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# Artificial intelligence for assisting diagnostics and assessment of Parkinson's disease—A review

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ABSTRACT

Artificial intelligence, specifically machine learning, has found numerous applications in computer-aided diagnostics, monitoring and management of neurodegenerative movement disorders of parkinsonian type. These tasks are not trivial due to high inter-subject variability and similarity of clinical presentations of different neurodegenerative disorders in the early stages. This paper aims to give a comprehensive, high-level overview of applications of artificial intelligence through machine learning algorithms in kinematic analysis of movement disorders, specifically Parkinson's disease (PD). We surveyed papers published between January 2007 and January 2019, within online databases, including PubMed and Science Direct, with a focus on the most recently published studies. The search encompassed papers dealing with the implementation of machine learning algorithms for diagnosis and assessment of PD using data describing motion of upper and lower extremities. This systematic review presents an overview of 48 relevant studies published in the abovementioned period, which investigate the use of artificial intelligence for diagnostics, therapy assessment and progress prediction in PD based on body kinematics. Different machine learning algorithms showed promising results, particularly for early PD diagnostics. The investigated publications demonstrated the potentials of collecting data from affordable and globally available devices. However, to fully exploit artificial intelligence technologies in the future, more widespread collaboration is advised among medical institutions, clinicians and researchers, to facilitate aligning of data collection protocols, sharing and merging of data sets.

## 1. Introduction

Healthcare is one of the most prominent fertile fields for development and implementation of advanced and emerging technologies, including artificial intelligence, wearable sensors, augmented and virtual reality, 3D printing and others [1–6]. Artificial intelligence (AI) is a growing field covering a wide range of technologies that aim to imitate cognitive functions and intelligent behaviour of humans [1]. AI is now ubiquitous, showing extraordinary abilities in countless areas, from autonomous vehicles to robot-assisted surgery. Although AI is a broad field, its recent growth has been greatly brought by new advances and improvements in machine learning [4]. Machine learning (ML) represents a subset of AI and includes powerful algorithms that provide systems with the ability to explore and find patterns within data, classify and predict outcomes by learning through experience [4]. ML has also found its significant place in healthcare, contributing to diagnostics, disease management, progression monitoring and outcome prediction [1]. This sort of approach has also penetrated neurology. ML algorithms coupled with wearable devices have addressed different challenges regarding neurodegenerative movement disorders, including Parkinson's disease (PD) [7].

A study investigating the accuracy of traditional methods for clinical diagnosis, using post-mortem neuropathological examination, found a clinical diagnosis of PD to have sensitivity and specificity of 88% and 68%, respectively [8]. Early diagnosis was particularly unreliable, correctly recognizing as PD only 26% of patients who were untreated or not clearly responsive, and 53% of those responsive to medication. The most important clinical features of PD are tremor, bradykinesia, rigidity, and postural instability [9]. These motor symptoms affect upper and lower extremities and hinder patients'

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performance of everyday routine tasks, which can be visible from the earliest stages of the disease. Therefore, evaluation of these symptoms through analysis of body movements represents a very important part of the clinical assessment and diagnosis of PD.

Since reliable diagnostics and early stage detection are one of the top priorities in medical practice [10], a lot of effort is being invested in the development of new methods for diagnostic support, which would increase the accuracy and minimize required time and resources. Information on the patient's condition (ON/OFF states, the occurrence of dyskinesias, falls) and symptoms (tremor, bradykinesia, freezing of gait) outside of clinical settings could provide physicians with deeper insight into patients' disease severity and progress, setting the path towards fully personalized treatment. Support tools based on the use of ML have great potential for clinical practice increasing accuracy, reliability and efficiency of clinical decision making and assessment [11]. Machine learning approaches are frequently used for outputting a diagnostic suggestion, using data collected from various media [12]. In addition, ML has found its application in real-time, remote monitoring and detection of PD severity, symptoms and response to therapy.

The aim of this paper is to give a comprehensive, high-level overview of the benefits that AI and specifically ML have brought to diagnosis and management of PD, as well as instrumentation and technologies which enabled it.

## 2. Methods

Selection criteria for presented publications were based on the implementation of machine learning algorithms for diagnosis and assessment of PD using data describing body motions, including movements of upper and lower extremities and whole-body movements. The search included both conventional machine learning and deep learning algorithms [13]. Most of the included studies applied conventional machine learning algorithms with supervised learning for finding desired patterns in the collected, labelled data. Those algorithms use hand-crafted features, extracted from the raw data by means of different signal processing techniques. In this paper, we included some of the most commonly used algorithms: Support Vector Machine - SVM (both linear and non-linear), Support Vector Regression - SVR, Naïve Bayes - NB, Logistic Regression – LR, Artificial Neural Network – ANN (including Probabilistic Neural Network – PNN, Radial Basis Function Neural Network – RBF NN, Extreme Machine Learning – EML and Dynamic Neural Networks - DNN), k-Nearest Neighbours - kNN, Linear Discriminant Analysis - LDA, Tree-based algorithms - TREE (including Decision Trees – DT, Random Forest – RF, Random Trees – RT, Ada Boost DT, C4.5 DT, BAG DT), Hidden Markov Models – HMM, Evolutionary algorithms (EVOL), whereas some researchers applied ensembles of different algorithms (ENS). Studies that are included are providing meaningful results, i.e. contributing to the challenges that need to be resolved in terms of detection and classification performance and providing promising results for remote monitoring of disease symptoms and response to therapy. The performance criteria were analysed together with dataset size and used instrumentation. We have selected the papers that included PD patients with specified disease stage and scores, such as Hoehn and Yahr score (H&Y), Unified Parkinson's Disease Rating Scale (UPDRS), especially part III that covers examination scores for upper and lower extremity motions [14]. The diagnosis was considered as early if the recruited patients had a H&Y score of 2 or less, unless stated otherwise. The observed instrumentation included systems providing arms and legs kinematic data, which included wearable systems and camera motion capture systems. We surveyed papers published between January 2007 and January 2019, within online databases including PubMed, Science Direct, and more, using combinations of the keywords given below. Articles were restricted to the English language. The initial query yielded 1100 papers and was filtered to 488 by the scope/subjects/methodology, from which 48 articles were found to be relevant and match our criteria. The following keywords were used for searching the literature: *Machine learning, deep learning, artificial intelligence, intelligent devices, smart systems, classification, pattern recognition, data mining.* The above keywords have been combined with the following: *neurodegenerative disorders, movement disorders, Parkinson's disease, wearables, diagnostics, freezing of gait, kinematic analysis, upper extremities, lower extremities, inertial sensors, motion capture, UPDRS, tremor, finger tapping, leg agility*.

## 3. Results

Based on the search and stated selection criteria, 48 publications were found which matched the abovementioned criteria and successfully applied ML to kinematic datasets acquired from patients with PD, 20 of which analysed upper extremity kinematics, 15 papers considered lower extremity kinematics, and 13 analysed kinematics of full body (upper and lower extremities concurrently). The implementation of ML for PD is organized in two subgroups: 1) algorithms for diagnostic support and 2) algorithms for disease monitoring and kinematic assessment.

### 3.1. Upper extremities

Intelligent algorithms are often applied on kinematic signals acquired from upper extremities of patients with PD for provision of additional diagnostic support, assessment of therapeutic effects and monitoring and evaluation of motor symptoms, especially hand tremor and bradykinesia [15,16].

Numerous research groups have investigated the implementation of different algorithms and instrumentation, as well as tested various protocols in order to find the optimal solution which would provide the best possible results in early-stage diagnostics, assessment of disease severity and monitoring, as well as PD progress prediction [15].

#### 3.1.1. Assisting diagnostics with advanced hand motion analysis techniques

A lot of effort has been put into the development of systems that use advanced algorithms for diagnosis and early diagnosis of PD based on the properties of hand movements. By using simple instrumentation, such as standard computer keyboards [17–19], smartphone integrated inertial sensors [20–22], electromagnetic sensors [23], wearable inertial sensors [24] and video camera [25], researchers have gathered motion data describing different tasks that are traditionally used for evaluation of PD in clinical settings. This primarily includes analysis of finger tapping and action/rest tremor tasks included in the standardized clinical UPDRS scale, part III [14]. Literature suggests that machine learning algorithms significantly improve differentiation between PD patients and healthy participants compared to results achieved in clinical practice. Studies differ in the number of recruited subjects, disease stages, applied analysis and instrumentation, showing increased accuracy of classification between PD patients and healthy controls (HC) for more advanced disease stages and larger datasets. The implementation of ML algorithms for PD diagnosis and their results when applied to upper limb kinematic data are shown in Fig. 1 (upper panel). Each study is shown as an individual marker, coded with shape, size and colour, representing different instrumentation, number of patients and performance measures respectively. The performance is presented in terms of sensitivity (Se), specificity (Sp) and accuracy (Ac). The figure shows the most frequently used or the most successful supervised ML algorithms obtained as a representative subset of all reviewed publications. Columns are organized alphabetically according to the used algorithm: ANN, ENS, EVOL, kNN, LR, NB, SVM and TREE.

Interesting observations can be made when comparing the sensitivity and specificity of the results obtained by some algorithms. Diagnostics based on tremor recordings provided by smartphones and processed by NB, LR and SVM algorithms provided the Se:Sp ratio of 56%:100%, 74%:100%, 56%:100%, respectively, proving these algorithms to have high credibility for identifying HC from PD, but leaving

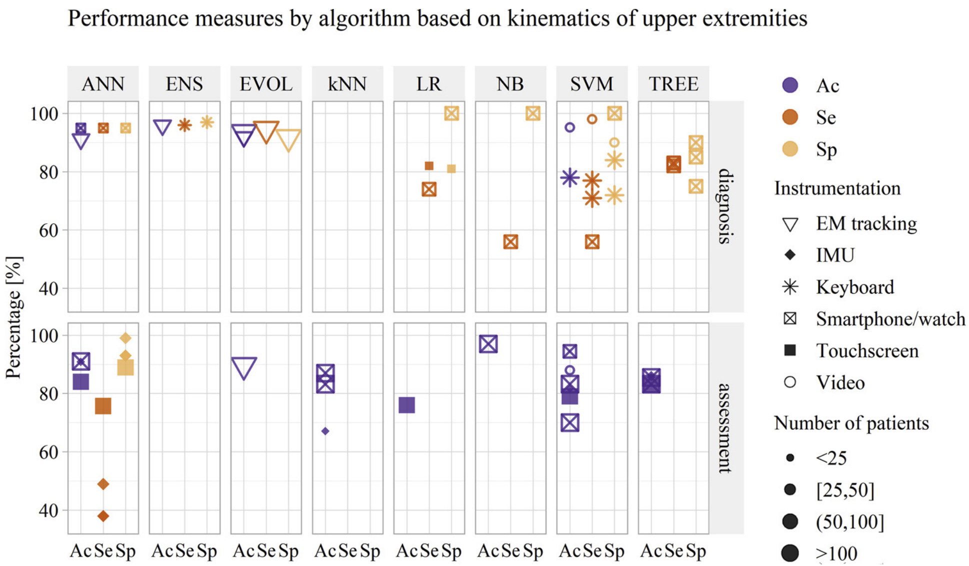


**Fig. 1.** Implementation of machine learning on upper extremity kinematic data for diagnosis (upper panel) and assessment (lower panel), showing top ML algorithms (one in each column), their performance (the horizontal axis shows the presented measure, the vertical axis shows its percentage value), used instrumentation (indicated by marker shape), and number of patients (indicated by marker size). ANN – Artificial Neural Network; ENS – Ensemble of different algorithms; EVOL – Evolutionary algorithms; kNN – k-Nearest Neighbours; LR – Logistic Regression; NB – Naïve Bayes; SVM – Support Vector Machine; TREE – Tree-based algorithms; Ac – Accuracy; Se – Sensitivity; Sp – Specificity; EM tracking - Electromagnetic tracking; IMU – Inertial Measurement Unit.

certain doubt as for whether all PD could be diagnosed [22]. BAG DT, AdaBoost, and C4.5 algorithms gave comparable results, and showed increased sensitivity and decreased specificity compared to the previous three algorithms [22], concretely with Se:Sp ratios of 82%:90%, 83%:85% and 83%:75%, respectively. When it comes to early diagnostics, researchers reported Ac = 95% based on tremor analysis using smartphone and Artificial Neural Networks [20], and Se = 96% paired with Sp = 97% based on keyboard typing analysis using an ensemble of 8 different ML models [18]. However, comparing algorithm performance is highly sensitive to the collected dataset and its pre-processing, as shown by Giancardo et al. [17] and Arroyo-Gallego et al. [19] who used a standard keyboard and SVR algorithms to detect early PD, and achieved Se:Sp of 71%:84%, and 77%:72%, respectively. It is particularly interesting that these results were achieved using recordings made by standard smartphones or computer keyboards which are nowadays globally present and affordable. This means there is a much greater potential for implementation of such standardized procedures in any setting - clinical or home, city clinic or rural medical office.

#### 3.1.2. Following disease progress and response to therapy

Another approach to this topic includes the use of intelligent algorithms for objective assessment of motor symptoms and a more efficient evaluation of disease severity based on the standard clinical tests. In clinical practice, those tests are visually observed and assessed by physicians, which may result in rough resolution and subjective evaluation [26]. Researchers have therefore been working on the development of ML-based systems for objective and automated evaluation of symptoms severity based on the standardized motor tasks, including tremor [27,28] and finger tapping [25,29] or other repetitive motions [30]. As the input to those intelligent algorithms, researchers have provided features describing clinically important parameters, such as tremor frequency [27], rhythmicity, frequency and amplitude of repetitive movements [30]. In Fig. 1, lower panel, we present results for most commonly used supervised ML algorithms for assessment of PD patients based on the upper extremity kinematic data. Results are presented in a similar manner as in Fig. 1, upper panel.

Cloud-based mobile applications that use ML have also been developed with the aim of increasing efficiency of examination of patients' motor abilities and symptoms severity [31,32]. Stamate et al. [32] developed CloudUPDRS - a mobile application that allows remote recording of UPDRS tasks, such as tremor, finger tapping, and gait. It integrates a deep learning algorithm for discrimination between high and low-quality recordings. Machine learning is also applied for detection and classification of patients' conditions and everyday activities [33,34] which can provide insight into medication efficiency and provide information that can be crucial for a patient-tailored treatment plan. Fisher et al. [34] applied Artificial Neural Networks on data derived from a wrist-worn accelerometer for automatic detection of asleep, ON, OFF and dyskinesia states in home settings. The results showed that different ON/OFF states and dyskinesia can be detected with low Se and high Sp (above 80%). Comparable results were obtained using deep learning algorithms [33]. Both conventional machine learning [35,36] and deep learning algorithms [36] were used for the detection and classification of bradykinesia and dyskinesia with high accuracy (ranging from 84% up to 90%).

### 3.2. Lower extremities

Advanced algorithms have also been applied to the development of new diagnostic and assessment systems that are based on the motion of the lower extremities [15]. Different approaches have been taken, covering a wide range of algorithms and instrumentation. In this paper, the focus is given on the use of ML algorithms for diagnostics, especially early-stage diagnostics, prediction and detection of motor symptoms influencing normal walking (such as freezing of gait, falls), prediction of disease severity and assessment of therapy response [15,16].

#### 3.2.1. Assisting diagnostics with advanced gait analysis techniques

Research groups have been working on developing the optimal algorithm for accurate diagnostics of PD, implementing different machine learning algorithms to datasets collected from infrared cameras (Kinect or motion capture with optical markers) [37–40], force sensors placed in shoe insoles or integrated into sensor walkways, [41–44], and inertial sensors positioned on leg segments, waist, or integrated in smart shoes [45–51]. A significant contribution was provided by studies that focused on algorithms for early PD diagnostics, where the kNN algorithm reached Ac = 85.5% [51]. Using SVM provided 85% or higher accuracy, confirmed by different studies [42,43]. LDA algorithm obtained Se:Sp of 88%:86% for early-stage PD diagnostics (defined by UPDRS score below 15) using walking data, while both parameters for mild stage PD (defined by UPDRS score above 20) were 100% using features extracted from data describing three different exercises [47]. Using RBF NN provided Se, Sp and Ac of 96.77%, 95.89%, and 96.39%, respectively, when applied on a PhysioBank dataset which included 93 PD patients with moderate or early disease stage [44]. In Fig. 2, upper panel, we present results for most commonly used supervised ML algorithms for assisting diagnosis of PD patients based on lower extremity kinematic data. Results are presented in a similar manner as in Fig. 1.

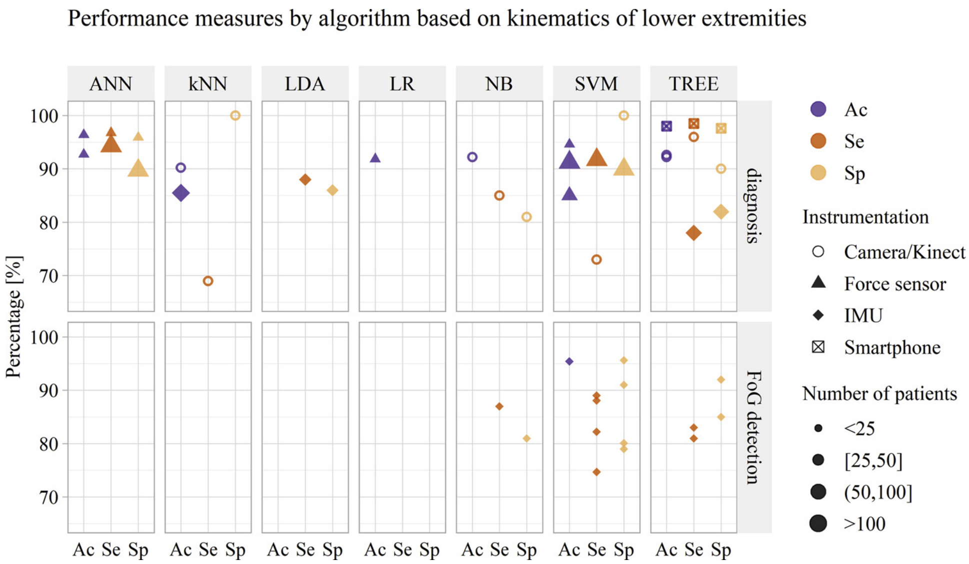


**Fig. 2.** Implementation of machine learning on lower extremity kinematic data for diagnosis (upper panel) and FOG detection (lower panel), showing top ML algorithms (one in each column), their performance (the horizontal axis shows presented measure, the vertical shows its percentage value), used instrumentation (indicated by marker shape), and number of patients (indicated by marker size). ANN – Artificial Neural Network; kNN – k-Nearest Neighbours; LDA – Linear Discriminant Analysis; LR – Linear Regression; NB – Naïve Bayes; SVM – Support Vector Machine; TREE – Tree-based algorithms; Ac – Accuracy; Se – Sensitivity; Sp – Specificity; IMU – Inertial Measurement Unit.

#### 3.2.2. *Following disease progress and response to therapy*

Another major field of application for machine learning algorithms is detection and prediction of freezing of gait (FoG) and falls. Wearable sensors have been particularly exploited [52], owing to their suitability for home use and recording along complicated paths with turns, doorways and narrow walkways. Sensors are typically mounted on the legs and waist [53–55], but sometimes also on the wrist and chest [56,57]. As smartphones have profoundly infiltrated our daily lives, with integrated inertial sensors, they also found their role as unobtrusive FoG detection equipment and gait-based diagnosis assistants [58]. Integration with a smart watch has also been suggested [59]. One of the most frequent approaches for FoG detection was using SVM algorithms. Polynomial kernel SVM provided Sp = 91% and Se = 89% for FoG detection, whereas these measures were Sp = 88% and Se = 75% for prediction of FoG events [55]. Other algorithms implemented for the same application were NB, RF, kNN, ANN, linear SVM and Extreme Gradient Boosting, but their performance was found to be lower compared to Polynomial kernel SVM [55]. Another study compared the performance of generalized and personalized FoG detection models based on SVM algorithms and showed that the generalized model reached Sp = 79% and Se = 74.7%, compared to Sp = 80.1% and Se = 88.1% obtained for personalized algorithms [54]. Using non-linear SVM introduced lower performance compared to linear SVM, showing accuracy of Ac = 94.2% compared to Ac = 95.4% [53]. Prediction of incoming FoG would further improve its management. Mazilu et al. [60] worked on identifying patterns in motion data using unsupervised learning, but they found significant variations between subjects. In Fig. 2, lower panel, we present summary results for the most commonly used ML algorithms for FoG detection in PD patients based on lower extremity kinematic data. Results are presented in a similar fashion as in Fig. 1.

Studies estimated fall frequency as well as demographic and clinical factors related to falling in a cohort of Serbian patients with PD and showed that 60% of 300 observed patients had falls in the 6-month period prior to the study [61,62]. Therefore, ML algorithms and smart wearable technologies found a significant role in fall detection and prediction. Although threshold-based algorithms are easier to implement and they are less computationally demanding, machine learning methods are prevalent due to much better prediction rates [63]. As for the type of systems used, wearable and camera-based systems are predominant methods for fall detection, the former being favoured [63,64].

Another implementation of ML for gait was shown by Jane et al. [41] who designed an automated scale for detecting the severity of gait disturbances according to the H&Y scale using a Q-backpropagated time-delay neural network on data collected by wearable sensors with the accuracy of about 90%. A SVM classifier was applied in one of the phases of the motor fluctuation (ON/OFF) detection using gait data recorded by 3D accelerometer sensor, which resulted in both Se and Sp above 90% [65]. Deep brain stimulation (DBS) effects on ground reaction force data were also assessed with machine learning algorithms: PNN, LR, and SVM, showing the positive effect of DBS on walking patterns, especially combined with medications [66].

### 3.3. *Upper and lower extremities*

Some research groups used data from both upper and lower extremities to analyse motion and extract features for early or mild PD diagnostics [38,46,49], PD staging [49,50], detection of FoG and/or dyskinesia [56,67], tremor [67–69], bradykinesia [58,68], as well as to perform assessment of dose-responsive dyskinesia [67].

A combination of inertial sensors on the dominant limbs with some other sensors (vibration, infrared, magnetic door, ambient light) on the dominant arm recorded data during daily activities for discerning between HC, PD patients with and without cognitive impairments, and patients with cognitive impairment (but no PD) [38]. Different results were reported, showing that these four groups can be discriminated with accuracy of 86% using the AdaBoost DT algorithm. Comparison of HC and PD patients based on inertial data acquired from upper and lower body parts resulted with accuracy ranging from 79.62% to 84.1% for LDA, NB, kNN, SVM (linear), SVM (non-linear) and DT, and accuracy above 90% for an ensemble of classifiers [50]. The authors also used SVM for discrimination between HC and PD patients with H&Y I, H&Y II, H&Y III with the accuracy of 94.5%, 87.75%, 93.63%, respectively. Other studies compared results for diagnosing PD patients with three disease stages based on a combination of H&Y and UPDRS scores (mild, moderate and severe) using inertial motion data from legs and wrists, with the help of three classifiers: EML, PNN, and kNN [49]. By using the kinematic data from upper and lower limbs, estimation of tremor severity was performed with HMM classifier achieving accuracy of 87% [69]. Tremor, bradykinesia, and dyskinesia can be assessed with performance above 90% using the SVM [68] and DNN [67]. Similar results were reported for FoG detection, reporting accuracy above 90% for NB, RF, DT and RT classifiers. In Fig. 3, we present results for most commonly used or most successful ML algorithms for diagnosis and assessment of PD patients based on both upper and lower extremity kinematic data. Results are presented in a similar manner as in Figs. 1 and 2.

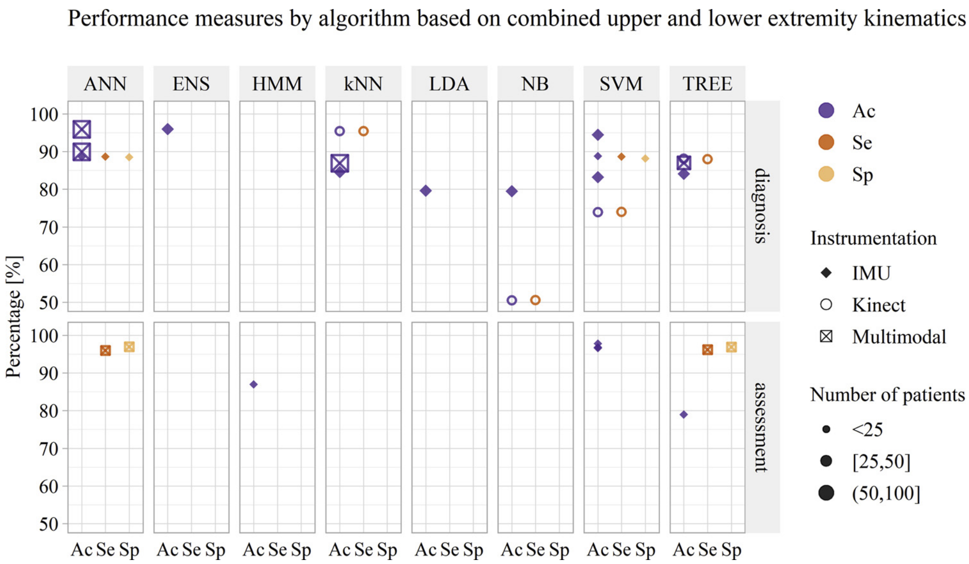


**Fig. 3.** Implementation of machine learning on both upper and lower extremity kinematic data for diagnosis (upper panel) and assessment (lower panel), showing top ML algorithms (one in each column), their performance (the horizontal axis shows presented measure, the vertical shows its percentage value), used instrumentation (indicated by marker shape), and number of patients (indicated by marker size). ANN – Artificial Neural Network; ENS – Ensemble of different algorithms; HMM – Hidden Markov Models; kNN – k-Nearest Neighbours; LDA – Linear Discriminant Analysis; NB – Naïve Bayes; SVM – Support Vector Machine; TREE – Tree-based algorithms; Ac – Accuracy; Se – Sensitivity; Sp – Specificity; IMU – Inertial Measurement Unit.

**Table 1**
A selection of papers providing promising results for different applications based on movements of different body parts, using different instrumentation, protocols and algorithms.

| Ref. | Goal | Type of observed motion | Body part | Instrumentation | Subjects | Algorithm | Best performance [%] | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Sp | Se | Ac |
| [29] | Diagnosis | Finger tapping | Up | EM tracking | 107 PD, 49 HC | EVOL | 91.8 | 94.6 | 93.5 |
| [18] | Diagnosis | Typing | Up | Keyboard | 20 PD (mild), 33 HC | ENS | 97 | 96 | |
| [20] | Diagnosis | Arm movements at rest, waving and walking | Up | Smartphone | 21 PD (> 1 year), 21 HC | ANN | 95 | 95 | 95 |
| [25] | UPDRS scoring | FT | Up | Video | 13 PD (UPDRS: 0-3) | SVM | | | 88 |
| [27] | UPDRS scoring | Hand tremor | Up | Smartphone | 52 PD | NB | | | 97 |
| [29] | UPDRS scoring | FT | Up | EM tracking | 107 PD, 49 HC | EVOL | | | ≥89.7 |
| [44] | Diagnosis | Gait | Low | Force sensor | 93 PD (mild and early), 73 HC | ANN | 95.89 | 96.77 | 96.38 |
| [45] | Diagnosis | Gait, Posture | Low | Smartphone | 10 PD, 10 HC | RF | 97.6 | 98.5 | 98.0 |
| [51] | Diagnosis | Gait | Low | IMU | 156 PD, 424 HC | kNN | | | 85.51 |
| [53] | FoG detection | Gait | Low | IMU | 20 PD (H&Y > 2) | Linear SVM | 95.6 | 82.2 | 95.4 |
| [40] | Diagnosis | Gait | Low | Camera system & force plate | 23 PD (H&Y: 2), 26 HC | RF | 90 | 96 | 92.6 |
| [67] | Classification of severity of motor disorders | Unconstrained activity | All | Multimodal | 19 PD, 4 non-PD | ANN | 97.1 | 94.9 | |
| [68] | Assessment | FtN, FT, HOC, HT, SIT, HA | All | IMU | 12 PD (H&Y: 2-3) | SVM | | | > 95 |
| [58] | Diagnosis | Gait, Posture, FT, RT | All | Smartphone | 10 PD, 10 HC | RF | 96.9 | 96.2 | |
| [50] | Diagnosis (PD - H&Y I) | Gait | All | IMU | 27 PD (H&Y:1-3), 27 HC | SVM | | | 94.5 |

PD – Parkinson's disease; HC – Healthy controls; UPDRS – Unified Parkinson's disease Rating Scale; H&Y – Hoen and Yahr scale; ANN – Artificial Neural Network; EVOL - Evolutinary algorithms; ENS – Ensemble of different algorithms; kNN – k-Nearest Neighbours; NB – Naïve Bayes; SVM – Support Vector Machine; RF – Random Forest; Ac – Accuracy; Se – Sensitivity; Sp – Specificity; IMU – Inertial Measurement Unit; EM tracking – Electromagnetic tracking; FtN – Finger to nose; FT – Finger tapping; HOC – Hand opening/closing; HT – Heel tapping; SIT – Sitting; HA – Hand alternating; RT – Reaction time.

The summarized results are presented in Table 1. The table comprises selection of papers presented in the review which are providing promising results for diagnosis and assessment of PD patients, using different algorithms, measurement protocols and instrumentations recording kinematic data from different body parts.

## 4. Discussion

In this paper, we presented some of the most prominent results from the field of artificial intelligence, specifically machine learning, applied with the goal of providing a more precise diagnosis and assessment of patients with PD. The paper focused on the implementation of commercial and off-the-shelf instrumentation for capturing motor patterns of upper and lower extremities.

The obtained results were found to be comparable for different sensor systems, which proves their equal potential for practical use in terms of classification and detection accuracy. However, the applicability of camera and motion capture systems are limited because they are more expensive and require dedicated space for recording. On the other hand, wearable sensor devices are affordable and allow monitoring in any environment. As shown, smartphones are also frequently used without any additional instrumentation, since they already have integrated inertial sensors, and they are globally available, enabling the easy realization of various assessment and assistive applications. They are an inexpensive option with simple wireless data transmission [71]. Although the quality of the sensors differs for different models, and battery life can be a burning issue, the obtained high accuracy results paired with usability and affordability, make smart wearable devices an important part of the future development of the telemonitoring of PD.

Machine learning applications in this field can be divided into two subgroups: 1) diagnostic support and 2) disease monitoring and assessment. The most commonly used algorithms are Support Vector Machine, k-Nearest Neighbours, Naïve Bayes, Artificial Neural Networks, Linear Discriminant Analysis, Tree-based algorithms (which includes Decision Trees, AdaBoost DT, Random Forest, Random Trees, and others).

Research has shown that simple wearable instrumentation in combination with supervised machine learning algorithms can provide significant diagnostic support and discriminate between PD patients and healthy subjects with accuracy above 90%. Artificial Neural Network proved to be the most successful algorithm for early diagnostics, reporting accuracy above 95% using features extracted from gait force patterns. This is especially important, since in early disease stages motor symptoms are not clearly visible and with delayed diagnostics the progression of the disease is unbridled. High-accuracy results are also obtained for detection of motor symptoms, disease stage and severity. Prediction of symptoms severity was successfully applied using various algorithms and sensors. However, Support Vector Machine combined with IMUs proved to be the most successful approach, with accuracy above 95%, as demonstrated for tremor, bradykinesia and dyskinesia.

The presented results could be considered as pilot studies for future full-scale implementations. Although numbers of participants in the presented studies are typically sufficient for finding statistical significances between groups, having few dozens of patients is not enough for full exploitation of machine learning and even less for deep learning algorithms. In addition, some analysed datasets consisted of simulated data (e.g. falls), usually with young people as subjects, contrary to the users and real-life situations they are designed for [63]. Furthermore, results obtained with different methodologies cannot be completely comparable if the recording conditions and applied methodologies are too diverse. Another challenge in the implementation of AI and ML can be incomplete or inappropriately labelled data. For the assessment of the disease symptoms, each recording must be correctly annotated, which is especially hard for recordings outside clinical settings. In cases where clinicians are not sure of the diagnosis (early disease stages), the provided reference labels may be incorrect, which could cause algorithms to learn wrong patterns from the data. One of the future strategies should include collecting data from multiple sources (different research groups, medical institutions, cities or countries) but with systematically and precisely defined methodologies in terms of used instrumentation, sensor placement and position, signal length, recording protocols, testing, data storing, and structured reporting [72].

There are already some relevant publicly available databases, such as PhysioNet, a database that contains ground reaction force data obtained during walking from 93 participants with mild to intermediate PD, and 73 HC, which allowed several research groups to test and verify their methods [41,42,44] As part of the FP7 project REMPARK, funded by the European Community, a database with movement data from 93 PD patients was developed for the assessment of motor symptoms and conditions [73]. The database contains information from three sources: annotations or data labelling, video recordings of patients' performance and data collected from wrist and waist worn inertial sensors. There are some available databases that contain clinical data for more than 8000 patients (out of which several thousand are PD), however, no similar database (in terms of size) comprising kinematic data is available [74]. Given these limitations, the validation of sensor-derived assessment and diagnostics of PD would benefit from increased and widespread collaboration among different research groups. Aligning data collection protocols, and sharing data sets among researchers would provide a good basis for the development of large-scale databases and more precise and clinically acceptable algorithms.

## 5. Conclusion

This systematic review presents an overview of studies investigating the use of artificial intelligence, specifically machine learning algorithms, for diagnostics, therapy assessments and progress prediction in PD based on kinematic data collected from upper and lower extremities and whole-body movements. Despite promising validation initiatives, study sample sizes are relatively small, the instrumentation is quite diverse both in type and positioning. Participant groups are often too heterogeneous regarding disease stage and symptoms. There is also a lack of consistency in outcome measures, methods of assessing validity, and form of reported results. Given these limitations, the validation of sensor-derived assessments of PD features would benefit from increased collaboration among researchers, aligning data collection protocols, sharing and merging data sets.

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## Declaration of Competing Interest

None.

## References

[1] F. Jiang, Y. Jiang, H. Zhi, Y. Dong, H. Li, S. Ma, Y. Wang, Q. Dong, H. Shen, Y. Wang, Artificial intelligence in healthcare: past, present and future, Stroke Vasc. Neurol. 2 (2017) 230–243.
[2] A. Holzinger, Machine Learning for Health Informatics. In Lecture Notes in Computer Science (including Subseries Lecture Notes in Artificial Intelligence and Lecture Notes in Bioinformatics), (2016) ISBN 978-3-319-50477-3.
[3] W.O. Contreras López, P.A. Navarro, S. Crispin, Intraoperative clinical application of augmented reality in neurosurgery: a systematic review, Clin. Neurol. Neurosurg. (2019).
[4] P. Hamet, Artificial intelligence in medicine, Metabolism 69 (2017) S36–S40.
[5] L. Li, F. Yu, D. Shi, J. Shi, Z. Tian, J. Yang, X. Wang, Q. Jiang, Application of virtual reality technology in clinical medicine, Am. J. Transl. Res. 9 (2017) 3867–3880.
[6] C.-Y. Liaw, M. Guvendiren, Current and emerging applications of 3D printing in medicine, Biofabrication 9 (2017) 024102.
[7] E. Rovini, C. Maremmani, F. Cavallo, How wearable sensors can support parkinson's disease diagnosis and treatment: a systematic review, Front. Neurosci. 11 (2017) 555.
[8] C.H. Adler, T.G. Beach, J.G. Hentz, H.A. Shill, J.N. Caviness, E. Driver-Dunckley, M.N. Sabbagh, L.I. Sue, S.A. Jacobson, C.M. Belden, et al., Low clinical diagnostic accuracy of early vs advanced Parkinson disease: clinicopathologic study, Neurology (2014).
[9] J. Jankovic, Parkinson's disease: clinical features and diagnosis, J. Neurol. Neurosurg. Psychiatry 79 (2008) 368–376.
[10] A. Berardelli, G.K. Wenning, A. Antonini, D. Berg, B.R. Bloem, V. Bonifati, D. Brooks, D.J. Burn, C. Colosimo, A. Fanciulli, et al., EFNS/MDS-ES recommendations for the diagnosis of Parkinson's disease, Eur. J. Neurol. (2013).
[11] David Gil, Magnus Johnson, Diagnosing Parkinson by using artificial neural networks and support vector machines, Glob. J. Comput. Sci. Technol. (2009).
[12] C.R. Pereira, D.R. Pereira, S.A.T. Weber, C. Hook, V.H.C. de Albuquerque, J.P. Papa, A survey on computer-assisted Parkinson's disease diagnosis, Artif. Intell. Med. (2018).
[13] S. Russel, P. Norvig, Artificial Intelligence—A Modern Approach, 3rd edition, (2012) ISBN 9780136042594.
[14] MDS UPDRS Rating Scale, (2019) Available online: https://www.movementdisorders.org/MDS-Files1/PDFs/Rating-Scales/MDS-UPDRS_English_FINAL.pdf (Accessed on Jan 31, 2019).
[15] E. Rovini, C. Maremmani, F. Cavallo, How wearable sensors can support parkinson's disease diagnosis and treatment: a systematic review, Front. Neurosci. (2017).
[16] C. Ahlrichs, M. Lawo, Parkinson's disease motor symptoms in machine learning: a review, Health Informatics—Int. J. (2013).
[17] L. Giancardo, A. Sánchez-Ferro, T. Arroyo-Gallego, I. Butterworth, C.S. Mendoza, P. Montero, M. Matarazzo, J.A. Obeso, M.L. Gray, R.S.J. Estépar, Computer keyboard interaction as an indicator of early Parkinson's disease, Sci. Rep. (2016).
[18] W.R. Adams, High-accuracy detection of early Parkinson's disease using multiple characteristics of finger movement while typing, PLoS One (2017).
[19] T. Arroyo-Gallego, M.J. Ledesma-Carbayo, I. Butterworth, M. Matarazzo, P. Montero-Escribano, V. Puertas-Martín, M.L. Gray, L. Giancardo, Á Sánchez-Ferro, Detecting motor impairment in early parkinson's disease via natural typing interaction with keyboards: validation of the neuroQWERTY approach in an uncontrolled At-Home setting, J. Med. Internet Res. (2018).
[20] L. Fraiwan, R. Khnouf, A.R. Mashagbeh, Parkinsons disease hand tremor detection system for mobile application, J. Med. Eng. Technol. (2016).
[21] D. Iakovakis, S. Hadjidimitriou, V. Charisis, S. Bostantzopoulou, Z. Katsarou,

L.J. Hadjileontiadis, Touchscreen typing-pattern analysis for detecting fine motor skills decline in early-stage Parkinson's disease, Sci. Rep. (2018).
[22] N. Kostikis, D. Hristu-Varsakelis, M. Arnaoutoglou, C. Kotsavasiloglou, A smartphone-based tool for assessing parkinsonian hand tremor, IEEE J. Biomed. Health Informatics (2015).
[23] M.A. Lones, S.L. Smith, J.E. Alty, S.E. Lacy, K.L. Possin, D.R.S. Jamieson, A.M. Tyrrell, Evolving classifiers to recognize the movement characteristics of parkinson's disease patients, IEEE Trans. Evol. Comput. (2014).
[24] M.D. Djurić-Jovičić, V.N. Bobić, M. Ječmenica-Lukić, I.N. Petrović, S.M. Radovanović, N.S. Jovičić, V.S. Kostić, M.B. Popović, Implementation of continuous wavelet transformation in repetitive finger tapping analysis for patients with PD, Proceedings of the 2014 22nd Telecommunications Forum (2014).
[25] T. Khan, D. Nyholm, J. Westin, M. Dougherty, A computer vision framework for finger-tapping evaluation in Parkinson's disease, Artif. Intell. Med. (2014).
[26] M. Djuric-Jovicic, N. Jovicic, S. Radovanovic, M. Jecmenica-Lukic, M. Belic, M. Popovic, V. Kostic, Finger and foot tapping sensor system for objective motor assessment, Vojnosanit. Pregl. (2018).
[27] O. Bazgir, S.H. Habibi, L. Palma, P. Pierleoni, S. Nafees, A classification system for assessment and home monitoring of tremor in patients with Parkinson's disease, J. Med. Signals Sens. (2018).
[28] H. Jeon, W. Lee, H. Park, H.J. Lee, S.K. Kim, H.B. Kim, B. Jeon, K.S. Park, Automatic classification of tremor severity in Parkinson's disease using awearable device, Sensors (Switzerland) (2017).
[29] C. Gao, S. Smith, M. Lones, S. Jamieson, J. Alty, J. Cosgrove, P. Zhang, J. Liu, Y. Chen, J. Du, et al., Objective assessment of bradykinesia in Parkinson's disease using evolutionary algorithms: clinical validation, Transl. Neurodegener. (2018).
[30] B.P. Printy, L.M. Renken, J.P. Herrmann, I. Lee, B. Johnson, E. Knight, G. Varga, D. Whitmer, Smartphone application for classification of motor impairment severity in Parkinson's disease, Proceedings of the 2014 36th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (2014).
[31] D. Pan, R. Dhall, A. Lieberman, D.B. Petitti, A mobile cloud-based Parkinson's disease assessment system for home-based monitoring, JMIR mHealth uHealth (2015).
[32] C. Stamate, G.D. Magoulas, S. Kueppers, E. Nomikou, I. Daskalopoulos, M.U. Luchini, T. Moussouri, G. Roussos, Deep learning Parkinson's from smartphone data, Proceedings of the 2017 IEEE International Conference on Pervasive Computing and Communications (2017).
[33] N.Y. Hammerla, J.M. Fisher, P. Andras, L. Rochester, R. Walker, T. Plötz, PD disease state assessment in naturalistic environments using deep learning, Aaai (2015).
[34] J.M. Fisher, N.Y. Hammerla, T. Ploetz, P. Andras, L. Rochester, R.W. Walker, Unsupervised home monitoring of Parkinson's disease motor symptoms using body-worn accelerometers, Park. Relat. Disord. (2016).
[35] M. Memedi, A. Sadikov, V. Groznik, J. Žabkar, M. Možina, F. Bergquist, A. Johansson, D. Haubenberger, D. Nyholm, Automatic spiral analysis for objective assessment of motor symptoms in Parkinson's disease, Sensors (Basel) (2015).
[36] B.M. Eskofier, S.I. Lee, J.F. Daneault, F.N. Golabchi, G. Ferreira-Carvalho, G. Vergara-Diaz, S. Sapienza, G. Costante, J. Klucken, T. Kautz, et al., Recent machine learning advancements in sensor-based mobility analysis: deep learning for Parkinson's disease assessment, Proceedings of the Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society (2016).
[37] C. Tucker, Y. Han, H. Black Nembhard, W.C. Lee, M. Lewis, N. Sterling, X. Huang, A data mining methodology for predicting early stage Parkinson's disease using non-invasive, high-dimensional gait sensor data, IIE Trans. Healthc. Syst. Eng. (2015).
[38] D.J. Cook, M. Schmitter-Edgecombe, P. Dawadi, Analyzing activity behavior and movement in a naturalistic environment using smart home techniques, IEEE J. Biomed. Health Informatics (2015).
[39] A. Procházka, O. Vyšata, M. Vališ, O. upa, M. Schätz, V. Mařík, Bayesian classification and analysis of gait disorders using image and depth sensors of Microsoft Kinect, Digit. Signal Process. Rev. J. (2015).
[40] F. Wahid, R.K. Begg, C.J. Hass, S. Halgamuge, D.C. Ackland, Classification of Parkinson's disease gait using spatial-temporal gait features, IEEE J. Biomed. Health Informatics (2015).
[41] Y. Nancy Jane, H. Khanna Nehemiah, K. Arputharaj, A Q-backpropagated time delay neural network for diagnosing severity of gait disturbances in Parkinson's disease, J. Biomed. Inform. (2016).
[42] M.R. Daliri, Chi-square distance kernel of the gaits for the diagnosis of Parkinson's disease, Biomed. Signal Process. Control (2013).
[43] M. Djurić-Jovičić, M. Belić, I. Stanković, S. Radovanović, V.S. Kostić, Selection of gait parameters for differential diagnostics of patients with de novo Parkinson's disease, Neurol. Res. (2017).
[44] W. Zeng, F. Liu, Q. Wang, Y. Wang, L. Ma, Y. Zhang, Parkinson's disease classification using gait analysis via deterministic learning, Neurosci. Lett. (2016).
[45] S. Arora, V. Venkataraman, S. Donohue, K.M. Biglan, E.R. Dorsey, M.A. Little, High accuracy discrimination of Parkinson's disease participants from healthy controls using smartphones, Proceedings of the ICASSP, IEEE International Conference on Acoustics, Speech and Signal Processing - Proceedings, (2014).
[46] Q.W. Oung, M. Hariharan, H.L. Lee, S.N. Basah, M. Sarillee, C.H. Lee, Wearable multimodal sensors for evaluation of patients with Parkinson disease, Proceedings of the Proceedings - 5th IEEE International Conference on Control System, Computing and Engineering (2016).
[47] J. Barth, J. Klucken, P. Kugler, T. Kammerer, R. Steidl, J. Winkler, J. Hornegger, B. Eskofier, Biometric and mobile gait analysis for early diagnosis and therapy monitoring in Parkinson's disease, Proceedings of the Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society (2011).
[48] J. Klucken, J. Barth, P. Kugler, J. Schlachetzki, T. Henze, F. Marxreiter, Z. Kohl, R. Steidl, J. Hornegger, B. Eskofier, et al., Unbiased and mobile gait analysis detects motor impairment in Parkinson's disease, PLoS One (2013).
[49] Q.W. Oung, H. Muthusamy, S.N. Basah, H. Lee, V. Vijean, Empirical wavelet transform based features for classification of Parkinson's disease severity, J. Med. Syst. (2018).
[50] C. Caramia, D. Torricelli, M. Schmid, A. Munoz-Gonzalez, J. Gonzalez-Vargas, F. Grandas, J.L. Pons, IMU-based classification of Parkinson's disease from gait: a sensitivity analysis on sensor location and feature selection, IEEE J. Biomed. Health Informatics (2018).
[51] F. Cuzzolin, M. Sapienza, P. Esser, S. Saha, M.M. Franssen, J. Collett, H. Dawes, Metric learning for Parkinsonian identification from IMU gait measurements, Gait Posture (2017).
[52] K.J. Kubota, J.A. Chen, M.A. Little, Machine learning for large-scale wearable sensor data in Parkinson's disease: concepts, promises, pitfalls, and futures, Mov. Disord. 31 (2016) 1314–1326.
[53] C. Ahlrichs, A. Samà, M. Lawo, J. Cabestany, D. Rodríguez-Martín, C. Pérez-López, D. Sweeney, L.R. Quinlan, G. Laighin, T. Counihan, et al., Detecting freezing of gait with a tri-axial accelerometer in Parkinson's disease patients, Med. Biol. Eng. Comput. (2016).
[54] D. Rodríguez-Martín, A. Samà, C. Pérez-López, A. Català, J.M.M. Arostegui, J. Cabestany, À. Bayés, S. Alcaine, B. Mestre, A. Prats, et al., Home detection of freezing of gait using support vector machines through a single waist-worn triaxial accelerometer, PLoS One (2017).
[55] N.K. Orphanidou, A. Hussain, R. Keight, P. Lishoa, J. Hind, H. Al-Askar, Predicting freezing of gait in Parkinsons disease patients using machine learning, Proceedings of the 2018 IEEE Congress on Evolutionary Computation (2018).
[56] E.E. Tripoliti, A.T. Tzallas, M.G. Tsipouras, G. Rigas, P. Bougia, M. Leontiou, S. Konitsiotis, M. Chondrogiorgi, S. Tsouli, D.I. Fotiadis, Automatic detection of freezing of gait events in patients with Parkinson's disease, Comput. Methods Programs Biomed. (2013).
[57] A.T. Tzallas, M.G. Tsipouras, G. Rigas, D.G. Tsalikakis, E.C. Karvounis, M. Chondrogiorgi, F. Psomadellis, J. Cancela, M. Pastorino, M.A. Waldmeyer, et al., Perform: a system for monitoring, assessment and management of patients with Parkinson's disease, Sensors (Switzerland) (2014).
[58] S. Arora, V. Venkataraman, A. Zhan, S. Donohue, K.M. Biglan, E.R. Dorsey, M.A. Little, Detecting and monitoring the symptoms of Parkinson's disease using smartphones: a pilot study, Park. Relat. Disord. (2015).
[59] V. Sharma, K. Mankodiya, F. De La Torre, A. Zhang, N. Ryan, T.G.N. Ton, R. Gandhi, S. Jain, Personalized parkinson disease interventions through synergy between a smartphone and a smartwatch, Proceedings of the Lecture Notes in Computer Science (including subseries Lecture Notes in Artificial Intelligence and Lecture Notes in Bioinformatics), (2014).
[60] S. Mazilu, A. Calatroni, E. Gazit, D. Roggen, J.M. Hausdorff, G. Tröster, Feature learning for detection and prediction of freezing of gait in Parkinson's disease, Proceedings of the Lecture Notes in Computer Science (Including Subseries Lecture Notes in Artificial Intelligence and Lecture Notes in Bioinformatics), (2013).
[61] T. Gazibara, T. Pekmezovic, D. Kisic Tepavcevic, A. Tomic, I. Stankovic, V.S. Kostic, M. Svetel, Fall frequency and risk factors in patients with Parkinson's disease in Belgrade, Serbia: a cross-sectional study, Geriatr. Gerontol. Int. (2015).
[62] T. Gazibara, D. Kisic Tepavcevic, M. Svetel, A. Tomic, I. Stankovic, V.S. Kostic, T. Pekmezovic, Near-falls in people with Parkinson's disease: circumstances, contributing factors and association with falling, Clin. Neurol. Neurosurg. (2017).
[63] R. Igual, C. Medrano, I. Plaza, Challenges, issues and trends in fall detection systems, Biomed. Eng. Online (2013).
[64] N. Pannurat, S. Thiemjarus, E. Nantajeewarawat, Automatic fall monitoring: a review, Sensors (Switzerland) (2014).
[65] A. Rodríguez-Molinero, A. Samà, D.A. Pérez-Martínez, C. Pérez López, J. Romagosa, À. Bayés, P. Sanz, M. Calopa, C. Gálvez-Barrón, E. de Mingo, et al., Validation of a portable device for mapping motor and gait disturbances in Parkinson's disease, JMIR mHealth uHealth (2015).
[66] A.M.S. Muniz, H. Liu, K.E. Lyons, R. Pahwa, W. Liu, F.F. Nobre, J. Nadal, Comparison among probabilistic neural network, support vector machine and logistic regression for evaluating the effect of subthalamic stimulation in Parkinson disease on ground reaction force during gait, J. Biomech. (2010).
[67] S.H. Roy, B.T. Cole, L.D. Gilmore, C.J. De Luca, C.A. Thomas, M.M. Saint-Hilaire, S.H. Nawab, High-resolution tracking of motor disorders in Parkinson's disease during unconstrained activity, Mov. Disord. (2013).
[68] S. Patel, K. Lorincz, R. Hughes, N. Huggins, J. Growdon, D. Standaert, M. Akay, J. Dy, M. Welsh, P. Bonato, Monitoring motor fluctuations in patients with parkinsons disease using wearable sensors, IEEE Trans. Inf. Technol. Biomed. 13 (2009) 864–873.
[69] G. Rigas, A.T. Tzallas, M.G. Tsipouras, P. Bougia, E.E. Tripoliti, D. Baga, D.I. Fotiadis, S.G. Tsouli, S. Konitsiotis, Assessment of tremor activity in the parkinsons disease using a set of wearable sensors, IEEE Trans. Inf. Technol. Biomed. (2012).
[71] M. Ashfak Habib, M.S. Mohktar, S. Bahyah Kamaruzzaman, K. Seang Lim, T. Maw Pin, F. Ibrahim, Smartphone-based solutions for fall detection and prevention: challenges and open issues, Sensors (Switzerland) (2014).
[72] D. Ravi, C. Wong, F. Deligianni, M. Berthelot, J. Andreu-Perez, B. Lo, G.Z. Yang, Deep learning for health informatics, IEEE J. Biomed. Health Informatics (2017).
[73] A. Sama, C. Perez-Lopez, A heterogeneous database for movement knowledge extraction in parkinson's disease, Eur. Symp. Artif. Neural Networks Comput. Intell. Mach. Learn. (2013).
[74] Clinical research database Available online:https://movementdisorders.ufhealth.org/research/clinical-research/clinical-research-database/ (accessed on Jan 31, 2019).