



Long-term ambulatory assessment of motor symptoms in movement disorders: a best-evidence review



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ABSTRACT

Introduction: Assessing movement disorders in daily life can provide information that might not be available during a short clinical visit. This review provides an overview of the currently available ambulatory registration methods to assess motor symptoms.

Methods: A systematic review was performed of ambulatory registration methods, registering motor symptoms for at least 24 h. The following characteristics were studied: study goal, study population, data acquisition, outcome measures, and data interpretation.

Results: For the classical subjective approach, a patient-kept diary, two types are widely applied: the ON/OFF diary to assess the medication response status in patients with Parkinson's Disease (PD), and the fall diary to assess fall frequency. Both diaries are established methods for clinical decision-making. However, both diaries have disadvantages, especially since self-report might not always agree with clinicians' ratings. An often-used alternative objective approach that employs accelerometry can assess activity levels and gait, monitor disease progression and distinguish between healthy controls and patients. However, accelerometry cannot reliably assess medication status in PD nor distinguish between different diseases. Also due to the heterogeneity in body locations for the accelerometer and outcome measures, there are no gold standards to rely on. Accelerometry to assess tremor can be used to obtain clinically valid measures. The combination of objective and subjective measurements is, at this point, mainly useful for scientific research.

Conclusion: Subjective measurements of ON/OFF status and fall frequency remain the most widely adopted long-term registration methods. Most other methods first need more validation in a clinical setting before they can be applied in patient care.

1. Introduction

Recently, there has been great interest in studying motor symptoms in movement disorders objectively [1–3]. Movement disorders can be broadly divided into two subtypes: hyperkinetic and hypokinetic movement disorders. Hypokinetic movement disorders, including Parkinson's disease (PD), have bradykinesia as a core feature. Hyperkinetic movement disorders, for example tremor, chorea, and myoclonus, are characterized by an increase in muscle activity.

Currently, the standard method to assess movement disorders is a clinical examination during an outpatient clinic visit [4]. Clinical rating scales, such as the Unified Parkinson's Disease Rating Scale (UPDRS), can standardize this. Such an assessment, however, only provides a snapshot of the patient's condition. Many symptoms are only present for part of the day [4]. For example, patients with PD can exhibit

response fluctuations with during parts of the day a good response to medication (ON time) and at other times no good response (OFF time), plus periods of medication-induced dyskinesias (ON with dyskinesias). Recalling such a fluctuating pattern accurately can be difficult for patients and can therefore result in an inaccurate estimate of the symptoms [5].

Monitoring patients for a longer period (hours, days) can provide a more accurate assessment of motor symptoms in daily life [4]. Moreover, increased insight into the pattern of movement-disorder symptoms during the day might help in studying factors contributing to symptom fluctuations. The classical approach for monitoring patients for a longer period is using a diary. An ON/OFF diary, for example, studies medication response in PD for a pre-specified interval [6]; a fall diary assesses the fall frequency by applying an event-related design [7]. Using measuring devices, movement disorder motor symptoms

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during daily life activities can be quantified objectively. Examples of measuring devices include accelerometers, measuring acceleration of a body part, and gyroscopes, measuring angular velocity. These methods can be used to study tremor, general activity, and gait patterns. Although such objective registrations have been applied for over 30 years [8], subjective measurements remain the primary assessment tools or endpoints in clinical care and research in PD [4]. However, there is growing awareness that objective measures might improve or complement subjective measures in capturing the full complexity of motor symptoms [1]. Furthermore, a recent study discovered a discrepancy between subjective and objective tremor measurements [9]. It can thus be questioned whether subjective or objective methods should be preferred, or whether they should be combined since they provide different information.

This review will provide an overview of the currently available ambulatory registration methods for motor symptoms in movement disorders. To do so, it will describe the characteristics, data acquisition, outcome measures and data interpretation of these registration methods, as well as describe the extent these registration methods have been applied scientifically and clinically.

2. Methods

A computerized MEDLINE search was performed on July 1, 2017, using combinations of text words and MeSH terms: Movement disorders [MeSH], movement disorders [title/abstract] ambulatory registration [MeSH] OR ("Monitoring, Ambulatory"[Mesh] OR ambula*[tiab] OR outpatient[tiab] OR home[tiab]) AND (Movement Disorders[Mesh] OR movement disorder*[tiab] OR chorea[tiab] OR myoclonus[tiab] OR dystonia[tiab] OR Parkinson*[tiab] OR bradykinesia[tiab] OR tremor*[tiab]) AND (registration*[tiab] OR monitor*[tiab] OR detect*[tiab] OR sensor*[tiab] OR acceleromet*[tiab] OR gyroscope*[tiab] OR magnetometer[tiab] OR diary[tiab] OR diaries[tiab] OR record*[tiab] OR regist*[tiab] OR wireless*[tiab])). Furthermore, the bibliographies of the studies were examined for relevant studies not covered in the search. The following criteria were applied: (1) only studies in English were reviewed; (2) studies needed to apply continuous ambulatory registration in the home environment for 24 h minimum, while subjects performed normal daily life activities; and (3) the studies focused on motor symptoms in movement disorders like tremor, gait disorders, myoclonus, dystonia, chorea, and bradykinesia. Ataxia was excluded since this diagnosis refers to a coordination problem rather than a hyperkinetic or hypokinetic movement disorder.

Data were extracted for the following items: (1) general information on the method, including type of device and brand; (2) study goal and symptom of interest; (3) study population, that is, number and characteristics of patients and controls; (4) data acquisition, that is, study length, part of the day with the device, bodily location of the device, and whether the device was ready to use (i.e., no further preparations necessary to begin the measuring period); (5) outcome measures; and (6) interpretation, that is, correlation of outcome parameters with a gold standard and whether the parameter measured reflected the symptom of interest.

3. Results

3.1. Description of search results

In total, 1090 studies were identified. After application of the inclusion and exclusion criteria, 52 studies remained; details are in Table 1. PD patients were included in all studies except one that concerned Huntington's disease [10]. In 33 studies, PD was studied exclusively. No studies involving myoclonus or dystonia were found. In 15 studies a diary was used: 11 on ON/OFF levels in PD and four on falls. Furthermore, in 28 of the 52 studies, accelerometry was used to study activity levels (14), gait (12), or tremor (2). Finally, eight studies used a

combination of a diary and accelerometry; one study used a method that did not fit in any of the categories (a gastrocnemius expansion measurement unit). In the following section, each of the methods assessing movement disorders in an ambulatory setting will be discussed separately.

3.2. Diary – ON/OFF levels in PD

3.2.1. Study goal and study population

The ON/OFF diary is used to measure the medication response in PD patients. Out of the 11 studies, four tried to validate the ON/OFF diary by comparing with a reference diary [6,11] or clinicians' ratings [12,13] and seven studied treatment effects [14–19]. All 11 studies assessed PD patients (Table 1).

3.2.2. Data acquisition

The measuring period varied between 24 h and four weeks. Diary use involves only waking time, by definition. In 10 studies, diaries had to be completed every 30 min and in one study every hour [13]. Four studies advised a training session to enhance reliability [6,12,13,19]. Seven studies mentioned the use of a paper diary; the other studies did not mention whether they used a paper or electronic diary (Table 1).

3.2.3. Outcome measures

Four studies used diaries with the items "ON" or "OFF" medication [14,16,17,20]; the other seven also included items on dyskinesia [6,11–13,18,19,21].

3.2.4. Data interpretation

Four studies used a gold standard for comparison. The first used a reference diary (*good* and *bad* period items) and found a better correlation when applying the new items *ON with* or *ON without troublesome dyskinesias* instead of the previous *ON without*, *ON with mild* or *ON with severe dyskinesias* [11]. In the second study, *good on time* (on time without dyskinesia or with nontroublesome dyskinesias) most strongly correlated with the patients' perceived duration of a good response as measured by a visual analog scale and overall motor response over the day [6]. The third and fourth studies used simultaneous clinicians' ratings and found a correspondence of 80% and a kappa of 0.62, respectively [12,13].

3.2.5. Summary

The ON/OFF diary has been used extensively in PD patients. With patients reporting medication response every 30 min, the outcome is meaningful for clinical practice. However, patient self-report and clinicians' ratings do not always correspond regarding the medication status of PD patients.

3.3. Diary – falls

3.3.1. Study goal and study population

Fall diaries are used to study the fall frequency and circumstances. One study aimed to identify modifiable predictors of falls in patients with Alzheimer's disease, Lewy body dementia, or vascular dementia [22]; another to assess the circumstances of falls in PD patients, patients with mild cognitive impairment, or patients with a history of idiopathic falls [7]; the third to study whether treadmill training reduced fall frequency in PD patients [23]; and the fourth to compare characteristics of community and home-based falls in PD patients [24].

3.3.2. Data acquisition

All studies used a long measuring period: 6, 12, or 14 months (Table 1). Three studies used exclusively paper diaries [7,22,24] whereas the fourth also provided the possibility of using a web-based calendar or smartphone application. The diaries had an event-related design: patients only completed the fall diary when they fell.

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