reliable method to induce FoG-like symptoms in a controlled fashion in PD participants with FoG.
Khobragade et al. [94]	The parameters are extracted from a non-invasively collected surface electromyography and accelerometer signals in 7 PD individuals.	The author describes the application of the LAMSTAR (LArge Memory STorage and Retrieval) neural network for the prediction of onset of tremor in PD.	A sensitivity of 100% and overall performance better than the previously proposed Back Propagation neural networks are obtained.

while simultaneously performing a secondary cognitive task.

Khobragade et al. [94] applied a Large-Memory Storage and Retrieval neural network for the prediction of onset of tremor in PD patients. The work demonstrated a fully automated deep brain stimulation system that can be applied on-demand, i.e. only when it is needed, since the usual treatments apply that stimulation continuously. Navarro et al. [95] proposed to employ an augmented reality-based approach that has been widely used in the field of rehabilitation to aid PD patients. The experiment was tested on 7 PD individuals, and showed that VR is a simple and suitable tool that should be encouraged to be used in PD patients. Table 5 summarizes the details of the main papers presented in this session.

2.6. Sensors

Jellish et al. [96] examined the ability of persons with PD when using a real-time feedback (RTFB) system to improve gait and postural impairments, being considered the hypotheses that the patients with PD are able to utilize RTFB to maintain their step length compared to their baseline value, and employ RTFB of their back angle to maintain a more upright posture. As such, it is possible to develop RTFB-based technologies and protocols to manage gait and posture during daily activities in clinics and/or at home.

Yoneyama et al. [97] proposed an accelerometer-based gait analysis considering single trunk-mounted accelerometer and an analytical algorithm for the assessment of gait behavior that may be context-dependent aiming to detect gait peaks from acceleration data. The study also aimed the analysis of multimodal patterns in the relationship between gait cycle and vertical gait acceleration. According to the authors, this was the first work that quantitatively demonstrated that PD patients may make different types of decisions on how to walk in daily environments.

Tay et al. [98] developed a wearable wireless PD monitoring and biofeedback system to address the above issues. Each one of the wearable device consists of a accelerometer, gyroscope, compass, flex-sensors, among other sensors, and accompanying communication via bluetooth and wi-fi to transmit data wirelessly to a computer. As such, a wearable gait monitoring system is able to process real-time captured sensory data and FoG events, and then trigger audio and vibration biofeedback to prevent or reduce freezing when FoG has occurred. The system's adaptive gyroscope-based FoG detection algorithm uses automated temporal gait analysis by means of wearable wireless sensors. By using this system, PD patients will be more aware of their risk of falling, and also benefit from the periodic cueing to pace their steps after a FoG occurrence, hence improving their quality of life. The system is mobile and hands-free, which allows the patient to walk freely for long periods of time and distance.

Mazilu et al. [99] investigated the correlation between wrist movement (arm movements) and FoG in PD during walking, and analyzed the possibility to detect FoG from wrist-attached wearable sensors. According to the authors, this is the very first time that wrist movements during walking are correlated with FoG in PD. Beyond this, they computed new features to describe FoG from wrist from ETHOS Inertial Measurement Units (IMU) on both wrists (FoG and wrist movement during the rest of walking) of 11 subjects of the CuPiD dataset. Finally, the authors evaluated the feasibility in detecting FoG using wrist-attached IMU in subject-dependent and -independent evaluation schemes using the FoG detection methods based on supervised machine learning. The work showed that FoG episodes can be detected using the wrist movements with a hit-rate of 90% in a subject-dependent evaluation scheme, suggesting that the wrist sensors can be a feasible alternative to the cumbersome placement on the legs.

Mazilu et al. [100] proposed the use of new sensor modalities to continuously monitor the FoG episodes in PD, being possible to be predicted before it happens by means of physiological data, namely electrocardiography (ECG) and skin-conductance (SC). The authors analyzed the variations of some specific features extracted from both ECG and SC for periods of data right before, during, and right after FoG events. Such features were then compared to normal walking events. Further, the authors deployed an anomaly-based method for predicting gait-freeze events using SC features and multivariate Gaussians, being able to predict 71.3% of FoG episodes with an average of 4.2 s right before that event has happened.

Lorenzi et al. [101] proposed a wireless headset sensing system based on Inertial Measurement Units designed for long-time monitoring of specific movement disorders. The system is composed of a single inertial sensor to be positioned laterally on the head, close to the ear. The headset allows emphasizing signals related to oscillations of the trunk, improving timely detection of the freezing of gait and timely auditory stimulation directly in the ear. With respect to other positions on the body, the headset has the maximum sensitivity to the trunk oscillations made by patients when moving, thus increasing dramatically the risk of falls. The identification of the motion features is performed using an artificial neural network, which obtained excellent results without the need of large number of samples.

Iuppariello et al. [77] tested the hypothesis that muscle vibration of splenius muscles can improve step initiation performance in patients with PD. According to the authors, no study has examined the contribution of proprioception to postural control in PD when a bilateral continue vibration train is applied to neck muscle groups. Thought this study, the authors show that a bilateral continue vibration train, applied to neck muscle groups, reduces postural instability by increasing stepping performance and specific posture related mechanisms, leading to a reduction in hesitation and increasing self-confidence to start walking.

Reinfelder et al. [102] evaluated a robust and automated phase segmentation method of the traditional Timed Up-and-Go (TUG) test, providing phase times for PD patients. The recordings were conducted with the Embedded Gait Analysis using a intelligent system consisting of two IMUs placed unobtrusively at the lateral side of each shoe. Also, the work validated a classification approach using SVM for separating the TUG test into resting (before sit to walk), sit to walk (first torso movement), forward walking (start of walking), first turn (end of forward walking), backward walking (end of first turn), second turn (end of backward walking), turn to sit (end of turning), and resting (end of turn to sit), obtaining an accuracy rate of 81.80%.

Dong et al. [103] proposed a wireless body area sensor network as a non-intrusive device to measure the activity of individuals with PD in order to understand their spontaneous movement in an un-observed environment. Tiny body sensors attached to lower limbs collect position and acceleration data in a periodic manner, and transmit them to a processing and storage node that can store data and transfer the information to the doctor's office via telecom network or wireless local area network. In order to measure the posture changes in a non-intrusively manner, they used low voltage flex sensors, pressure sensors, accelerometers and gyroscopes to build a networked sensor device that can be worn by a person to detect posture and gait changes. Adaptive fractal and frequency domain analysis for cued and spontaneous movements detection were used either.

Jellich et al. [96] presented a study about people with Parkinson's disease that have difficulty while walking, and showed an increased variability in step time and step length, which are associated with higher risk of falls. Based on this rationale, the authors developed a treadmill-based rehabilitation system that has the ability to provide real-time feedback. Their results suggested that persons with PD can effectively follow feedback of posture via the presentation of visual feedback of back angle. Dai et al. [73] develop a sensor-based quantitative assessment method to analyze the features of parkinsonian tremors, where the current possibilities of inertial sensor technology and motion-tracking algorithms can be used to implement quantitative assessments of these tremors. The authors adopted a time-frequency signal analysis algorithm to detect tremor states. Trojaniello et al. [104] proposed a comparative analysis of selected single inertial measurement units for estimating gait temporal parameters in different pathological gait conditions. The results showed the acceleration signals were filtered before being processed using the Z-method. The Z-method, including a preliminary filtering of the acceleration signals, seems to be preferred when analyzing Parkinson's Disease populations.

Yang et al. [92] conducted a study on the correlation of hand tremors using laser signals, i.e. Laser Line Triangulation Measurement (LLTM). The work considered four different modes of hand tremors, being the analysis performed off-line. The results showed a significant correlation among different tremor frequencies. McCandless et al. [105] investigated the effect of three different devices of cueing when applied to 20 PD patients with freezing of gait. Also, 10 cameras and 4 force platforms were used in the experimental section. They compared three devices (Laser Cane, sound metronome and vibrating metronome) against the walking stick and no intervention. In the tests, 12 of 20 patients had freezing incidents. The study identified patterns among the devices, being the best improvement obtained by Laser Cane.

Shao et al. [106] introduced a case study of a 77-years old PD patient with hand contracture. The authors submitted the patient to a therapy using the game “Microsoft Fligth Simulator X”, where the patient reached significant decreasing in the hand contracture. This work proposed an individualized therapy computer-based either. Volpe et al. [107] presented a study about the under water gait therapy. The work used a software that performs a 3D analysis of the gait. After three weeks of under water gait therapy, the results showed significant improvement in the gait speed and cadency.

Finally, Qiang and Marra [108] used the telemedicine to the treatment of PD patients to reduce cost in the travel, as well as to provide a better therapy and patient satisfaction. After the initial treatment, the patients answered a satisfaction questionnaire, and 85% preferred continuing with telemedicine, thus showing the importance of the telemedicine in the patient satisfaction. Table 6 summarizes the details of the main papers presented in this session.

2.7. Web applications

Kraepelien et al. [109] investigated the feasibility and preliminary effects of internet-based cognitive behavioral therapy for depression and anxiety on 9 patients with PD while exploring the effects on non-motor symptoms. Concerns about some PD-specific health and quality of life, insomnia, plus the participant's involvement, satisfaction, and subjective evaluation of the treatment were also considered. The patients reported lower values of hospital anxiety and depression after internet-based cognitive behavioral therapy, but levels of inactivity were rather high. The participants suggested the treatment can be improved by adding more therapist support.

Pasluosta et al. [24] presented a review about some existing wearable technologies and the Internet-of-things applied to Parkinson's disease with an emphasis on how this technological platform may lead to a shift in the paradigm, being mindful the transition that is coming along with the technological revolution. In terms of diagnostics and treatment, they discussed the wearable technologies, their main concepts and applications, as well as the new possibilities using machine learning and artificial intelligence.

Ferreira et al. [110] identified relevant parameters thought assessment tools in six domains (gait, bradykinesia/hypokinesia, tremor, sleep, balance and cognition) using a system to evaluate people with PD at home. Yang et al. [111] evaluated a virtual reality system for balance training at home, which seemed to be more effective than the conventional home balance to improve walking and quality of life in PD. Table 7 summarizes the details of the main papers presented in this session.

3. Dataset description

In this section, we introduce some datasets used in the aforementioned works, as well as how they were designed to cope with Parkinson's Disease.

3.1. HandPD Dataset

The *HandPD Dataset* was designed by Pereira et al. [19], being composed of images extracted from handwriting exams of 92 individuals divided in two groups: (i) the first one contains 18 exams of healthy people, named *control group*, with 6 male subjects and 12 female individuals; (ii) the second group contains 74 exams of people affected with Parkinson's disease, named *patients group*, having 59 male subjects and 15 female ones. The images were collected at the Faculty of Medicine of Botucatu, São Paulo State University, Brazil.

In order to compose the dataset, each subject is asked to fill a form in order to fulfil some task, such as drawing circles, spirals and meanders. Fig. 2 displays an exam of a 56 years-old male patient, in which we can observe the tremor inherent to Parkinson's disease. Note the patient is required to perform 6 distinct activities (a–f), which consist in the repetition of several operations in accordance with certain drawings.

After filling the forms out, they are digitized for the further extraction of spirals and meanders. Such step is performed by hand, where each drawing is cropped to the minimum bounding box (or close to it). Later, the cropped spiral and meander images are numbered as follows: 1, 2, 3, 4 concerning the spirals from left to right, and 5, 6, 7, 8 concerning the meanders from left to right. Therefore, the entire dataset is composed of 736 images labeled in two groups: patients (296) and control (72). Also, the dataset comprises 368 images from each drawing, i.e. spirals and meanders.[5]

[5] http://wwwp.fc.unesp.br/papa/pub/datasets/Handpd/.

Table 6
Works based on sensor.

References	Dataset	Study proposal	Results
Jellish et al. [96]	Eleven subjects (mean age 67 ± 8 years) with mild-to-moderate PD were evaluated.	To present a real-time feedback system to improve gait and postural impairments.	Changes in back angle and step length due to feedback were compared using Friedman non-parametric tests with Wilcoxon.
Yoneyama et al. [97]	They recorded acceleration data from 13 healthy, 26 PD, and 26 mild cognitive impairment or dementia subjects.	To present a gait analysis method developed with new metrics capable of quantifying ambulatory gait and their extraction procedures from acceleration data.	The authors found that the normal, PD, and MCI/dementia groups show characteristic walking patterns, which can be distinguished from one another by the developed gait measure set.
Tay et al. [98]	A total of 8 PD patients had their gait data collected at NNI clinic using the PD logger system streamed to an iPad.	To present a real-time PD monitoring and biofeedback system using low-cost wearable sensors (e.g. accelerometers, gyroscope and magnetic compass).	The developed system aims at aiding the patients to be more aware of the risk of falling.
Mazilu et al. [99]	Experiments on data from 11 subjects.	To investigate the correlation between wrist movement and freezing of gait in Parkinson's disease.	The author states that FoG can be detected only by using data from IMUs attached to the wrist with a hit-rate of 90%.
Iuppariello et al. [77]	Four major scientific databases were searched: the OVIDmedline, CINAHL, PsycINFO, and SCOPUS.	Thought this study, the authors showed that a bilateral continue vibration train, applied to neck muscle groups, reduces postural instability.	Aan average improvement of 52% across all outcome measures.

Table 7
Works based on web applications.

References	Dataset	Study proposal	Techniques/results
Kraepelien et al. [109]	A total of 9 patients with PD with morbid symptoms on the relevant subscale of Hospital Anxiety and Depression Scale (HADS), of either depression (HADS-D > 7) or anxiety (HADS-A > 7) received 12 weeks of internet-based cognitive behavioral therapy (ICBT).	To investigate the feasibility and preliminary effects of ICBT for depression and anxiety in PD.	The results suggested that ICBT could be a feasible way to alleviate depression and anxiety in PD.
Yang et al. [111]	A total of 13 patients in each group were used.	To compare the virtual reality balance training in the participants' home setting.	Virtual reality balance training is more effective than the conventional home balance training.
Ferreira et al. [110]	A total of 233 patients, caregivers and physicians.	A 2-round Delphi study was conducted to select a core of parameters and assessment tools to be applied. This process included patients, caregivers and movement disorders specialists.	An agreed set of measuring parameters, tests, tools, and devices were considered to be part of a system to evaluate patients at home.

3.2. Parkinson's Progression Markers Initiative Dataset – PPMI

The Michael J. Fox Foundation (MJFF)[6] has been an essential driver for the PD biomarkers initiative. Such foundation developed a clinical study to verify progression markers in Parkinson's disease, the so-called *Parkinson's Progression Markers Initiative Dataset* – PPMI, which emerged as a model for following multiple cohorts of significant interest, and it is being conducted at a network of clinical sites around the world. The study is designed to establish a comprehensive set of clinical, imaging and biosampled data to be used to define biomarkers of PD progression. Once these biomarkers are defined, they can be used in therapeutic studies, which is the ultimate goal of this research work.[7]

3.3. Parkinsonian Disease Handwriting Dataset – PaHaw

The *Parkinson's Disease Handwriting Database* – PaHaW[8] consists of multiple handwriting samples from 37 parkinsonian patients, being 19 men and 18 women. In regard to the control group, the dataset contains 38 individuals, being 20 men and 18 women. The database was acquired in cooperation with the Movement Disorders Center at the First Department of Neurology,[9] Masaryk University and St. Anne's University Hospital in Brno, Czech Republic.

Each individual was asked to fill a form, and the completed template was shown to the subjects, as well as no restrictions about the number of repetitions of syllables/words in the tasks or their heights were given. A conventional ink pen was held in a normal fashion, allowing for immediate full visual feedback. The signals were recorded using the Intuos 4M (Wacom technology) digitizing tablet with 200 Hz of sampling frequency.

The signals were digitized on-the-fly, since the individual exerts pressure on the writing surface during the movement. The perpendicular pressure exerted on the tablet surface was also recorded. The recordings started when the pen touched the surface of the digitizer, and finished when the task was completed.

3.4. Parkinson Speech Dataset

The *Parkinson Speech Dataset* database consists of exams performed with 20 PD patients, being 6 female and 14 male. The healthy individuals comprise 20 people, being 10 female and 10 male who appealed at the Department of Neurology in Cerrahpasa Faculty of Medicine, Istanbul University.[10]

From all subjects, multiple types of sound recordings (26 voice samples including sustained vowels, numbers, words and short sentences) are taken. The voice samples are selected by a group of neurologists from a set of speaking exercises that aim at leading to more powerful sound of PD patients [112]. The recording step was achieved

[6] http://www.ppmi-info.org/fundingpartners.
[7] http://www.ppmi-info.org/access-data-specimens/download-data/.
[8] https://www.researchgate.net/publication/289525377_Parkinson's_Disease_Handwriting_Database_PaHaW.
[9] http://bdalab.utko.feec.vutbr.cz.
[10] http://archive.ics.uci.edu/ml/datasets/Parkinson + Speech + Dataset + with + + Multiple + Types + of + Sound + Recordings.

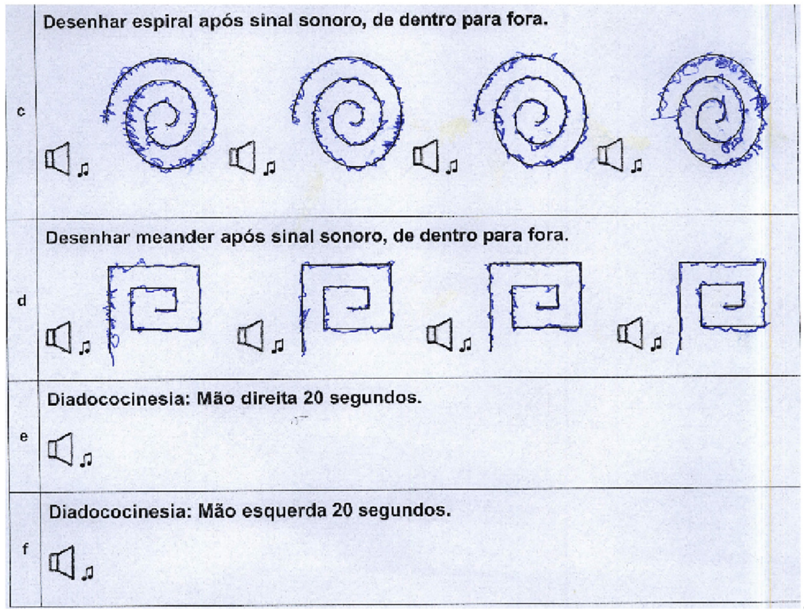

Fig. 2. Handwriting exams filled out by a 56-years old PD patient. Adapted from [19].

by a Trust MC-1500 microphone with a frequency range between 50 Hz and 13 kHz.

During the collection of data, 28 PD patients were asked to say only the sustained vowels “a” and “o” three times, which makes a total of 168 recordings. The test group consists of patients who are suffering from PD for 0 to 13 years, and individual ages vary between 39 and 79.

3.5. CuPiD dataset

The CuPiD dataset contains 24 h of sensing data collected from Inertial Measurement Units [113] attached on both wrists of 18 subjects with Parkinson's disease, which performed different walking protocols in a laboratory setting designed to provoke FoG, including walking with 360- and 180-degrees turns, walking in straight lines and passing narrow corridors, or walking across the crowded hospital halls [114]. The idea was analyze whether the hand movements during walking correlate with freezing of gait episodes or not.

The data collection system contained 9 wearable ETHOS Inertial Measurement Units [115] attached on different parts of the body, one electrocardiogram sensor, a galvanic skin response sensor and a near-infrared spectroscopy sensor. The dataset was designed by collecting data from the IMUs attached on both wrists of the subjects.

3.6. ^{18}F-DMFP-PET dataset

The Fluorine-18 ais a radioisotope, which is an important source of positrons, and desmethoxyfallypride is a moderate affinity dopamine D2 receptor/D3 receptor antagonist often used in medical research [116]. Such substance has been used in human studies [117] as a positron emission tomography (PET) radiotracer. Therefore, such chemical compounds give the name to the dataset.

Introduced in the 80s with main application in the field of oncology, positron emission tomography is focused on neurodegenerative diseases and is currently applied in PD analyzes. Using the neuroimaging modality that allows the analysis of striatal dopamine, the ^{18}F-DMFP-PET database allows assessing the glucose metabolism of the brain, and it contains data from 87 individuals diagnosed with parkinsonism. The image is acquired one hour after the injection of the radiopharmaceutical into the individual to compose the dataset.

3.7. New Spanish speech corpus dataset

The dataset presented by Orozco-Arroyave et al. [118], consists of speech samples used for the analysis of people with PD. Speech recordings of 100 Spanish native speakers were used, being 50 of them diagnosed with PD and the other 50 stand for healthy controls. Also, the data comprises a balanced set with 25 men and 25 women on each group.

The recording of speech has different tasks to analyze the several aspects of the voice of the individual, as the use of the techniques of phonation, articulation and prosody. The experiments were performed using the SVM classifier, obtaining an accuracy of 91.3%. Another experiment considering only the phonation of the 5 Spanish vowels was also considered, and with good results concerning the detection of presence or absence of PD.

4. Discussion

Fig. 3 summarizes the amount of works considered in this review separated by area of interest, where we have: Web Aplication (WA), Sensors, Virtual and Augmented Reality (VAR), Smartphone Devices (SD), Signal Analyses and Processing (SAP), Image Analysis and Processing (IAP) and Machine Learning (ML). Clearly, the great majority of works focus on signal analysis and processing, followed by sensor-based studies. Actually, most works are related to speech analysis, which makes sense to find a number of papers that make use of signal analysis to aid PD recognition. Also, a lot of works employ sensors for data acquisition, thus making signal analysis even stronger.

Although machine learning-related papers are outnumbered by others, a considerable number of works related to signal analysis make use of some sort of artificial intelligence either, thus increasing the number of papers that employ machine learning to aid PD recognition. We have observed that image-based data for PD identification have being poorly explored, since we have the problem of digitizing the forms for the further application of image processing techniques, which are strongly dependent on the quality of the input images, and thus more prone to errors.

Smartphone devices can contribute to alleviate the errors induced during image acquisition by using applications that use touch-based sensors, which digitize the exams in real-time. However, we did not find many works on this subject. The fewer number of papers refers to

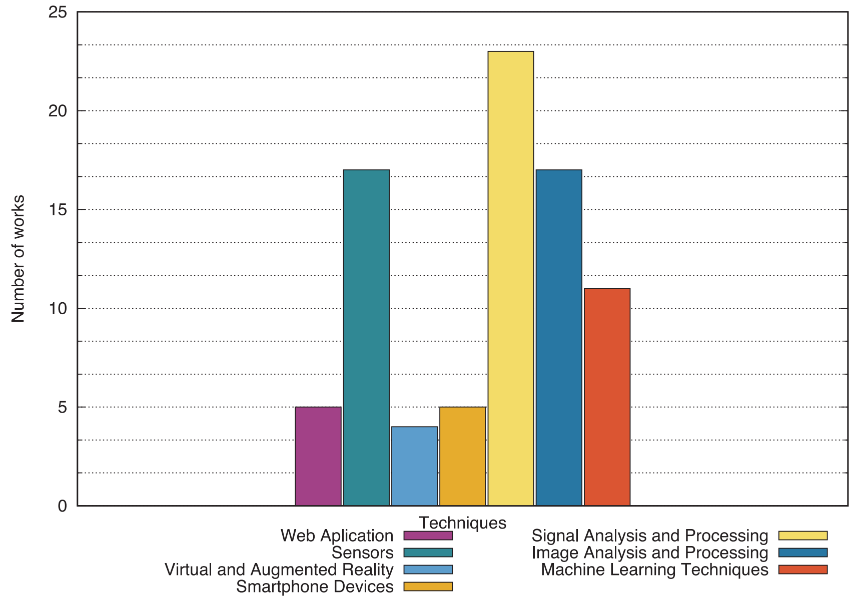

Fig. 3. Summarization of the works considered in this review.

virtual and augmented reality. Although such environments are quite suitable, some of them are expensive to design and maintain. However, in-home devices such as Kinect seem to be a game-changing.

Recently, the NPJ/Parkinson's Disease journal[11] pointed out that both sensors- and smartphone device-based applications to aid PD treatment have grown considerably. With such devices, it is possible to monitor the amount of severity of the disease at home, as well as some therapeutic activities and games can be used for the treatment. Nowadays, tablets and smart phones usually contain a lot of sensors that can measure tremors and orientation. Trister et al. [119] claimed that such mobile-oriented systems would ideally evaluate all aspects of the disease through a series of measures captured on activities, thus being able to consider a more detailed view into the day-to-day variability that patients may describe. Bot et al. [120] used the ResearchKit provided by Apple to collect data from PD patients using an iPhone. The study interrogated aspects of movement disorders by means of surveys and sensor-based recordings from healthy and PD individuals. The authors stated that such works are in the very early beginning.

Actually, some past works have used technology to handle PD treatment either. In 2011, Nemedi et al. [121] presented a web-based system to monitor PD patients remotely. The system was composed of three main parts: (i) a handheld computer to collect data, (ii) a sever for information storage, and (iii) an interface to visualize and interpret the results. Westin et al. [122] presented a system composed of a touch screen-equipped computer for assessment of PD patients at home. The proposed approach highlighted the treatment has been effective in two patients, both in self-assessments, tapping tests and spiral scores.

In 2014, Hariharan et al. [13], presented a study about PD identification using a hybrid approach composed of Gaussian Mixture Model, Principal Component Analysis, and several other techniques over University of California-Irvine (UCI) machine learning datasets. The experiments showed the combination of feature pre-processing, feature reduction/selection methods and classification leads to very good results.

5. Conclusions

In the last years, the amount of people with Parkinson's Disease has increased considerably, which turns out to be one of the world's major health problem up to date. The use of artificial intelligence and machine learning techniques have presented promising results, thus becoming a fundamental aid to cope with PD early detection.

In this work, we presented a review concerning Parkinson's Disease detection and monitoring by means of recent technologies. The main contribution of this work is to consider very recent works dating from 2015 and 2016 mostly. Several approaches based on image and signal analysis, smartphone devices, virtual and augmented reality, sensors and web-based application were considered, as well as some datasets widely used in the literature.

We have observed the great majority of works make use of signal analysis, which are often acquired by on-body sensors, thus making both kind of tools the most used ones in the papers considered in this review. Also, machine learning-driven works have been widely referred either, since most works, even using signal- or image-based data, require some sort of decision-making mechanism supported by artificial intelligence. Similarly, we believe the smartphones and tablets will begin to play an important role in the future, since e-health research kits are constantly being developed, and to monitor patients at home seems to be the most promising direction towards Parkinson's Disease understanding.

Conflict of interests

The author declares that they have no conflict of interest.

Acknowledgements

The authors are grateful to FAPESP grants #2013/07375-0, #2014/16250-9, #2014/12236-1, and #2016/19403-6, Capes, as well as CNPq grants #470571/2013-6, #306166/2014-3, #301928/2014-2, #304315/2017-6, and #307066/2017-7. This material is based upon work supported in part by funds provided by Intel® AI Academy program under Fundunesp Grant No.2597.2017.

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