R E V I E W

Quantitative Wearable Sensors for Objective Assessment of Parkinson's Disease

Walter Maetzler, MD,[1,2]* Josefa Domingos,[3] Karin Srulijes, MD,[1,2] Joaquim J. Ferreira, MD, PhD,[3] and Bastiaan R. Bloem, MD, PhD[4]

[1]Hertie Institute for Clinical Brain Research, Department of Neurodegeneration, Center of Neurology, University of Tuebingen, Tuebingen, Germany
[2]German Center for Neurodegenerative Diseases (DZNE), Tuebingen, Germany
[3]Laboratory of Clinical Pharmacology and Therapeutics and Instituto de Medicina Molecular, Faculty of Medicine, University of Lisbon, Lisbon, Portugal
[4]Radboud University Nijmegen Medical Centre, Donders Institute for Brain, Cognition and Behaviour, Department of Neurology and Parkinson Centre Nijmegen, Nijmegen, The Netherlands

ABSTRACT: There is a rapidly growing interest in the quantitative assessment of Parkinson's disease (PD)-associated signs and disability using wearable technology. Both persons with PD and their clinicians see advantages in such developments. Specifically, quantitative assessments using wearable technology may allow for continuous, unobtrusive, objective, and ecologically valid data collection. Also, this approach may improve patient-doctor interaction, influence therapeutic decisions, and ultimately ameliorate patients' global health status. In addition, such measures have the potential to be used as outcome parameters in clinical trials, allowing for frequent assessments; eg, in the home setting. This review discusses promising wearable technology, addresses which parameters should be prioritized in such assessment strategies, and reports about studies that have already investigated daily life issues in PD using this new technology. © 2013 *Movement* Disorder Society

Key Words: outcomes; Parkinson's disease; quantitative motor assessment; wearable devices

Clinical visits provide only a brief snapshot of the condition that persons with Parkinson's disease (PD) present in that particular situation. However, PD is notorious for its fluctuations, which may occur both within and across days. Moreover, performance during the clinical visit does not always reflect how patients perform at home. A well-known example is freezing of gait, which is often difficult to elicit in the examination room, even in patients who are severely debilitated by frequent freezing episodes at home.[1] Other events are by definition absent during routine clinical visits, such as nighttime disability caused by axial akinesia.[2] Measuring such disease-related outcomes objectively (fairly, without bias or external influence), continuously (without interruption), unobtrusively (not involving direct elicitation of data from the user), and with high ecological validity (approximating the real world that is being examined, for example, at the patients' homes), could boost the efficiency and clinical relevance of those visits, and improve patient management. This clinical wish appears to coming within reach with the advent of new, wearable technology that can quantitatively collect, analyze, and deliver data to both the patient and doctor. The relevance and accessibility of these data acquired from wearable technology is improving thanks to the development of sophisticated software and web-based applications (eg, see Memedi et al.[3]). Objective recordings from wearable sensors may better help to capture meaningful data than information from surveys, paper, and diaries that is retrospectively assessed[4] and prone to recall and other sources of bias. In addition, consistency of symptom ratings may differ considerably between patient and doctor. Indeed, trained observers' and patients' ratings have surprisingly low agreement.[5,6]

From a scientific and methodological perspective, there is also great interest in such assessment strategies. For example, in some negative clinical trials, small effects may have been missed because the clinically based outcomes were unable to detect them (discussed in Maetzler et al.[7] and Parkinson Progression Marker Initiative[8]). Use of wearable technique in future clinical trials might offer a way to detect such subtle changes more readily through a high responsiveness to change. This could potentially be important, eg, when evaluating potential disease-modifying agents, because even small effects offer a proof of concept that the intervention at least achieved some biological effects. An additional advantage for clinical trials is the ability of wearable devices to measure outcomes at multiple time points, enhancing the statistical power.

Overall, continuous assessments of disease-associated signs and disabilities of persons with PD, eg, in the home environment, are urgently required as they probably have high ecological validity. The technique is still in its infancy, and many aspects, including validity, reliability, and data security issues must be considered before such assessment strategies can be applied routinely. From our point of view the following symptoms and signs are particularly relevant in this respect:

Motor disabilities;
    Axial disability (gait and transfer deficits, freezing of gait, balance deficits, and falls);
    Distal bradykinesia;
    Dyskinesias;
    Tremor;
    Dysarthria;
    Sedentary lifestyle and physical inactivity;

Non-motor disabilities;
    Sleep disturbances; and
    Autonomic dysfunctions

Table 1 reviews wearable assessment tools that have already been used to detect some of these signs and symptoms, with a particular focus on studies that assessed responsiveness of therapy, and on techniques that were tested in an everyday environment. A discussion about device-assisted detection strategies cannot be comprehensive (and there are indeed examples of emerging—also not body-worn—objective measures of disability in people with PD[9]), but based on some illustrative examples, we aim to give readers a feel for the current status and potential applications of this new and potentially important wearable technology.

Motor Disabilities

Axial Signs

Axial signs such as postural instability and gait deficits, including freezing of gait (FOG), have long been considered as late symptoms of PD. However, using new assessment strategies and algorithms, it is becoming clear that at least some gait and balance parameters can be altered in early or even preclinical stages of PD.[10–12]

Gait and Transfer Deficits

PD is characterized by a hypokinetic gait, with slow and shuffling steps, as well as an asymmetrically reduced arm swing.[13] This hypokinetic gait usually improves with dopaminergic medication,[14] with deep brain stimulation (DBS),[15] and with a variety of physical therapy interventions, including high-amplitude movements,[16] dancing,[17] and Nordic Walking.[18,19] It would be helpful for clinicians to be reliably informed about the progression of gait disability and the therapeutic effects of applied interventions. However, gait assessment during a typical clinical visit is mostly only qualitative, subjective, and brief.

In recent years, wearable technical solutions have markedly enhanced the quality of gait assessment. For example, a small device with acceleration and angular velocity sensors worn on the shank has been used to assess stride length over a 24-hour period.[20] The investigators found a 100% agreement between the stride length measurement assessed with the wearable sensors, and video observation. Others have used pressure-sensitive foot insoles as sensors, and developed a different outcome, namely a coefficient representing the variability and inaccuracy in phase generation.[21,22] Their results showed that gait variability was larger in persons with PD than in controls. This is relevant because gait variability can be used as marker to help predict the risk of future falls.[23–25]

Collection of disease-relevant gait data may even be possible using a single wearable sensor. For example, stride-to-stride variability in PD patients can be assessed using the acceleration signal of the vertical axis derived from a sensor that is worn at the lower back.[26] Moreover, the authors found that automated frequency-based measures solely from the vertical acceleration signals differentiated PD patients from controls, and also distinguished between PD patients in their on and off state with acceptable accuracy.[26] Interestingly, this difference was also visible when the participants walked around the medical center, suggesting that frequency-based analysis approaches could provide ecologically valid estimates of stride-to-stride variability even under everyday circumstances.[26] Acceptable accuracy for the detection of on/off phases has also been demonstrated for the parameter stride length, assessed with an unobtrusive inertial measurement unit worn at the left shank.[27]

Data derived from angular velocity transducers attached to the lower back indicate that turning when walking is slower, and that trunk movements are slower in untreated early-to-moderate PD patients,

TABLE 1. Selection of quantitative assessment tools for PD-associated signs and symptoms

Signs/symptoms	Body location of the sensor(s)	Raw signal(s)	Most promising parameter(s)	Device(s) used	References
Gait and transfers	Left shank	Acceleration and angular velocity	Stride length	Xsens Technologies B.V. (Enschede, The Netherlands); gait monitor (IM Systems, Baltimore, MD, USA)	27[a], 20[b]
	Soles of feet	Foot pressure	Phase coordination index of gait cycle	Custom-made force-sensitive insoles	21,22
	Lower back	Acceleration of the vertical axis	Frequency-based measures of gait	ADXL330® (Analog Devices, Norwood, MA, USA)	26[b]
	Lower back	Acceleration (Smartphone)	Cadence, interstride autocorrelation, step time variability	Smartphone (HTC, Android) and Dynaport Hybrid® (Mc Roberts, the Netherlands)	59[d]
	Forearms, shanks, thighs and sternum	Acceleration and angular velocity	Cadence, peak arm swing velocity, arm swing yaw, peak trunk horizontal velocity, turning duration, turn-to-sit duration	Physilog® (BioAGM, La Tour-de-Peilz, Switzerland)	58
	Lower back	Acceleration	Time- and amplitude-based measures of sit-to-stand and stand-to-sit	ADXL330® (Analog Devices)	57
	Shanks, wrists, sternum	Angular velocity (sternum: with acceleration signal)	Peak arm velocity, arm swing range of motion and asymmetry, cadence, peak trunk rotation velocity and rotation range of motion, turning velocity	Physilog® (BioAGM)	29
	Lower back	Angular velocity	Walk peak roll velocity, total turning duration, turn peak yaw and roll velocity	SwayStar™ (Balance Int. Innovations GmbH, Iseltwald, Switzerland)	28
	Forearm	Acceleration	Arm swing asymmetry, maximal cross-correlation and instantaneous relative phase of bilateral arm swing	Triaxial G-Link accelerometers (MicroStrain, Inc.; Williston, VT, USA)	30
Freezing of gait	Knee	Angular velocity	Spectral analysis of knee signal	Custom-made goniometers	39
	Left shank	Acceleration	Spectral analysis of vertical leg acceleration	Stride monitor (IM Systems)	40
	Shank, tight, waist	Acceleration	Spectral analysis	Custom made real-time wearable system	41[c]
Balance	Lower back	Acceleration	Velocity, JERK, acceleration, frequency-based measures	Xsens	51
	Lower back	Angular velocity	Displacement, velocity	SwayStar™ (Balance Int.)	52,53[a]
	Lower back	Acceleration	Peak trunk acceleration during anticipatory postural adjustments towards the stance leg	Xsens	56
	Lower back	Acceleration	Hilbert-Huang transformation of postural parameters	DynaPort MiniMod® (McRoberts, The Hague, The Netherlands)	80
Falls	Front pants pocket	Acceleration	Movements being faster than defined thresholds	Smartphone (HTC, Android)	65[e]
Distal bradykinesia	Wrist	Acceleration	Movements made with lower acceleration and amplitude and with longer intervals between movements	Parkinson's Kinetigraph (Global Kinetics Corporation, Melbourne, Australia)	68[a]
	Finger and wrist	Acceleration and angular velocity	Speed, amplitude and rhythm of UPDRS bradykinesia tasks	Kinesia™ (Cleveland Medical Devices Inc., Cleveland, OH, USA)	69[a]
	Forearms	Angular velocity	Period, speed and range of movement	Physilog® (BioAGM)	67

(Continued)

TABLE 1. *Continued*

Signs/symptoms	Body location of the sensor(s)	Raw signal(s)	Most promising parameter(s)	Device(s) used	References
Dyskinesia	Shoulder	Acceleration	Time- and frequency-domain properties of the signal	EGAS-FS-25 (Entran ltd, Watford, UK)	76
	Wrists, shanks, chest, waist	Acceleration and angular velocity	Energy distribution over the frequency spectrum, nonlinear properties of the signal	ANCO devices (Athens, Greece)	75
	Upper arms and legs, wrist, sternum	Acceleration	Segment velocity, neural networks	ADXL-202 (Analog Devices, Norwood, MA, USA)	74
	Wrist	Acceleration	Movements of normal amplitude and acceleration but with shorter periods without movement	Parkinson's Kinetigraph	68[a]
Tremor	Finger and wrist	Acceleration and angular velocity	Not applicable	Kinesia™	69[a]
	Wrist	Acceleration	Tremor frequency	MicroMini Motionlogger (Ambulatory Monitoring, Ardsely, NY, USA)	79[a]
	Forearms	Angular velocity	Tremor period and amplitude	Physilog® (BioAGM)	67
	Lower back	Acceleration	Hilbert-Huang transformation of postural parameters	DynaPort MiniMod®	80
Physical activity	Lower back	Acceleration	Walking steps, duration of walking periods	DynaPort MoveMonitor®	87
	Lower back	Acceleration	Time spent on activities including walking, cycling, standing, sitting, lying	DynaPort MoveMonitor®	88
	Shanks, trunk	Acceleration	Time spent on activities such as walking, standing, sitting, lying	Physilog® (BioAGM)	89
	Wrist	Acceleration	Activity counts and steps	MicroMini Motionlogger	91[b]
Sleep	Lower back	Acceleration	Physical activity, body posture	DynaPort MiniMod®	94
	Wrist	Acceleration	Activity counts	MicroMini Motionlogger	91[b]
Autonomic dysfunction	Chest	Ambulatory 24-hour ECG	Low- and high-frequency component	24-hour ECG (Fukuda-Denshi, Tokyo, Japan)	91[b]
	Wrist	Acceleration	Resting activity in bed/out of bed	MicroMini Motionlogger	91[b]

Most of the available studies compared the usability of wearable devices to distinguish PD patients from controls, and were performed in a clinical environment.
[a]Studies that measured responsiveness to therapy.
[b]Studies that were performed under everyday conditions.
[c]Studies that measured the progression, change, and/or variability of symptoms in PD patients.
[d]Compared timed-up-and-go measures of a Smart-phone with those of a sensor specifically designed for movement analyses.
[e]Not evaluated in PD patients.
 ECG, electrocardiogram; JERK, derivate of acceleration; PD, Parkinson's disease; UPDRS, Unified Parkinson's Disease Rating Scale.

compared to controls.[28] Reduced arm swing and arm swing asymmetry are also hallmarks of PD. A recent study[29] found a reduced peak arm swing velocity on the more affected side of untreated early-to-moderate PD patients compared to controls using a gyroscope attached to the dorsum of each wrist. Similar results were found by use of accelerometers attached to the forearms.[30]

Freezing of Gait

Freezing of gait (FOG) is a disabling phenomenon characterized by brief episodes during which patients are unable to generate effective forward-stepping movements. It is one of the most important factors that constrain quality of life in PD.[31] Moreover, FOG now appears to be 1 of the most important causes of falls.[32,33] FOG is a treatable condition. For example, off-period FOG responds relatively well to medication, but in rare cases levodopa can worsen FOG.[34] Also, nonmedical interventions such as cueing strategies[35] and robot-assisted gait training[36] can reduce FOG frequency and severity.

All these aspects argue for an evaluation of FOG. However, it can be extremely difficult to elicit FOG episodes when examining affected PD patients in the hospital,[1] because examinations are typically performed under "ideal" circumstances (wide open

corridors, even terrain, well-lit environment) that are unlikely to elicit FOG, and the sheer knowledge of being observed can suppress the sign. This underscores the need for continuous assessments, preferably in the home environment of the patient.

What techniques are currently available to detect FOG? A broadly studied approach aims to assess FOG by evaluating the spatiotemporal kinematic parameters of gait.[37,38] For example, 1 laboratory-based study examined people with PD who had to avoid suddenly appearing obstacles while walking on a moving treadmill, a paradigm known to elicit FOG.[39] Gait kinematics were assessed using motion analysis, based on feedback of goniometers. With a frequency-based approach that has previously been shown to detect FOG accurately in PD,[40] even very subtle FOG episodes could be detected with acceptable sensitivity and high specificity, compared to judgment by 2 movement disorders specialists in a video analysis.[39] The detection of such subtle FOG is potentially relevant because they might serve as a marker for more severe FOG, making the transformation of this technology into ambulatory assessment highly demanding.

The first attempts to detect FOG online during ecologically valid real-life conditions with wearable devices are promising. In a recent study, 237 FOG events were detected with a sensitivity of 73% and a specificity of 82%, compared to judgment by professional physiotherapists in a post hoc video analysis.[41] These devices can potentially be used even for online cueing of actual FOG events.[42]

Balance Deficits

Balance impairment in PD greatly affects quality of life. The response to medical therapy is complex, as some elements of postural control may improve, others are resistant to treatment, and still others may in fact worsen.[43,44] Balance deficits may also improve with specific physical therapy interventions, such as strength and balance training[45] or, with a lower level of evidence, tai chi.[46] A notorious problem that hampers further development of better treatment strategies is the lack of reliable and sensitive clinical outcome measures, including the subjective scoring of the test outcome (judging the number and quality of the compensatory stepping reactions).[47] It would therefore be helpful to have an unobtrusive quantitative "mobile" assessment of balance control, in order to detect deficits as early as possible, and to monitor progression.

Wearable technology is now available to detect even subtle balance deficits. Most approaches aim to measure sway of the trunk or the body's centre of gravity, as a derivative of balance control, assuming that less sway equates with better balance performance (note that this is not necessarily true, as some have argued

that under certain circumstances, large sway excursions are actually useful, for example to "probe" the environment[48,49]; moreover, in PD patients dyskinesia has been shown to relevantly influence balance parameters[50]). For example, a linear accelerometer attached to the lower back can be used to detect mild postural sway abnormalities in early-stage, untreated PD patients during quiet stance, and the results are comparable with those of a more expensive, laboratory-based static posturography assessment (force plates).[51]

It is also possible to detect postural sway with wearable sensors while subjects are moving about freely; eg, while walking. For example, a combination of 2 angular sensors, again attached to the lower back, has been used to measure trunk sway in the pitch (anterior-posterior) and roll (medial-lateral) plane, while subjects performed a variety of everyday gait and balance tasks.[52] The results showed that persons with PD have larger anterior-posterior and medial-lateral angular velocity deviations at the trunk when performing stance tasks, compared to controls. When this device is rotated 90 degrees, 1 of the sensors now measures rotations in the yaw plane (vertical axis), and this is highly relevant because this permits assessment of axial turning during walking (now recognized as the most common precipitant of FOG). The same device was recently used to determine balance differences in PD patients before and after biofeedback training, suggesting that this kind of training has beneficial effects on trunk stability.[53]

Anticipatory postural adjustments represent another interesting balance parameter associated with an increased risk of freezing and falling. In order to allow for stepping movements, anticipatory weight shifts are necessary to "free up" the swing leg. Laboratory-based assessments had demonstrated that these anticipatory postural adjustments are reduced in persons with PD.[54,55] Using a sensor at the lower back, it was found that anticipatory postural adjustments toward the stance leg (as measured from the peak trunk acceleration) were smaller in untreated PD patients compared to control individuals,[56] also indicating that wearable technology is able to detect changes of this parameter.

Combined Assessments

Combinations of axial movements such as transfers, gait, turning, and balance reflect a more true-to-life condition. The timed up and go (TUG) test is a widely used clinical paradigm to test such combinations. However, the usefulness of this test is limited by the fact that only the total time to perform all these different and complex movements is measured. A number of studies evaluating subcomponents of the TUG (eg, sit-to-stand and stand-to-sit transfer[57]) by using wearable sensors have recently been published. One study

found that, when comparing early PD patients with controls, total TUG time was similar between the groups but cadence, angular velocity of arm swing, turning duration, and time to perform turn-to-sits differed significantly.[58]

Such objective gait assessments may now become readily available to a wide audience through the use of commercially available smart-phones with built-in accelerometers. Such devices can be used to quantify performance on the TUG, and in fact equally good as a device that was specifically developed for movement analysis.[59] We expect that smart-phones will soon develop into pervasive, low-cost tools for continuous quantitative assessment of movement and mobility.

Fall Events

Falls are usually defined as "events where subjects inadvertently come to rest on a lower level."[60] There is an enormous interest to monitor falls because of the associated morbidity (injuries, loss of independence) and even mortality.[61] Fall frequency should therefore be 1 of the most relevant outcome parameters in future disease progression studies and clinical trials. Particularly the latter application is becoming increasingly important, in light of exciting new evidence for therapeutic interventions that may reduce falls, including cholinesterase inhibitors[62] and strength and balance training.[45,63]

Falls are sporadic, episodic events, so prolonged monitoring is necessary to capture these rare incidents in individuals with low risk of falling. Importantly, being able to record the actually occurring fall would theoretically open up avenues for "online" fall prevention, for example by attaching an inflatable device that would be activated to cushion the impact of the fall once its onset was recorded. The first experience with falls detection during everyday life is becoming available, for example by use of a single sensor with accelerometers worn at the lower back.[64] Moreover, it is possible to determine a fall by extracting data from the triaxial accelerometer of smart-phones, which is evaluated with several threshold-based algorithms and position data.[65]

Distal Bradykinesia

Bradykinesia describes slowness in the execution of a movement, and is a cardinal motor symptom of PD that generally responds well to dopaminergic medication and DBS, with distal bradykinesia showing the best response.[66] Thus, assessment of this feature can be used as a reflection of the effectiveness of medical treatment. Moreover, it would be helpful to have an objective measure for bradykinesia, alongside (or perhaps even instead of) the semiquantitative and subjective assessment that is now used in clinical practice. For this purpose, assessment of distal bradykinesia

with wearable sensors could help to improve the monitoring of medical treatment, aiming to achieve better control with reduction of off phases and fluctuations.

Aspects of distal bradykinesia have already been measured with wearable devices.[67] Moreover, recent results indicate that ecologically valid detection of bradykinesia during the day is feasible. Griffiths et al.[68] measured bradykinesia in people with PD and controls during a 10-day period at home using a wrist-worn device, coupled with sophisticated software to analyze the recorded signals, and found clear differences between the groups, as well as a high correlation to the Unified Parkinson's Disease Rating Scale, motor par (UPDRS-motor, Part III) score, and improvement in scores in response to changes in medication. Similar results were obtained with a motion capture device worn on 1 finger and the wrist when PD patients were asked to perform bradykinesia items of the UPDRS at home.[69]

Dyskinesias

Dyskinesias are a disabling adverse effect of long-term L-dopa treatment. These occur in approximately 50% of PD patients after a mean of 5 years of L-dopa treatment, and include peak-dose and diphasic dyskinesias, and dystonia.[70,71] New treatment options are becoming available,[72] but evaluation during a clinical visit is prone to bias because dyskinesias are typically influenced by emotional changes. Moreover, single assessments during a clinical visit offer insufficient insight into the nature and severity of dyskinesias that occur in daily life. This makes it particularly relevant to measure dyskinesias continuously and quantitatively in the home setting.

Assessment of dyskinesias using wearable technique appears to be a promising approach. Accuracies of 84% and higher for the correct classification of dyskinesias were reported using multiple body-worn sensors.[73–75] Even a single device worn at the shoulder[76] showed good agreement with simultaneously performed rating scores that were made by experienced neurologists. Results of a recent study using a single wrist-worn sensor suggest that dyskinesia could be quantified also in a home setting[68]; however, this needs further evaluation. It should also be noted that studies using wearable technique did not differentiate between dyskinesia subtypes, such as ON, OFF, and diphasic dyskinesias, and did not report about occurrence or absence of therapy-associated dystonias. However, we cannot exclude that clever analytical algorithms may in future be able to separate the more dystonic type of dyskinesias (as in diphasic dyskinesias) from the more choreatic peak-dose dyskinesias. This would certainly be a great help to clinicians, because making this distinction based on history taking can be very difficult.

Tremor

Although tremor is not seen as 1 of the main quality of life–constraining signs of PD,[31] evaluation of tremor remains relevant because it is easily recognized by the social environment and because it can be very incapacitating for individual patients. Moreover, quantification of tremor can provide accurate information about the efficacy of medical therapy as tremor responds relatively well to dopaminergic medication. Such a quantitative evaluation cannot easily be performed during the typically short-lived patient–doctor consultations, but requires an objective continuous quantitative assessment; eg, with wearable sensors.

The first results using either the Wii remote,[77] or triaxial accelerometers placed at 4 different positions on the body[78] showed an acceptable accuracy in detecting the severity of tremor. Feasibility of tremor detection in PD has been demonstrated by use of small sensors located at the wrist,[79] forearm,[67] and lower back,[80] as well as—in a home setting—a finger-worn motion sensor combined with a wrist-worn command module.[69] A downside of all published studies is that none reported whether the applied systems were able to differentiate between distinct subforms of tremor (eg, resting tremor vs action tremor) under everyday conditions.

Dysarthria

An estimated 70% to 90% of people with PD develop speech or voice disorders, specifically hypokinetic dysarthria.[81] Depending on their specific symptom profile, dopaminergic medication and DBS can alter specific parameters of speech in individual patients. For example, specific DBS settings that offer major motor improvements may lead to dysarthric side effects. Being able to objectively assess and analyze speech and voice would be a great advantage for both patients and clinicians, for example to track the treatment response. To date, researchers have mainly collected quantitative speech data using head-mounted or desktop microphones, combined with solid-state digital recording devices[81] or computer-integrated software.[82] However, it is conceivable that wearable technique such as smart-phone–based sensors with adequate analysis software can deliver objective speech information as well.

Sedentary Lifestyle and Physical Inactivity

Mobility and physical activity are among the most important factors capable of maintaining good quality of life.[83] In people with PD and elderly without parkinsonism, regular physical activity potentially has preventive effects; eg, regarding occurrence of cardiovascular events, diabetes mellitus, dementia, depression and sleep disturbances,[84] flexibility, balance and muscle strength,[45,85] and falls.[86] Currently we have the unsatisfying situation that neither the patient nor the doctor has an objective feedback about these parameters.

Wearable sensors can give an estimate of mobility and physical activity by defining, eg, number and intensity of certain activities such as walking and performing transfers in a defined time period. Pilot validation studies suggest that wearable sensors can be used as simple and objective tools to assess mobility in the patient's own environment. Walking periods and number of steps were appropriately detected by a single sensor at the lower back,[87] as were activities such as walking, cycling, standing, sitting, and lying.[88,89] However, accuracy of such activity sensors for long-term monitoring of walking distances seems still to be limited.[90] Interestingly, by use of a wrist-worn sensor in a home setting, it was recently shown that people with PD have lower physical activity levels than controls.[91]

Non-Motor Disabilities

Sleep Disturbances

Almost two-thirds of persons with PD suffer from complex sleep disturbances that severely affect their quality of life.[92] Insomnia is most common, followed by rapid eye movement (REM) sleep behavior disorder (RBD), excessive daytime sleepiness, and restless legs syndrome.[93] Currently, assessment of sleep is only possible with questionnaires or time- and resource-consuming polysomnography that cannot be provided to the whole PD community. Thus, quantitative and more easy-to-use assessment tools are needed.

The first results using wearable technique such as triaxial accelerometers are promising. In a laboratory-based study with healthy individuals and patients with obstructive sleep apnea syndrome,[94] body posture scores of a single accelerometer worn at the lower back, and the polysomnography position reached an intraclass correlation of 0.84. In people with PD, movement patterns during sleep have been shown to be accessible with a single sensor at home.[91]

Autonomic Dysfunction

People with PD often suffer from autonomic dysfunction. Orthostatic hypotension, impaired heart rate variability, sexual and gastrointestinal dysfunction, sialorrhea, and sweating are among them.[95] They have an enormous impact on quality of life of affected patients, and are extremely difficult to assess, in particular in a clinical setting. Although autonomic dysfunction is generally difficult to treat, at least some of the symptoms are treatable; eg, with increased physical activity.[95,96]

Wearable sensors may be an elegant option to offer an ecologically valid continuous and quantitative assessment of autonomic symptoms. As shown with a 24-hour ambulatory electrocardiograph (ECG) and a sensor worn at the

wrist for 7 days in the home environment to measure circadian regulation of heart rate variability and resting activity, PD patients had lower activity levels when out of bed and higher activity levels when in bed, compared to controls.[91] Moreover, PD patients had a lower total frequency component and a reduced low-frequency/high-frequency ratio of the heart rate variability.[91] This suggests that the circadian rhythm of the autonomic nervous system is altered in PD, and that continuous assessment of physical activity and heart rate variability using wearable technique are promising outcome variables for the evaluation of the autonomic system.

Conclusion

It is increasingly possible to assess PD-related signs with wearable technical devices that are relatively unobtrusive, cheap, and which offer objective recordings over prolonged periods under ecologically valid circumstances. However, the currently available techniques have not yet found their way into routine clinical assessment. We expect this to change drastically in the near future, in light of a rapidly growing interest among PD patients, clinicians, and methodologists, aiming to pragmatically collect objective and ecologically relevant data to evaluate therapeutic effects and to rate disease severity. Wearable technical devices can provide potentially relevant, factual, accurate, and continuous health data that are less open to subjective interpretation. Ultimately, such techniques will help to overcome the drawbacks that are inherent to single or multiple "snapshot" assessments in current clinical practice and clinically oriented research. ■

References

1. Snijders AH, Haaxma CA, Hagen YJ, Munneke M, Bloem BR. Freezer or non-freezer: clinical assessment of freezing of gait. Parkinsonism Relat Disord 2012;18:149–154.

2. Louter M, Munneke M, Bloem BR, Overeem S. Nocturnal hypokinesia and sleep quality in Parkinson's disease. J Am Geriatr Soc 2012;60:1104–1108.

3. Memedi M, Westin J, Nyholm D, Dougherty M, Groth T. A web application for follow-up of results from a mobile device test battery for Parkinson's disease patients. Comput Methods Programs Biomed 2011;104:219–226.

4. Stone AA, Shiffman S, Schwartz JE, Broderick JE, Hufford MR. Patient compliance with paper and electronic diaries. Control Clin Trials 2003;24:182–199.

5. Goetz CG, Stebbins GT, Blasucci LM, Grobman MS. Efficacy of a patient-training videotape on motor fluctuations for on-off diaries in Parkinson's disease. Mov Disord 1997;12:1039–1041.

6. Davidson MB, McGhee DJ, Counsell CE. Comparison of patient rated treatment response with measured improvement in Parkinson's disease. J Neurol Neurosurg Psychiatry 2012;83:1001–1005.

7. Maetzler W, Liepelt I, Berg D. Progression of Parkinson's disease in the clinical phase: potential markers. Lancet Neurol 2009;8: 1158–1171.

8. Parkinson Progression Marker Initiative. The Parkinson Progression Marker Initiative (PPMI). Prog Neurobiol 2011;95:629–635.

9. Surangsrirat D, Thanawattano C.Android application for spiral analysis in Parkinson's disease. Proceedings of IEEE Southeastcon Orlando 2012:1–6. Available at: http://ieeexplore.ieee.org/stamp/stamp.jsp?tp=&arnumber=6196943&isnumber=6196883. Accessed July 31, 2013.

10. Maetzler W, Hausdorff JM. Motor signs in the prodromal phase of Parkinson's disease. Mov Disord 2012;27:627–633.

11. Maetzler W, Mancini M, Liepelt-Scarfone I, et al. Impaired trunk stability in individuals at high risk for Parkinson's disease. PLoS One 2012;7:e32240.

12. Mirelman A, Gurevich T, Giladi N, Bar-Shira A, Orr-Urtreger A, Hausdorff JM. Gait alterations in healthy carriers of the LRRK2 G2019S mutation. Ann Neurol 2011;69:193–197.

13. Snijders AH, van de Warrenburg BP, Giladi N, Bloem BR. Neurological gait disorders in elderly people: clinical approach and classification. Lancet Neurol 2007;6:63–74.

14. Rochester L, Baker K, Nieuwboer A, Burn D. Targeting dopasensitive and dopa-resistant gait dysfunction in Parkinson's disease: selective responses to internal and external cues. Mov Disord 2011;26:430–435.

15. Deuschl G, Schade-Brittinger C, Krack P, et al. A randomized trial of deep-brain stimulation for Parkinson's disease. N Engl J Med 2006;355:896–908.

16. Ebersbach G, Ebersbach A, Edler D, et al. Comparing exercise in Parkinson's disease—the Berlin LSVT(R)BIG study. Mov Disord 2010;25:1902–1908.

17. Hackney ME, Earhart GM. Short duration, intensive tango dancing for Parkinson disease: an uncontrolled pilot study. Complement Ther Med 2009;17:203–207.

18. Reuter I, Mehnert S, Leone P, Kaps M, Oechsner M, Engelhardt M. Effects of a flexibility and relaxation programme, walking, and nordic walking on Parkinson's disease. J Aging Res 2011;2011: 232473.

19. Fritz B, Rombach S, Godau J, Berg D, Horstmann T, Grau S. The influence of Nordic Walking training on sit-to-stand transfer in Parkinson patients. Gait Posture 2011;34:234–238.

20. Moore ST, Dilda V, Hakim B, Macdougall HG. Validation of 24-hour ambulatory gait assessment in Parkinson's disease with simultaneous video observation. Biomed Eng Online 2011; 10:82.

21. Plotnik M, Giladi N, Hausdorff JM. A new measure for quantifying the bilateral coordination of human gait: effects of aging and Parkinson's disease. Exp Brain Res 2007;181:561–570.

22. Plotnik M, Giladi N, Hausdorff JM. Bilateral coordination of gait and Parkinson's disease: the effects of dual tasking. J Neurol Neurosurg Psychiatry 2009;80:347–350.

23. Hausdorff JM, Rios DA, Edelberg HK. Gait variability and fall risk in community-living older adults: a 1-year prospective study. Arch Phys Med Rehabil 2001;82:1050–1056.

24. Nakamura T, Meguro K, Sasaki H. Relationship between falls and stride length variability in senile dementia of the Alzheimer type. Gerontology 1996;42:108–113.

25. Verghese J, Holtzer R, Lipton RB, Wang C. Quantitative gait markers and incident fall risk in older adults. J Gerontol 2009;64: 896–901.

26. Weiss A, Sharifi S, Plotnik M, van Vugt JP, Giladi N, Hausdorff JM. Toward automated, at-home assessment of mobility among patients with Parkinson disease, using a body-worn accelerometer. Neurorehabil Neural Repair 2011;25:810–818.

27. Moore ST, MacDougall HG, Gracies JM, Ondo WG. Locomotor response to levodopa in fluctuating Parkinson's disease. Exp Brain Res 2008;184:469–478.

28. Visser JE, Voermans NC, Oude Nijhuis LB, et al. Quantification of trunk rotations during turning and walking in Parkinson's disease. Clin Neurophysiol 2007;118:1602–1606.

29. Zampieri C, Salarian A, Carlson-Kuhta P, Aminian K, Nutt JG, Horak FB. The instrumented timed up and go test: potential outcome measure for disease modifying therapies in Parkinson's disease. J Neurol Neurosurg Psychiatry 2010;81:171–176.

30. Huang X, Mahoney JM, Lewis MM, Guangwei D, Piazza SJ, Cusumano JP. Both coordination and symmetry of arm swing are reduced in Parkinson's disease. Gait Posture 2012;35:373–377.

31. Ellis T, Cavanaugh JT, Earhart GM, Ford MP, Foreman KB, Dibble LE. Which measures of physical function and motor impairment best predict quality of life in Parkinson's disease? Parkinsonism Relat Disord 2011;17:693–697.

32. Kerr GK, Worringham CJ, Cole MH, Lacherez PF, Wood JM, Silburn PA. Predictors of future falls in Parkinson disease. Neurology 2010;75:116–124.

33. Latt MD, Lord SR, Morris JG, Fung VS. Clinical and physiological assessments for elucidating falls risk in Parkinson's disease. Mov Disord 2009;24:1280–1289.

34. Espay AJ, Fasano A, van Nuenen BF, Payne MM, Snijders AH, Bloem BR. "On" state freezing of gait in Parkinson disease: a paradoxical levodopa-induced complication. Neurology 2012;78:454–457.

35. Nieuwboer A, Kwakkel G, Rochester L, et al. Cueing training in the home improves gait-related mobility in Parkinson's disease: the RESCUE trial. J Neurol Neurosurg Psychiatry 2007;78:134–140.

36. Lo AC, Chang VC, Gianfrancesco MA, Friedman JH, Patterson TS, Benedicto DF. Reduction of freezing of gait in Parkinson's disease by repetitive robot-assisted treadmill training: a pilot study. J Neuroeng Rehabil 2010;7:51.

37. Nieuwboer A, Fabienne C, Anne-Marie W, Kaat D. Does freezing in Parkinson's disease change limb coordination? A kinematic analysis. J Neurol 2007;254:1268–1277.

38. Nieuwboer A, Dom R, De Weerdt W, Desloovere K, Fieuws S, Broens-Kaucsik E. Abnormalities of the spatiotemporal characteristics of gait at the onset of freezing in Parkinson's disease. Mov Disord 2001;16:1066–1075.

39. Delval A, Snijders AH, Weerdesteyn V, et al. Objective detection of subtle freezing of gait episodes in Parkinson's disease. Mov Disord 2010;25:1684–1693.

40. Moore ST, MacDougall HG, Ondo WG. Ambulatory monitoring of freezing of gait in Parkinson's disease. J Neurosci Methods 2008;167:340–348.

41. Bachlin M, Plotnik M, Roggen D, Giladi N, Hausdorff JM, Troster G. A wearable system to assist walking of Parkinson s disease patients. Methods Inf Med 2010;49:88–95.

42. Bachlin M, Plotnik M, Roggen D, et al. Wearable assistant for Parkinson's disease patients with the freezing of gait symptom. IEEE Trans Inf Technol Biomed 2010;14:436–446.

43. Beuter A, Hernandez R, Rigal R, Modolo J, Blanchet PJ. Postural sway and effect of levodopa in early Parkinson's disease. Can J Neurol Sci 2008;35:65–68.

44. Mancini M, Rocchi L, Horak FB, Chiari L. Effects of Parkinson's disease and levodopa on functional limits of stability. Clin Biomech (Bristol, Avon) 2008;23:450–458.

45. Goodwin VA, Richards SH, Henley W, Ewings P, Taylor AH, Campbell JL. An exercise intervention to prevent falls in people with Parkinson's disease: a pragmatic randomised controlled trial. J Neurol Neurosurg Psychiatry 2011;82:1232–1238.

46. Li F, Harmer P, Fitzgerald K, et al. Tai chi and postural stability in patients with Parkinson's disease. N Engl J Med 2012;366:511–519.

47. Munhoz RP, Li JY, Kurtinecz M, et al. Evaluation of the pull test technique in assessing postural instability in Parkinson's disease. Neurology 2004;62:125–127.

48. Corna S, Tarantola J, Nardone A, Giordano A, Schieppati M. Standing on a continuously moving platform: is body inertia counteracted or exploited? Exp Brain Res 1999;124:331–341.

49. Carpenter MG, Murnaghan CD, Inglis JT. Shifting the balance: evidence of an exploratory role for postural sway. Neuroscience 2010;171:196–204.

50. Chung KA, Lobb BM, Nutt JG, McNames J, Horak F. Objective measurement of dyskinesia in Parkinson's disease using a force plate. Mov Disord 2010;25:602–608.

51. Mancini M, Horak FB, Zampieri C, Carlson-Kuhta P, Nutt JG, Chiari L. Trunk accelerometry reveals postural instability in untreated Parkinson's disease. Parkinsonism Relat Disord 2011;17:557–562.

52. Adkin AL, Bloem BR, Allum JH. Trunk sway measurements during stance and gait tasks in Parkinson's disease. Gait Posture 2005;22:240–249.

53. Nanhoe-Mahabier W, Allum JH, Pasman EP, Overeem S, Bloem BR. The effects of vibrotactile biofeedback training on trunk sway in Parkinson's disease patients. Parkinsonism Relat Disord 2012;18:1017–1021.

54. Burleigh-Jacobs A, Horak FB, Nutt JG, Obeso JA. Step initiation in Parkinson's disease: influence of levodopa and external sensory triggers. Mov Disord 1997;12:206–215.

55. Rocchi L, Chiari L, Mancini M, Carlson-Kuhta P, Gross A, Horak FB. Step initiation in Parkinson's disease: influence of initial stance conditions. Neurosci Lett 2006;406:128–132.

56. Mancini M, Zampieri C, Carlson-Kuhta P, Chiari L, Horak FB. Anticipatory postural adjustments prior to step initiation are hypometric in untreated Parkinson's disease: an accelerometer-based approach. Eur J Neurol 2009;16:1028–1034.

57. Weiss A, Herman T, Plotnik M, et al. Can an accelerometer enhance the utility of the timed up & go test when evaluating patients with Parkinson's disease? Med Eng Phys 2010;32:119–125.

58. Salarian A, Horak FB, Zampieri C, Carlson-Kuhta P, Nutt JG, Aminian K. iTUG, a sensitive and reliable measure of mobility. IEEE Trans Neural Syst Rehabil Eng 2010;18:303–310.

59. Mellone S, Tacconi C, Chiari L. Validity of a Smartphone-based instrumented timed up and go. Gait Posture 2012;36:163–165.

60. Hauer K, Lamb SE, Jorstad EC, Todd C, Becker C, Group P. Systematic review of definitions and methods of measuring falls in randomised controlled fall prevention trials. Age Ageing 2006;35:5–10.

61. Kannus P, Sievanen H, Palvanen M, Jarvinen T, Parkkari J. Prevention of falls and consequent injuries in elderly people. Lancet 2005;366:1885–1893.

62. Chung KA, Lobb BM, Nutt JG, Horak FB. Effects of a central cholinesterase inhibitor on reducing falls in Parkinson disease. Neurology 2010;75:1263–1269.

63. Ashburn A, Fazakarley L, Ballinger C, Pickering R, McLellan LD, Fitton C. A randomised controlled trial of a home based exercise programme to reduce the risk of falling among people with Parkinson's disease. J Neurol Neurosurg Psychiatry 2007;78:678–684.

64. Klenk J, Becker C, Lieken F, et al. Comparison of acceleration signals of simulated and real-world backward falls. Med Eng Phys 2011;33:368–373.

65. Sposaro F, Tyson G. iFall: an Android application for fall monitoring and response. Conf Proc IEEE Eng Med Biol Soc 2009;2009:6119–6122.

66. Fahn S, Oakes D, Shoulson I, et al. Levodopa and the progression of Parkinson's disease. N Engl J Med 2004;351:2498–2508.

67. Salarian A, Russmann H, Wider C, Burkhard PR, Vingerhoets FJ, Aminian K. Quantification of tremor and bradykinesia in Parkinson's disease using a novel ambulatory monitoring system. IEEE Trans Biomed Eng 2007;54:313–322.

68. Griffiths RI, Kotschet K, Arfon S, et al. Automated Assessment of bradykinesia and dyskinesia in Parkinson's disease. J Parkinsons Dis 2012;2:47–55.

69. Mera TO, Heldman DA, Espay AJ, Payne M, Giuffrida JP. Feasibility of home-based automated Parkinson's disease motor assessment. J Neurosci Methods 2012;203:152–156.

70. Olanow CW, Stern MB, Sethi K. The scientific and clinical basis for the treatment of Parkinson disease (2009). Neurology 2009;72(21 Suppl 4):S1–S136.

71. Fox SH, Lang AE. Levodopa-related motor complications—phenomenology. Mov Disord 2008;23(Suppl 3):S509–S514.

72. Gottwald MD, Aminoff MJ. Therapies for dopaminergic-induced dyskinesias in Parkinson disease. Ann Neurol 2011;69:919–927.

73. Tsipouras MG, Tzallas AT, Rigas G, Bougia P, Fotiadis DI, Konitsiotis S. Automated levodopa-induced dyskinesia assessment. Conf Proc IEEE Eng Med Biol Soc 2010;2010:2411–2414.

74. Keijsers NL, Horstink MW, Gielen SC. Automatic assessment of levodopa-induced dyskinesias in daily life by neural networks. Mov Disord 2003;18:70–80.

75. Tsipouras MG, Tzallas AT, Fotiadis DI, Konitsiotis S. On automated assessment of levodopa-induced dyskinesia in Parkinson's disease. Conf Proc IEEE Eng Med Biol Soc 2011;2011:2679–2682.

76. Manson AJ, Brown P, O'Sullivan JD, Asselman P, Buckwell D, Lees AJ. An ambulatory dyskinesia monitor. J Neurol Neurosurg Psychiatry 2000;68:196–201.

77. Mamorita N, Iizuka T, Takeuchi A, Shirataka M, Ikeda N. Development of a system for measurement and analysis of tremor using a three-axis accelerometer. Methods Inf Med 2009;48:589–594.

78. Rigas G, Tzallas AT, Tsalikakis DG, Konitsiotis S, Fotiadis DI. Real-time quantification of resting tremor in the Parkinson's disease. Conf Proc IEEE Eng Med Biol Soc 2009;2009:1306–1309.

79. Schlesinger I, Benyakov O, Erikh I, Suraiya S, Schiller Y. Parkinson's disease tremor is diminished with relaxation guided imagery. Mov Disord 2009;24:2059–2062.

80. Mellone S, Palmerini L, Cappello A, Chiari L. Hilbert-Huang-based tremor removal to assess postural properties from accelerometers. IEEE Trans Biomed Eng 2011;58:1752–1761.

81. Chenausky K, Macauslan J, Goldhor R. Acoustic analysis of PD speech. Parkinsons Dis 2011;2011:435232.

82. Skodda S, Gronheit W, Schlegel U. Intonation and speech rate in Parkinson's disease: general and dynamic aspects and responsiveness to levodopa admission. J Voice 2011;25:e199–e205.

83. Acree LS, Longfors J, Fjeldstad AS, et al. Physical activity is related to quality of life in older adults. Health Qual Life Outcomes 2006;4:37.

84. Speelman AD, van de Warrenburg BP, van Nimwegen M, Petzinger GM, Munneke M, Bloem BR. How might physical activity benefit patients with Parkinson disease? Nat Rev Neurol 2011;7:528–534.

85. Hirsch MA, Farley BG. Exercise and neuroplasticity in persons living with Parkinson's disease. Eur J Phys Rehabil Med 2009;45: 215–229.

86. Sherrington C, Whitney JC, Lord SR, Herbert RD, Cumming RG, Close JC. Effective exercise for the prevention of falls: a systematic review and meta-analysis. J Am Geriatr Soc 2008;56:2234–2243.

87. Dijkstra B, Zijlstra W, Scherder E, Kamsma Y. Detection of walking periods and number of steps in older adults and patients with Parkinson's disease: accuracy of a pedometer and an accelerometry-based method. Age Ageing 2008;37:436–441.

88. Pitta F, Troosters T, Spruit MA, Decramer M, Gosselink R. Activity monitoring for assessment of physical activities in daily life in patients with chronic obstructive pulmonary disease. Arch Phys Med Rehabil 2005;86:1979–1985.

89. Salarian A, Russmann H, Vingerhoets FJ, Burkhard PR, Aminian K. Ambulatory monitoring of physical activities in patients with Parkinson's disease. IEEE Trans Biomed Eng 2007;54:2296–2299.

90. Speelman AD, van Nimwegen M, Borm GF, Bloem BR, Munneke M. Monitoring of walking in Parkinson's disease: validation of an ambulatory activity monitor. Parkinsonism Relat Disord 2011;17: 402–404.

91. Niwa F, Kuriyama N, Nakagawa M, Imanishi J. Circadian rhythm of rest activity and autonomic nervous system activity at different stages in Parkinson's disease. Auton Neurosci 2011;165:195–200.

92. Iranzo de Riquer A, Bergareche A, Campos V. Sleep disorders in Parkinson disease. Neurologist 2011;17:S38–S42.

93. Barone P, Antonini A, Colosimo C, et al. The PRIAMO study: a multicenter assessment of nonmotor symptoms and their impact on quality of life in Parkinson's disease. Mov Disord 2009;24:1641–1649.

94. Bossenbroek L, Kosse N, Ten Hacken N, Gordijn M, Van der Hoeven J, De Greef M. Validation of the DynaPort MiniMod during sleep: a pilot study. Percept Mot Skills 2010;111:936–946.

95. Seppi K, Weintraub D, Coelho M, et al. The Movement Disorder Society evidence-based medicine review update: treatments for the non-motor symptoms of Parkinson's disease. Mov Disord 2011; 26(Suppl 3):S42–S80.

96. Schmitz-Hubsch T, Pyfer D, Kielwein K, Fimmers R, Klockgether T, Wullner U. Qigong exercise for the symptoms of Parkinson's disease: a randomized, controlled pilot study. Mov Disord 2006; 21:543–548.