Innovative Methods for the Detection of Parkinson's Disease

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Abstract:
Parkinson's Disease has had a significant impact on patients with the disease, and there have been recent advancements in early detection methods. These modalities include using EEG measures, gait measures, and acoustic measures. EEG measures are capable of identifying abnormalities in subcortico-cortical circuits in Parkinson's Disease patients. Acoustic measures can identify vocal irregularities, such as increased variations in fundamental frequency (jitter measure) and amplitude (shimmer measure) in the voices of Parkinson's Disease patients. Gait measures indicate that slow gait speed and increased cadence may serve as indicators of Parkinson's Disease. These three modalities were selected due to their simplicity and accessibility, in contrast to more costly and less accessible modalities like FMRIs and MRIs. This review examines the current knowledge in each of these areas and explores their potential for early detection and assessment of the severity of Parkinson's Disease. The review also covers machine learning applications with each modality and the advantages and limitations of each method. Multiple studies are provided for each modality, and the different parameters they measure are explored as well.

Introduction:

Parkinson's Disease (PD) is a progressive disorder of the central nervous system characterized by a significant decrease in dopamine levels due to damage to nerve cells, resulting in various symptoms including tremors, stiffness, vocal abnormalities, and postural instability. Early diagnosis of PD is crucial for understanding and effectively managing the condition to enhance patients' quality of life. Timely identification of the disease can facilitate the discovery of treatments to slow its progression, thereby providing a therapeutic window to mitigate its impact. While traditional diagnostic methods rely on clinical and neurological assessments and are effective in detecting PD at more advanced stages, three modalities, in particular, have emerged as promising tools for identifying the disease at its earliest stages and are gaining increasing recognition in the field. These three modalities are acoustic measures, gait measures, and electroencephalography (EEG) measures.

Identifying PD in its early stages poses a significant challenge in the field of neurotechnology, and these three modalities offer distinct methods to address this challenge. Acoustic measures involve the analysis of voice recordings to extract specific measures, including fundamental frequency (the rate at which vocal folds vibrate when making voiced speech sounds) and amplitude (the strength of the vibrations transmitted in a voice). These measures provide valuable insights into the voice variations present in PD patients, such as increased breathiness or altered pitch. Utilizing acoustic measures is particularly effective for early-stage PD analysis, as it allows for the detection of subtle voice differences that might otherwise go unnoticed. This approach significantly accelerates the identification of PD, detecting even the slightest variations before other clinical symptoms manifest.

Gait analysis involves assessing the movement patterns of individuals to detect PD. Common PD symptoms, such as tremors, manifest in these movement patterns, resulting in asymmetric and hesitant movements as individuals attempt to compensate for the tremors. Gait analysis has the potential to detect Parkinson's disease in its early stages by identifying subtle

alterations in movement patterns, even before noticeable tremors develop. Therefore, sudden changes in gait patterns could serve as an early indicator of the disease, even in the absence of other typical symptoms.

EEGs are utilized to assess brain functioning to diagnose PD. The identification of PD involves the assessment of reduced low-frequency brain waves within the frontal brain region, as well as the monitoring of specific wavelengths and determining reduced band activity, which is then correlated with PD-related decline. PD is characterized by excessive beta band activity in the motor cortex and basal ganglia, leading to the bradykinesia observed in PD patients. Additionally, EEG analysis encompasses the examination of cortical connectivity and synchronization, both of which are typically disrupted in PD. Abnormal thalamocortical dysrhythmia, indicating the presence of PD, can be rapidly identified through EEGs by detecting abnormal coherence and phase relationships between brain regions. Furthermore, EEGs provide evidence of reduced connectivity between the motor cortex and other brain regions in PD patients, aligning with the motor symptoms observed in EEG assessments. These are all examples of the types of EEG measurements that can be used to identify PD. Overall, EEGs have established themselves as a precise diagnostic tool for early-stage PD, offering valuable insights into specific abnormal brain regions long before the emergence of overt disease symptoms, thereby enabling the early detection of PD through distinct brain wave patterns.

Acoustic, gait, and EEG measures demonstrate efficacy in detecting Parkinson's disease by directly addressing the motor, neurological, and vocal disturbances, which serve as indicators of the condition. Furthermore, all three methods are non-invasive and cost-effective (i.e., they do not necessitate the use of elaborate or expensive equipment). These diagnostic tools can be employed in a clinical environment or remotely, thereby offering a practical means for early detection. The utilization of these methods crucially also facilitates the assessment of disease progression. Gait measures can help identify increased abnormal movement patterns to gauge the extent of disease advancement, while EEG measures can determine the rate of reduction in band activity to infer whether disease progression is decelerating. Moreover, EEGs are a more practical alternative to advanced imaging techniques like fMRI and MRI, which may provide detailed brain images but are less effective in capturing real-time dynamics for disease monitoring. Acoustic measures have the capacity to identify heightened pitchiness or breathiness in speech, indicating disease progression, and can be conveniently administered and repeated due to minimal data collection efforts. Additionally, acoustic measures offer a novel approach to disease analysis, focusing not on functional changes in the brain but on how these changes influence speech and establish a link between cognitive decline and motor manifestations in the voice, similar to gait measures. These three modalities excel in Parkinson's disease detection by providing real-time insights and employing a multifaceted approach to disease study, thus proving to be more cost-effective than alternative methods. Their usability outside of clinical settings further accentuates their time-saving potential for researchers, medical professionals, and patients. This review paper thoroughly explicates the characteristics of each modality and their respective outcomes.

Acoustic Measures:

Acoustic measures play a crucial role in the identification of PD by allowing for the analysis of an individual's voice for potential indicators of dysphonia (impairment in the ability to speak). Tremors, a key symptom of PD, can manifest in the voice as shaky, breathy, or pitchy characteristics. One commonly used tool for this analysis is the multi-dimensional voice program

(MDVP), which calculates up to 33 vocal parameters. Essential measures utilized in voice analysis include jitter (which assesses fundamental frequency variation), shimmer (assessing amplitude variation), Noise-to-Harmonics ratio (NHR), detrended fluctuation analysis (DFA) for signal variation, and period pitch entropy (PPE) for nonlinear assessment of fundamental frequency variation. Individuals with PD demonstrate higher jitter measures compared to healthy controls, indicative of reduced voice stability. Furthermore, PD patients exhibited elevated shimmer measures, reflecting increased variability in voice loudness, hoarseness, and breathiness. Meanwhile, NHR measures tend to be higher, and HNR measures are lower, denoting diminished tonal quality in PD patients' voices.

Little et al. (2008) conducted a noteworthy study to support the findings discussed above. This study demonstrates the diverse ways in which vocal measures impact the voices of individuals with PD. Ranging from irregular pitch to heightened hoarseness, PD patients' voices manifest more irregularities than those of healthy individuals. This highlights the potential of acoustic measures in identifying early-stage PD, given that recording a voice is non-invasive and could serve as a potential biomarker. The pronounced disparity in measures is evident, with jitter levels ranging from 1.2% to 1.5% in PD patients, as opposed to below 1% in healthy controls (Little et al., 2008). Notably, the study achieved an accuracy of 91.4%, underscoring the efficacy of acoustic measures in Parkinson's classification (Little et al., 2008). The combination of the various acoustic measures in this experiment is designed to provide comprehensive insights. For instance, greater jitter correlates with increased shimmer, and higher abnormalities in both aspects are associated with heightened voice irregularities, aligning with PD symptoms. Findings indicate noticeable variations in the mean fundamental frequency (f0), max f0, min f0, jitter, and median intensity of speech between PD patients and healthy controls. Specifically, PD patients exhibit a lower start f0, lower max f0, higher mid f0, and higher-end f0. This suggests a reduction in vocal fold frequency vibrations among PD patients, likely due to reflexive laryngeal muscle contraction in PD. Additionally, PD patients display quicker speech patterns and shorter duration in reading the same sentence as healthy controls, attributed to muscle stiffness arising from dopamine depletion in the basal ganglia, affecting the controllability of laryngeal muscles which, in turn, impacts rhythm and timing. Reduced airflow from the lungs to the vocal cords resulted in breathy and occasionally hoarse voices in PD patients. Moreover, PD patients exhibit lower HNR, higher jitter values, and fundamental frequency, indicating stiff vocal folds due to laryngeal musculature firmness.

A study by Yang et al. (2020) provided additional evidence to support these findings. The severity of the disease was best measured by the slope of maximum pronunciation to the ending of a phrase, median intensity, and duration, all showing significant differences between PD patients and the control group. Furthermore, PD patients demonstrated higher median intensity in vocalization, and PD patients with the highest values of median intensity had the disease in its most advanced stages, potentially indicating increased disease severity (Yang et al, 2020). The findings showcase the abnormal changes in the voices of PD patients, suggesting the potential use of specific vocal measures in identifying PD. The research emphasizes the importance of these vocal parameters in distinguishing between healthy controls and PD patients, making PD easier to identify.

The presence of dysphonia in patients adversely affects their quality of life, with subsequent implications for their mental well-being. By utilizing acoustic measures to promptly detect PD, efforts can be made to mitigate the progression of dysphonia in patients, thereby preserving their quality of life. This trend of PD patients exhibiting more voice irregularities is

consistent with previous findings and is reported to have a negative impact on the patient's perception of self and lower scores on the Beck Depression Inventory (Silva et al., 2012). A study by Silva et al. (2012) uses 27 male voice recordings to showcase how having dysphonia negatively affects the outlook on life. These findings showcase the importance of acoustic measures in early PD detection, as the fundamental frequency and jitter measures served as objective indicators of the PD group's more erratic voice, attributed to the tremors associated with PD. Early identification of PD could also facilitate interventions such as voice therapy for patients, thereby alleviating stress.

Machine learning, in combination with acoustic measures, may offer a further understanding of PD. Employing machine learning models to enhance acoustic analysis, by training the models to accurately identify PD based on data, could streamline the research process significantly. A study conducted by Bang et al. (2013) analyzed seven female PD patients and seven female healthy individuals. The participants were asked to vocalize extended corner vowels thrice for five seconds at a comfortable voice level. Praat, which stands for Phonetic and Acoustic Analysis Toolkit Program, was employed for annotating the acoustic speech signals. Through the input of voice samples into Praat, distinctions between healthy and PD groups were discerned, facilitating the clear identification of the disease-afflicted group. Utilizing the Praat program, the results indicated that female PD patients exhibited increased jitter and NHR. The F1 and F2 measures in PD patients revealed asymmetric centralization of unrounded vowels in positions of the tongue, signifying reduced vowel space areas (Bang et al., 2013). F1 measures are related to vowel heigh, where a higher F1 measure indicates a lower vowel. F2 measures are related to vowel backness, where a higher F2 measure indicates a more frontal vowel. This asymmetrical centralization of the tongue, affecting voice tone and loudness, is characteristic of hypokinetic dysarthria, a condition involving deficits in respiration, phonation, articulation, and prosody. Notably, the study findings support previous research, particularly in relation to jitter, shimmer, and NHR. Moreover, the utilization of the Praat program for data analysis emerged as a key focus of this study. Little et al. (2008), previously cited, also utilized the Praat program for traditional acoustic measures, highlighting the potential of integrating software programs to expedite the analysis of acoustic measures. This approach optimizes the model’s ability to swiftly identify PD, enhancing the prospects of acoustic measures serving as a biomarker for the disease. While pharmacological and neurosurgical approaches have not extensively utilized voice characteristics for diagnosing Parkinson’s, features such as jitter, shimmer, and NHR could serve as objective variables for assessing speech disorders associated with PD.

Gait Measures:

Gait measures constitute a vital method employed for the analysis of movement patterns between two distinct points. In the context of PD, these measures offer insights into the impact of the condition on an individual's walking ability. Gait measures assume a significant role in the identification of PD, as they detect bradykinesia, reduced arm swing, postural instability, and shuffling steps, all of which are key indicators of the disease. Bradykinesia is a PD symptom that impairs motor control and can cause slow movements or freezing. Deviations of a patient's values from those of healthy controls are indicative of an elevated likelihood of PD, with increasingly abnormal values suggesting advancement to more severe stages of the disease. Furthermore, gait measures can serve as potential biomarkers for early-stage PD, given that abnormal walking patterns represent symptomatic manifestations. Consequently, the

progression of the disease can be tracked by the increasing prominence of alterations in walking patterns, characterized by slower and stiffer movements due to muscular involvement and a reduction in stride length.

The line of progression, a crucial gait measurement parameter, outlines the central trajectory between the left and right footprints. Under normal circumstances, the right foot remains to the right of the line of progression, while the left foot stays to the left. In PD, both feet may become aligned exactly along the mid-line or exhibit slight asymmetry. In addition to gait velocity, another crucial measurement is cadence, defined as the number of steps taken per minute. While the average cadence ranges from 80 to 90 steps per minute, individuals with PD exhibit reduced step count. This gait pattern is characterized by rigidity, decreased movement speed (bradykinesia), diminished stride length, and irregular accelerations during walking. Gait analysis is closely linked to PD due to the impact of motor symptoms on walking patterns. Bradykinesia, for instance, leads to reductions in gait speed and step length, while tremors and muscle rigidity further exacerbate gait irregularities, particularly affecting parameters like cadence and stride time.

When examining gait, wearable sensor systems stand out as the most widely utilized method of analysis. These systems provide objective measurements of gait parameters, allowing for a clear differentiation between healthy individuals and those with PD. For instance, common PD symptoms such as increased stride time and reduced step length can be effectively monitored and quantified through the use of wearable sensors. These sensors capture the relevant data, which, when stored, can be leveraged to analyze PD symptoms, offering valuable insights into the impact of PD on muscles, particularly in the context of walking.

Brognara et al. (2019) conducted research utilizing wearable sensor systems for gait analysis, focusing on spatio-temporal parameters. The use of inertial sensors for diagnostic purposes in a clinical setting was a primary area of examination (Brognara et al., 2019). A review of 36 articles highlighted the most prevalent parameters for spatiotemporal gait analysis, including gait speed (present in 90% of the articles), cadence (61%), stride length (52.8%), stride time (41.7%), and step time (27.8%) (Brognara et al., 2019). Although parameters such as step length, right-left asymmetry, double support, stance, and swing time were also considered, they were not as commonly observed. The review underscored the potential of gait analysis with wearable sensors in the identification of PD, as the values observed in PD patients markedly differed from those of healthy individuals.

Importantly, additional studies also revealed that gait parameters were susceptible to changes and mirrored the progressive nature of Parkinson's Disease, as captured by the wearable sensor system. Schlachetzki et al. (2017), utilized wearable sensors positioned laterally on both shoes, to study 190 PD patients and 101 healthy controls. Reduced foot clearance, indicative of shuffling, was particularly evident, with controls exhibiting an average foot clearance of around 14.3 centimeters, while PD patients had significantly reduced foot clearance at an average of 10.6 centimeters. Reduced foot clearance may elevate the risk of tripping as it relates to the foot's height during the swing phase. Furthermore, PD patients exhibited a 21.5% reduction in the heel-strike angle, a 7% reduction in normalized stride length, a 5% increase in stride time, and decreased cadence and gait velocity, highlighting a slower walking pattern (Schlachetzki et al., 2017). These findings underscore how gait analysis, with its quantitative values, can serve as an objective method to diagnose Parkinson's Disease and track its progression. The study also emphasizes the pivotal role of wearable sensors in gait

measurement for PD, as these sensors serve as the primary data collection component for subsequent analysis.

The comparison of gait values between PD patients and healthy controls reveals significant differences. Utilizing gait data as a biomarker for PD proves to be particularly beneficial due to these differences. Objective quantitative gait parameters exhibit notable variances from normal values as the disease progresses through its stages. Identifying the stage of PD in a patient could serve as a valuable tool in evaluating treatment approaches, and employing gait parameters for this purpose could reduce the risk of inaccuracies. Analysis of these parameters can also provide insight into the level of muscle rigidity in PD patients. Findings that individuals in the more advanced stages of PD exhibited slower walking speed and shorter, shuffling steps compared to those in the early stages. Moreover, these advanced-stage patients displayed a wider base of support while walking, presumably to compensate for postural instability (Hass, Malczak, Nocera, Stegemöller, Shukala, Malaty, et al., 2012). Their average walking speed of 0.88 m/s was notably slower than that of the healthy older population, whose average values ranged from 1.06 m/s to 1.22 m/s. Research reveals that severely affected patients walked at an average speed of 24% slower than those with milder symptoms Hass, Malczak, Nocera, Stegemöller, Shukala, Malaty, et al., 2012). While gait speed is a widely recognized parameter, other gait parameters also hold the potential for predicting fall risk and mobile stability in PD patients. For example, the swing phase in a walking cycle typically constitutes 40% of the cycle. However, severely affected female PD patients displayed a swing phase of only 30%, substantially increasing their risk of falling and indicating the presence of smaller, shuffling steps. These findings come from research conducted by Hass, Malczak, Nocera, Stegemöller, Shukala, Malaty, et al. (2012), who used 310 individuals with idiopathic Parkinson's Disease.

The marked differences between the values for the two groups, particularly in parameters such as the swing phase, emphasize the reliability of gait parameters as a diagnostic tool. Walking speed, stride length, swing time, and hip excursion tend to be diminished in patients with PD. Conversely, the cadence and double support time exhibit an increase in PD patients compared to their healthy counterparts (Zanardi, da Silva, Costa, et al., 2021). Furthermore, PD patients demonstrate slower walking speeds and smaller steps in comparison to matched healthy controls, underscoring the marked differences in gait between the two groups. Research by Zanardi, da Silva, Costa, et al. (2021) reiterates the conclusions drawn from previous studies, highlighting the significant anomalies in gait parameters in PD patients as compared to healthy controls. This reaffirms the pivotal role of gait as a distinguishing identifier of PD, as the discrepancies in gait metrics delineate the symptoms of PD.

EEG Measures:

EEGs are a medical procedure involving the application of electrodes to the scalp to record the brain's electrical activity. This diagnostic tool is precious in the identification of PD as it directly captures brain activity. EEG readings involve the analysis of postsynaptic potential, which is derived from the interactions of thousands of neurons, reflecting various brain wave patterns. The signals obtained from EEG procedures are amplified, digitized, and subsequently transmitted to an electronic device for storage and data analysis. Moreover, the main frequency bands analyzed encompass delta (0.5 - 4 Hz), theta (4 - 8 Hz), alpha (8 - 12 Hz), and beta (16 - 30 Hz) waves. Notably, individuals with PD exhibit distinguishable angles and sharpness in their brain waves compared to those of healthy counterparts. Consequently, EEGs can unveil

abnormalities in dopaminergic subcortico-cortical circuits within PD patients. This can importantly serve as an indicator of disease severity and aid in pinpointing the primary brain regions affected, along with potential side effects.

EEG data, specifically the analysis of signals from the frontal regions of the brain, is highly valuable for identifying abnormalities in brain activity. The higher density of cortical neurons in the frontal region allows for more detailed readings, making it particularly useful in the study of PD. Reading data from these frontal regions shows how EEG can be a useful biomarker for PD. In a study conducted by Sahota et al. (2023), PD was characterized from EEG data as a "15-variate series of band power and peak frequency values/coefficients," (Sahota et al., 2023). Band power refers to specific ranges within the power spectral density, while peak frequency indicates the frequency coefficients that peak in power spectral density. The study involved recording participants in a wakefulness state, as well as in all four stages of the sleep cycle (N1, N2, N3, REM). Upon collecting data from both healthy individuals and PD patients, the researchers compared the length in epochs of all five stages from PD patients and the controls (Sahota et al., 2023). They then computed the band power and peak frequency values and, using a trained classifier, they tried to predict the accuracy of the predictions made. The results indicated that the classifier trained on the Right Temporal region achieved 85% accuracy, while the Left Frontal region achieved 78% accuracy. In contrast, the baseline models performed less accurately, with the highest accuracy reaching only 73% (Sahota et al., 2023). These findings can be attributed to the significant involvement of the frontal regions in motor control and executive functions, as well as their extensive cortical folding, which results in stronger electrical signals detectable on the scalp. Notably, the classifier accuracy revealed that the N1 data type was significantly better in recall than the other sleep stages. N1 data represents the lightest sleep stage and is shown to be the most significant data type. This suggests that it can potentially indicate restlessness in patients with early-stage Parkinson's, as they may struggle to fall asleep as quickly as before. The study underscores the clear potential of EEG data as a biomarker for PD, given its ability to analyze brain activity and detect abnormalities in comparison to healthy controls. Furthermore, the relatively small sample size of 19 healthy controls and 11 PD patients in this study highlights the need for future research with larger sample sizes to further establish the efficacy of EEGs as a biomarker, particularly in the context of monitoring brain activity during sleep cycles. The small sample size could affect the accuracy of the experiment.

Quantitative electroencephalography (qEEG) represents an important modality for assessing cognitive decline in PD. By leveraging purely quantitative and objective values, qEEG analysis offers insight into cognitive impairment in PD patients. The uniformity and objectivity of qEEG measures present the potential for early and accurate recognition of PD-related cognitive decline. Given that certain quantitative values serve as clear indicators of PD, early identification of these values could position qEEG as a potential biomarker. QEEGs can be used to identify cognitive decline in PD. QEEG processes EEG data mathematically to see relevant information. Conventionally, EEG data is qualitatively analyzed, but qEEG has parameters. Several steps are required, such as collecting the EEG data, preprocessing (removing EEG noise), and mathematically processing the “clean” EEG data. Linear and nonlinear processing techniques are used, where linear techniques use EEG data as a stationary process, and nonlinear uses EEG data as an irregular occurrence (Cozac et al., 2016). An example of linear processing is spectral analysis, which is decomposing EEG signals into component frequencies and calculating the oscillation amplitude at each frequency (Cozac et al., 2016). Studies usually

focus on spectral features of cognitive states in PD and use them to identify the difference between Parkinson's Disease with normal cognition (PD-NC) and Parkinson's Disease with dementia (PD-D). Global delta and theta powers (increased in PD-D patients) and peak background frequency (decreased in PD-D patients) were most useful in differentiating between PD-NC patients and PD-D patients. Focusing on functional connectivity features of cognitive states in PD was another use of qEEG, where PD-D patients had higher global field synchronization in theta frequency range and lower global field synchronization in the alpha 1 range. Cozac et al. (2016) showed how qEEGs can be used to analyze spectral and connectivity markers in PD patients to differentiate the levels of cognitive decline in them and find if they have dementia or not. Slower EEG frequencies are indicative of a decline in cognition, characterized by increases in the "slow" frequency bands (delta and theta), while the "fast" frequency bands (alpha and beta) show a decrease, which serves as an additional marker of cognitive decline (Shirahige et al., 2020). Connectivity measures reveal alterations in the frequency ranges of theta, alpha, and beta. There is a discernible decrease in connectivity patterns within the parietal-temporal-occipital regions of the brain, which corresponds to cognitive decline. The data is objective and identifies specific values that indicate PPD, notably the deceleration of "fast" frequency bands. This underscores the potential of EEG data, particularly qEEG data, as a valuable standardized biomarker. Motor symptoms in PD patients suggest a deceleration of cortical activity during both resting and complex movement action states, in contrast to healthy controls (Shirahige et al., 2020). Additionally, a lower dominant frequency and heightened theta power are observed in PD patients. Shirahige et al. (2020) supported the previous findings.

Although there are limitations such as a non-reduced sample size and a high risk of bias, the findings of the study suggest a deceleration of cortical activity during movement. Nonetheless, a larger controlled trial is necessary for this study, specifically incorporating a blinded qEEG analysis to prevent biases. These two qEEG studies present an alternative approach for evaluating the severity and potential diagnosis of PD. By examining band waves during resting and movement states, identifying PD patients with decreasing "fast" band waves and increasing "slow" band waves may serve as a potential biomarker for the disease. The deceleration of cortical activity could be a reliable indicator of the presence of PD, and identifying spectral features could also help identify additional conditions alongside Parkinson's, such as dementia. In summary, the findings indicate that qEEG (quantitative electroencephalography) serves as a plausible and objective biomarker for PD. This is particularly relevant to EEGs, as qEEG involves a specific data analysis approach that minimizes potential bias.

EEG analysis can be effectively conducted using machine learning techniques. By inputting EEG data into artificial intelligence and a machine learning model, the time and effort required for analysis can be significantly reduced. Machine learning techniques applied to EEG data have shown promising results in identifying progression markers of PD at a relatively low cost. The classification results have demonstrated high accuracy, with values exceeding 90% in many studies. As machine learning techniques continue to evolve, they have the potential to become one of the primary methods for detecting Parkinson's Disease by analyzing EEG data to identify abnormalities indicative of the disease. It is important to note that machine learning techniques require a substantial amount of data for training to achieve optimal accuracy and recall. Therefore, the involvement of a larger number of PD patients in EEG studies is crucial for further training the machine learning models. Additionally, the quality of EEG signals plays a

vital role in obtaining accurate results, as any signal disruption can significantly impact the findings. Research conducted by Maitín, Ana María, Alvaro José García-Tejedor, and Juan Pablo Romero Muñoz (2020) provides evidence that machine learning models related to EEGs constitute a growing field, yielding precise results and hold the potential to serve as a significant biomarker for tracking disease progression. Keller et al. (2020) conducted a study analyzing tsallis entropy and the band power of theta, alpha, beta, delta, and gamma bands in baseline, with eyes-open and eyes-closed conditions using EEGs. The study encompassed 42 cognitively normal PD patients matched with 24 healthy controls based on age, sex, and education. This analysis relied on statistical software, emphasizing the potential of combining EEGs and machine learning for advancements in Parkinson's Disease analysis. This underscores the potential for machine learning, in conjunction with EEG data, to expedite the analysis of results, as observed in its ability to discern cognitive deterioration in PD patients based on the provided EEG data. The utilization of EEGs alongside machine learning models presents as a promising asset in PD research due to its high accuracy in disease identification, with the approach of training the models emerging as a rapidly embraced concept in this domain.

Discussion:

The different modalities each present distinct advantages and disadvantages when applied to the identification of PD. Acoustic measures, for example, are closely associated with the motor symptoms of PD and function as a sensitive tool for early-stage detection due to their ability to capture subtle changes. When paired with machine learning techniques, the use of acoustic measures accelerates the identification process by enabling the detection of abnormal jitter, shimmer, NHR, and other vocal irregularities found in PD patients. Software such as Praat and MDVP are particularly employed in this context. This approach also offers the potential for personalized vocal therapy interventions aimed at enhancing the voice and overall quality of life for PD patients. Ongoing efforts are focused on the development of applications that facilitate at-home voice recordings for real-time analysis using machine learning models, allowing patients to monitor their results. Notably, the accuracy of such models has achieved 92% (Carrón et al., 2021). Patients are advised to record in semi-controlled conditions for accurate results.

However, it is important to note that utilizing acoustic measures for PD identification also presents drawbacks. Variations in voice changes among patients create a significant challenge in establishing consistent diagnostic criteria, potentially compromising result reliability. However, the probability of this occurrence is low, as most parameters, such as jitter and NHR, generally produce similar results across multiple studies. PD patients typically exhibit higher jitter and NHR values, and this pattern remains consistent. Moreover, factors like age, gender, environment, and the presence of concurrent diseases or vocal disorders can introduce confounding variables in acoustic measurements, potentially leading to misdiagnoses. Older individuals tend to have higher jitter and shimmer measures, and high measures in these areas from older individuals could lead to inaccurate readings. Additionally, the overlap of PD-related voice deterioration with symptoms of other neurological conditions in advanced stages further complicates the specificity of PD identification, while the limited sample size in existing studies should also be considered. In the investigation conducted by Bang et al. (2013), a total of 14 female participants were examined, whereas in the study performed by Silva et al. (2012), a total of 27 male participants were examined. It is important to note that smaller sample sizes may lead to reduced statistical power, increased chance of bias, and failure to represent the

entire population. Consequently, small sample sizes may fail to detect subtle effects in PD that could be found in larger sample sizes. Enhancing acoustic measures may involve the standardization of parameters as a critical step toward advancement, and increasing the sample size across various experiments may facilitate the identification of previously undiscovered features.

Gait measures play a crucial role in identifying PD as they directly assess motor symptoms, including tremors, which are among the most prevalent indications of the condition. Analyzing parameters such as gait speed, stride length, and cadence facilitates the detection of irregular walking patterns, making indications of PD readily identifiable. Utilizing wearable gait sensors further enhances the accessibility and application of gait measures beyond clinical settings. The precision and non-invasive nature of gait measures not only leaves a minimal margin for errors but also provides an effective means for tracking disease progression. Certain parameters, such as decreasing step count and higher cadence, could provide explicit indications of the advancement of the disease. As gait measures are quantitative and objective, the standardization of the parameters is increased. Moreover, ongoing developments in wearable gait sensor systems and the potential integration of machine learning with gait analysis, illustrated by initiatives such as those pursued by Tekscan, indicate promising advancements in gait analysis technology.

However, like all assessment methods, gait analysis has its limitations. Factors such as age, physical fitness, and musculoskeletal conditions can impact gait parameter variability, unrelated to PD. In older individuals, gait velocity decreases and cadence increases due to weaker calf muscles, leading to shortened step length. Conversely, in PD patients, these changes are attributed to tremors. As PD progresses, the symptoms, including tremors, become more pronounced, resulting in more prominent gait abnormalities. This would lead to challenges in relying solely on gait analysis for assessing early-stage PD, as finding the abnormalities would require further precision. Combining gait analysis with other modalities, such as EEG readings, is an effective approach to enhance the accuracy of PD diagnosis and monitoring. Furthermore, conducting additional clinical studies involving gait analysis in PD patients could unveil previously unidentified parameters, ultimately contributing to a deeper understanding of the disease and more accurate assessment methodologies.

EEGs present several advantages as a valuable tool for investigating PD. It provides direct insights into the brain's electrical activity, offering comprehensive information beyond motor symptoms by revealing the impact on brain structure. EEGs are easily accessible and non-invasive, making them a superior alternative to fMRIs and MRIs, which are more challenging to obtain for analysis. EEGs effectively detect alterations in neural oscillations and connectivity, both indicative of PD. Specific changes in beta and alpha rhythms, associated with motor control and cognitive functions, are readily identifiable in EEGs, potentially indicating early signs of PD. Furthermore, the high temporal resolution of EEGs enables real-time monitoring of disease progression. By examining brain activity in the frontal regions, which house a substantial number of neurons, insights into the effect of PD on these areas and the deterioration of motor control can be gained. Utilizing quantitative EEG analysis (qEEG) provides a more detailed and objective assessment of neural dysfunctions. Integration of qEEGs with machine learning holds promise for enhancing early PD detection by identifying changes in brain waves. Additionally, EEGs are being employed to assess patient responses to PD treatments, such as medication or deep brain stimulation (DBS), offering further understanding of disease progression and therapy efficacy.

EEGs and qEEGs also present certain limitations. EEGs have limited spatial resolution and have difficulty precisely localizing neural abnormalities. This impacts the ability to identify specific affected brain regions and bands. Additionally, EEG signals can be influenced by external factors, known as noise, which complicates data analysis by introducing artifacts. While they excel at detecting changes in neural activity, EEGs and qEEGs do not offer comprehensive information on the extent of neurodegeneration, unlike fMRIs or MRIs. Advancements in EEG technology involve signal processing techniques to eliminate artifacts and reduce noise, as well as the use of high-density EEG arrays with increased electrodes for improved spatial resolution. Continuous EEG monitoring could track changes in brain activity throughout the progression of Parkinson's disease, providing valuable insights.

The potential of AI in PD is substantial. Previous research has highlighted the combination of machine learning with acoustic, gait, and EEG measures to facilitate the analysis of these modalities. Acoustic measures have benefited from tools like Praat to enhance data collection and ensure precise results. Machine learning has been crucial in assessing gait measures by determining differences in the movements of PD patients and healthy individuals. Moreover, EEG measures have shown machine learning models with over 90% accuracy in correctly identifying the disease. With further advancements in AI technology and an increased understanding of PD, the identification of the disease could potentially become more convenient, even within a home environment. The collaboration between AI and these modalities holds significant promise in striving for improved PD patient identification.

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