

# A Wearable Neuromonitoring Platform to Map Motor and Neural Biomarkers of Gait Dysfunction in People with Parkinson's Disease across Daily Life

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**Abstract**— A majority of individuals with advanced Parkinson's disease develop severe gait and balance deficits that significantly restrict mobility, independence, and quality of life. Despite impressive technological advances, gait impairments remain poorly understood and notoriously hard to treat. Most attempts to characterize gait deficits or to identify neural biomarkers of gait dysfunction have been confined to well-controlled, sophisticated laboratory settings. However, such environments fail to capture many critical contextual factors that exacerbate gait deficits in real-world conditions, such as stress, fatigue, or unexpected distractions and environmental constraints. Replicating these unpredictable conditions in laboratory settings remains a significant challenge. To address this, we developed a wearable neuromonitoring platform integrating (i) smart, sensorized shoes with embedded microchips running A.I. algorithms for online gait quality assessment, along with (ii) wireless recordings of local field potentials from chronically implanted electrodes for deep brain stimulation. This platform enables continuous monitoring of motor and neural biomarkers of gait function and dysfunction across activities of daily life. 13 participants with advanced Parkinson's disease were monitored during a comprehensive set of out-of-laboratory locomotor tasks, both in the ON and OFF medication conditions. Our platform allowed to assess gait quality, quantify modulations in response to medication, fatigue, and context-specific demands, and to map the underlying neural correlates. This neuromonitoring platform offers valuable possibilities for refining neuromodulation protocols and supporting closed-loop therapies for gait impairments in real-life conditions.

**Keywords**—Parkinson's disease, gait deficits, neural biomarkers, closed-loop therapies, out-of-laboratory conditions

## I. INTRODUCTION

Gait and balance deficits are among the most prevalent and debilitating symptoms of advanced Parkinson's disease [1]. Abnormalities such as shuffling steps, festination, postural instability or freezing of gait (FOG) not only reduce mobility and independence, but also elevate the risk of falls and related comorbidities, significantly diminishing quality of life and life expectancy [2]. Despite their high prevalence, the mechanisms underlying gait deficits remain poorly documented, and their multifactorial symptomatology very hard to treat [1]. Standard therapies, including dopaminergic replacement pharmacotherapies such as L-DOPA or continuous

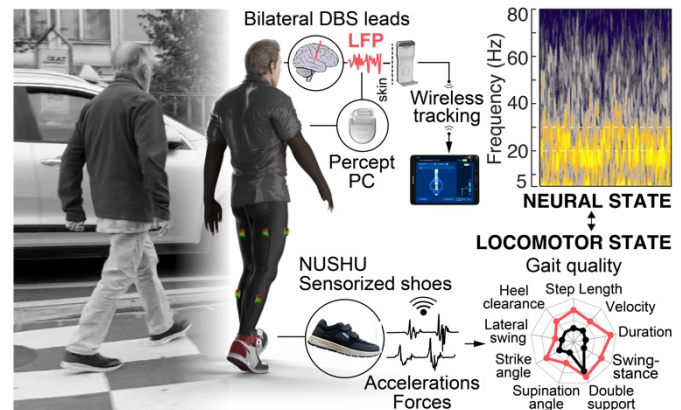


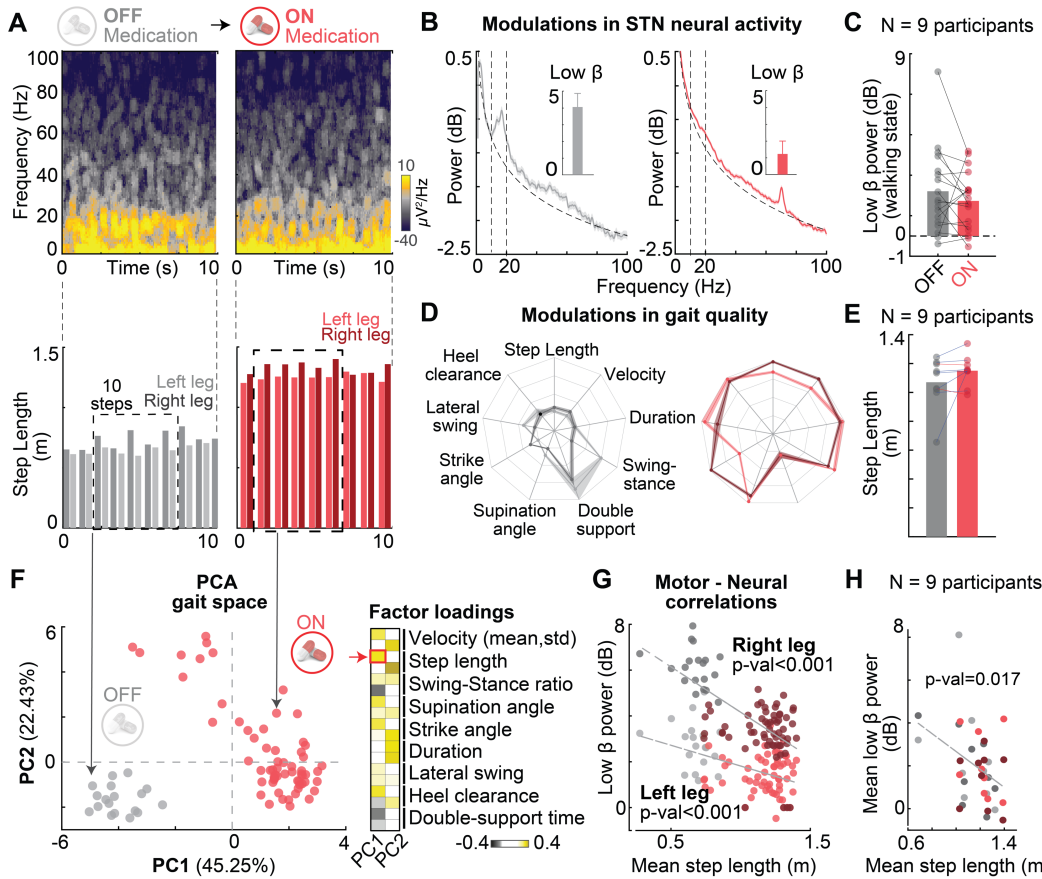
Figure 1. Wearable neuromonitoring platform to map neural and motor states

deep brain stimulation (DBS) of the subthalamic nucleus (STN) exhibit modest and inconsistent efficacy for many gait impairments [3-6]. The dynamic nature of these deficits—which are often episodic and context-dependent—poses additional challenges. The development of new interventions targeting gait deficits must thus be based on a better understanding of the time-varying and context-specific neuronal processes that contribute to locomotor dysfunction in real-life conditions [7]. Such therapy optimizations may encompass personalization of pharmacological regimens, or implementation of closed-loop DBS or spinal cord stimulation protocols capable of dynamically adapting the delivery of stimulation to sudden episodic changes in symptom severity [8-10].

So far, the study of gait dysfunction in PD has been mainly restricted to well-controlled, sophisticated laboratory settings. However, in real-life conditions, gait deficits are exacerbated by unpredictable factors like distractions, stress, and sudden physical or cognitive effort, such as navigating busy environments, tight corridors, or multi-tasking [11]. These conditions are hard to replicate in laboratory settings. Instead, advances in wearable sensor technologies allow to monitor symptoms in ecological settings, providing continuous readouts of gait quality during daily life activities, thus offering a better characterization of symptom variability [12]. Concurrently, DBS technologies now allow to record local field potentials (LFPs) from chronic DBS electrodes, making it possible to monitor neural biomarkers over long periods of time [8,13,14].

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**Figure 2. L-DOPA-related modulations in motor and neural measures of gait quality.**

**A.** Illustrative examples of raw spectrograms of STN LFP recordings, aligned with gait-cycles, as recorded with the wearable neuromonitoring platform, both in the OFF- (left) and ON-medication (right) conditions. **B.** Power spectral density of STN LFP when walking, OFF and ON medication, and quantification of low beta power. **C.** Cross-participant changes in low beta power mediated by medication. Dots represent the mean power for each participant. **D.** Gait parameter values (mean  $\pm$  SEM) during the OFF (left) and ON (right) medication condition. **E.** Cross-participant changes in step-length with medication. Dots represent the mean value for each participant and condition. **F.** PCA on 18 gait parameters. Each dot in the PC space represents a group of five consecutive right and left steps. Factor loadings indicate the contribution of each gait parameter to each PC. **G.** Correlation analysis of low beta band power and step length during different medication conditions. **H.** Cross-participant correlation analysis between low beta power and step length. Dots represent the mean value for each participant and condition.

Despite these technological advances, no study to date has integrated high-resolution LFP recordings with detailed gait characterization in daily life conditions.

To address this gap, we developed a novel, wearable neuromonitoring platform capable of continuously tracking motor and neural biomarkers associated with gait function and dysfunction during real-life activities. This platform combines synchronous recordings from last-generation DBS neurostimulators endowed with ‘sensing’ functionalities (Percept™ PC, Medtronic, USA) and from sensorized shoes capable of computing on-the-fly precise, medical-grade gait quality analyses [15] (NUSHU, Magnes AG, Switzerland).

We tested this platform on 13 individuals with advanced PD as they performed a broad range of locomotor tasks representative of daily life activities, both in the ON and OFF medication condition. We mapped motor and neural biomarkers associated with locomotor states and gait quality measures, and we assessed how these biomarkers evolved in response to L-DOPA, fatigue, or task-specific motor demands.

Our results assert the utility of this platform for capturing the full complexity of gait impairments in PD, paving the way for optimizing interventions and deploying closed-loop therapies in real-world conditions.

## II. METHODS

### A. Experimental design

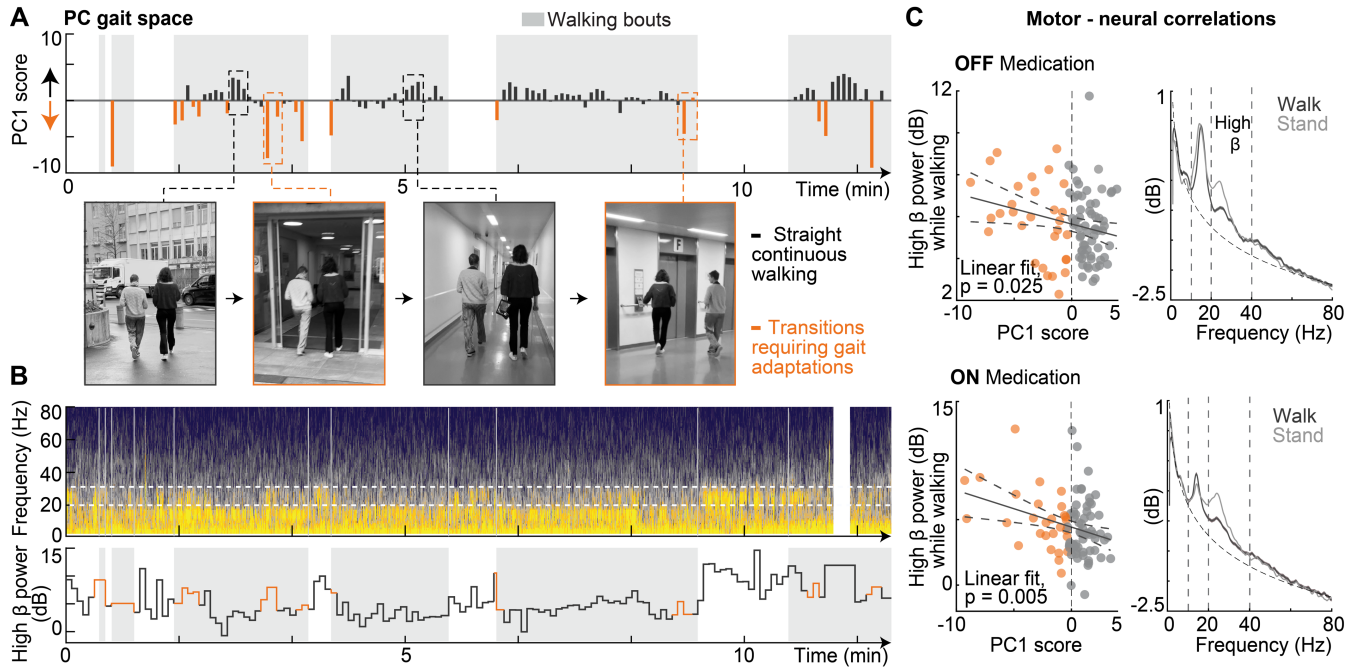
All procedures were approved by the Ethics Committee of the Canton de Vaud, Switzerland (ref PB\_2017-00064). Fourteen

individuals with advanced PD (12 males, 2 females; mean age: 66 years; mean MDS UPDRS III score: 40 OFF L-DOPA, 18 ON L-DOPA; mean disease duration: 12 years) were enrolled in the study. They all provided informed consent prior to participation in the tasks. Recordings were performed within 7 days post-DBS surgery. All participants received bilateral STN DBS directional leads (Sensight™, Medtronic, USA) and a Percept™ PC implantable neurostimulator (Medtronic, USA) in the right chest area. Participants recorded in the OFF-medication condition were withdrawn from their usual dopaminergic medication the night before the recordings (>12h). For recordings conducted ON-DBS and ON-medication, stimulation amplitudes and medication dosages were maintained at the optimal levels defined by the neurologist managing each participant at the time of the recording. Among the 13 participants, nine were recorded in both ON and OFF medication states, three in the ON-medication state only, and one in the OFF-medication state only.

### B. Neuromonitoring platform

We assessed the accuracy of our wearable neuromonitoring platform to capture neural and motor biomarkers associated with changes in gait quality in real life conditions. All recordings were performed during walking activities either outdoors or within hospital corridors. These combined:

**Gait recordings:** All recordings were conducted using the *Generic* recording mode of the NUSHU Research Application. This mode enabled continuous, unrestricted data collection during sessions lasting several hours. After completion of



**Figure 3. Context-related modulations in motor and neural measures of gait quality.** **A.** PC1 over the course of a 15-minute walking task involving bouts of continuous walking in corridors and outdoors, as well as transitions to enter elevators, cross doors or navigate obstacles. Each bar represents a group of 10 consecutive right and left steps. Positive PC1 scores capture bouts of straight walking (grey), whereas negative PC1 scores capture changes in gait parameters during transitions requiring gait adaptations, e.g. when crossing doors (orange). **B.** Raw spectrogram of STN LFP (top) and average high beta power (bottom) aligned to PC1 gait scores. **C.** Quantification of context-related changes in beta power, both in the OFF- (top) and ON-medication condition (bottom). Correlation analyses of high beta power and gait PC1 score highlight STN modulations with locomotor demands; Power spectral density of STN LFP comparing locomotor states (walking, dark grey and standing, light grey) indicate clear STN modulations associated to distinct motor-states.

recordings, data was extracted from the shoes, uploaded to the cloud and post-processed to derive gait parameters.

NUSHU computed the following nine parameters for each right and left gait-cycle: velocity, stride length, swing-stance ratio, supination angle, duration, lateral swing, toe clearance, heel clearance and double support time. They also provided the timestamps of individual ‘heel off’, ‘toe off’, ‘heel strike’, and ‘flat foot’ gait events, along with information about whether the participant was ‘walking’ or not (‘rest’ state).

**LFP recordings:** LFPs were recorded using the *BrainSense Streaming* mode of the Percept<sup>TM</sup> PC (sampling frequency: 250 Hz) using as ‘sensing’ contact pair the one surrounding the electrode chosen by the neurologist as clinically optimal.

**Synchronization of gait and LFP recordings.** Both systems used internet-synchronized network timestamps to align neural and gait recordings. Precision was <1s, which was suitable to align locomotor states.

### C. Analyses of gait quality

All analyses were performed in MATLAB.

**Principal component analysis (PCA):** PCA was applied to both the mean and standard deviation of each gait parameter, calculated over groups of ten consecutive left and right steps. We used the first two components of the PC space to visualize the main changes in gait over time and across conditions. Factor loadings contributing to each PC were used to identify

the gait parameters that more robustly explained differences between the conditions.

**Within-subject statistical comparisons:** Significant differences in gait quality between ON and OFF medication states, as well as between right and left gait-cycles, were evaluated using two-sample t-tests for each gait parameter.

**Cross-subject statistical comparisons:** To assess gait changes across participants, mean values of each gait parameter were computed for each subject. Paired t-tests were used to determine differences between ON vs. OFF conditions.

### D. Analyses of neural biomarkers

**Raw spectrograms:** Spectrograms of LFP signals were computed using multitaper decomposition using the Chronux library (<http://chronux.org/>), covering the spectral range from 5 to 125 Hz (3 tapers, 1s window with 50ms overlap).

**Artefacts in LFP signals:** For participants exhibiting ECG-related artefacts (N=1), we applied a denoising algorithm based on singular value decomposition [16] to isolate and clean neural signals.

**Computation of band power:** Power spectral density (PSD) profiles for each walking sequence were computed using the ‘pwelch’ function in MATLAB (1s window, 500ms overlap). After removal of the aperiodic component [17], band power values were derived as the area under the curve (AUC) of the PSD within the low beta (10-20 Hz) and high beta (20-40 Hz) bands. Computations were performed separately for the ‘walking’ and ‘rest’ states, ON or OFF L-DOPA

**Task-related modulations in band power:** To assess task-related changes in brain activity, band power was computed over the same time-intervals as for the PCA, i.e. groups of 10 consecutive left and right steps. During the ‘rest’ condition, band power was computed using 5 s windows.

**Correlations:** Pearson correlation and linear models were used to extract relationships between gait parameters and LFP band-power values.

### III. RESULTS

The wearable neuromonitoring platform was able to monitor motor and neural biomarkers of gait quality in real life conditions, and to capture changes induced by (i) medication, (ii) context-related constraints, and (iii) fatigue, as they emerged in the context of out-of-laboratory activities.

#### A. L-DOPA-related modulations

L-DOPA significantly improves motor control, including many features of gait and balance. However, in advanced stages of PD, the effects of L-DOPA often fluctuate in time due to the intermittent nature of medication intake. Fluctuations can significantly affect key aspects of gait and balance. For instance, postural instability can worsen at peak dose, whereas the incidence of FOG episodes and shuffling gait can increase as medication wears-off. Our platform must effectively capture continuous changes in gait quality in response to L-DOPA, and allow to map modulations in the underlying neural signatures (**Fig. 2**).

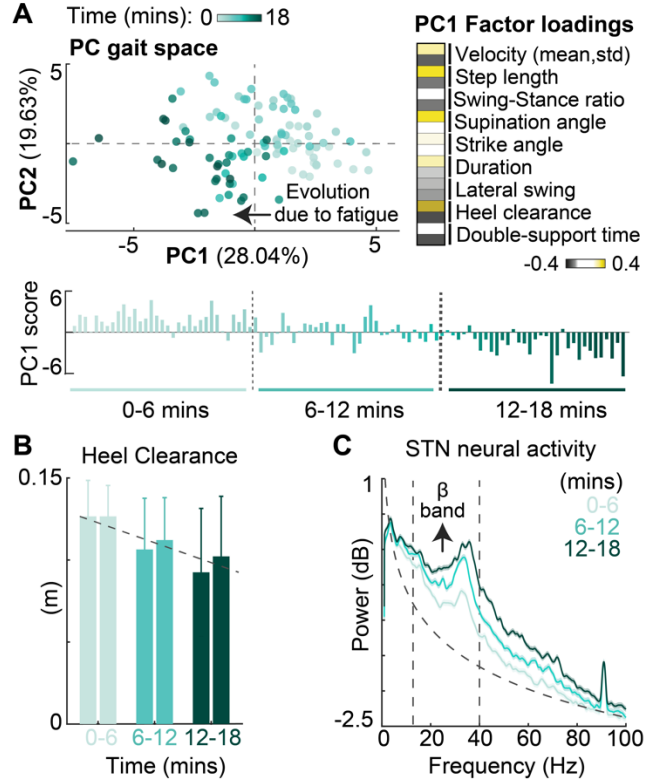
Across all our participants, L-DOPA led to improvements in all 9 bilateral gait parameters. Among those, PCA analyses identified longer step length, faster walking speed, and more balanced swing-to-stance ratio as the primary contributors to these enhancements. Additionally, right-left asymmetries and step-to-step variability were significantly reduced.

Concurrently, LFP recordings exhibited a marked decrease in low-beta power ON L-DOPA, consistent with previous observations on the effects of dopaminergic pharmacotherapy on STN LFP at rest [16,17]. These low-beta modulations strongly correlated with the aforementioned gait parameters, consistently across participants, supporting the idea that L-DOPA-induced changes in well-defined spectral biomarkers contribute to improved locomotor function.

These results pave the way for gait therapies that may adapt in real-time to dopamine pharmacokinetics. They also highlight the potential to identify and monitor patient-specific residual gait deficits that may be refractory to L-DOPA, and which may inform the use of alternative therapeutic interventions, such as spinal cord stimulation, to target them.

#### B. Task-related modulations

During prolonged recordings outdoors, our neuromonitoring platform reliably detected gait adaptations associated with task-related constraints, particularly when crossing doors, entering elevators, or navigating obstacles. These ‘transitions’ typically require increased attentional effort and careful control of walking patterns. These added cognitive



**Figure 4. Fatigue-related modulations in motor and neural measures of gait quality.** **A.** PC analysis on the 18 gait parameters computed by the NUSHU sensorized shoes over the course of a walking activity lasting 18 minutes. Each dot of the PC space represents a group of 10 consecutive right and left steps. Factor loadings indicate the contribution of each gait parameter to PC1. **B.** Bar plot showing heel clearance (mean  $\pm$  STD) at three different time-periods over the duration the task. **C.** Power spectral density of STN LFP during the same three time-periods.

and motor demands can often exacerbate the emergence of FOG episodes. PCA analyses automatically extracted these transitions from the changes induced in gait parameters, which were reflected in PC1 scores that were positive during continuous steady-state straight walking, and negative during gait adaptations linked to transitions (**Fig. 3**).

We then aligned PC1 scores with STN neural activity. High-beta power exhibited strong correlations with context-related gait adaptations. Concretely, high-beta decreased during continuous straight walking compared to transitions. It also displayed reduced power during walking as compared to standing. These observations suggest that modulations in that spectral band reflect locomotor demands, capturing the type and difficulty of gait activities. These patterns were preserved ON- and OFF-L-DOPA.

The ability to isolate and study neural modulations arising during episodic events is crucial for advancing our understanding and prevention of deficits such as FOG in real life, including the design of therapies that dynamically cope with the unpredictability of context-related constraints in closed-loop.

#### C. Fatigue-related modulations

Finally, our monitoring platform accurately captured the progressive deterioration of gait quality during prolonged walking tasks that are susceptible to fatigue. Over time, PC1

scores exhibited a gradual decline, shifting from positive to negative values, reflecting a gradual reduction in step length, walking speed, and heel clearance, as well as an increased variability in most gait parameters. Thus, PCA automatically captured the worsening in gait throughout the task (**Fig. 4**).

Analyses of the corresponding neural modulations revealed a gradual increase in beta power over the course of the task, suggesting that rising beta activity may be associated with fatigue-induced declined in locomotor performance.

These motor and neural biomarkers may be used to automatically regulate DBS or spinal cord stimulation therapies to better compensate for fatigue in daily life conditions.

#### IV. DISCUSSION

We developed and validated a wearable neuromonitoring platform to uncover motor and neural biomarkers of gait dysfunction in daily life. This platform accurately monitored changes in gait quality and STN neural modulations due to L-DOPA, fatigue, or context-related constraints. Albeit studied in isolation, these three aspects are certainly intertwined in real-life conditions, and may need to be accounted for concurrently when developing therapies that effectively target gait deficits.

STN LFP biomarkers may also be combined with EEG and/or other wearable sensors for monitoring electrophysiological and motor readouts of gait.

The system's user-friendly design is intended to maximize adherence, including during everyday activities. Subthalamic nucleus LFPs are recorded directly from implanted DBS leads, while wearable sensors are discreetly embedded in conventional-looking shoes that can be worn as part of patients' daily routines.

Overall, our gait neuromonitoring platform has the potential to help assess the efficacy of gait therapies over long periods of time, and to guide the optimization of closed-loop protocols in out-of-laboratory environments.

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