

An Artificial Intelligence Based Effective Diagnosis of Parkinson Disease Using EEG Signal



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Abstract This study focuses on the use of human bio-signals for the early diagnosis of PD (Parkinson's disease). EEG (Electroencephalography) and EMG have been used to examine human brain and muscle signals to learn more about the functional and neurological alterations of Parkinson's patients. Parkinson disease (PD) is a neurological illness that typically affects people over the age of 50. Dopamine, a neurotransmitter, is depleted in the substantia nigra as a result. As this neurotransmitter is released, the person's muscles begin to contract. Reduced dopamine production causes a loss of brain and muscle coordination, which manifests as unsteady limb movement in a person with PD. The underlying aetiology of PD can be validated by studying the functional and neural alterations using EEG and correlating the results with EMG. It will explain the origin of the wide range of early-stage motor and non-motor PD symptoms. The EEG and EMG results for detecting early-stage PD were validated using other radiological data, such as a Brain Magnetic Imaging signal. The mathematical model for PD diagnosis was developed utilising an ANN and a graphical user interface. The ANN-designed classifier achieved a near-perfect accuracy rate of 100% while testing its ability to distinguish between an early-stage PD patient and a control subject using a dataset consisting of electroencephalogram and electromyogram readings as input features.

Keywords AI · Parkinson disease · EEG · EMG · ANN

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1 Introduction

The human brain is the most important organ in the body for processing sensory information. The brain is the central processing unit and command and control centre of the body. It is responsible for a wide variety of bodily processes. Everything is taken into account, including but not limited to sight, hearing, speech, memory, intelligence, emotion, and cognitive ability.

While studying human electrical activity, it is normal practise to collect impulses from the scalp. The endocrine system, which is comprised of a complex network of neurons and hormones, is responsible for regulating and coordinating the operations of the body. Motor nerves are another type of neuron that are responsible for transmitting signals to effectors from the brain and spinal cord [1]. The cerebral cortex, the cerebellum, and the brainstem are the three primary components that make up the rest of the brain.

The cerebrum is the largest region of the brain and is roughly divided in half along the lines that separate the two hemispheres. The processing of sensory information from the senses of touch, sight, and sound, as well as language, cognition, emotion, instruction, and motor control, are just few of the numerous functions that the cerebrum is responsible for. At this point, the brain can be broken down into four different regions. Other parts of the brain include the occipital, parietal, frontal, and temporal lobes [2].

The cerebellum plays a role in the coordination of many bodily functions, including muscular movement and the upkeep of different body positions. Its location is below the brain.

The brainstem's primary function is to link the spinal cord to the higher brain regions (cerebrum and cerebellum). It helps keep things like heart rate and core body temperature steady. Little human body functions like puking, digestion, and sleep cycles are also tracked [3].

1.1 Disease of the Nervous System

Neurodegenerative disorders refer to diseases that predominantly impact brain neurons. Neurons like these make up the brain and spinal cord [4].

- Parkinson Disease: The loss of dopamine in the human brain's substantia nigra over time causes a chronic neurodegenerative illness known as PD. This causes the individual's brain and muscles to stop working together effectively. Most people with PD are over the age of 50. The prevalence of PD increases with age, with 93.1 cases per 100,000 persons diagnosed between the ages of 70 and 79, and 17.4 cases per 100,000 people diagnosed between the ages of 50 and 59, according to a statistical analysis.
- Alzheimer's disease (AD): AD has a wide range of effects on cognitive abilities and typically manifests in middle age. Dementia is the main culprit in this case.

The gradual decline in memory and cognition caused by Alzheimer's disease can make it difficult, if not impossible, for a patient to engage in the routine tasks required to maintain daily functioning. Instances of dementia can take several forms. Dementias include those caused by Lewy bodies, diseases of the frontotemporal lobes, and stroke [5]. Alzheimer's disease and vascular dementia, for example, might occur concurrently in some persons, creating a condition called mixed dementia.

- Huntington's disease (HD): HD causes involuntary movement and mental decline in affected individuals. Huntington illness typically appears in people's 30 and 40 s, but it can occur at any age. A transformation in the Huntington gene is the underlying cause of autosomal dominant inheritance. The Huntington gene describes the protein's ancestry. An aberrant gene is formed when the number of CAG (cytosine-adenine guanine) triplet repeats in the coding for the Huntington protein increases. In most cases, genetic testing is used to identify Alzheimer's disease.

1.2 *Bio-signal Consequence*

The electroencephalogram, sometimes known as an EEG, is a analytical method that does not include any offensive measures. In order to quantify the activity of the EEG, microvolts and frequencies up to 30 Hz are used. The EEG is useful in the diagnosis of a wide variety of neurological conditions. Electroencephalograms, sometimes known as EEGs, are non-invasive diagnostic tools used by medical professionals to diagnose a wide range of abnormalities that can occur in the brain [6]. There is a lack of standardisation in the application of EEG techniques in medical research when it comes to clinical applications. This can be problematic. On the other hand, research into mental health disorders, which is both more prevalent and commonly utilised, demonstrates the opposite pattern. EEG scans are recordings made of a person's brainwaves made using scans of their head. Any electrical activity that was detected on an EEG but did not originate in the brain is referred to as an artefact. There are two basic categories that can be used to describe artefacts, physiological and non-physiological [7]. An artefact is a glitch that occurs during the process of analysing the signal coming from the brain. The genesis of non-physiologic artefacts may be traced back to non-biological causes, whereas the origin of physiologic artefacts can be traced back to the human body. Artifacts have the potential to affect a number of statistical metrics used to evaluate the quality of an EEG, including the mean, median, distribution, standard deviation, and signal-to-noise ratio. It is possible to lessen the impact of artefacts by carefully planning the EEG procedure, engaging in intensive training prior to the examination, making use of a response of an appropriate rejinder device [8].

1.3 Symptoms

- Bradykinesia, literally “slow motion,” is one of the utmost communal motor indications. A marked slowing or stopping of spontaneous movement is what we call bradykinesia, and it can cause an individual to appear unusually silent and to lose some of their facial expression.
- The limbs, neck, and trunk become stiff and unyielding when rigidity is present. Muscles tend to lengthen during movement and relax afterward.
- In the case of a tremor, the shaking of body parts and eases when the affected limb or body part moves. Those with PD and their loved ones may notice that the affected person has a tremor.
- Someone who experiences postural instability has a tendency to lose their balance while standing [9].

Non-motor Symptoms

- Neuropsychiatric: These indications are communal in PD and are associated with an enlarged maintenance load and an amplified hazard of entering a nursing home, both of which have substantial effects on quality of life and regular working.
- Impulse control disorders (ICDs) are seen in a subset of people with PD, and are most often linked to increased gambling, eating, sex, and shopping.
- Sleep disturbance: Sleep disturbances are common in PD and may stem from a wide variety of causes. Sleep problems can occur both at night and during the day [10].

Reducing the presence of artefacts in an EEG can be done in a number of ways. The majority of their uses are in clinical diagnosis, scientific study, and brain-computer interface (BCI) technology. Such examples are ICA and discrete wavelet transformations (DWT). Correcting the recorded EEG with independent component analysis is a reliable procedure, much like second-order blind identification (SOBI). Extended information maximisation (InfoMax) and an adaptive mix of independent component analysers (AMICA) are two further methods that can be used [11].

An orderly exchange of information takes place between the neurons that make up the cortex. In an electroencephalogram, oscillatory communications between the cortex of the brain and the subcortical processes can be detected as sinusoidal rhythmic activity. This communication linkage is more likely to take place whenever the brain is not actively engaged in any task. As the cortex is actively engaged in a task, its electrical activity begins to desynchronize, and lower amplitude, faster electrical pulses begin to predominate. This continues until the task is completed, at which point the brain returns to its normal resting condition [12]. The PDR is the example of this that is the most well-known to a wide audience. The back of a person’s head will demonstrate an oscillating rhythm ranging from 8.5 to 12 Hz when the eyes are closed, the individual is awake, and they are comfortable. When you open your eyes, a stream of visual information is given to the brain. This stimulates the visual cortex, which is located at the back of your head. At activation, the visual cortex momentarily falls out of sync with the thalamus so that it can process the most

recent visual information. As a consequence of this disagreement, the PDR will be absent for an extended period of time.

Muscular contractions and relaxations captured when a human was moving freely under their own volition. Compound action potentials, also known as CMAPs, and motor evoked potentials, also known as MEPs, are both induced by cortical and PNS stimulation, respectively. In addition to providing stimulation to the brain, the PNS also monitors the integrity of the external motor system. The health of the corticospinal circuit can be evaluated with the help of transcranial magnetic stimulation, often known as TMS [13]. Weakness or numbness in a muscle detected by electromyography that can be linked back to an illness or injury to the neurological system or to any of the nerves that supply that muscle. This can be caused by a disease or injury to any of the nerves that supply that muscle. EMG is capable of diagnosing a wide variety of disorders.

2 Related Work Done

The authors created a DNN to detect freezing of gait (FoG) in PD patients during unrehearsed situations. The PD patient's three ACC sensors and one surface EMG sensor fed data into the DNN, creating the input features. While the EMG sensor is attached to the shin, the forearm of the other. By the end of the study, they determined that the custom FoG detector had a second-by-second sensitivity of 83% and a specificity of 97% [14].

With the use of sensors, researchers were able to construct a portable, efficient gait analysis system to assess the level of impairment in PD patients based on their walking patterns. There were a total of 16 healthy participants, 14 people in the early stages of PD, and 13 people in the intermediate stages of PD. Sport shoes equipped with gyroscopes and accelerometers were requested for gait analysis. A wireless signal recording device used for acquisition. With a sensitivity of 88% and a specificity of 86%, the system distinguished PD patients from healthy controls [15]. It also ranked participants with gait impairments in terms of how mild or severe they were.

Using an AI system, researchers could tell PD patients from control people. This research makes use of human voice recordings from a range of individuals. The maximum training and testing accuracy (95.38% and 94.72%, respectively) were achieved using an adaptive Neuro-Fuzzy classifier in combination with linguistic hedges [16].

Myotonometry was used to assess patients with PD for passive muscle dysfunction. Muscle resting surface and mechanomyography electrical activity reports and offline amplitude analyses. Higher levels of PD were associated with increased stiffness in the Bicep Brachii (BB) muscle. A positive link between the parkinsonian rigidity score and passive stiffness values of Bicep Brachii was found using the Spearman correlation coefficient. The EMG and MMG amplitudes of the BB muscle

did not significantly differ between groups, nor did the relevance of these measures correlate strongly with the patients' rigidity ratings [17].

By determining the ideal biceps brachii loading levels, the authors analysed sEMG characteristics of the biceps brachii in PD patients and compared it to control old and young people. When contrasted with the UPDRS and finger-tapping scores, these factors shed light on the nature of PD [18]. The biggest discrepancy occurred in isometric elbow flexion when no weights were used. There is little to no discernible difference in the overt characteristics of EMG between elderly and youthful people.

A Portuguese adaptation of the CERAD neuropsychological battery, the modified Hoehn and Yahr scale for PD, was used to assess 32 people with PD and 26 people without the condition [19]. They tested people using the Mini-Mental State Exam and the Clinical Dementia Rating scales. Resting state EEG band amplitude in absolute and relative terms.

There were a total of four groups studied: one healthy group, one with PD (composed of seven people), one with dementia (ten people), one with mild cognitive impairment (fifteen people), and one with no mental abnormalities (fifteen people). When comparing healthy individuals to those with PD, the qEEG found no noteworthy differences without causing any noticeable disruptions in cognitive function [20]. Those with mild cognitive impairment showed a rise in posterior theta absolute and relative amplitude, while those with dementia showed an increase in posterior delta absolute and relative amplitude. The researchers found that eEEG is a promising new method for evaluating cognitive decline in PD.

During the on-medication phase, the authors examined EMG and MMG alterations in the biceps and triceps brachii of PD patients holding an absolute submaximal load [21]. The biceps brachii of PD participants was found to have a higher amplitude and the median muscle activation frequency (MMAF) was found to be lower for both forces. When in PD the median frequency of electrical muscle stimulation of the triceps brachii muscle increased. In addition to showing differences between PD and healthy subjects, the MMG was unaffected by physiological postural tremor, suggesting that this condition is a valuable tool for neuromuscular examination [22–24].

Two popular classifiers, ANN and SVM, were evaluated and compared for their classification accuracy (SVM). In PD patients, it helped them distinguish their gait pattern at the walking speed of their choosing. Features of gait were determined, including their location and velocity in space and time and their kinematics in space and time [25–27]. Intragroup and intergroup normalisation were used to pre-process these features. Based on the data fed into the classifiers, the elements' efficacy was determined. The results demonstrated that both the ANN and the SVM classifier achieved a high rate of accuracy while using basic spatiotemporal as a feature during intragroup normalisation [28].

Researchers analysed PD patients' EEG sub-bands using wavelet Energy and Overall Wavelet Entropy. This is accomplished through a multi-resolution decomposition of EEG, which was originally based on a discrete wavelet transform during the ice-age. PD patients that experience freezing while walking can be identified by the Back Propagation Neural Network classifier. It demonstrated almost 75% average

values for precision, awareness, and specificity. The data presented here show that EEG can be used for FOG diagnosis and treatment in the future [29].

Authors researched on EEG and EMG in PD utilising multi-block Partial Least Squares (mbPLS) during the sinusoidal squeezing test. The researchers discovered a connection between EEG electrodes that mirrors the activity of the skeletal muscle. It found that the occipital area of PD patients was more connected than that of healthy controls [30].

The authors investigated the feasibility of detecting PD via vocal cues. The accuracy of the k-nearest-neighbourhood classifier was 92.46% while utilising tenfold validation. While k is the closest, post-processing achieved a 96.83% success rate in identifying a single individual [31].

Changes in temporal microstate variables that connect with different motor functions were used to detect aberrant brain dynamics in drug-free patients. They arrived at a few findings that could aid in PD identification efforts [32].

Patients with PD were tested with a visual oddball paradigm task to determine the event-related responses. By means of a 32-channel direct current (DC) EEG recording equipment, we can study the brain's electrical activity. Twice a year following the initial assessment, PD patients underwent additional cognition testing and EEG readings. Seven locations were chosen. This early study revealed a gradual weakening of event-related theta strength in PD patients [33]. Patients were not different from one another in terms of neurocognitive assessments.

In order to learn the similarity in tremor severity between surface EMG signals, they built S-Net, a lightweight and computationally effective convolution neural network. Evaluations with 147 individuals diagnosed with PD demonstrate that their method significantly outperforms the status quo. In addition, their method is simple and might be used to create useful applications [34].

3 The Objective of the Research Work

Examining the clinical interpretations of patients with PD at the Stage 1 and Stage 1.5 levels of the disease according to the Modified Staging.

- To observe and analyse outward symptoms of Parkinson's disease.
- Imaging studies (CT and MRI) confirm the diagnosis of PD to support this.
- To create a mathematical model using EMG and EEG connection to
- Quantitate the drug-induced improvement in Parkinson's disease.

4 The Proposed Work

Electrical activity was recorded from the Extension Carpis Ulnaris and the Flexor Digitorum Superficialis of the hand during flexion and extension of the wrist. In addition to the bio signal features, clinical data sheets, demographic information,

and SpO₂ levels were obtained from each and every individual. The clinical data sheet contained the MMSE, the GDS, and the Fatigue Severity Scale (FSS). The information contained in these fact sheets was utilised in order to zero in on a broad spectrum of non-motor symptoms. We inquired about age, gender, occupation, nutrition, smoking, drinking and depression, usage of well water, history of brain injury, and history of exposure to insecticides. It was clear from the results whether or not the patient had problems falling or staying asleep. A graphical user interface and an artificial neural network were utilised in the creation of the mathematical model for PD diagnosis. Using a dataset that included readings from an electroencephalogram and an electromyogram as input features, the artificial neural network (ANN) classifier that was developed achieved an almost perfect accuracy rate of 100% while being tested on its capacity to differentiate between an early-stage PD patient and a control subject. When it comes to following the evolution of an illness in its early stages, clinicians will find this model to be a very helpful tool. This app will not only monitor how far along the condition has gone, but it will also monitor how well the patient is doing both before and after taking any medications that have been prescribed. The model will operate as a centralised centre for the speedy diagnosis of a variety of motor and non-motor symptoms that are linked with PD. This one-of-a-kind approach has the potential to become a practical instrument in the not-too-distant future for the diagnosis of PD and other neurodegenerative disorders.

Figure 1 illustrates the proposed block diagram. PD is a neurological condition that typically strikes adults over the age of 50. Dopamine, a type of neurotransmitter, is lost in the substantia nigra of the human brain as a consequence of this condition. Dopamine production slows down, which causes a loss of brain and muscle coordination in people with Parkinson's disease, which in turn causes limb motions to become disorganised. In addition, the individual has postural instability as well as bradykinesia and tremors in numerous parts of their body, such as their hands, legs, and lips. The investigation of the functional and the neurological changes utilising EEG in combination with EMG will justify the root cause of PD from the brain to the muscles. It will provide an explanation for the numerous motor and non-motor symptoms that are present in the early stages of Parkinson's disease. The results obtained for the early-stage detection of PD using EEG and EMG were verified using a variety of radiological data's such as Brain Magnetic Imaging (MRI)/Computerized tomography (CT) etc.

5 Result and Analysis

In order to identify motor symptoms, components of patients' electroencephalograms and electromyograms were obtained, as were those of control participants. Patients with early-stage PD were involved in this learning. The bio-signals were used to derive a great number of characteristics, both in the time domain and the frequency domain. Properties of the electroencephalogram (EEG) include the autocorrelation function, the Shannon entropy, the kurtosis, the variance, the RMS, the standard

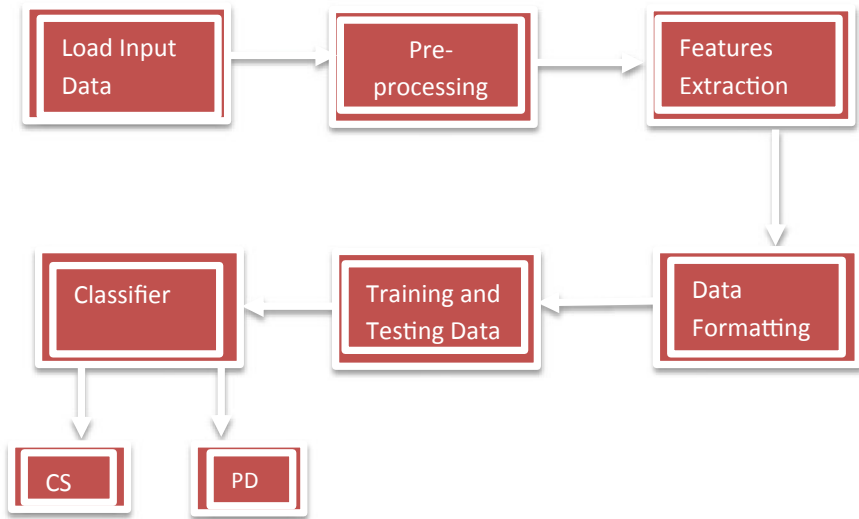


Fig. 1 The proposed block diagram

deviation, the median frequency, the mean frequency, the standard deviation, and the length of the waveform. Recordings of the subject’s frontal and temporal regions of the EEG were made. The following EMG parameters were retrieved: Power, Variation, Variability, Root Mean Square, Waveform Length, Median Frequency, Mean Frequency, Percent Maximum Voluntary Contraction, and Grip Strength. Table 1 lists the comparison for PD and CS stages performance.

The preceding graph shown in Fig. 2 demonstrates that those who have PD have much greater rates of depression than the general population (7–14 points). The GDS scores of healthy controls, on the other hand, can range anywhere from 0 to 7, indicating a significantly lower level of depression than that seen in PD patients.

A person who does not have PD has substantially more grip strength than a person who does have the condition, as can be seen in the bar graph that came before it. A person who has PD will notice a gradual weakening of their muscles as the condition advances. This will have an influence on the individual’s ability to grasp and grip objects as the condition progresses.

The presented results provide an illustration of the development of cognitive decline seen in PD. People with PD have cognitive impairment if they have scores between 16 and 24 on the Mini-Mental State Examination (MMSE), while healthy

Table 1 Comparison for PD and CS stages performance

S. No.	Stage	GDS	Grip strength	MMSE	FSS	SpO ₂
1	PD	12	25	20	6	10
2	CS	6	68	30	2	35

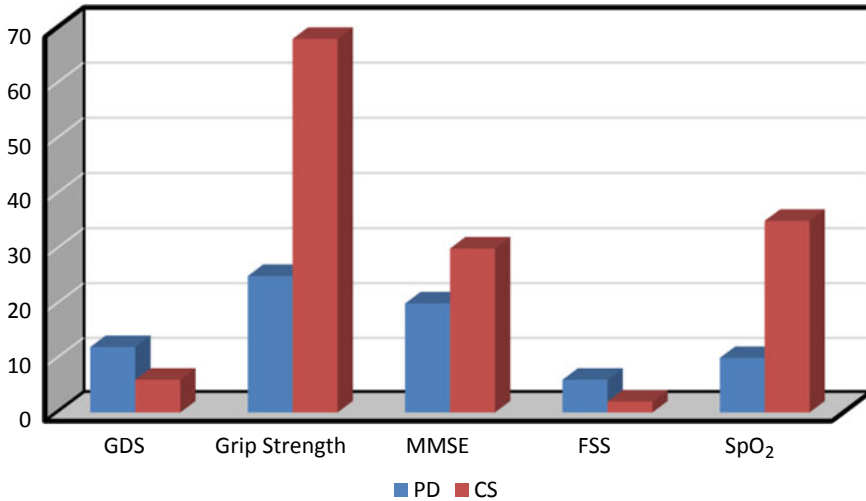


Fig. 2 Comparison for PD and CS stages performance

controls receive scores between 24 and 32, which suggest that they do not have such impairment.

We just looked at a comparison of the patients' levels of exhaustion in the graph that came before it. A person living with PD is more worn out than a member in the control group. As they become worn out so easily as a consequence of this, they are unable to carry out the regular responsibilities that are expected of them.

The graph displayed a significant disparity between the SpO₂ levels of a patient with PD and those of a healthy control participant. This research suggests that a person with PD typically has trouble sleeping due to the gradual decline in the amount of oxygen that is supplied to the brain. Table 2 lists the variance of Lyapunov Exponent and Inverse Lyapunov Exponent.

This reveals that the spatio-temporal correlation is one of the factors that contribute to lower correlations between neurons in the brains of people with PD.

Table 2 Variance of Lyapunov exponent and inverse Lyapunov exponent

PD	Lyapunov Exponent	Frontal	5.63
		Temporal	2.879
	Inverse Lyapunov Exponent	Frontal	0.1435
		Temporal	0.1278
CS	Lyapunov Exponent	Frontal	2.89
		Temporal	3.43
	Inverse Lyapunov Exponent	Frontal	0.6609
		Temporal	0.279

The findings of an electromyography (EMG) study revealed that healthy controls performed better than patients with PD in terms of root mean square, waveform length, power, and modified mean frequency. As the condition progresses, the person's muscles will begin to waste away, and it will become increasingly difficult for them to move their limbs. The findings provide new insight into the factors that contribute to the underlying cause of muscle weakness and difficulties with walking.

6 Conclusion

The fundamental objective of this research is to develop a unified model that can identify PD based on many different EEG and EMG characteristics. The neural network can be taught using any one of a large number of different instructional methods.

According to the findings of our study, we are aware that electroencephalogram (EEG) and electromyogram (EMG) data were collected with the intention of diagnosing Parkinson's disease, and that a satisfactory identification rate was achieved. In contrast, we have combined the information obtained from EEG and EMG into a single dataset that is then used as input to a classifier. This dataset contains both raw and processed data.

It is not possible to evaluate the effectiveness of classification by comparing the degrees of accuracy attained by using various types of classifiers. In order to train a classifier, we made use of a variety of EEG and EMG time domain and frequency domain data, and the combination of these three types of data led to the highest classification rate of all of the cases that we examined (only EEG or EMG features). When compared to other types, the recognition rate is maximum 98.9%, when a combination of EEG and EMG information is used as the input to the network.

References

1. Yuvaraj, R., Acharya, U.R., Hagiwara, Y.: A novel PD diagnosis index using higher-order spectra features in EEG signals. *Neural Comput. Appl.* **30**(4), 1225–1235 (2018)
2. Yuvaraj, R., Murugappan, M., Acharya, U.R., Adeli, H., Ibrahim, N.M., Mesquita, E.: Brain functional connectivity patterns for emotional state classification in Parkinson's disease patients without dementia. *Behav. Brain Res.* **298**, 248–260 (2016)
3. Yuvaraj, R., Murugappan, M., Ibrahim, N.M., Omar, M.I., Sundaraj, K., Mohamad, K., Satiyan, M.: On the analysis of EEG power, frequency and asymmetry in PD during emotion processing. *Behav. Brain Funct.* **10**(1), 12 (2014)
4. Wang, G., Shepherd, S.J., Beggs, C.B., Rao, N., Zhang, Y.: The use of kurtosis denoising for EEG analysis of patients suffering from Alzheimer's disease. *Bio-Med. Mater. Eng.* **26**(s1), S1135–S1148 (2015)

5. Wang, K.-L., Burns, M., Xu, D., Hu, W., Fan, S.-Y., Han, C.-L., Zhang, J.-G.: Electromyography biomarkers for quantifying the intraoperative efficacy of deep brain stimulation in Parkinson's patients with resting tremor. *Front. Neurol.* **11** (2020)
6. Urigüen, J.A., Garcia-Zapirain, B.: EEG artifact removal—state-of-the-art and guidelines. *J. Neural Eng.* **12**(3), 031001 (2015)
7. Vanegas, M.I., Ghilardi, M.F., Kelly, S.P., Blangero, A.: Machine learning for EEG-based biomarkers in Parkinson's disease. Presented at the 2018 IEEE International Conference on Bioinformatics and Biomedicine (BIBM) (2018)
8. Venuto, D.D., Annese, V.F., Defazio, G., Gallo, V.L., Mezzina, G.: Gait analysis and quantitative drug effect evaluation in Parkinson disease by jointly EEG/EMG monitoring. Presented at the 2017 12th International Conference on Design & Technology of Integrated Systems in Nanoscale Era (DTIS) (2017)
9. Um, T.T., Pfister, F.M.J., Pichler, D., Endo, S., Lang, M., Hirche, S., Kulić, D.: Data augmentation of wearable sensor data for PD monitoring using convolutional neural networks. [arXiv: 1706.00527](https://arxiv.org/abs/1706.00527) (2017)
10. Thilakvathi, B., Devi, S.S., Bhanu, K., Malaippan, M.: EEG signal complexity analysis for schizophrenia during rest and mental activity. *Biomed. Res.* **28**(1), 1–9 (2017)
11. Tuncer, T., Dogan, S., Acharya, U.R.: Automated detection of PD using minimum average maximum tree and singular value decomposition method with vowels. *Biocybern. Biomed. Eng.* **40**(1), 211–220 (2020)
12. Stefanis, L., de Andrade, J.B.C., Mohr, J.P.: Brain arteriovenous malformation and amyotrophic lateral sclerosis: a review based on published cases. *SN Comprehensive Clin. Med.* 1–5 (2020)
13. Alam Khan, Z., Feng, Z., Uddin, M.I., Mast, N., Ali Shah, S.A., Imtiaz, M., Mahmoud, M.: Optimal policy learning for disease prevention using reinforcement learning. *Sci. Program.* **2020**, 1–13 (2020)
14. Hussain, M., Koundal, D., Manhas, J.: Deep learning-based diagnosis of disc degenerative diseases using MRI: a comprehensive review. *Comput. Electr. Eng.* **105**, 108524 (2023)
15. Segura-Aguilar, J., Paris, I., Muñoz, P., Ferrari, E., Zecca, L., Zucca, F.A.: Protective and toxic roles of dopamine in Parkinson's disease. *J. Neurochem.* **129**(6), 898–915 (2014)
16. Ruonala, V., Pekkonen, E., Airaksinen, O., Kankaanpää, M., Karjalainen, P.A., & Rissanen, S.M.: Levodopa-induced changes in electromyographic patterns in patients with advanced Parkinson's disease. *Front. Neurol.* **9**(35). <https://doi.org/10.3389/fneur.2018.00035> (2018)
17. Santos-García, D., de Deus Fonticoba, T., Castro, E.S., Díaz, A.A., McAfee, D., Catalán, M., Mir, P.: Non-motor symptoms burden is strongly correlated to motor complications in Parkinson's disease patients. *Euro. J. Neurol.* (2020)
18. Ricciardi, C., Amboni, M., De Santis, C., Ricciardelli, G., Improta, G., Iuppariello, L., Cesarelli, M.: Classifying different stages of PD through random forests. Presented at the Mediterranean Conference on Medical and Biological Engineering and Computing (2019)
19. Qin, Z., Jiang, Z., Chen, J., Hu, C., Ma, Y.: sEMG-based tremor severity evaluation for PD using a light-weight CNN. *IEEE Signal Process. Lett.* **26**(4), 637–641 (2019). <https://doi.org/10.1109/LSP.2019.2903334>
20. Raethjen, J., Govindan, R., Muthuraman, M., Kopper, F., Volkman, J., Deuschl, G.: Cortical correlates of the basic and first harmonic frequency of Parkinsonian tremor. *Clin. Neurophysiol.* **120**(10), 1866–1872 (2009)
21. Aktürk, T., Yıldırım, E., Hanoğlu, L., Yılmaz, N.H., Yener, G.G., Güntekin, B.: A longitudinal investigation of event related EEG brain oscillations in patients with Parkinson's disease. *Anatomy Int. J. Exper. Clin. Anatomy* **13** (2019)
22. Al-Fahoum, A.S., Al-Fraihat, A.A.: Methods of EEG signal features extraction using linear analysis in frequency and time-frequency domains. *ISRN Neurosci.* (2014)
23. Camara, C., Isasi, P., Warwick, K., Ruiz, V., Aziz, T., Stein, J., Bakstein, E.: Resting tremor classification and detection in PD patients. *Biomed. Signal Process. Control* **16**, 88–97 (2014)
24. Chakraborty, S., Aich, S., Sim, J.-S., Jang, D.-J., Joo, M.-I., Kim, H.-C.: Detection of neurodegenerative disease in ageing adults: a systematic review. *TEST Eng. Manage.* **82**, 8982–8990 (2020)

25. Chaudhuri, K.R., Schapira, A.H.: Non-motor symptoms of Parkinson's disease: dopaminergic pathophysiology and treatment. *Lancet Neurol.* **8**(5), 464–474 (2009)
26. Chen, X., Wang, Z.J., McKeown, M.J.: A three-step multimodal analysis framework for modeling corticomuscular activity with application to Parkinson's disease. *IEEE J. Biomed. Health Inform.* **18**(4), 1232–1241 (2014). <https://doi.org/10.1109/JBHI.2013.2284480>
27. Chiang, J., Wang, Z.J., McKeown, M.J.: A multiblock PLS model of cortico-cortical and corticomuscular interactions in Parkinson's disease. *Neuroimage* **63**(3), 1498–1509 (2012)
28. Chu, C., Wang, X., Cai, L., Zhang, L., Wang, J., Liu, C., Zhu, X.: Spatiotemporal EEG microstate analysis in drug-free patients with Parkinson's disease. *NeuroImage Clin.* **25**, 102132 (2020)
29. Cockrell, J.R., Folstein, M.F.: Mini-mental state examination. *Principles and practice of geriatric psychiatry*, 140–141 (2002)
30. Feng, Y., Liu, Y., Liu, Z., Liu, W., Yao, Q., Zhang, X.: A novel interval iterative multi-thresholding algorithm based on hybrid spatial filter and region growing for medical brain MR images. *Appl. Sci.* **13**(2), 1087 (2023)
31. Dong, M., Husain, M., Brooks, D., Wilson, M., Craven, M., Destrebecq, F., Aps, B.: Alzheimer's disease (ad) detect and prevent-presymptomatic ad detection and prevention, (2020)
32. Dorszewska, J.: Genetic factors in Parkinson's disease. *Curr. Genomics* **14**(8), 485 (2020)
33. Duda, R.O., Hart, P.E., Stork, D.G.: *Pattern Classification*. John Wiley & Sons (2012)
34. Salankar, N., Koundal, D., Chakraborty, C., Garg, L.: Automated attention deficit classification system from multimodal physiological signals. *Multimedia Tools Appl.* 1–16 (2022)