Gait & Posture 38 (2013) 109–114

Contents lists available at SciVerse ScienceDirect

Gait & Posture

journal homepage: www.elsevier.com/locate/gaitpost

Quantitative analysis of gait and balance response to deep brain stimulation in Parkinson's disease

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ARTICLE INFO

Article history:
Received 21 September 2011
Received in revised form 24 October 2012
Accepted 30 October 2012

Keywords:
Parkinson's disease
Deep brain stimulation
Gait
Balance
Motion sensors

ABSTRACT

Gait and balance disturbances in Parkinson's disease (PD) can be debilitating and may lead to increased fall risk. Deep brain stimulation (DBS) is a treatment option once therapeutic benefits from medication are limited due to motor fluctuations and dyskinesia. Optimizing DBS parameters for gait and balance can be significantly more challenging than for other PD motor symptoms. Furthermore, inter-rater reliability of the standard clinical PD assessment scale, Unified Parkinson's Disease Rating Scale (UPDRS), may introduce bias and washout important features of gait and balance that may respond differently to PD therapies. Study objectives were to evaluate clinician UPDRS gait and balance scoring inter-rater reliability, UPDRS sensitivity to different aspects of gait and balance, and how kinematic features extracted from motion sensor data respond to stimulation. Forty-two subjects diagnosed with PD were recruited with varying degrees of gait and balance impairment. All subjects had been prescribed dopaminergic medication, and 20 subjects had previously undergone DBS surgery. Subjects performed seven items of the gait and balance subset of the UPDRS while wearing motion sensors on the sternum and each heel and thigh. Inter-rater reliability varied by UPDRS item. Correlation coefficients between at least one kinematic feature and corresponding UPDRS scores were greater than 0.75 for six of the seven items. Kinematic features improved ($p < 0.05$) from DBS-OFF to DBS-ON for three UPDRS items. Despite achieving high correlations with the UPDRS, evaluating individual kinematic features may help address inter-rater reliability issues and rater bias associated with focusing on different aspects of a motor task.

1. Introduction

Parkinson's disease (PD) causes both motor and non-motor signs, but is primarily recognized by resting tremor, rigidity, and bradykinesia (slowness of movement) [1]. However, other manifestations such as balance and gait disturbances, especially in advanced patients, can be debilitating and may lead to increased fall risk [2].

As PD advances and patients become potential candidates for deep brain stimulation (DBS), targeted symptoms for surgical management typically include tremor and medication-responsive bradykinesia, rigidity, and freezing of gait in the presence of intolerable control due to motor fluctuations and dyskinesia. In general, compromised gait and balance is more difficult to manage with DBS, and as patients advance into later stages of the disease, these impairments become more common and problematic. The same set of stimulation parameters may not address all of the cardinal motor signs of PD regardless of disease severity. In addition, as severity increases, response to specific stimulation parameters may change. Strategies to better treat these more complex symptoms have been proposed. Moreau et al. demonstrated that high-frequency (>100 Hz) stimulation improved tremor and bradykinesia, but was not as effective for gait and balance. In contrast, low-frequency (60 Hz) stimulation with proportionally higher-amplitude settings resulted in greater improvement in gait [3]. Currently, there are no standardized DBS programming guidelines for gait and balance. To further this point, in a study of 108 DBS patients, primarily diagnosed with PD, subjects sought referral to a movement disorder specialist after experiencing unsatisfactory symptomatic benefit. Gait and balance was the second leading complaint (34.3%) [4]. Therefore, developing improved neuromodulation tools for improving gait and balance is still needed. This may be especially beneficial as new stimulation targets are being investigated including the

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http://dx.doi.org/10.1016/j.gaitpost.2012.10.025

pedunculopontine nucleus; a brain region believed to play an important role in locomotion function, specifically initiation and modulation of gait [5–7].

A wide range of clinical rating scales have been developed to quantify and rate gait and balance impairment. The Unified Parkinson's Disease Rating Scale (UPDRS) is the standard clinical evaluation for PD, including DBS programming. A study conducted by Kerr evaluated multiple gait and balance clinical scales and their ability predict fall risk, a measure of functional gait impairment [8]. The motor section of the UPDRS (UPDRS-III) motor examination differentiated between fallers and non-fallers ($p < 0.012$) with a sensitivity and specificity of 0.64 and 0.60, respectively. The Tinetti Mobility Test (TMT) was predictive of prospective falls ($p < 0.001$) with a sensitivity and specificity of 0.67 and 0.59, respectively. Kegelmeyer also reported that the TMT correlated with the UPDRS-III ($r = -0.45$, $p < 0.05$) and resulted in a sensitivity and specificity of 0.76 and 0.66, respectively [9].

Although clinical rating scales have been shown to correlate with fall risk, inter-rater reliability may introduce bias and washout important features of gait and balance that may respond differently to PD therapies. Espay demonstrated that clinicians differentially weighed amplitude and speed deficits when rating UPDRS-III upper extremity bradykinesia tasks [10]. It was also shown that angular velocity, a measure of speed, improved more in response to dopaminergic medication than excursion angle or variability in tapping angular velocity, measures of amplitude and rhythm, respectively [11].

Motion sensor technology has been previously commercialized as a general activity monitor to quantify gait. The ActivPal (Pal Technologies, Scotland, UK), AMP 331 (Dynastream Innovations, Alberta, Canada), and StepWatch (Orthocare Innovations, Seattle, WA) are examples of single unit accelerometer sensors which output various gait measures (e.g. cadence, walking speed). In contrast, we investigated a motion capture system that utilized multiple upper and lower body-worn motion sensor units to capture kinematic features specific to the gait and balance task subset of the UPDRS and changes in these features in response to DBS. Three hypotheses were tested: (1) UPDRS gait and balance items are compromised by lack of inter-rater reliability, (2) UPDRS is not sensitive enough to capture specific aspects of gait and balance, and (3) sensor-based kinematic features significantly change in response to DBS during a typical clinical visit.

2. Methods

This work was approved by the institutional review board in which this study was performed, and all subjects gave prior informed consent. All clinical investigations were performed in accordance with the ethical standards of the Declaration of Helsinki (2008).

2.1. Technology overview

KinetiSense™ (Great Lakes NeuroTechnologies Inc., Cleveland, OH) captures synchronized three-dimensional kinematic data from five sensor units (Fig. 1). Each sensor unit contains three orthogonal accelerometers for measuring linear acceleration (a_x, a_y, and a_z) and three orthogonal gyroscopes for measuring angular velocity (ω_x, ω_y, and ω_z). The command module provides power and streams data to a computer at 128 samples per second.

2.2. Data collection protocol

Forty-two subjects (31 males, 11 females, 67 ± 13 years old) diagnosed with idiopathic PD in accordance with UKPDS Brain Bank criteria [12] with varying gait and balance impairment were recruited from a movement disorders center (Cleveland, OH). All subjects were on dopaminergic medication during the study and twenty subjects had also previously undergone DBS surgery. A motion sensor unit was positioned on each heel using a U-shaped shoehorn, on the central anterior aspect of each quadriceps muscle using an elastic Velcro strap, and on the base on the sternum using double-sided adhesive electrode washers (Fig. 1).

The movement disorder center clinician or nurse practitioner guided subjects through seven items of the UPDRS-III to evaluate gait and balance impairment: (1) toe tapping, (2) leg agility, (3) arising from chair, (4) gait, (5) freezing of gait, (6) postural stability, and (7) posture [13]. Non-DBS subjects were each evaluated once while DBS subjects were evaluated twice, first with stimulation turned on using parameters from the previous clinical visit and again within a minute of turning the stimulation off, typical of the time allotted in a routine clinical visit. While motor tasks were performed, kinematic data were transmitted wirelessly and recorded to a laptop, and subjects were videotaped for later clinician scoring.

These videos were randomized and loaded onto a secure online server. Three movement disorder neurologists were blinded to stimulation state and rated the videos per UPDRS guidelines. Scores were averaged across raters to minimize variability. Agreement between clinicians was measured based on the correlation coefficient between scores given by each combination of two of the three clinical raters.

2.3. Kinematic feature extraction

Kinematic data collected from the KinetiSense device were processed into a range of quantitative features based on our previous studies evaluating speed, amplitude, and rhythm deficits of upper extremity hand movement motor tasks [10,11] and other work using sensors to quantify gait [14,15]. These studies also showed that variability over time and the logarithm of these features were correlated to clinician ratings and indicators of gait impairment. Correlation coefficients were calculated between the quantitative features and mean clinician

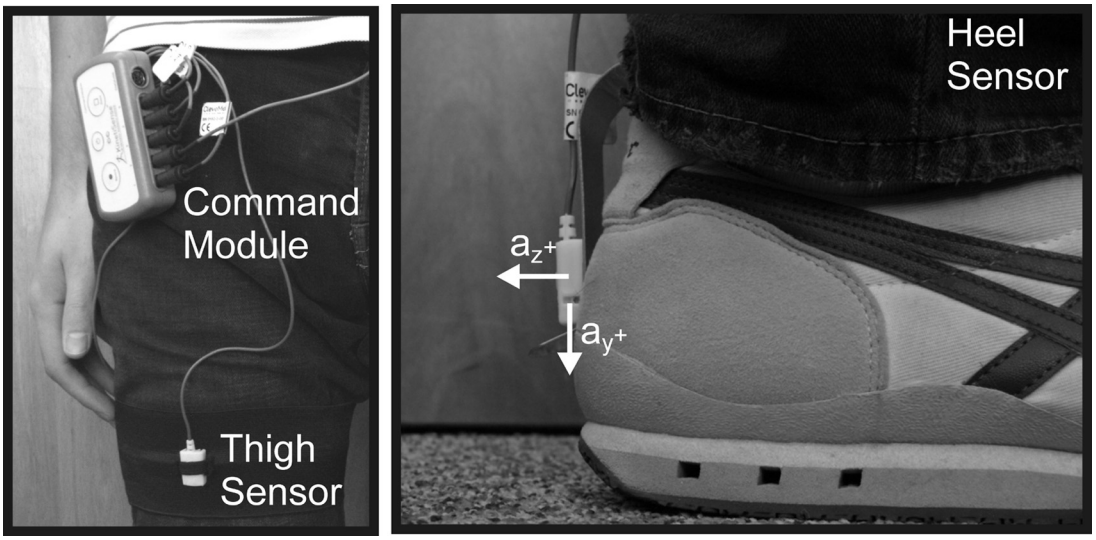

Fig. 1. KinetiSense™ (Great Lakes NeuroTechnologies Inc., Cleveland, OH) consists of a command module and five motion sensor units, each containing three orthogonal accelerometers and three orthogonal gyroscopes. One sensor unit was positioned on each heel, one on each thigh, and one on the sternum.