Human Movement Science 58 (2018) 185–194

Contents lists available at ScienceDirect

Human Movement Science

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

Full Length Article

Motor output complexity in Parkinson's disease during quiet standing and walking: Analysis of short-term correlations using the entropic half-life

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ARTICLE INFO

Keywords:
Motor output
Complexity
Center of pressure
Gait
Parkinson's disease

ABSTRACT

Parkinson's disease (PD) is associated with alterations in motor outputs such as center of pressure (CoP) adjustments during quiet standing and foot kinematics during walking. Previous research suggests that the complexity of motor outputs reflects the number of control processes stabilizing a specific movement, providing a measure that is linked to the neurological control of the movement. The Entropic Half Life (EnHL) represents a new method for assessing motor output complexity. We hypothesized that there will be a lack of neuromuscular control pathways for PD patients, resulting in a decrease in motor output complexity. We computed the EnHL of CoP adjustments during quiet standing and foot kinematics during walking of 70 PD patients and 33 age-matched controls. Patients with PD showed longer EnHL values compared to controls, suggesting a tighter motor control. Excluding vision led to a decrease of EnHL of CoP in both groups. EnHL was correlated with spatio-temporal gait parameters. We compared EnHL with the pull test and the timed up-and-go test. No significant differences were present in the pull test, yet motor output complexity was correlated with the timed up-and-go test. The results suggest a reduced complexity in motor outputs of PD patients affecting distinct motor functions.

1. Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by the cardinal motor symptoms bradykinesia, tremor, rigidity and postural instability (Jankovic, 2008). These motor symptoms resulting from a disrupted motor control by the extrapyramidal system of the CNS are reflected in neuromuscular motor outputs such as center of pressure (CoP) adjustments during quiet standing and foot kinematics during walking. Neuromuscular motor outputs are the result of the interaction of multiple control strategies of the central and peripheral nerve system with the muscular system. This suggests multiple control pathways, which results in many degrees of freedom that are part of the control processes stabilizing a specific movement. Thus, all possible solutions that lead to a proper controlled movement can be referred to as the solution space of the neuromuscular motor control. A greater

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https://doi.org/10.1016/j.humov.2018.02.005
Received 15 September 2016; Received in revised form 8 February 2018; Accepted 8 February 2018
Available online 12 March 2018
0167-9457/

number of degrees of freedom of a solution space thus represents one aspect that increases motor output complexity, which can be used to infer impairments in motor control. Lipsitz and Goldberger postulated that the complexity of the output of any physiological process, as a result of the interaction of the involved biological mechanisms, is directly related to its adaptability and flexibility to external perturbations, and that this complexity is reduced with both aging and disease (Lipsitz & Goldberger, 1992). Measures of the complexity in CoP adjustments and foot kinematics during static and dynamic motor functions are sensitive to the subject's neuromuscular control state, and may complement the diagnosis of neurodegenerative disorders such as PD.

Examining the excursion of the human CoP during quiet standing is a well-established method to study balance and postural control (Johnson et al., 2013; Mancini & Horak, 2011). In this context, nonlinear analysis of CoP excursions has been employed to assess postural instability in the elderly (Kilby, Slobounov, & Newell, 2014), PD (Schmit et al., 2006), and multiple sclerosis (Negahban, Sanjari, Mofateh, & Parnianpour, 2013). The main motivation for using nonlinear methods is that they are able to quantify the variability in CoP adjustments, which is not possible by using mean values such as CoP sway length, CoP mean velocity, or CoP area. Within the battery of nonlinear methods, the entropic half-life (EnHL) is a new methodology to measure short-term temporal correlations of time series (Zandiyeh & Von Tscharner, 2013), which has been successfully applied to the analysis of CoP excursions in healthy populations during quiet standing (Baltich, von Tscharner, & Nigg, 2015; Baltich, von Tscharner, Zandiyeh, & Nigg, 2014; Federolf, Zandiyeh, & von Tscharner, 2015). The EnHL is defined as the time scale at which the signal's entropy reaches the half maximal value. The maximal entropy indicates that the signal is fully random, lower than random signals represent more regular signals. At the scale represented by the EnHL the measure becomes most sensitive to changes of motor output complexity. According to the current view, a decreased motor output complexity corresponds to a decreasing number of physiological mechanisms that are responsible for lowering of the degrees of freedom of the solution space and thus increase EnHL (Enders, von Tscharner, & Nigg, 2014). On the contrary, complexity is reflected in a non-random phase of the signal. Randomizing the phase, thus eliminating its complex structure, lowers the EnHL (Enders et al., 2014; von Tscharner, Zandiyeh, & Federolf, 2016). Further, the EnHL increases if the interventions on the CoP occur less frequently and thus previous processes altering the CoP adjustments remain related to present adjustments for a much longer time (Baltich et al., 2015).

EnHL is therefore a variable most sensitive to changes in neuromuscular control mechanisms that generate motor output complexity. For example, an increased EnHL in CoP adjustments was documented in a cohort of healthy young subjects when their somatosensory information was challenged by standing on a foam surface (Baltich et al., 2014). Thus, disruption of the somatosensory information increases the EnHL of CoP excursions and hence the dependency of current to previous adjustments on larger time scales. This points to a decrease in system output complexity as proposed by Lipsitz and Goldberger (Lipsitz & Goldberger, 1992). By contrast, analysis of CoP excursions during a single limb stance demonstrated an increased EnHL of CoP excursions in younger compared to old subjects (Baltich et al., 2015). This finding showed that aging leads to a significantly lower EnHL in the anterior posterior direction. Thus, the more demanding control leads to a higher motor output complexity in healthy older subjects when the assessment is performed with the challenge of a single limb stance (Baltich et al., 2015). In line with this, specific task constrains have been proposed to influence complexity in difference physiological outputs (Manor & Lipsitz, 2013; Vaillancourt & Newell, 2002, 2004).

Accessing the dynamics of human locomotion parameters such as foot kinematics and stride-interval correlations complements the quiet standing analysis of motor control mechanisms in humans (Dingwell & Cusumano, 2000; Hamacher, Singh, Van Dieen, Heller, & Taylor, 2011; Hausdorff, 2007). For example, a breakdown of the long-range correlations of the stride-to-stride fluctuations (e.g., hundreds of strides) was detected in PD patients (Hausdorff, 2009). Patients with Huntington's disease also showed a reduction of the stride-interval correlations (Hausdorff, 2007). A reduction in long-range correlations was observed as a reduction in the scaling fractal exponent α of a de-trended fluctuation analysis of stride variability for unhealthy subjects (Hausdorff, 2009; Hausdorff et al., 2000). Because α is inversely proportional to 1/EnHL, the decay of α could be viewed as a decrease in EnHL (von Tscharner et al., 2016) and could conceivably arise from a loss of predictability in the long range scale that accompanies disease progression.

Based on these findings and on the assumption that the neuromuscular control of PD patients occurs with less degrees of freedom, one could hypothesize that (1) EnHL of CoP and stride (gait) variability should increase in subjects suffering from PD, (2) EnHL correlates with spatio-temporal gait parameters, and (3) EnHL correlates with clinical balance outcomes. To test this hypothesis, we examine a population of 33 healthy subjects and 70 patients with sporadic PD to investigate short-term temporal dependencies using EnHL as a measure of motor output complexity in (1) postural adjustments during quiet standing with and without visual feedback, and (2) in the fluctuation of foot kinematics during straight gait. Vision was removed during quiet standing experiments to eliminate visual compensation in patients with PD. Because the combined study of balance control during quiet standing and gait performance has proven useful to comprehend motor control in several models (Hendrickson, Patterson, Inness, McIlroy, & Mansfield, 2014; Lewek, Bradley, Wutzke, & Zinder, 2014; O'Connor & Kuo, 2009; Titianova & Tarkka, 1995), we also explore whether a correlation exists between motor output complexity and spatio-temporal gait parameters. Finally, since postural control is impaired in PD, motor output complexity was further analyzed against two standard clinical balance tests, namely, the pull test (PT) and the timed up-and-go (TUG) test.

2. Methods

2.1. Participants

Seventy sporadic PD patients (61.2 ± 11.3 years old) with a Unified Parkinson's Disease Rating Scale part III (UPDRS-III) score (Goetz et al., 2007) of 16.8 ± 7.4 and Hoehn and Yahr (H&Y) stage (Goetz et al., 2004) 2.2 ± 0.8, and 33 age-matched controls