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SYSTEMATIC REVIEW ARTICLE

Machine Learning Applications in the Study of Parkinson's Disease: A Systematic Review

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Abstract: ***Background*:** Parkinson's disease is a common neurodegenerative disorder that has been studied from multiple perspectives using several data modalities. Given the size and complexity of these data, machine learning emerged as a useful approach to analyze them for different purposes. These methods have been successfully applied in a broad range of applications, including the diagnosis of Parkinson's disease or the assessment of its severity. In recent years, the number of published articles that used machine learning methodologies to analyze data derived from Parkinson's disease patients have grown substantially.

***Objective*:** Our goal was to perform a comprehensive systematic review of the studies that applied machine learning to Parkinson's disease data

***Methods*:** We extracted published articles in PubMed, SCOPUS and Web of Science until March 15, 2022. After selection, we included 255 articles in this review.

***Results*:** We classified the articles by data type and we summarized their characteristics, such as outcomes of interest, main algorithms, sample size, sources of data and model performance.

***Conclusion*:** This review summarizes the main advances in the use of Machine Learning methodologies for the study of Parkinson's disease, as well as the increasing interest of the research community in this area.

Keywords: Parkinson's disease, machine learning, deep learning, artificial intelligence, systematic review, bioinformatics.

1. INTRODUCTION

Parkinson's disease (PD) is the second-most common neurodegenerative pathology with a global 0.3% prevalence overall, but an over 3% prevalence in the population over 80 years old [1]. People with PD (PwP) present both, motor and non-motor symptoms, including bradykinesia, rigidity, tremor, depression or dementia, among many others [2]. At the present time, there is no cure for PD, although some treatments improve the symptoms [3]. These treatments include rehabilitative therapies, pharmacological interventions (*e.g.*, levodopa a.k.a. L-DOPA) and deep brain stimulation (DBS), a surgical treatment consisting of the placement of electrodes on the subthalamic nucleus (STN) or the globus pallidus interna of the brain.

Several types of data are used for diagnosis, symptom evaluation and other clinical and research aims related to PD. Many of these data consist of neuroimaging techniques such as positron emission tomography (PET), I-ioflupane single-photon emission computed tomography (SPECT) and magnetic resonance imaging (MRI). Molecular data, including omics data such as genomics, transcriptomics and proteomics, are being increasingly used in this field, providing very valuable information about the molecular mechanisms involved in PD [4]. Other common types of data, especially for early diagnosis, are extracted from voice, gait, handwriting and other tasks. There are different public repositories of PD experimental data, such as Parkinson's Progression Markers Initiative (PPMI) [5], an international project that

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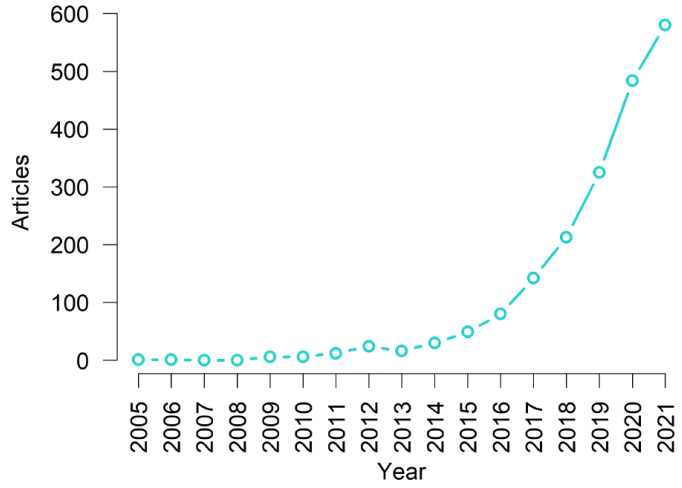

Fig. (1). Articles of ML applied to PD from 2005 to 2021. The search was performed at the SCOPUS database on 15th March 2022 using the query *("Machine Learning" OR "Deep Learning") AND Parkinson*.

generates clinical, neuroimaging, omics and other kinds of data longitudinally.

In this context, machine learning (ML) methodologies have a great potential to analyze and extract information from those large, complex and heterogeneous data. ML is an area of Artificial Intelligence (AI) that learns from input data to make predictions on new data (*e.g.*, diagnosis of a disease). A variety of ML algorithms can be used to analyze different kinds of data with different advantages and disadvantages (see [6] for an updated review on this topic). Furthermore, Deep Learning (DL) is a subset of ML algorithms that uses artificial neural networks (ANN), which are based on biological neural networks and can perform particularly complex tasks with large amounts of data.

The use of ML approaches to analyze data derived from PwP has increased exponentially in recent years. A search in the SCOPUS database of the terms related to ML and PD returns more than 2.000 published articles on these topics, most of them since 2015 (Fig. **1**). Remarkably, none of the articles was published before 2005, evidencing the recency of application of ML to PD data analysis.

Previous reviews on this topic focus only on diagnosis [7-9] and monitoring [10], excluding other applications such as assessing symptoms or improving the treatments. Other reviews cover only specific types of data like the generated by sensors [11, 12], kinematic analyses [13], or omics studies [14, 15] and focused only on DL methodologies [16]. Furthermore, many of those reviews are not systematic and/or are outdated. In this study, we present an updated and comprehensive systematic review of the applications of ML methodologies to PD for a broad range of applications and data types.

2. MATERIALS AND METHODS

For conducting the systematic review of literature, we followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines [17], a standard procedure that guarantees good practices and reproducibility in systematic reviews.

We performed the same search in 3 different literature databases: PubMed, SCOPUS, and Web of Science (WoS) Core Collection. In the three cases, we searched the term *("Machine Learning" OR "Deep Learning")* and *Parkinson*. All searches were performed on March 15th, 2022. In PubMed, we searched the terms in all fields and saved the results as a NBIB file; in SCOPUS, we searched the term in the article title, abstract and keywords and saved the results as a RIS file; in WoS, we searched the term in the topic field, which includes title, abstract, author keywords and keywords plus, and saved the results as a RIS file. We used the licenses from the University of Granada to search and export the results from the WoS and SCOPUS databases.

To process the search results, we used the revtools R package [18] to load and integrate all the obtained bibliography in the R statistical language environment. We excluded the duplicated articles with the same digital object identifier (DOI), the same PubMed ID or the same title.

The inclusion criteria were original research published in scientific journals which used PD data from human subjects that were analyzed using ML approaches. We excluded *in vitro* studies, articles with an unclear or incomplete description of the data and methods, articles not written in English, case reports, reviews, letters, conference articles and meta-analyses. Furthermore, we excluded articles that use ML methods only in specific analytical steps during the data processing (*e.g.*, normalization), but they are not relevant for generating the main outcomes. We did not restrict the results by publication date nor location. We did not apply a minimum sample size threshold as inclusion criteria.

The retrieved articles were grouped by the type of analyzed data to facilitate the state-of-the-art assessment in different fields. When ML and other methods were used in an article, we only described the objectives and results of the analyses performed with ML methods. Commonly, different ML algorithms are compared to select the one with the best

outcome. In these cases, only the algorithms and results for the best-performing analyses are included in the tables.

For each reviewed article, we compiled the type of data used and its source, the number of PwP and healthy controls (HC) included, the main objectives and results (generally, the accuracy of the models due to it is the most commonly reported metric) and the ML algorithms used to get the main results. The included performance metrics correspond preferably to external validation data or internal test sets.

To compare the performance of the used methodologies in each data modality, we calculated the mean of the reported accuracies, which is the most common metric provided. Therefore, we excluded the articles that do not report accuracy. Furthermore, for each data type, we only considered those algorithms used by at least three studies to avoid biased results obtained from too few works. Finally, we focused on the works that do classification tasks to avoid comparing results from different types of analyses.

3. RESULTS

3.1. Systematic Review

A PRISMA diagram showing the process of the systematic review of literature is presented in Fig. (**2**). First, we retrieved 4327 articles from PubMed, SCOPUS and WoS. 3135 of these papers were identified to be duplicated and were discarded, retaining 1192 records. Then, we screened the titles and abstracts of these records, excluding the article types that did not meet our inclusion criteria (conference papers, reviews, book chapters, meta-analyses, and so on) as well as retracted articles and manuscripts written in a language other than English. We retained 477 articles, eight of which do not have the full text available. Finally, we performed a full-text screening to assess their eligibility in this review. We excluded 163 articles because they were out of the scope of this review (*e.g.*, ML methods were not used, or PD data was not analyzed) and 51 articles because the methods and/or results were insufficiently described. Two hundred and fifty-five articles were finally included in the review.

3.2. Algorithms Used

A variety of ML methodologies were used in the selected articles (Table **1**) [19-37]. Classical ML algorithms such as support vector machine (SVM) (n=73), random forest (RF) (n=43), K-Nearest neighbors (KNN) (n=21) and logistic regression (LoR) (n=20) have been broadly used.

SVM consists of mapping the training data to spatial points maximizing the distance between categories [19]. The category of a new sample is predicted based on the region where its data is mapped.

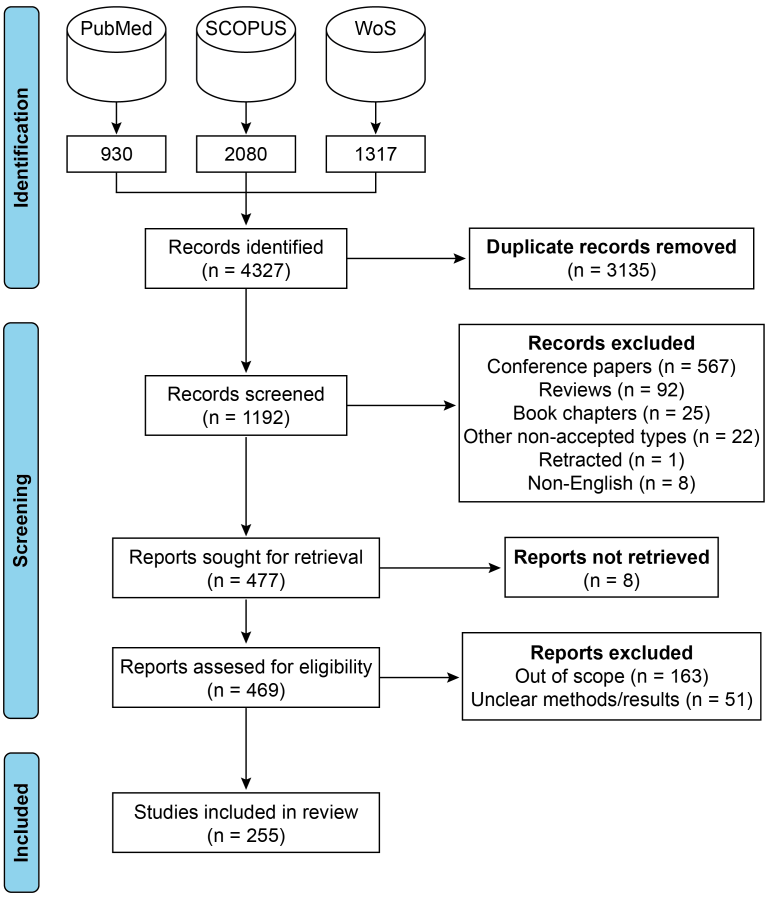

Fig. (2). PRISMA diagram of the identification and screening process. In each step, the number of studies excluded for different reasons is indicated. 255 studies were included in the review.

Table 1. Algorithms used in the reviewed articles. The table contains the abbreviation and whole names, a reference to get more information and the number of times used in the selected articles.

Abbreviation	Name	Reference	Times Used
Classical ML Algorithms			
AdaBoost	Adaptive Boosting	[22]	6
DT	Decision tree	[20]	12
EN	Elastic Net	[23]	2
KNN	K-Nearest neighbors	[24]	21
LDA	Linear discriminant analysis	[25]	7
LoR	Logistic regression	[26]	20
LR	Linear regression	[27]	3
NBC	Naive Bayes classifier	[28]	6
RF	Random forest	[21]	43
SVM	Support vector machine	[19]	73
SVR	Support vector regression	[29]	4
XGBoost	eXtreme Gradient Boosting	[30]	8
DL Algorithms			
CNN	Convolutional neural network	[31]	37
DNN	Deep Neural Network	[32]	6
ELM	Extreme Learning Machine	[33]	4
FNN	Feed-forward neural network	[32]	7
LSTM	Long short-term memory	[34]	9
MLP	Multilayer perceptron	[32]	4
PNN	Probabilistic neural network	[35]	3
RNN	Recurrent neural network	[36]	8
SAE	Stacked autoencoder	[37]	2

RF is based on decision trees (DTs), which is a prior ML method that follows a series of boolean conditions to label the samples depending on the input data [20]. In RF, several DTs are constructed following a bagging approach, each one with a random subset of training samples and features [21]. Predictions on new samples are based on the majority voting of the DTs for classification and their mean value for regression.

KNN predicts new samples depending on the k most similar samples according to a distance metric [24]. It can be also used for classification and regression. KNN is simple and easy to understand, although it is not efficient and is sensitive to outliers.

Similar to linear regression, LoR is a predictive technique that uses independent factors to predict the dependent variable, with the exception that the dependent variable should be categorical, regardless of whether the independent factors are numerical or categorical [25]. LoR makes use of the logistic function to model the conditional probability.

Regarding DL methods, the most used approach is the convolutional neural network (CNN) [31]. CNNs are ANN designed for analyzing grid-like data, such as images. A typical CNN has a convolution layer, a pooling layer and a fully connected layer. CNNs work similarly to a long dimensionality reduction process, associating the input data with the outputs.

3.3. Selected Articles Overview

After reviewing the 255 selected articles, we split them by the type of data used (Supplementary Tables **1-9**). We identified nine main types of data: neuroimaging, voice recordings, gait, movement, handwriting, electrical activity, omics, video and clinical data. Data that cannot be classified into those groups were assigned to the category "other" (Supplementary Table **10**). Finally, we grouped the studies that use a combination of more than one data modality (Supplementary Table **11**). The two most common goals of the included articles are diagnosis (including differential diagnosis of PD and other pathologies) and symptom evaluation. Fig. (**3**) shows the number of times that each goal was accomplished with each type of data.

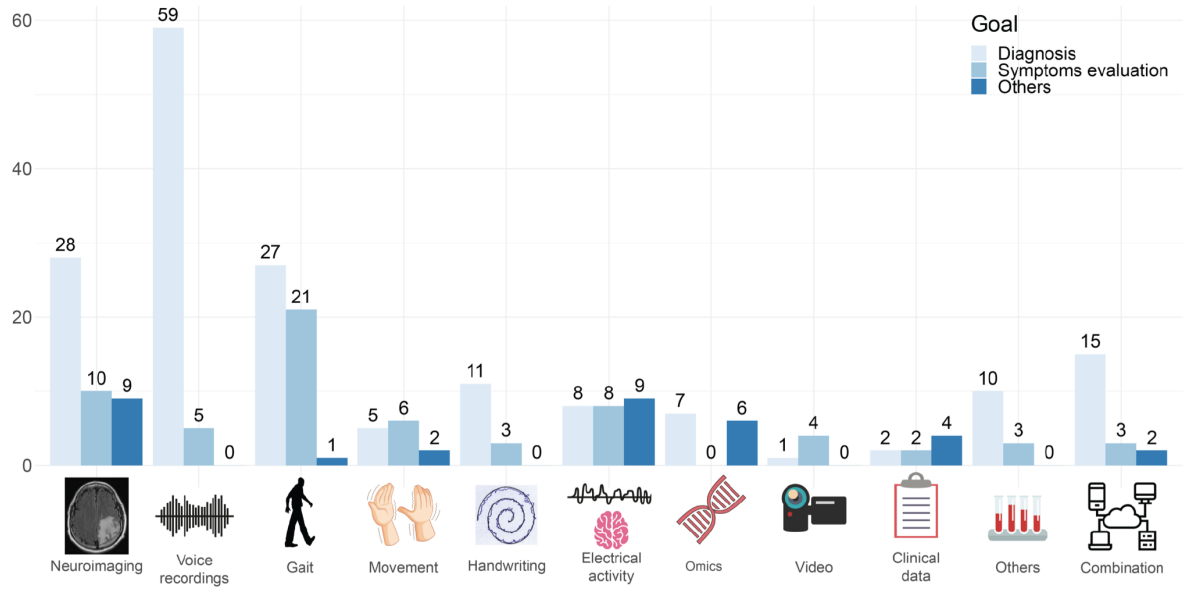

Fig. (3). Number of times that diagnosis, symptoms evaluation and other goals were pursued in studies using different data types. MRI was obtained from The Cancer Imaging Archive [40], the spiral pattern from HandPD [41] and some graphical elements were downloaded from Freepik (https://www.freepik.com/).(*A higher resolution / colour version of this figure is available in the electronic copy of the article*).

Regarding the reported results, most articles use accuracy, which is the ratio between correct predictions and the total number of samples. Other metrics commonly used are the area under the receiver operating characteristic curve (AUC), the area under the precision-recall curve (AUPR), the positive predictive value (PPV), the negative predictive value (NPV) and the root mean squared error (RMSE), among others. In the following sections, we review the articles classified in each category.

3.4. Neuroimaging

Medical imaging of the brain is a common approach for the diagnosis and evaluation of PwP, especially for differentiating PD and other parkinsonisms [3]. As such, it is one of the data types that attracted more attention in the application of ML to PD, not only for building predictive models, but also for data processing steps such as harmonization and regularization. We selected 43 studies that use neuroimaging data (Supplementary Table **1**). Among the specific techniques to obtain neuroimaging data, MRI is by far the most used one (it was used in 35 studies). Other used techniques were dopamine transporter scan (DatSCAN), SPECT, diffusion tensor imaging (DTI) and fluorodeoxyglucose (FDG) PET. In addition, to perform automatic classification of PwP and HC from their neuroimaging data, ML accomplished other purposes like predicting the progression of the disease [38, 39], to differentiate PD from other pathologies, like Alzheimer's disease (AD) [42-48] and to evaluate the symptoms, for instance predicting the Unified PD Rating Scale (UPDRS) scores [49, 50], used to assess the severity of the disease. Remarkably, 16 studies used DL algorithms for their analyses, evidencing the capability of neural networks like CNN to exploit imaging data. The only public source of neuroimaging data used in these studies was PPMI, which was used in 22 articles. The mean sample size for PD groups is 197.00.

3.5. Voice Recordings

Speech disorders are a common symptom of PD, affecting up to 89% of PwP [51], and they are one of the early indicators of the disease [52]. We identified 64 studies using voice recordings (Supplementary Table **2**), most of them for diagnostic goals (n=59). The five remaining studies used these data for assessing the severity of the disease [53-57]. The mean sample size for PD groups is 81.77. A high number of methods, including both classical ML and DL algorithms, were used to analyze these data. The University of California Irvine (UCI) Machine Learning Repository [58] is a collection of public datasets intended for the development and testing of ML methods. Among other data, this repository contains voice recordings of PwP and HC that were used in 41 of the selected articles.

3.6. Gait

Most PwP have their gait affected by the disease [2]. Among the gait problems that usually arise, freezing of gait (FOG), which consists of sudden moments when patients can't move their feet, affects notably their quality of life since it commonly causes falls and higher dependency [59]. Gait patterns are usually collected by devices such as wearable sensors and, more recently, smartphones. We identified 42 articles that used gait data, mainly for diagnosis and detecting FOG (Supplementary Table **3**). The mean sample size for PD groups is 63.19. The most common source of public gait data was the PhysioNet database [60], a resource containing complex physiological signals datasets. Among other data, PhysioNet contains gait data collected from PwP

and HC that was used in 17 articles. Other sources of public gait data were the UCI Machine Learning Repository (n=4) and mPower [61] (n=2), a study based on a smartphone application that collects data from PwP.

3.7. Movement

Motor disorders like tremors or bradykinesia (slowness of movement) are another hallmark of PD [62]. We found 12 studies that use movement sensor data to evaluate these motor disorders and for diagnosis, among other goals (Supplementary Table **4**). The mean sample size for PD groups is 25.92. Most studies (n=10) used classical ML methods to analyze this type of data, especially RF. All studies collected their own data, which may explain the lower mean sample size compared to other data types with public data available.

3.8. Handwriting

Many of the common symptoms of PD affect handwriting and different writing exams are usually used in hospitals to evaluate patients [63]. Fourteen studies used ML to analyze handwriting data (Supplementary Table **5**), most of them for automatic diagnosis of PD (n=11). The mean sample size in these studies is 76.86 for PD groups. Some public data sources were used, such as HandPD [41] and NewHandPD [63], which contain patterns like spirals and meanders drawn by PwP and HC.

3.9. Electrical Activity

Electroencephalography (EEG) is a non-invasive technique that permits measuring brain activity that has been used to diagnose PD [64]. On the other hand, during the DBS surgical procedure, microelectrodes are used to locate the STN, which is a very small region in the brain where an electrode must be implanted to succeed with this treatment. The microelectrode recordings (MERs) permit measuring the electrophysiological signals of the brain to achieve this task. Twenty-four studies applied ML to these kinds of data to achieve a non-invasive diagnosis of PD and to improve the STN location during DBS, among other goals (Supplementary Table **6**). For this data type, the mean sample size in PD groups is 40.75. Only one study used public data from OpenNeuro [65], a neuroinformatics database that contains, among other data, EEGs from PwP and HC.

3.10. Omics Data

Omics experiments enable the study of whole biological systems such as the genome (genomics), the transcriptome (transcriptomics), the metabolome (metabolomics) or the proteome (proteomics). Particularly, due to the known contribution of genetic factors to the risk of developing PD [66], genomics approaches such as genome-wide association studies (GWAS) are especially useful to get insight into the molecular mechanism of this disease. In these GWAS, sequence variants (*e.g.*, single nucleotide polymorphisms (SNPs)) are correlated to the studied phenotypes, such as the risk of developing PD,

Thirteen studies used ML to analyze omics data (Supplementary Table **7**). The most common omic type was genomics (n=5), followed by transcriptomics (n=4). Remarkably, five of the articles [67-71] focused on studying the molecular mechanisms of PD, evidencing the potential of omics data for this purpose. Only one study [72] employed a DL approach to analyze the data. Some specific omics data repositories, like Gene Expression Omnibus (GEO) [73] and dbGaP [74] were used as data sources. The mean sample size for PD groups is 1098.15,

3.11. Video

Five studies analyzed video data with ML methods, mostly to evaluate the symptoms of PwP, but also for diagnosis [75] (Supplementary Table **8**). DL and classical ML algorithms were used in these articles an equal number of times. No public data sources were used in these studies. The mean sample size is 111.40 for the PD groups.

3.12. Clinical Data

Eight studies used ML to analyze clinical information such as demographic data (*e.g.*, age) or laboratory measurements (*e.g.*, cerebrospinal fluid biomarkers) for different purposes (Supplementary Table **9**). Only classical ML methods were used to analyze these data. PPMI was the data source for all the studies that used public data (n=5). The mean sample size for PD groups is 352.00.

3.13. Other Types

Thirteen studies used data types that cannot be classified in any of the previous categories (Supplementary Table **10**). Some examples of these data are interactive tests performed with smartphone applications [76, 77] or specific laboratory tests such as flow cytometry [78] or bioelements analysis [79]. All these articles used ML for diagnosis or symptom evaluation. Only one study [80] used a DL approach to analyze the data. One study used public data from The Partners Healthcare Research Patient Data Registry [80]. The mean sample size in PD groups is 699.62, although this amount is biased by the high number of patients included in one of the studies [80].

3.14. Data Combination

Seventeen studies combined more than one data type in their analyses (Supplementary Table **11**). Eleven of these articles used classical ML approaches, while five used DL and one used both. Some of the public resources presented in previous sections are used in these articles, such as UCI Machine Learning Repository, mPower or PPMI. The mean sample size for PD in these studies is 450.76.

3.15. Algorithms Comparison

After selecting the studies to be compared (see Section 2), four data modalities contained at least two algorithms to be compared: neuroimaging, voice recordings, gait and handwriting. The method with highest mean accuracy for

Table 2. Algorithms with the highest performance for each analyzed data type and number of studies considered to calculate the mean accuracy.

Data Type	Algorithm	Number of Studies	Mean Accuracy
Neuroimaging	CNN	5	95.76 %
Voice recordings	RF	3	94.01 %
Gait	CNN	3	99.16 %
Handwriting	CNN	3	98.15 %

neuroimaging, gait and handwriting data is CNN, and for voice recordings data is RF (Table **2**).

4. DISCUSSION

In this article, we summarized the methods and outcomes of 255 articles published recently in scientific journals that used ML methodologies to analyze data derived from PwP. For each article, we provide details about data characteristics and data sources, algorithms used, sample size and the main outcomes. This summarization permits us to easily compare studies both within and between data types. We detected an imbalance in the data types utilization due to various factors. In the first place, data types that are non-invasive (*e.g.*, neuroimaging) and/or relatively cheaper (*e.g.*, gait measurements) are generated more commonly than invasive and/or more expensive data modalities (*e.g.*, omics data). In addition, the availability of public data repositories also endorses the publication of works using those data. For instance, the voice recordings from UCI Machine Learning Repository were used in 41 of 64 (64.06%) studies that analyzed this data type.

During the screening process, we discarded several articles (n=51) that failed to report basic details about the followed methodology and results, such as the sample size, the source of the data or even the type of data analyzed. This is a concerning problem that compromises the reproducibility of those works and brings into question their scientific quality. Nevertheless, few articles provide the code necessary to reproduce the analyses. Although we did not exclude articles for this reason, it would be recommendable to share such code to increase the reproducibility of these works.

Most articles reported accuracy as the main (or unique) performance metric of their models. Although accuracy is easy to calculate and interpret, it has limitations and it has been reported that it is an over-optimistic metric, especially for multiclass and imbalanced datasets [81]. Since many of the reviewed studies have unmatched case and control counts, accuracy may not be the better performance metric for these studies. Other metrics, such as Matthew's correlation coefficient, have been reported to be more reliable scores [82] and their implementation would provide a more realistic assessment of the ML outcomes. Furthermore, the standardization of the reported metrics in these works would facilitate the comparison between studies, which would be very valuable to assess which methods and data types have better performance for different goals.

Many classical ML and DL algorithms have been used in the selected articles, especially the former (Table **1**). Classical ML methods are easier to implement and require less computational resources and training time than DL [83]. For these reasons, it is not surprising that most reviewed articles used these approaches (n=191, 74.90%). Nevertheless, the number of works that used DL is also remarkable (n=79, 30.98%), suggesting that this approach also has a large potential to be applied in PD research. CNN is, by far, the most used ANN architecture in these works, indicating that it is particularly useful for analyzing these data.

We compared the reported accuracy of different algorithms between the studies that performed classification tasks with PD data. Apparently, CNN overcome other approaches when neuroimaging, gait and handwriting data are analyzed, while RF was the best one among the works that analyzed voice recordings. However, these results should be treated with caution due to the limitations of our analysis: accuracy may be an inflated metric to estimate the performance of the models, some studies calculate the accuracy with internal test sets and others with external validation sets and the number of studies compared is small. Therefore, different methods should still be tested in order to determine which algorithm works better in each dataset and analysis.

Since this review is focused on data generated from patients, some ML contributions to the study of PD are not included, such as drug development. Nevertheless, we would like to remark the importance of ML in other fields. For instance, quantitative structure-activity relationship (QSAR) uses ML approaches for associating chemical structures of compounds to biological activities, driving the discovery of novel drug candidates [84-87]. These methods have been used to find leucine-rich repeat kinase 2 (LRRK2) inhibitor candidates [88-90], which is a promising treatment due to its increased kinase activity in a significant proportion of PD patients [91].

Overall, both the number of published articles and their generally good performance demonstrates the feasibility of ML techniques to achieve different goals with diverse data modalities in the field of PD. However, the proposed models are rarely validated with new cohorts and most of them have not been translated into clinical practice so far.

CONCLUSION

In this article, we systematically reviewed the published works that used ML approaches for analyzing PD data without filtering by data type or by goal. We grouped the selected articles by data modalities and provide summary tables with information about the data, methodology, objectives and results. As far as we know, this is the first systematic review containing a comprehensive selection of articles, including those with goals other than diagnosis. This review may serve as the basis for later updates since the increasing number of published articles in this field will make it necessary to publish updated reviews to keep informing about its state-of-the-art.

LIST OF ABBREVIATIONS

AD	=	Alzheimer's Disease
AdaBoost	=	Adaptive Boosting
AI	=	Artificial Intelligence
ANN	=	Artificial Neural Networks
AUC	=	Area Under The Receiver Operating Characteristic Curve
AUPR	=	Area Under The Precision-Recall Curve
CNN	=	Convolutional Neural Network
DatSCAN	=	Dopamine Transporter Scan
DBS	=	Deep Brain Stimulation
DL	=	Deep Learning
DNN	=	Deep Neural Network
DOI	=	Digital Object Identifier
DT	=	Decision Tree
DTI	=	Diffusion Tensor Imaging
EEG	=	Electroencephalography
ELM	=	Extreme Learning Machine
EN	=	Elastic Net
FDG	=	Fluorodeoxyglucose
FNN	=	Feed-Forward Neural Network
FOG	=	Freezing of Gait
GEO	=	Gene Expression Omnibus
GWAS	=	Genome-Wide Association Studies
HC	=	Healthy Controls
KNN	=	K-Nearest Neighbors
LDA	=	Linear Discriminant Analysis
LRRK2	=	Leucine-Rich Repeat Kinase 2
LSTM	=	Long Short-Term Memory
LR	=	Linear Regression
LoR	=	Logistic Regression
MER	=	Microelectrode Recording
ML	=	Machine Learning
MLP	=	Multilayer Perceptron
MRI	=	Magnetic Resonance Imaging
NBC	=	Naive Bayes Classifier
NPV	=	Negative Predictive Value
PD	=	Parkinson's Disease
PET	=	Positron Emission Tomography
PNN	=	Probabilistic Neural Network
PPMI	=	Parkinson's Progression Markers Initiative
PRISMA	=	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PPV	=	Positive Predictive Value
PwP	=	People with Parkinson's Disease
QSAR	=	Quantitative Structure-Activity Relationship
RF	=	Random Forest
RMSE	=	Root Mean Squared Error
RNN	=	Recurrent Neural Network
SAE	=	Stacked Autoencoder
SNP	=	Single Nucleotide Polymorphism
SPECT	=	Single-Photon Emission Computed Tomography
STN	=	Subthalamic Nucleus
SVM	=	Support Vector Machine
SVR	=	Support Vector Regression
UCI	=	University of California Irvine
UPDRS	=	Unified Parkinson's Disease Rating Scale
WoS	=	Web of Science
XGBoost	=	eXtreme Gradient Boosting

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

The data supporting the findings of the article is available in the PubMed, SCOPUS, and Web of Science (WoS) Core Collection.

STANDARDS OF REPORTING

PRISMA guidelines and methodology were followed.

FUNDING

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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SUPPLEMENTARY MATERIAL

Supplementary material is available on the publisher's website along with the published article.

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