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Motion Sensors to Assess and Monitor Medical and Surgical Management of Parkinson's Disease

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Abstract

Patients with Parkinson's Disease (PD) often suffer from a resting tremor, bradykinesia, rigidity, postural instability and gait difficulty. Determining a patient's candidacy for Deep-Brain Stimulation (DBS) surgery and tracking their clinical response postoperatively requires that the frequency, duration, and severity of these symptoms be characterized in detail. Conventional means of assessing these symptoms, however, rely heavily on patient self-reporting, which often fails to provide the necessary level of detail. Wearable accelerometers are a novel tool that can detect and objectively characterize these movement abnormalities both in the clinical setting as well as in the patient's home environment. In this article, we review the role of accelerometers in surgical candidate selection, recording and predicting falls, recording and predicting freezing of gait, evaluating surgical outcomes, and evaluating postoperative recovery and in altering DBS settings. While accelerometry has yet to make it into the mainstream clinic, there is great promise for this technology in monitoring Parkinson's patients.

Keywords: Accelerometer; Connected devices; Deep brain stimulation; Parkinson's disease; Monitoring; Movement disorders; Activity tracking

Introduction

Parkinson's Disease (PD) affects over 1 million people in the U.S. alone and approximately 1% of individuals over age 60 [1,2]. The cardinal features of idiopathic PD-resting tremor, bradykinesia, rigidity-are often accompanied by postural instability, gait difficulty, dementia, and autonomic dysfunction in the later stages of the disease [3,4].

The motor symptoms are challenging to measure objectively, both outside of and within the clinical or research setting. To help guide treatment, patients are asked to record the details of their symptoms in diaries, but these often lack accuracy, especially in those PD patients who are cognitively impaired [5]. In the clinical setting, concerns over inter-rater reliability on subjective Parkinson's motor examinations such as the Unified Parkinson's Disease Rating Scale (UPDRS), can diminish their clinical effectiveness [6]. Furthermore, tests isolated to clinic visits only provide a brief, limited view of a patient's illness.

There is a great need for low cost systems able to provide objective measurement of a patient's movement in the hospital, clinic, and longitudinally at a patient's home. Fortunately, there has been tremendous technological progress in the field of movement quantification.

Researchers have used technology to objectively characterize a wide range of movement abnormalities including those related gait, tremor, and changes in posture [7]. In the more recent studies that have quantified movement, most have used accelerometers, which tend to be cheaper, less cumbersome, and more widely available. Others have used sensors that measure the force of contact with the ground, such those integrated into the insoles of shoes [8], as well as specialized treadmills [9], magnetometers [10], and visual-based systems such as the camera-guided 3-D-kinematic system (VICON Oxford Metrix) [11]. However, many of these technologies are very expensive, and any associated cables, wires, and cumbersome measurement devices attached to limbs often disturb the patient's natural gait. Furthermore, most can only be used for short distances and for short periods of time in the office [12], and thus are not ideal for longer-term monitoring that would provide longitudinal data.

Accelerometers are capable of providing information about the direction, frequency and intensity of movement. An accelerometer records this data in a single directional plane, and may be combined with another one or two accelerometers oriented in different planes to collect and integrate data on two or three axes. Several studies have used devices that contain both accelerometers and gyroscopes [13,14], which can assess changes in orientation and posture by measuring angular displacement [7]. Recent advancements have allowed for small, lightweight, devices that can be worn extended periods of time, and this data can electronically be transmitted to a patient's health care team. Accelerometers are regularly being incorporated into smart watches, smart-wristbands, smartphones, Google glass, smart clothing and many more devices that are rapidly being released onto the market.

Accelerometers, as well as the other devices mentioned above, are useful for patients at various stages of PD, but there is even more potential for their use in individuals with advanced PD, especially

those who have undergone or who are being evaluated for Deep Brain Stimulation (DBS). DBS is a neurosurgical procedure used to treat advanced idiopathic PD, and several randomized controlled trials have shown that it improves motor function in patients with advanced, levodopa responsive PD [15,16]. Certain studies have sought to use accelerometers to guide PD care in DBS patients.

In patients with advanced PD, due to the frequent changes in the response to levodopa, high risk of falls, potential for rapid deterioration, and overall difficulty of objective assessment of chronic PD among a large multidisciplinary team, accelerometers may be uniquely suited to objectively assess and monitor patient symptoms. This data may then guide treatment for, in particular, the motor component of PD.

Although numerous applications of accelerometry in the treatment and rehabilitation of PD populations, especially in the DBS population, have been studied, to date no all-encompassing literature review exists. In this article, we review the role that accelerometry has played in, and its application to, surgical candidate selection, recording and predicting falls as well as freezing of gait, evaluating surgical outcomes, evaluating postoperative recovery and in altering DBS settings.

Surgical Candidacy Selection

Wearable accelerometers may be useful in providing baseline information to determine which patients are most likely to benefit from DBS. Typical indications for DBS in PD patients are worsening of the patient's cyclical on-off medication motor fluctuations; an unpredictable amount of time a given dose of a dopaminergic agent will improve symptoms; and/or severe levodopa-induced dyskinesias [17]. This represents a large patient population, since roughly 40% of patients will experience dyskinesias and/or on-off motor fluctuations within 4-6 years of beginning levodopa therapy [18].

A clinical improvement during the "on" period when given a dopaminergic agent supports a diagnosis of PD and strongly predicts whether a patient will benefit from DBS [19,20]. Patients who do not show significant improvement may have parkinsonism from causes other than Parkinson's Disease, and thus are not good DBS candidates. Determining the degree of this improvement, however, is challenging.

Outside the clinical context, determining the levodopa response duration and frequency of on-off fluctuations, as well as the degree of motor disturbances such as dyskinesia, relies on patient-reports and diaries. Subjective responses, poor diary compliance and adherence are significant sources of error, especially since a large proportion of PD patients have some degree of cognitive impairment [21]. In the hospital and outpatient clinical setting, the Unified Parkinson's Disease Rating Scale (UPDRS) motor scores are used, which are very subjective [6].

Wearable accelerometers may provide an objective measure of a patient's movement on a second-by second basis, which may allow accurate measurement of the frequency and duration as well as characterize the type of aberrant movement. Triaxial accelerometers provide three-dimensional output and more detailed analysis of motion compared to bi- or single-plain accelerometry. In the short-term lab or research environment, subjects will typically have numerous sensors on all different limbs and locations. For feasibility sake, in the home environment typically only one sensor is placed on the belt or sacrum to gauge general movement and on the lower leg itself to assess a patient's gait. For tremors, smart gloves or hand sensors are typically placed. In addition, they can be worn over extended periods of time in a hospital or long term at home. Many accelerometers are integrated with transistors that allow them to stream data directly to physicians or to other internet based systems such as personal smartphones. While other devices require a manual downloading onto a personal computer, future devices will hopefully be able to send alerts to the health care team for immediate intervention if a patient falls or has a freezing of gait (FOG) event.

Accelerometers are capable of detecting even mild gait impairments and subtle differences in stride length over time which can reliably capture fluctuations of efficacy associated with levodopa therapy [22,23]. Furthermore, using six strategically placed accelerometers, Keijsers et al. were able detect on-off states with a 97% sensitivity and specificity [24]. For rapid assessment of levodopa responsiveness in the clinic setting, accelerometers have been used to gauge a precision grip-and-lift task and quantify overall movement to objectively gauge responsiveness to levodopa [25,26].

Dyskinesias can also be quantified via accelerometry, and can therefore clarify a potential need for DBS [27,28]. By aiding in the assessment of initial levodopa responsiveness, later motor fluctuations, and dyskinesias, accelerometers have the potential to play a crucial role in guiding selection and optimal timing for DBS treatment [29-40] (Table 1).

Device	Company	Citation	Clinical Application	Weight (g)	Dimensions (mm)
DynaPort® MiniMod	McRoberts (The Hague, The Netherlands)	Dijkstra, et al. [23]	Gait, Posture	44.5 g	84x50x8
DynaPort® Hybrid System	McRoberts (The Hague, The Netherlands)	Weiss, et al. [39]	Fall risk	74	87x45x14
DynaPort® Micromod	McRoberts (The Hague, The Netherlands)	Palmerini, et al. [38]	Timed up and go	44.5	84x50x8
Body Sensor AGYRO®	ANCO S.A. (Athens, Greece)	Tripoliti, et al. [13]	Freezing of Gait	*	36.5x48.5x10.5
KinetiSense®	Great Lakes NeuroTechnologies, Inc. (Cleveland, OH)	Mera, et al. [14]	Tremor, levodopa-induced dyskinesia	10	22x16x10

Table 1: Validated Acclerometers Used in Patients with Parkinson's Disease. *Information unavailable.

Fall Risk and Prediction

Wearable accelerometers provide a means of detecting as well as predicting falls, which are a major cause of pre- and post-operative morbidity. Falls are typically related to gait and postural impairment, which often contribute more to the disease burden than the cardinal symptoms [29]. Unfortunately, DBS targeting the conventional brain regions-the Subthalamic Nucleus (STN) and the Globus Palladus internus (GPi)-may not improve the debilitating gait and postural symptoms [30,31]. In fact, in a large multicenter trial comparing DBS of the STN and GPi versus best medical therapy, there was an increased incidence of falls in the DBS group [15]. However, the authors postulated that this might actually be related to the improved mobility that was observed. In contrast, DBS targeting the pedunculopontine nucleus likely has very little effect on the cardinal symptoms but may significantly mitigate freezing and falling. Two small trials, each with 6 patients, targeting pedunculopontine stimulation, demonstrated a significant decrease in falls and freezing among PD patients suggesting that the pedunculopontine nucleus likely modulates these symptoms [32,33].

While DBS patients have advanced Parkinson's Disease and the higher fall risk that this entails, there is some evidence that the stimulation therapy itself may result in more falls through increased mobility or other mechanisms. Thus, rehabilitative physicians and physical therapists must remain especially vigilant about falls in this patient population.

Conventional clinical tests struggle to accurately predict fall risk among PD patients [34]. One of the most common clinical tests used to assess fall risk and characterize a patient's ability to live independently is a timed 'up and go' exam. In this test, the patient is timed rising from a chair, walking three meters, turning around, walking back to their chair, and sitting back down. Patients who take longer to perform this task are considered more likely to fall. Palmerini et al. and Weiss et al. demonstrated that using an accelerometer to objectively quantify 'up and go' movement compared to timing alone is superior at differentiating PD patients with a history of falling from controls [35–38]. A brief, 'up and go' exam in a clinic, however, provides only a limited perspective of a patient's longitudinal symptom severity. To resolve this challenge, Weiss et al. used accelerometry on patients, over three days, comparing patients who had a history of falls to patients with no prior falls. Sensor-derived measures of gait, such as step to step variability, were superior to an in clinic 'up and go' exam at predicting fall risk over one year follow-up [39]. Adding these sensors, therefore, may enhance the efficacy of the 'up and go' test to predict fall risk.

Freezing of Gait (FOG)

Freezing of gait (FOG), is the paroxysmal interruption of movement that may occur when the patient initiates gait, turns, or negotiates an obstacle [40]. Although DBS may initially improve FOG, 45% of DBS patients continue to experience FOG events [41]. Moreover, despite DBS treatment, FOG worsens over 5-10 year follow-up, consistent with the natural history of the disease [31]. Conventional means of assessing the frequency and duration of FOG, such as the new Freezing of Gait Questionnaire, have not been shown to correlate with the severity of FOG [42], and self-reported measures may be subject to a recall bias, and, as mentioned, may be inaccurate in the cognitively impaired.

Accelerometers have been used to detect FOG events, and are able to wirelessly transmit this data to health professionals. Initially, cumbersome devices with sensors in multiple regions of the body-only suitable for research settings-were able to detect FOG events with specificities and sensitivities in the 80%-90% range. In a recent pilot study of 25 patients, a simple, cheap, lightweight sensor, which also contained a gyroscope, was placed on the subjects' lower leg, and was highly sensitive and 67% specific for detecting FOG events [13,40]. Another smaller study by Niazmand et al. used smart-pants, which have wireless accelerometers embedded into pants that a patient may wear at home. The smart-pants had a 88.3% sensitivity and 85.3% specificity for detecting FOG events [12]. Given that FOG is difficult to predict, clinical consultation may only provide a limited snapshot of FOG symptoms. Therefore, outpatient assessment in the patient's home environment is important to guiding personalized treatment.

Outcomes Prediction

The general rehabilitation and ambulatory activity after DBS surgery can be assessed via accelerometry. Accelerometers have been shown to objectively quantify different physical activities in this postoperative population [43]. Rochester et al. demonstrated that accelerometry detected an increase in total time spent walking from 6 weeks preoperatively to 6 months post-DBS surgery. This correlated with improved postoperative motor function outcome measures such as the Nottingham Extended Activities of Daily Living Index, although the total number of steps per day did not increase [44]. This suggests there tends to be improvements in diversity and flexibility of walking patterns.

Personalized Deep-Brain Stimulation

Wireless monitoring of postoperative ambulation and other forms of movement may provide an objective way to not only gauge outcome after surgery, but also assess the need to alter DBS settings such as the voltage, impulse duration, and frequency [45].

Although DBS has been shown to reduce the incidence and severity of dyskinesias occurring during the "on" period, device over-stimulation may itself cause mild dyskinesia as well as paresthesias, dizziness, facial contractions, and hemiballismus. As a result, patients often require adjustments of DBS settings at frequent follow-up visits [15,46]. Mera et al. showed in post-DBS patients that a wrist-worn accelerometer, which also included a built-in gyroscope, can objectively assess dyskinesia within the hours following a dose of levodopa [14]. In another study, Obwegeser et al. used accelerometers to demonstrate and objectively quantify the positive impact DBS has on reducing tremors [47]. This information may be collected in the outpatient setting to guide adjustment of DBS settings.

Current DBS technology is considered 'open loop' in that the implanted lead supplies constant electrical stimulation and does not respond to any particular stimulus. Novel systems of 'closed loop' DBS that tailor stimulation to physiological alterations or physical symptoms are actively being investigated. Basu et al. devised a novel system and algorithm that combines accelerometers with Electromyography to predict an ensuing tremor. Using their algorithm the DBS unit could theoretically be turned off until it detects the onset of a tremor, at which point it would turn back on [48]. This can provide feedback to guide automated adjustment of DBS settings.

Conclusions

As accelerometers have improved, so have the plethora of sophisticated devices incorporating their technology. Smart watches, smart-wristbands, smartphones, Google glass, smart clothing and many more devices are rapidly being released onto the market, and all have accelerometers. The accelerometer is quickly transitioning from a place of relative obscurity, to a common tool accessible to the masses.

Due to advances in and increased availability of accelerometers, there has been a great deal of research using this novel technology to assess and monitor the symptom burden of numerous Parkinson's patients. In our review, we found that there is strong evidence that accelerometers can aid in surgical selection of ideal candidates and timing of DBS surgery and in assessing fall risk, freezing of gait and dyskinesia. This information can help manage the appropriate DBS settings.

Despite these advances, wearable accelerometers are not yet abundant within the clinical domain. Their use is likely to increase in the near future, as repeated studies show their potential attributes to patient care. In the future, accelerometers that have been validated to detect certain movement abnormalities may be used to direct immediate and automated interventions based off their feedback. For instance, closed loop DBS using accelerometry seems feasible and accelerometers on Google glass could detect a fall and automatically contact help. Ultimately, accelerometers show great potential in the care of Parkinson's Disease patients in the preoperative selection and postoperative management following DBS.

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