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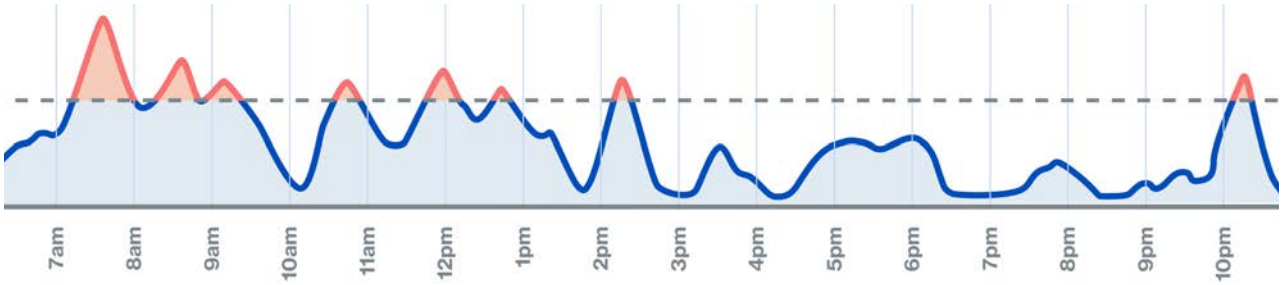


Benefits of objectively measuring Parkinson's disease motor symptoms

Parkinson's disease (PD) is a complex neurological disorder characterized by progressive motor symptoms that affect a patient's mobility, balance and quality of life. The gold standard for evaluating PD symptoms has primarily relied on subjective assessments during in-clinic visits using rating scales like the Unified Parkinson's Disease Rating Scale (UPDRS). This approach, however, has specific limitations, leading to often incomplete disease progression evaluation.

First-generation approach – in-person clinical evaluation

The most common method today to determine the existence and progression of PD is through in-person clinical evaluation. These are typically 20- to 30-minute clinic appointments that occur relatively infrequently. During the appointment, the clinician questions the patients about their symptoms and overall well-being while observing the patient and carrying out a physical examination. Based on this information, the clinician may determine the symptom rating.

Clinical rating scales are used to quantify the symptoms, impairment and disability [1]. The Unified Parkinson's Disease Rating Scale (UPDRS) has been one of the principal tools used to evaluate PD motor symptoms and is still used widely today. Using this method, clinicians assess various motor symptoms based on observations, patient-reported experiences and their expertise.

An in-person clinical evaluation using rating scales, when appropriate and within the allocated appointment time, is the current gold standard in evaluating PD

severity and tracking the progression of the disease. However, according to clinicopathological studies in the UK and Canada, diagnostic accuracy of the method is low. [6]

The UPDRS was originally developed in the 1980s to evaluate various aspects of PD, including motor and non-motor experiences in daily living and motor complications. The Movement Disorder Society recently made changes to the UPDRS to take a more holistic approach, adding non-motor elements, such as mood and behavior. [3]

Another commonly used rating scale is Hoehn and Yahr, originally created in 1967 to evaluate the disease severity by combining deficiency and disability based on bilateral motor involvement and compromised balance and gait. The simple scale describes PD stages from 1 to 5 based on motor impairment severity and disability. The scale has gained acceptance due to its ease of use, although it does not fully reflect a person's degree of impairment when it comes to handling daily living activities. [1]

Shortcomings of in-person clinical evaluation

In-person clinical evaluations during time-restricted appointments, however, have inherent limitations. The assessment performed in a clinical environment does not mirror day-to-day symptoms, which may vary during the day or even between days. In-clinic evaluations only capture a "snapshot" of the symptoms at a specific moment in time. In addition, the evaluations are highly subjective. [4]

Subjectivity

The evaluation is highly dependent on subjectivity across human examiners, as it relies heavily on the clinician's own expertise, skills and experience. The in-clinic evaluation is subject to interpretability issues and recall bias, including a risk of assessment disagreement among the professionals working on the same patient case [1]. In addition, many elements depend greatly on the patient's memory and the ability to describe the symptoms experienced, either during the appointment or with the help of a symptom diary. Also, information entered in diaries is often unclear. A study by Erb et al. [2] found that 38% of all participants who were to complete a motor symptom diary at home missed about 25% of the possible entries, while the average delay time was more than 4 hours. To create an optimized and personalized PD treatment plan, objective evaluation of the patients' symptoms and overall condition is crucial.

Time limitations

Clinic visits generally tend to happen infrequently, restricting comprehensive patient monitoring and timely intervention. Clinic visits are also often restricted by short consultation times, limiting the length of evaluation to the duration of the appointment. Some signs of disease progression may remain unnoticed during the examination. Furthermore, this overlooks typical motor symptom fluctuations that patients may experience at home and between appointments.

Non-home environment

The clinic environment and potential travel to the clinic can also impact the patient's condition and

the evaluation of symptoms during the appointment. In many cases, patients also strive to perform at their best during medical evaluation, known as the Hawthorne effect in which patients modify their behavior in response to their awareness of being observed. Therefore, assessment in a non-home environment can easily lead to decisions that do not accurately represent the daily symptoms the patient experiences at home.

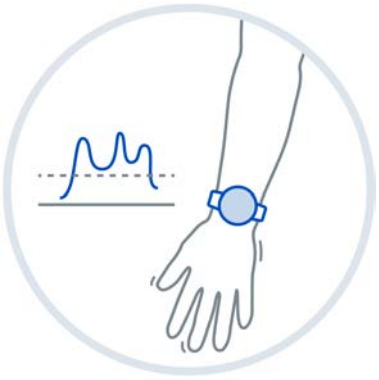
Long-term follow-up challenges

Lack of continuous, objective monitoring hinders a more complete understanding of the treatment effectiveness over extended periods. The optimal management of PD motor symptoms and their complications depends primarily on consistent symptom detection in frequent intervals, leading to enhanced treatment decisions.

Decisions, often made based on short-term evaluations and subjective information, can detrimentally affect the treatment plan by not considering a comprehensive, longer-term view of symptom occurrence and evolution over time.

First-generation approach

- ⊖ Subjectivity
- ⊖ Time limitations
- ⊖ Non-home environment
- ⊖ Long-term follow-up challenges



Second-generation approach – adding motion measurement

Over the last decades, methods using motion measurement have been developed to overcome the shortcomings of the first-generation approach. They provide a non-invasive method to measure the movements of PD patients, even in a home environment.

Methods using motion measurement are not intended to replace the first-generation approach but to complement it. The approach can help clinicians get more insight into a patient's condition at home.

Motion measurement uses dedicated wearable devices with motion sensors or accelerometer data from a smartwatch to quantify physical movements when assessing a patient's symptoms.

Over the past years, an increasing number of new wearable solutions have been launched to measure and monitor movement disorder symptoms, showing promising results in research trials. These wearable devices can be used either during a clinic visit or remotely. [1]

Studies show that remote and continuous monitoring plays a crucial role in the treatment quality a patient receives by allowing medical professionals to better track disease progression and adjust medication. Additionally, remote and continuous monitoring with wearable devices plays a significant role in reducing healthcare system costs and raising patient satisfaction. [1]

Advantages of symptom monitoring with wearable motion sensors

Recently, wearable devices have started to be used in clinical practice for monitoring a patient's PD-related motor symptoms during daily activity. Statistical analysis has shown potential in symptom detection, and the correlation between the severity and the expert evaluations has been high.

Objective measurement of patients' physical movements

The use of accelerometers allows physical movement data to be captured unobtrusively during the patient's daily life. The devices used are easy to wear and provide data about the patient's visible movement.

Collection of data over a longer period of time

Wearable devices also help to collect motion data over extended periods of time. This enables a more holistic view of a patient's condition overall. Many of the wearable devices can also monitor medication adherence and overall activity levels.

Measurement in a familiar environment

Measurement in a familiar, in-home and everyday environment allows to best capture the patient's day-to-day condition, including fluctuations. It enables the patient to perform regular daily activities naturally, without having to strive to attain the best results for evaluation purposes.

Regular measurements allow better treatment outcome follow-up

Regular assessments of the patient's symptoms allow clinicians to identify patterns and trends, and better understand the progression of the disease. Regular measurement also helps clinicians to objectively follow the effectiveness of the treatment and maintain a better care balance for the patient.

Limitations of the second-generation approach with motion measurement only

Despite offering objective data on the patients' physical movements, this second-generation approach also has specific limitations.

Measurement data includes only visible physical motion

Wearable devices for motion measurement capture only physical movement that is also visible. These devices are not able to capture motor symptoms that are not yet visible to the human eye.

No information on root cause of movement

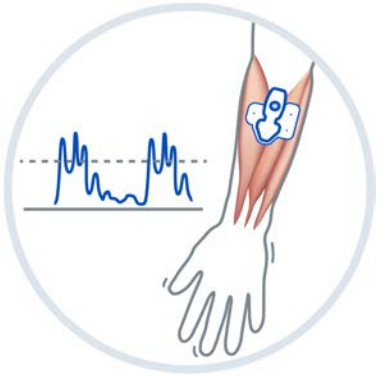
The approach does not measure the root cause of the movement that originates in the brain and moves through the motor nerves to the muscles. Without being able to determine the root cause of the observed movement, it is difficult to specify whether the movement is voluntary or involuntary – or if it is caused by PD or relates to another movement disorder. This hinders a deeper understanding of the symptomatology.

Limitations on accuracy

When a patient's motion is measured during everyday life, the amount of movement measured is extensive. The measurement includes both voluntary movement and movement caused by external sources, creating an inherent source for false positive and false negative outcomes for symptom analysis. To overcome this issue, extended measurement time as well as increased result averaging are typically needed. This extends the burden on the patient due to the length of the measurement. Additionally, it reduces the time resolution and makes the interpretation and use of findings more difficult.

Second-generation approach

- ⊕ Objective measurement of patients' physical movements
- ⊕ Collection of data over a longer period of time
- ⊕ Measurement in a familiar environment
- ⊕ Regular measurements allow better treatment outcome follow-up
- ⊖ Measurement data includes only visible physical motion
- ⊖ No information on root cause of movement
- ⊖ Limitations on accuracy



Third-generation approach – advanced technology combining EMG and motion measurement

The first articles about measuring PD-related motor symptoms with electromyography (EMG) date back to the 1980s. During the past 15 years, this method has gained more interest and systematic study.

Now that the technology combining EMG and motion measurement has been able to take advantage of wearable devices, it has become a viable option to monitor PD motor symptoms in a home environment.

The combination of **EMG and motion measurement**, aiming to complement the first- and second-generation approaches, offers advanced precision technology to attain high accuracy in objective symptom measurement. This is called the third-generation technology.

This third-generation approach uses dedicated wearable devices to add the measurement of neuromuscular signals to motion measurement for deeper insight into muscle activity. This approach allows an objective and more comprehensive understanding of a patient's motor symptoms. It provides clinically

meaningful and actionable data to plan treatment and empowers clinicians to make evidence-based treatment decisions for better patient outcomes.

The approach uses a small, non-invasive measurement device worn on the forearm or upper arm. It can be applied by a nurse or assistant either in-clinic or at home. The measurement device is worn during the day and night to provide a comprehensive overview of the symptoms and track possible differences in symptom behavior.

EMG measures the electrical muscle activity causing a person's movement. It detects issues with motor coordination, motor nerves, muscles and the communication between them. [5]

EMG has been used to objectively evaluate the different motor symptoms of PD, such as tremor, rigidity and bradykinesia, and indicates how the disease modifies the muscle activity patterns during rest periods or different types of movement. It provides valuable insight for making data-driven decisions about both muscle function and motor control that are affected by the disease. [5]

The third-generation approach combining EMG and kinematic measurements revolutionizes the accuracy of measured symptom data. It supports an earlier detection of motor symptoms and helps to objectively evaluate the symptoms, including the variation in severity at different points in time. It also allows to objectively measure the effects of different therapies.

With this high degree of symptom data accuracy, the third-generation approach supports clinicians in developing personalized treatment plans for optimal symptom control, including the follow-up of the treatment effectiveness, in a way that has not been possible before.

Unparalleled advantages of the third-generation approach

The third-generation approach combining EMG and kinematic measurements offers unique and unparalleled advantages that have not been attained by any other approach alone.

Differentiate between visually similar symptoms

This approach enables identification and differentiation of visually similar symptoms, such as different types of tremors, for example. It can also differentiate between symptoms that patients find hard to distinguish or have documented incorrectly.

Separate symptoms from voluntary and externally caused movements

The third-generation approach differentiates intentional movements from unintentional or externally caused movements, which aids clinicians in getting an accurate and clear picture of the patients' condition and improving treatment planning and outcomes.

Isolate PD from other movement disorders

The EMG signal analysis can indicate PD-specific symptoms, which helps in distinguishing them from symptoms of other movement disorders.

Detect and measure rigidity

This technology enables the detection and measurement of rigidity, a symptom especially critical in the assessment of PD. Having a better understanding of the associated rigidity aids in optimizing treatment planning.

Differentiate side effects

This approach also helps in distinguishing PD symptoms from side effects of the medications used for treatment. This allows clinicians to intervene appropriately, when necessary.

Detect symptoms not yet physically visible

The third-generation approach helps clinicians identify symptoms that are not yet visible or physically apparent, such as internal tremor, enabling them to detect symptoms earlier and offer the patient proactive disease management and earlier symptom intervention.

One of the most valuable advantages of this approach is that it allows findings to be cross-validated between the two technologies – EMG and kinematic measurement. This leads to more meaningful and holistic clinical insight when making therapeutic decisions and treatment plans for PD patients.

Third-generation approach

- ⊕ Differentiate between visually similar symptoms
- ⊕ Separate symptoms from voluntary and externally caused movements
- ⊕ Isolate PD from other movement disorders
- ⊕ Detect and measure rigidity
- ⊕ Differentiate side effects
- ⊕ Detect symptoms not yet physically visible

Attaining a more comprehensive symptom evaluation through advanced technology

Objective measurement methods, particularly the integration of EMG with kinematic measurement, represent a significant advancement in evaluating the specific symptoms related to PD. They complement the gold standard by providing accurate and objective data to validate patient evaluations and treatment plans.

Adamant Health has introduced advanced third-generation technology based on wearable surface EMG and 3D accelerometry that adds clinically meaningful data to the existing evaluation method by analyzing muscle activity and movement over a longer period of time.

Collecting, processing and using recorded EMG signals for analysis is challenging due to the vast amount of data that can be obtained with the measurement method. Adamant Health's unique, clinically validated and research-based data-analysis technology frees clinicians from analyzing and interpreting EMG signal results by providing easy-to-read reports from all data collected. This limits additional workloads on clinicians.

The Adamant Health symptom reports give a clear picture of a patient's symptoms and accurate insight into the patient's condition, enabling clinicians to communicate better with patients and their families and to make better-informed decisions for improved patient outcomes.

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