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Research article

Plantar cutaneous function in Parkinson's disease patients ON and OFF L-dopa

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HIGHLIGHTS

- It is unclear if plantar cutaneous function is disrupted in Parkinson's disease (PD).
- Sensitivity and lower-limb reflexes were assessed in PD patients ON/OFF L-dopa.
- Plantar cutaneous function was similar to healthy age-matched control groups.
- Intact function in PD supports the use of therapeutics (e.g., vibrating insoles).

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ABSTRACT

While Parkinson's disease (PD) is traditionally viewed as a motor disorder, there is mounting evidence that somatosensory function becomes affected as well. However, conflicting reports exist regarding whether plantar sensitivity is reduced in early-onset PD patients. Plantar sensitivity was assessed using monofilaments and a gold-standard, two-interval two-alternative forced choice vibrotactile detection task at both 30 and 250 Hz. Lower-limb cutaneous reflexes were assessed by delivering continuous, sinusoidal vibration at 30 and 250 Hz while recording muscle activity in Tibialis Anterior. We found no evidence of elevated plantar thresholds or dysfunctional lower-limb cutaneous reflexes in PD patients ON medication. We also found no acute effect of ceasing L-dopa intake on either plantar sensitivity or cutaneous reflexes. Our finding of intact cutaneous function in PD supports the further exploration of therapeutics that enhance plantar sensitivity to minimize postural instability, a source of considerable morbidity in this clinical population.

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1. Introduction

PD is one of the most prevalent neurodegenerative disorders, characterized by increasing motor impairment that includes hallmark symptoms of bradykinesia, rigidity, tremor, and postural instability [1]. Although some aspects of motor deficits with PD could be related to central or peripheral changes in somatosensory function, evidence for altered skin sensitivity, particularly in the lower limb, is limited, and unclear. Decreased plantar sensitivity could contribute to postural instability and falls, a source of considerable morbidity in PD. Moreover, stimulating the plantar surface of the feet with vibrating [2], or textured [3] insoles may have therapeutic implications.

Previously, Prätorius et al., [4] found increased plantar monofilament (MF) and 30 Hz vibrotactile detection thresholds in PD patients (ON medication) relative to controls, in addition to a correlation between vibrotactile thresholds and UPDRS motor examination (UPDRS-ME) scores. However, with more stringent

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testing, Doty et al., [5] found that plantar MF thresholds did not differ between PD patients and controls, nor did they observe an acute effect of L-dopa. The discrepancy between these previous studies might have to do with disease duration, as Prätorius et al. [4] tested a PD patient group with a mean disease duration of 9.5 years (SD 7.1), while Doty et al. [5] state that their patient group's motor symptoms had been present for only 2 years or less. However, despite having shorter disease duration, the PD patient group tested by Doty et al. [5] had more severe motor symptoms based on mean UPDRS-ME scores. Given these previous reports, it remains unclear whether disease duration or symptom severity has a larger impact on plantar sensitivity.

Here we re-investigated plantar cutaneous sensitivity in an early-onset PD patient group with disease duration not statistically different from Prätorius et al. [4], but with more severe motor symptoms than previous plantar cutaneous studies. We also take a more rigorous psychophysical approach than previous studies [4,5], and further examine the acute effect of L-dopa on plantar sensitivity and lower-limb cutaneous reflexes. Given the anatomical observation that PD patients suffer from peripheral neuropathy [6], we predicted PD patients ON L-dopa would have greater tactile detection thresholds and weaker lower-limb cutaneous reflexes than a group of healthy controls. Given the absence of any acute effect of the L-dopa on plantar sensitivity [5], we predicted that thresholds would not differ OFF medication compared to ON.

2. Methods

Thirteen PD patients (8 men, 5 women; mean age = 72.6, SD = 7.7) and twenty-two healthy age-matched controls (9 men, 13 women; mean age = 68, SD = 6.9), with no known history of neurological disease or injury participated in this study. Mean disease duration was 6.5 years (SD = 4.8 years). All patients had prescriptions for levodopa-carbidopa. PD patients were examined twice during the same day: 1) after overnight withdrawal of all antiparkinson medication (OFF) with minimum withdrawal time of at least 12 h for L-dopa and 18 h for DA agonists, and 2) and during their best clinical condition (ON), about one hour after intake of their regular L-dopa dosage. Patients were clinically examined using the UPDRS-ME scale [7] prior to each testing session. Experimental protocols were explained to each participant and their written, informed consent was obtained. All procedures were approved by the University of British Columbia's Clinical Research Ethics Board.

Tactile stimuli were delivered bi-laterally on the medial forefoot near the first metatarsal head, at a location 80% of the length (from heel to toe) and width (lateral to medial border) of the foot, while participants were blindfolded. To estimate MF thresholds, the gram force level was adjusted across 20 trials using a 4-2-1 adaptive staircase procedure [8], with the threshold taken as the average of the 1-step reversal points. Vibrotactile detection thresholds at 30 and 250 Hz were measured using a two-interval two-alternative forced choice detection task (see Fig. 1). Analog voltage signals were generated in LabVIEW, and sent via multifunctional data acquisition hardware (PXI-6225-to-BNC-2090, National Instruments, USA) to a 300C ASI model dual-mode lever arm motor system (Aurora Scientific, Canada). Probe tip diameter was 1.5 mm. Contact force was maintained near 10 g; trials with mean force outside the 5–15 g range were discarded. Probe tip displacement, contact force, and voltage commands were digitized at 5 kHz using an A/D board controlled through Spike 2.0 (Power 1401; Cambridge Electronic Design, United Kingdom)(Fig. 1B).

For vibrotactile threshold estimates, stimulus amplitude was adaptive adjusted across 40-trial testing blocks following the Bayesian adaptive procedure [9,10], and we parameterized psychometric curves as modified Weibull functions [11]. Thresholds were defined as the peak-to-peak probe tip displacement (in μm) at which the participant could correctly detect the vibration with 75% probability (half-way between chance and perfect performance). 75%-correct threshold values were extracted using the same mathematical approach as Peters et al., [12,13]. Testing blocks were discarded if it was more probable that the participant was guessing, rather than performing the detection task, based on the Guessing Bayes Factor [10,12], with a criterion value of 1.

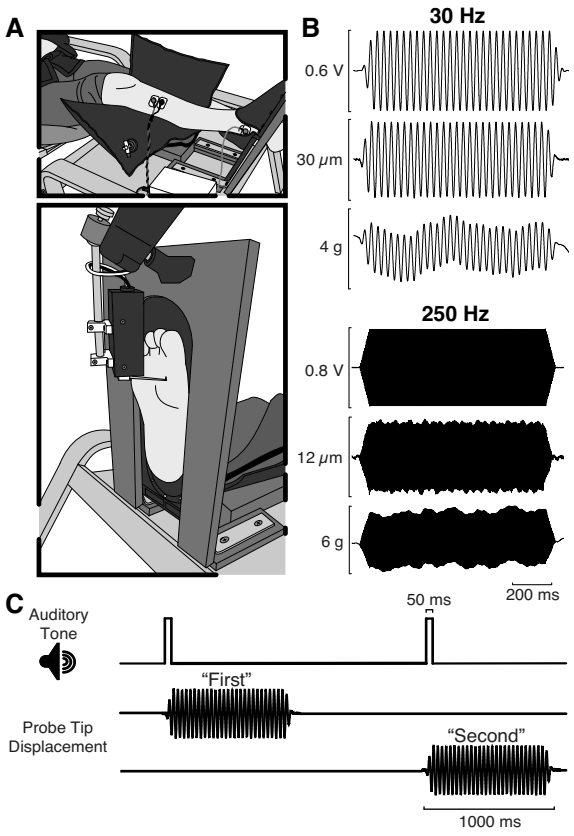

Fig. 1. Experimental setup, vibratory stimuli, and 2IFC trial timeline. A. Top: side schematic view of a participant's leg in the footrest/leg support setup. Bottom: front view of the exposed plantar surface of the foot, as well as the motor used for delivering vibrations. B. Sample 30 Hz (upper three traces) and 250 Hz (lower three traces) vibrations. Top: voltage command sent to the motor. Middle: probe tip displacement. Bottom: contact force. C. Timeline depicting the series of events that occurred on each 2IFC vibrotactile trial. The participant was presented with sequential 50-ms auditory tones denoting the two stimulus intervals. A 1-s vibration was delivered randomly during either the first or second interval, and the participant was required to determine which interval contained the stimulus.

To evoke cutaneous reflexes we used 30 and 250 Hz continuous, sinusoidal vibration for 5 min applied to the same skin location as the sensitivity testing. Only the more affected side was tested in PD patients. Stimulus amplitude was set to 0.2 mm for 30 Hz and 0.02 mm for 250 Hz (approximately 20 times perceptual threshold for young adults). EMG was recorded from Tibialis Anterior (TA) while participants isometrically dorsiflexed with 10–15% of their maximum volitional contraction. Contact force during reflex testing varied between 0–50 g (tolerance range of the vibrator) due to difficulty remaining still during dorsiflexion. Reflex coupling strength was assessed based on the gain, coherence, and cumulant density computed between the stimulus displacement and EMG time series [14,15] using Neurospec 2.0 (segment length = 0.4096 s; frequency resolution = 2.4414 Hz).

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