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ORIGINAL ARTICLE

Hands–feet wireless devices: Test–retest reliability and discriminant validity of motor measures in Parkinson's disease telemonitoring

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Background: Telemonitoring, a branch of telemedicine, involves the use of technological tools to remotely detect clinical data and evaluate patients. Telemonitoring of patients with Parkinson's disease (PD) should be performed using reliable and discriminant motor measures. Furthermore, the method of data collection and transmission, and the type of subjects suitable for telemonitoring must be well defined.

Objective: To analyze differences in patients with PD and healthy controls (HC) with the wearable inertial device SensHands–SensFeet (SH–SF), adopting a standardized acquisition mode, to verify if motor measures provided by SH–SF have a high discriminating capacity and high intraclass correlation coefficient (ICC).

Methods: Altogether, 64 patients with mild-to-moderate PD and 50 HC performed 14 standardized motor activities for assessing bradykinesia, postural and resting tremors, and gait parameters. SH–SF inertial devices were used to acquire movements and calculate objective motor measures of movement (total: 75). For each motor task, five or more biomechanical parameters were measured twice. The results were compared between patients with PD and HC.

Results: Fifty-eight objective motor measures significantly differed between patients with PD and HC; among these, 32 demonstrated relevant discrimination power (Cohen's $d > 0.8$). The test–retest reliability was excellent in patients with PD (median ICC = 0.85 right limbs, 0.91 left limbs) and HC (median ICC = 0.78 right limbs, 0.82 left limbs).

Conclusion: In a supervised environment, the SH–SF device provides motor measures with good results in terms of reliability and discriminant ability. The reliability of SH–SF measurements should be evaluated in an unsupervised home setting in future studies.

KEYWORDS
biomechanical parameters, motor function assessment, Parkinson's disease, subclinical motor abnormalities, telemedicine, telemonitoring, wearable sensors

1 | INTRODUCTION

Parkinson's disease (PD) is the second-most prevalent neurodegenerative disorder. In its advanced stages, it is associated with significant disability, increased caregiver burden, and significant healthcare costs for the community.[1,2] An improvement in the evolution of the disease and a reduction in caregiver burden can be achieved by avoiding late or incorrect diagnoses and managing motor symptoms from the early clinical stage of the disease.[3]

Before motor symptoms become evident[4–6] and lead to diagnosis according to specific diagnostic criteria,[7] PD has a preclinical phase of at least 5–7 years. If the disease is diagnosed in its preclinical phase, neuroprotective therapies would be started immediately with a possible benefit. Thus, the disease could have an improved course, resulting in a lower caregiver burden.[8–11]

The main motor symptoms of PD include tremor at rest, bradykinesia, rigidity, and postural instability, variously combined with each other.[7] Motor performance slowly worsens over time, and the treatment response decreases with the appearance of dyskinesias and motor fluctuations.[12] Parkinson's disease is associated with a broad spectrum of non-motor symptoms (e.g., hyposmia, fatigue, anxiety, apathy, depression, cognitive dysfunction, pain, hallucinosis, autonomic dysfunction, and complex behavioral disorders), sometimes influenced by therapy, in association with or without motor fluctuations.[12]

Considering the number of symptoms and the variability with which they can occur during the day, it is easy to understand why the patient's assessment in a hospital setting can greatly differ from when the patient resides at home.[13,14] Therefore, during outpatient visits, the clinician asks the patient and caregiver the 24-h symptom profile and how it changes over time. However, the reported information can be influenced by concomitant factors such as anxiety, depression, and cognitive impairment, and some patients with PD are not fully aware of their symptoms and cannot distinguish between signs of PD and other symptoms.[15]

The available clinical assessment tools for PD, such as the Hoehn and Yahr (HY) scale,[16] Movement disorders society—Unified Parkinson's Disease Rating Scale (MDS-UPDRS),[17] PD Questionnaire-39 (PDQ-39),[18] and 24-h motor diaries,[19] have well-known limitations.[3] The HY scale is used to measure functional disability in PD; however, it has low sensitivity.[3] The MDS-UPDRS is a clinical scale that requires a relatively long administration time (30 min). Furthermore, it is partially unreliable owing to patient and/or caregiver recall bias. Moreover, motor scores of the MDS-UPDRS part III are affected by the ability and experience of the examiner[3] and demonstrate high inter- and intra-rater variability when administered by nurses vs. neurologists.[20,21] Some limitations have also been suggested for the PDQ-39 because of the complexity of grouping items into scales with inherent interpretation problems.[22] Finally, 24-h clinical diaries are also prone to recall bias. Considering these premises, recent literature on motor assessment in PD has suggested that the current motor assessment system is archaic, imprecise, and frustrating.[23]

By using wearable wireless sensors (WWS), reliable quantification of a patient's motility can be obtained both in supervised (i.e., hospital, PD clinic) and unsupervised settings (i.e., home). In recent years, motor monitoring of PD using WWS in an unsupervised setting has received increasing attention. However, conclusive evidence that wireless technology has an actual impact on clinical outcomes is lacking.[14,24] Hence, 24/7 monitoring with wireless sensors has critical issues. The patient wore the equipment approximately 24/7, with potential psychological and privacy influences. The sensors cannot be positioned 24/7 on strategic points for fine motion detection of the fingers and hands (e.g., sensors on distal phalanges). Furthermore, the accelerometers and gyroscopes of the sensors are sensitive to any movement of the body (e.g., voluntary, automatic, physiological, pathological), although they do not distinguish the type of movement, much less the underlying cause (e.g., tremor from neurological disease vs. voluntary movements made with the arm; tremor transmitted to the body by a tool or other). The accelerations recorded by the sensors are processed using calculation algorithms that extrapolate motion indices, which are consequently rather coarse. Furthermore, 24/7 acquisitions were limited to some aspects of motor skills, such as walking and/or balance, tremor, and dyskinesia. Accordingly, to date, no general agreement on a reliable, valid, sensitive, transportable, and economical device for assessing the motor functions of patients with PD exists.[3] Furthermore, other types of devices (which do not analyze 24/7) evaluate only a few motor skills (e.g., walking).[25]

Thus, we developed a SensHands–SensFeet (SH–SF) device for motor monitoring of patients with PD. Precise motor measurements can be obtained in approximately 30 min. Monitoring can be repeated over time according to clinical needs (e.g., several times a day, once a week, a month) without major disturbances in the quality of daily life.

The SH–SF device can simultaneously record the movements from the four limbs; has wireless sensors placed on the distal ends of the phalanges of the fingers, thus providing information on fine motor skills; analyzes standardized motor exercises listed in the MDS-UPDRS III as well as other limb agility motor tasks; the calculation algorithms of the SH–SF system provides precise analytical motor measurements and not surrogate measures; and the sensors are worn for the time necessary for the acquisition of the predefined motor tasks.[26] The SH–SF device has been used to evaluate motor function in prodromal PD individuals.[27]

The following recommendations for the development of telemonitoring have recently been suggested: identifying a precise method of data collection, determining specific types of participants wherein good telemonitoring results can be expected, and evaluating the reliability of the data that will be used for telemonitoring.[14]

Accordingly, this study aimed to evaluate the reliability of the SH–SF device in a supervised setting in patients with mild-to-moderate PD, following a standardized motor task protocol. In particular, we aimed to identify reliable motor measures as they are highly discriminating (patients with PD vs. HC) and have high test–retest intraclass correlation coefficient (ICC) values.

2 | MATERIALS AND METHODS

2.1 | Study population

This cross-sectional study included 50 HC and 64 patients with mild-to-moderate PD (HY scale 1–2) enrolled between January 2019 and April 2020. The demographic and clinical characteristics of the HC and patients with PD are presented in Table 1.

The inclusion criterion was being right-handed because identifying a significant number of left-handed participants (HC and PD) can be difficult. The exclusion criteria were the presence of clinically significant impairments or diseases other than PD that could affect motor functions (e.g., atypical parkinsonism, osteoarthritis, or polyneuropathies) and having motor fluctuations and difficulty in walking independently since this study aimed to ascertain the reliability of the motor measures provided by the SH–SF device. The inclusion and exclusion criteria are listed in Table S1.

Patients with PD underwent a comprehensive neurological evaluation. Part III of the MDS-UPDRS was performed by a neurologist with expertise in movement disorders within a maximum of 7 days from the detection of the motor pattern with wearable devices; all patients were assessed without withdrawing antiparkinsonian medication and in the "on" state.

Written informed consent was obtained from all the participants before study initiation. The study (acronym CASANOVA, approved by the Ethical Committee of Tuscany Region, Area Vasta Nord Ovest, Italy, n°13,055/09.10.18, notified as n°1288/2019) was conducted in accordance with the International Conference of Harmonization Guideline for Good Clinical Practice and the Declaration of Helsinki.

2.2 | Sensor systems

The inertial sensor device SH–SF was used to evaluate and analyze the motor parameters. The SH–SF consists of two pairs of devices as follows: SansFoot devices are placed over the dorsum of the subject's feet, with an elastic ensuring adherence between the foot and the sensor, and SensHand devices are composed of three sensors, placed over the thumb, index, and middle fingernails, connected through spiral cables, with a coordination unit placed within a wrist bracelet that also contains a sensor. The processing algorithms for each motor measure used information from different sensors.[26] The details on the SH–SF sensors and algorithms are provided in the Data S1.

2.3 | Motor tasks evaluated with sensors

Once the sensor devices were worn, the participants were asked to perform 14 motor tasks, which were divided as follows: upper limb motility: thumb/forefinger tapping (THFF), thumb/middle finger tapping (THMF), forefinger tapping (FTAP), hand opening/closing (OPCL), and forearm pronation/supination (PSUP); lower limb motility: leg agility (HEHE), toe tapping with heel pin (TTHP), heel tapping with toe pin (HTTP), and heel–toe tapping (HETO); tremor: rest tremor of the upper limbs (HRST) and postural tremor of the upper limbs (POST); and gait: gait evaluation (GTAF); 360° rotation (ROTA); arm swing during gait (GTAH).

Most of these motor tasks are also performed in the MDS-UPDRS part III (THFF, OPCL, PSUP, HEHE, TTHP, HRST, POST, and GTAF) or evaluated during other tasks (e.g., GTAH). Others are not present in the MDS-UPDRS III (THMF, FTAP, HTTP, HETO, and ROTA).

Before execution of each motor task, the participants received specific training from a neurologist. The acquisition was conducted in a supervised setting with a clinician. A strictly standardized modality of execution and detection of the motor tasks was adopted. Most motor tasks had a predetermined execution and acquisition time (e.g., thumb–index finger tapping), while other tasks did not have a fixed time, and the end of the procedure coincided with the completion of the exercise (e.g., walking test).

The work procedure for the motor tasks at a fixed time had a total duration of 16 s and included four steps. First, the participant assumed with the limbs in the specific position foreseen for that motor task and remained stationary in that position (e.g., the fingertip index against that of the thumb for thumb–index tapping). The neurologist (or the neurophysiopathology technician) selected the motor task to be recorded on the control program interface (installed on a dedicated notebook) and started the procedure by pressing the enter key.

TABLE 1 Demographic characteristics of PD patients and healthy controls

Group	*N*	Age mean (SD)	Males (%)	Female (%)	HY mean (SD)	MDS-UPDRS III total score mean (SD)	Months from diagnosis (SD)	LEDD mean (SD)	MDS-UPDRS III mean scores for the right upper limb (SD)
Healthy controls	50	65.5 (2.7)	39 (78.0)	11 (22%)	-	-	-	-	-
PD patients	64	66.6 (8.8)	40 (62.5)	24 (37.5)	1.86 (0.73)	15.7 (8.88)	20.8 (17.21)	308.57 (232.6)	4.3 (2.13)

Abbreviations: HY, Hoehn and Yahr scale; LEDD, levodopa equivalent daily dose; MDS-UPDRS, Movement disorders society—Unified Parkinson's Disease Rating Scale; PD, Parkinson's disease; SD, standard deviation.

Second, the device calibrated the sensors for 3 s. Third, the device automatically emitted the start sound at which both movement and acquisition with the wireless sensors were initiated. This phase lasted 10 s, at the end of which the device automatically generated a sound signal to stop movement and acquisition. At this signal, the participant stopped the movement and assumed the starting position with the limbs. Last, the device performed again the sensor calibration for 3 s, and then emitted a final sound signal, after which it was possible to move on to the acquisition of another motor task. The duration of the movement and its acquisition was 10 s, while the calibration of the instrument was 6 s (3 s each before and after the execution of the movement).

Motor exercises without a fixed time (e.g., walking test) had the following procedure. First, the participant assumed the position foreseen for that motor task and remained stationary (e.g., standing for the walking test). The neurologist (or the neurophysiopathology technician) selected the motor task to be recorded on the program interface and started the procedure by pressing the enter key. Second, the device calibrated the sensors for 3 s. Third, the device automatically emitted the start sound at which both movement and acquisition with the wireless sensors were initiated. When the participant finished the motor task (e.g., the participant walked 15 m), the participant stopped as in the initial position (e.g., standing above the strip on the ground that marks the 15-m walk), and the neurologist stopped the acquisition. Last, the device performed the final calibration of the sensors for 3 s, then emitted a final sound signal, after which it was possible to move on to the acquisition of another motor task.

Instructions on how to execute the motor tasks are provided in Table S2.

The entire protocol was conducted in an outpatient clinic, and the gait evaluation tasks were performed in a well-lit corridor. The participants were examined twice consecutively to obtain two repeated measurements for each participant. For comparisons between groups, the mean value of the repeated measures was used. A detailed description of the measured biomechanical parameters is presented in Table 2.

2.4 | Statistical analysis

Motor measures detected in one limb of patients with PD were compared with that in the same limb of HC. To avoid comparing measures obtained from HC with measures obtained from a non-involved limb in an early stage patient with PD, only parameters obtained from limbs with an MDS-UPDRS score >0 were recorded for patients with PD. Therefore, the numerousness of measures relating to a specific motor task was different between patients with PD and HC and between the right and left limbs (these differences have been considered in the statistical analysis).

Variables and results are described as mean and standard deviation, median, and interquartile range (IQR) or absolute frequency and percentage, as appropriate. Comparison of continuous variables between HC and patients with PD was performed using an analysis of variance (ANOVA) or Welch ANOVA when the homogeneity of variances was not met. As the analysis of biomechanical parameters required multiple comparisons, statistical significance was adjusted using the Benjamini and Hochberg approach.[28] The discrimination power of the motor measures between patients with PD and HC was calculated using Cohen's *d* as a measure of the effect size. Cohen's *d* values were interpreted using the following criteria: <0.2 was not relevant; 0.2–0.49 was small; 0.5–0.79 was medium; 0.8–1.29 was relevant; and >1.29 was very relevant.[29]

The agreement between the two measures of the same task obtained from each participant (intra-subject reproducibility) was calculated as the ICC using a two-way mixed model with measures of absolute agreement. The ICC data were interpreted using the following criteria: values 0.41–0.6 indicate moderate agreement; 0.61–0.8 indicate strong agreement; and >0.8 indicate near complete agreement.[30] For each ICC, the 95% confidence interval was calculated.

Data analysis was performed using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp.). A two-sided *p*-value <.05 was considered significant.

MDS-UPDRS III mean scores for the right lower limb (SD)	MDS-UPDRS III mean scores for the left upper limb (SD)	MDS-UPDRS III mean scores for the left lower limb (SD)	% of PD patients with right upper limb MDS-UPDRS III score >0	% of PD patients with right lower limb MDS-UPDRS III score >0	% of PD patients with left upper limb MDS-UPDRS III score >0	% of PD patients with left lower limb MDS-UPDRS III score >0	% of PD patients with MDS-UPDRS III score >0 for right limbs	% of PD patients with MDS-UPDRS III score >0 for left limbs
-	-	-	-	-	-	-	-	-
2.2 (0.97)	3.9 (1.95)	2.4 (1.04)	84.4	71.9	81.2	65.6	86.9	82.8

3 | RESULTS

Of 14 motor tasks that were evaluated, 75 biomechanical parameters were extracted. Overall, 58 of the 75 motor parameters acquired were significantly different between the patients with PD and HC for either one or both limbs. Thirty-two motor measures were highly discriminating (HC vs. patients with PD) for both the right and left limbs (Cohen's *d*: 0.8–1.3). Five measures were highly discriminating on the right (Cohen's $d \geq 0.8$) and slightly less discriminating on the left. Six measures were highly discriminating on the left (Cohen's $d \geq 0.8$) and slightly less discriminating on the right. The four measures were sufficiently discriminating on both sides (Cohen's *d*: 0.5–0.79). Finally, 11 motor measures were weakly discriminating (Cohen's *d*: 0.2–0.49) on one or both sides of the body. The findings are detailed in Tables 3–6, respectively. In all 14 exercises explored using biomechanical sensors, at least one significantly different parameter between patients and controls was detected.

The most discriminating objective measures (Cohen's $d \geq 0.7$) of the upper limb movements, both for the right and left side of the body, were: (1) the number of taps in thumb–index finger and thumb–middle finger tapping (TF_Taps, TM_Taps); (2) the integral calculation of accelerations during thumb–index finger and thumb–middle finger tapping (TF_IAV, TM_IAV); (3) opening and closing speed of the index tapping on the table and amplitude of movement (FF_wo, FF_wc, FF_Exc); (4) number of opening–closing movements of the hand, opening–closing speed, and integral calculation of the accelerations of that movement (OC_Taps, OC_wo, OC_wp, OC_IAV); and (5) all motor measures of pronosupination of the hand (PS_Taps, PS_Exc, PS_wp, OC_ws, PS_IAV). For the lower limbs, biomechanical parameters that demonstrated a very significant discrimination (Cohen's $d \geq 0.8$) between patients with PD and HC were: (1) the number of taps performed with the heel (pivot at the forefoot) (HH_Taps); (2) the forefoot and heel excursion (HT_ExcT, HT_ExcH) in heel–toe tapping; and (3) three measures of the agility of the lower limb (peak in power spectral density – HE_Peak, average signal power from accelerometer PSD – HE_Power, integral of magnitude of the total acceleration vector in heel tapping, HE_IAV).

The GTAF indicated that patients with PD had a longer time to complete the task (GT_Time) with a greater number of steps (GT_Strd); the foot was lifted less from the ground (GT_H), with a reduction in the dorsal–plantar excursion of the ankle (GT_Ang). For all parameters, the effect size was moderately to very relevant (Cohen's *d*: 0.5–1.7).

Three measures of the rotation test, rotation strides (RO_Strd), rotation time (RO_Time), and stance phase (RO_STT), had a high discriminating capacity (Cohen's $d \geq 0.9$).

For tremor measurements, some parameters of POST were very discriminant: accelerometer % power in band 3.5–7.5 Hz (PT_Perc1A), gyroscope % power in band 3.5–7.5 Hz (PT_ Perc1G), and integral of magnitude of the total acceleration vector in POST (PT_IAV) (Cohen's *d*: 0.8–1.2).

Seventeen biomechanical parameters did not indicate significant differences between patients with PD and controls in either the right or left limb (Table S3).

Regarding the ICC for all significantly discriminating biochemical parameters, the ICC was 0.78 (IQR = 0.17) for the right limbs and 0.82 (IQR = 0.17) for the left limbs of the HC. In patients with PD, the median ICC was 0.85 (IQR = 0.12) for the right limbs and 0.91 (IQR = 0.11) for left limbs. In Tables S4 and S5, we report the ICCs for each biomechanical parameter recorded in HC and patients with PD, respectively.

4 | DISCUSSION

To our knowledge, SH–SF is the first reported wearable wireless device for Parkinson's disease with sensors also positioned at the distal ends of the first three fingers, which simultaneously acquires from the sensors at the feet and hands (e.g., during walking).

The standardized procedure allowed the execution of the exercises to be uniform and to obtain clear acquisition input from other movements, thus favoring good performance of the algorithms dedicated to the calculation of motor measures.

This method newly allows recording multiple types of motor tasks in approximately 30 min to obtain 58 significantly different objective motor measures (patients with PD vs. HC), of which 32 with high discriminating power and excellent ICC values.

Not all measures provided by the SH–SF system demonstrated good discriminating capacity between patients with PD versus HC, suggesting that the data provided by wearable sensors (or other types of instruments) would require preliminary reliability testing before being used in clinical practice.

The reasons why some motor measures did not discriminate between the two groups varied on a case-by-case basis.

The thumb–index and thumb–middle tapping width measurements were not significant. The SH–SF system processes these measurements without using information derived from the sensors placed on the thumb. This simplification does not affect some calculations, such as the number of taps, but could significantly affect the calculation of the amplitude of the movement (during tapping, the thumb moves although less than the index or middle finger). Therefore, in the future, algorithms dedicated to the calculation of the amplitude of these tapping movements will have to be integrated with the information coming from the thumb sensors (already positioned in the SH–SF system).

Regarding the tapping movement of the index on the table, the measures of tapping number and integral calculation of the accelerations were not significant. New algorithms will have to be developed that are more suitable for the study of fast movements with small excursions, such as those of this motor task. Additionally, the extent of hand opening and closing was not significantly different between the patients with PD and HC. Some people perform this movement by completely closing their hand (fist), while others perform the motor task without flexing the third phalanx over the second

TABLE 2 Biomechanical parameters

Tasks evaluated	Movement	Motor measurement	Abbreviation	Unit of measure
Upper limb motility	Thumb–forefinger tapping (THFF)	Taps number	TF_Taps	No.
		Amplitude of forefinger movement	TF_Exc	degrees of arc (°)
		Closing velocity	TF_wc	(°/s)
		Opening velocity	TF_wo	(°/s)
		Integral of magnitude of the total acceleration vector (IAV)	TF_IAV	(m/s)
	Thumb–middle finger tapping (THMF)	Taps number	TM_Taps	No.
		Amplitude of forefinger movement	TM_Exc	(°)
		Closing velocity	TM_wc	(°/s)
		Opening velocity	TM_wo	(°/s)
		Integral of magnitude of the total acceleration vector (IAV)	TM_IAV	(m/s)
	Forefinger tapping (FTAP)	Taps number	FF_Taps	No.
		Amplitude of forefinger movement	FF_Exc	(°)
		Closing velocity	FF_wc	(°/s)
		Opening velocity	FF_wo	(°/s)
		Integral of magnitude of the total acceleration vector (IAV)	FF_IAV	(m/s)
	Hand opening/closing (OPCL)	Hand opening–closing movements	OC_Taps	No.
		Amplitude of opening/closing movement	OC_Exc	(°)
		Closing velocity	OC_wc	(°/s)
		Opening velocity	OC_wo	(°/s)
		Integral of magnitude of the total acceleration vector (IAV)	OC_IAV	(m/s)
	Forearm pronosupination (PSUP)	Pronosupination movements	PS_Taps	No.
		Amplitude of pronosupination movements	PS_Exc	(°)
		Supinating velocity	PS_ws	(°/s)
		Pronation velocity	PS_wp	(°/s)
		Integral of magnitude of the total acceleration vector (IAV)	PS_IAV	(m/s)
Lower limbs motility	Lower limb agility-Heel tapping (HEHE)	Average signal power from accelerometer PSD	HE_Power	m^2/s^2
		Fundamental frequency	HE_Freq	(Hz)
		Peak in power spectral density	HE_Peak	Energy/Hz
		Integral of magnitude of the total acceleration vector (IAV)	HE_IAV	(m/s)
	Toe tapping heel pin (TTHP)	Taps number	TT_Taps	No.
		Toe angle	TT_Exc	(°)
		Integral of magnitude of the total acceleration vector (IAV)	TT_IAV	(m/s)
	Heel tapping—toe pin (HTTP)	Taps number	HH_Taps	No.
		Heel angle	HH_Exc	(°)
		Integral of magnitude of the total acceleration vector (IAV)	HH_IAV	(m/s)
	Heel–toe tapping (HETO)	Taps number	HT_Taps	No.
		Heel frequency	HT_freqH	(taps/s)
		Toe frequency	HT_freqT	(taps/s)
		Heel angle	HT_ExcH	(°)
		Toe angle	HT_ExcT	(°)
		Integral of magnitude of the total acceleration vector (IAV)	HT_IAV	(m/s)

(Continues)

TABLE 2 (Continued)

Tasks evaluated	Movement	Motor measurement	Abbreviation	Unit of measure
Tremor	Rest tremor (HRST)	Average signal power from accelerometer power spectral density (PSD)	RT_PwrA	m^2/s^2
		Accelerometer fundamental frequency	RT_freqA	Hz
		Accelerometer % power in band (3.5–7.5 Hz)	RT_Perc1A	%
		Average signal power from gyroscope PSD	RT_PwrG	$degrees^2$
		Gyroscope fundamental frequency	RT_freqG	Hz
		Gyroscope % power in band (3.5–7.5 Hz)	RT_Perc1G	%
		Integral of magnitude of the total acceleration vector (IAV)	RT_IAV	m/s
	Postural tremor (POST)	Average signal power from accelerometer PSD	PT_PwrA	m^2/s^2
		Accelerometer fundamental frequency	PT_freqA	Hz
		Accelerometer %power in band (3.5–7.5 Hz)	PT_Perc1A	%
		Accelerometer %power in band (8–12 Hz)	PT_Perc2A	%
		Average signal power from gyroscope PSD	PT_PwrG	$degrees^2$
		Gyroscope fundamental frequency	PT_freqG	Hz
		Gyroscope %power in band (3.5–7.5 Hz)	PT_Perc1G	%
		Gyroscope %power in band (8–12 Hz)	PT_Perc2G	%
		Energy expenditure	PT_IAV	m/s
Gait	Gait (GTAF)	Gait time	GT_Time	s
		Gait strides	GT_Strd	No.
		Stride time	GT_StrdT	s
		Swing time	GT_SWT	s
		Stance time	GT_STT	s
		Relative stance	GT_RS	%
		Angular excursion	GT_ANG	degrees of arc (°)
		Stride height indicator	GT_H	indicator in approx. cm
	Rotation (ROTA)	Rotation time	RO_Time	s
		Rotation frequency	RO_Freq	(strides/s)
		Rotation strides	RO_Strd	No
		Stance time	RO_STT	s
		Relative stance	RO_RS	%
	Arms swinging (GTAH)	Movements	GT_Taps	No.
		Movement amplitude	GT_Exc	(°)
		Front velocity	GT_wf	(°/s)
		Back velocity	GT_wb	(°/s)
		Integral of magnitude of the total acceleration vector (IAV)	GT_IAV	(m/s)

("bye–bye"-like finger movement). This inhomogeneity in execution may have influenced the significance of this measure. Asking patients to perform this task in a uniform way (i.e., "bye–bye" closure, instead of clenching a "fist") may improve the discriminating capacity of this measure. Moreover, calculation algorithms for this measure must be revised.

Of the 16 measures concerning tremor (at rest and postural), seven were not significant (Table S3). This could partly be due to the intrinsic high variability of the tremor and its dependence on physiological factors (e.g., anxiety and tiredness), which may also exacerbate physiological tremors in HC.

Furthermore, tremor variability during the examination could influence the subsequent retest, possibly explaining why tremor measurements with good discriminating capacity occasionally presented inhomogeneous ICC values that ranged from 0.13 (poor) to 0.97 (good).

An improvement in measures of tremor at rest could be obtained by making more prolonged acquisitions (e.g., 26 s instead of 16 s for

POST) and/or by detecting tremor during a condition that favors its onset, such as hand tremors that occur during walking.

The most discriminating measures of POST were those that investigated the 3.5–7.5 Hz frequency band, where the parkinsonian tremor was placed (effect size: 0.5–1.2). This may be due to the reappearance of Parkinsonian tremors during posture maintenance.

The following gait measures did not significantly differ between patients with PD and HC: stride time, swing time, and stance time. Hence, these measures may not be suitable for differentiating HC from patients with mild-to-moderate PD.

Del Din et al.[31] have reported that the variability and asymmetry of gait measurements were significant in prodromal PD. Unfortunately, we did not perform this analysis, although we have identified bilaterally very discriminating walking measures with good ICC values as follows: walking time of 15 m, number of steps, foot lift index from the ground, and dorso–plantar excursion of the ankle (effect size: 0.5–1.7; ICC: 0.90–0.98).

The relative stance (ratio between the duration of the stance phase and the walking cycle) was a sufficiently reliable measure for the left lower limb (effect size: 0.5; ICC of HC: 0.94; patients with PD: 0.90), whereas on the right, this measure was not significant.

In this study, we identified other significant motor measures only for one side of the body (Tables 3–6); of the 58 measures with medium–high discriminating capacity (Cohen's $d \geq 0.5$), 50 were for the right side of the body and 54 for the left. This slightly lower number of significant motor measures for the right limbs may be due to the fact that the dominant side of the body (i.e., right side in our sample) may benefit from more efficacious motor compensation mechanisms in the early stages of PD.

Nevertheless, this slight difference might disappear by investigating a larger sample, including participants with left-side dominance, for which we currently have a multisite study in progress that also includes left-handed participants, and the variability and asymmetry of motor measures will be evaluated.

The speed of the pendular backward movement of the upper limbs during walking was not significantly different between HC and patients with PD, in contrast to that of the forward movement. This difference could depend on the mild disease severity of the included patients with PD and/or on the limited sample size. However, the kinetics of the backward pendular movement could also explain the difference in results; it has a shorter oscillation time than the forward movement and occurs in favor of gravity, and fewer muscles are involved compared to when the oscillation of the arm was towards the front.[32,33]

Normative data for SH–SF parameters were obtained once the study sample was increased. This allowed us to obtain aggregate reference values for the limbs stratified by age and sex. Once normative values are obtained, a quantitative score of disease severity can be obtained, which would help clinicians to monitor motor impairment and provide appropriate treatment. With such reliable motor measures available, artificial intelligence algorithms will soon be implemented to automatize and optimize the process of data dimensionality reduction and data aggregation, providing clinicians with few parameters to be used in clinical practice.

Overall, this study demonstrates that the SH–SF device provides many reliable and discriminating motor parameters in a supervised setting. We hope that such measures (or some of them) will soon be detected during clinical checks in specialized settings. Such standardized motor measures would help clinicians to objectively monitor the course of the disease over time or even motor fluctuations that occur in patients with PD. Furthermore, such motor measures could help to identify patients at risk for PD (e.g., those with idiopathic hyposmia) who have an idiopathic deflection of motor performance that is not clinically evident (potential preclinical PD).[27]

The SH–SF device has already been used in supervised experiments for the quantitative and objective assessment of motor performance for the diagnosis and monitoring of PD.[26]

Since we have verified that the SH–SF system provides reliable and discriminating motor measures, this will also be used for patients with motor fluctuations and in more advanced stages of the disease in a supervised setting.

Before adopting the SH–SF device for telemonitoring, verifying that the system is also reliable to be used in an "unsupervised" home setting is necessary. Motor performance can be influenced by several factors (e.g., degree of vigilance and motivation), and these influences vary from a supervised clinical setting to an unsupervised home setting.[13] Consequently, a new project (OLIMPIA, Tuscany Region: J44120000760009) that aimed to verify the correlation of motor parameters obtained under different conditions is underway.

The patient will undergo training by specialized staff; furthermore, specific information material (paper and multimedia) will be provided.

Before the self-acquisition of each motor exercise, an avatar (displayed on the tablet screen of the SH–SF kit) demonstrates how the exercise must be performed. Additionally, the development of automatic recognition algorithms for the correct positioning of sensors was used.

Considering that the SH–SF device will provide reliable parameters in an unsupervised setting, the following home use scenario can be assumed: (1) evaluating the percentage of amelioration to a dopaminergic stimulation test in de novo drug-naïve patients with PD; (2) in a motor-compensated patient with PD, monitoring (approximately 30 min) once a month should be performed in order to assess the course of the disease; and (3) in patients with motor fluctuations, several self-acquisitions should be conducted daily in order to optimize dopaminergic therapy.

The strength of this study is the highly standardized and easily repeatable method of performing and acquiring motor tasks. This facilitates the analytical work of calculation algorithms. The SH–SF wearable sensors are another advantage because they allow the acquisition of motor information for each of the four limbs while simultaneously walking.

However, this study had some limitations. First, the study had a relatively small sample size, and only right-handed participants were included; this will be amended during the extension of the study in

TABLE 3 Motor measurement values of upper limbs motility in healthy control subjects and in PD patients

			Right					
Movement	Motor parameter	Group	*N*	Mean	SD	Min.	Max.	Effect size (*d*)
Thumb-forefinger tapping (THFF)	TF_Taps	C	50	45.4	7.5	29.0	58.5	1.2[a]
		P	54	32.9	12.4	8.5	57.5	
	TF_wc	C	50	165.0	83.4	40.3	353.1	0.3
		P	54	141.6	98.4	26.1	439.1	
	TF_wo	C	50	137.4	70.6	33.5	303.5	0.2
		P	54	124.3	83.3	25.2	373.2	
	TF_IAV	C	50	134.2	18.2	106.6	183.6	0.9[a]
		P	54	116.8	19.6	86.1	182.1	
Thumb-middle finger tapping (THMF)	TM_Taps	C	49	46.1	7.2	31.0	60.0	1.2[a]
		P	52	34.4	11.4	13.5	56.0	
	TM_wc	C	49	147.6	71.1	38.1	323.9	0.4
		P	52	121.2	72.5	30.8	391.8	
	TM_wo	C	49	177.9	85.1	43.8	392.5	0.5
		P	52	138.3	86.4	17.3	473.3	
	TM_IAV	C	49	150.8	21.9	101.5	203.5	1.2[a]
		P	52	120.3	26.6	92.2	200.1	
Forefinger tapping (FTAP)	FF_wo	C	49	97.2	43.4	12.6	226.5	1.4[a]
		P	26	45.4	23.2	16.8	131.6	
	FF_wc	C	49	116.5	52.0	2.3	262.8	1.4[a]
		P	26	53.3	29.3	11.2	157.5	
	FF_Exc	C	49	14.0	7.2	2.2	34.1	1.1[b]
		P	26	7.1	4.2	1.6	18.8	
Hand opening/closing (OPCL)	OC_Taps	C	50	35.7	6.9	24.5	56.0	1.3[a]
		P	53	24.0	10.6	6.5	50.5	
	OC_wc	C	50	555.3	159.4	146.6	920.8	0.8[a]
		P	53	420.0	171.0	129.6	830.8	
	OC_wo	C	50	656.3	184.8	180.2	1097.3	1.0[a]
		P	53	449.0	210.0	129.9	943.1	
	OC_IAV	C	50	254.9	58.7	153.2	435.3	1.8[a]
		P	53	156.6	53.5	98.1	292.3	
Forearm prono-supination (PSUP)	PS_Taps	C	49	22.6	5.9	13.0	37.0	0.7
		P	53	17.4	8.5	5.5	38.0	
	PS_Exc	C	49	156.2	27.9	102.2	220.3	1.3[a]
		P	53	117.3	32.3	45.0	190.5	
	PS_ws	C	49	613.1	118.8	351.6	915.1	2.0[a]
		P	53	360.5	137.8	127.0	742.4	
	PS_wp	C	49	688.0	144.7	381.9	1002.1	2.0[a]
		P	53	371.4	164.9	100.8	876.3	
	PS_IAV	C	49	154.6	31.5	109.2	225.6	1.6[a]
		P	53	114.2	19.0	92.0	200.9	

Note: Statistical significance between the two groups investigated (*p* adjusted) and discriminant capacity (effect size). C: control group; P: PD patients group; Effect size: Cohen *d*.

[a]Cohen $d > 0.8$ bilaterally.

[b]Cohen $d > 0.8$ unilaterally.

*$p < .05$.

Abbreviations: PD, Parkinson's disease; SD, standard deviation.

	Left						
p (adjusted)	*N*	Mean	SD	Min.	Max.	Effect size (*d*)	*p* (adjusted)
<.00001*	50	43.8	6.9	30.5	55.0	1.5[a]	<.00001*
	51	29.7	11.0	12.0	55.5		
.2410	50	197.8	86.0	75.4	396.3	0.6	.0109*
	51	146.0	96.5	14.9	374.1		
.4428	50	165.2	72.0	59.3	315.3	0.5	.0359*
	51	129.6	79.9	19.5	303.4		
.00003*	50	153.4	24.1	119.0	216.9	1.2[a]	<.00001*
	51	124.1	25.5	95.8	198.3		
<.00001*	49	43.5	6.6	32.5	54.5	1.3[a]	<.00001*
	52	31.7	11.1	11.5	56.0		
.921	49	186.3	80.5	56.9	397.5	0.7	.0014*
	52	128.2	86.0	25.9	368.3		
.0346*	49	224.2	95.8	73.6	480.9	0.8[b]	.0003*
	52	145.6	102.8	29.0	438.6		
<.00001*	49	154.3	26.1	103.7	210.0	1.2[a]	<.00001*
	52	122.5	27.8	96.8	197.2		
<.00001*	50	117.3	43.7	46.3	226.2	1.0[a]	.0007*
	26	73.4	48.6	26.2	216.7		
<.00001*	50	139.3	51.5	50.3	266.7	1.0[a]	.0007*
	26	85.3	60.1	27.1	260.9		
.00002*	50	18.0	8.1	6.1	38.3	0.7	.0075*
	26	11.9	8.5	3.2	39.3		
<.00001*	50	33.6	6.5	16.5	53.5	1.1[a]	<.00001*
	52	23.6	11.6	6.0	51.0		
.0002*	50	611.3	157.4	229.3	928.8	0.9[a]	.00003*
	52	450.4	188.3	141.3	818.5		
<.00001*	50	715.4	185.8	285.2	1094.5	1.1[a]	<.00001*
	52	473.3	235.3	146.2	967.9		
<.00001*	50	263.9	60.2	148.9	391.6	1.3[a]	<.00001*
	52	172.9	73.8	104.4	372.1		
.0012*	49	22.0	6.0	11.0	38.5	0.7	.0046*
	49	17.2	8.5	4.0	38.5		
<.00001*	49	154.0	33.5	59.4	245.8	1.4[a]	<.00001*
	49	109.7	30.9	41.7	181.2		
<.00001*	49	589.4	147.6	261.2	920.0	1.9[a]	<.00001*
	49	333.1	123.5	144.1	623.4		
<.00001*	49	652.4	177.7	282.8	1088.2	1.9[a]	<.00001*
	49	335.9	148.0	99.1	651.2		
<.00001*	49	153.85	36.1	108.9	251.9	1.5[a]	<.00001*
	49	112.9	14.24	87.2	158.6		

TABLE 5 Motor measurement values of tremor in healthy control subjects and in PD patients

			Right							Left						
Movement	Motor parameter	Group	*N*	Mean	SD	Min.	Max.	Effect size (*d*)	*p* (adjusted)	*N*	Mean	SD	Min.	Max.	Effect size (*d*)	*p* (adjusted)
Rest tremor (HRST)	RT_Perc1A	C	50	28.8	6.6	10.3	53.1	0.7	.0025*	49	28.5	3.9	17.1	35.1	0.5	.0177*
		P	53	33.8	8.2	16.4	57.2			52	31.5	7.1	24.2	76.0		
	RT_Perc1G	C	50	34.1	9.4	16.4	78.7	0.8[a]	.0002*	49	34.1	8.7	21.2	70.8	0.6	.0078*
		P	53	46.2	18.4	10.6	92.1			52	41.1	14.2	13.2	90.1		
	RT_PwrG	C	48	0.4	0.9	0.0	5.1	0.4	.0700	49	0.3	0.6	0.0	3.2	0.4	.0488*
		P	50	4.0	12.1	0.5	7.5			52	2.5	6.9	0.3	47.0		
	RT_IAV	C	50	99.5	3.1	93.6	107.1	0.6	.0300*	49	98.6	1.8	95.8	103.5	1.0[a]	.00002*
		P	53	101.7	3.9	93.9	108.0			52	101.6	4.0	95.1	107.8		
Postural tremor (POST)	PT_Perc1A	C	50	21.7	7.8	8.8	36.6	1.0[b]	<.00001*	50	19.4	6.7	6.5	37.7	1.2[b]	<.00001*
		P	54	34.1	15.4	11.6	78.9			51	31.8	13.4	10.4	77.6		
	PT_Perc2A	C	50	38.5	12.6	16.6	68.7	0.6	.0079*	50	37.4	11.9	17.8	71.2	0.5	.0347*
		P	54	30.9	13.5	8.1	63.3			51	31.7	12.4	8.3	66.9		
	PT_Perc1G	C	50	23.7	5.7	13.1	38.7	1.0[b]	<.00001*	50	23.9	8.1	8.0	48.3	1.0[b]	.00003*
		P	54	38.8	19.2	10.7	92.1			51	36.2	16.3	11.6	76.4		
	PT_Perc2G	C	50	32.4	10.6	15.5	60.5	0.5	.0177*	50	29.9	13.5	1.5	73.3	0.4	.0724
		P	54	25.4	15.9	0.8	74.1			51	24.3	14.2	4.1	72.5		
	PT_IAV	C	50	98.7	1.9	94.3	101.6	0.9[b]	.0150*	50	99.3	2.1	92.3	101.6	0.8[b]	.0001*
		P	54	101.8	4.6	93.9	110.3			51	102.1	4.2	94.8	108.4		

Note: Statistical significance between the two groups investigated (*p* adjusted) and discriminant capacity (effect size). C: control group; P: PD patients group; Effect size: Cohen *d*.

[a]Cohen $d > 0.8$ unilaterally.

[b]Cohen $d > 0.8$ bilaterally.

*$p < .05$.

Abbreviations: PD, Parkinson's disease; SD, standard deviation.

TABLE 6 Motor measurement values of gait, standing rotation and swing of the arms, in healthy control subjects and in PD patients

			Right							Left						
Movement	Motor parameter	Group	*N*	Mean	SD	Min.	Max.	Effect size (*d*)	*p* (adjusted)	*N*	Mean	SD	Min.	Max.	Effect size (*d*)	*p* (adjusted)
Gait (GTAF)	GT_Strd	C	49	11.3	1.3	9.0	14.5	0.6	.0081*	50	11.2	1.2	9.0	14.0	0.9[a]	.0007*
		P	46	13.7	5.2	10.5	44.5			42	14.0	4.5	8.5	34.5		
	GT_Time	C	49	12.0	1.7	8.2	15.5	0.6	.0086*	50	11.7	1.6	8.1	14.9	0.9[a]	.0005*
		P	46	14.7	6.0	10.0	48.5			42	15.1	5.3	9.0	33.7		
	GT_H	C	49	0.2	0.1	0.0	0.4	0.9[a]	.0008*	50	0.1	0.1	0.1	0.4	0.5	.0282*
		P	20	0.1	0.0	0.0	0.2			19	0.1	0.0	0.0	0.2		
	GT_Ang	C	49	73.9	9.6	52.9	92.7	0.6	.0127*	50	91.1	7.0	71.8	104.2	1.7[a]	<.00001*
		P	46	67.4	12.7	17.5	93.0			42	72.9	14.1	30.4	95.5		
	GT_RS	C	49	69.9	1.3	67.7	72.8	0.2	.2683	50	69.6	1.4	66.7	73.1	0.5	.0489*
		P	46	69.5	2.0	64.4	73.7			42	70.7	3.1	67.0	82.2		
Rotation (ROTA)	RO_Strd	C	50	3.4	0.6	1.5	5.5	1.0[b]	.00005*	50	3.5	0.7	2.0	5.5	1.0[b]	.0002*
		P	45	5.2	2.5	3.0	18.0			41	5.5	2.9	3.0	18.5		
	RO_Time	C	50	2.5	0.7	1.6	4.0	1.2[b]	.00001*	50	2.6	0.6	1.2	4.0	1.0[b]	.0002*
		P	45	4.2	2.0	2.0	13.5			41	4.9	3.4	1.8	18.2		
	RO_STT	C	50	1.2	0.5	0.1	2.3	0.9[b]	.0002*	50	1.1	0.4	0.2	2.3	0.9[b]	.0017*
		P	45	2.0	1.2	0.5	6.7			41	2.6	2.5	0.6	13.3		
	RO_Freq	C	50	1.4	0.3	0.9	2.2	0.3	.1813	50	1.4	0.3	0.9	2.9	0.7	.0073*
		P	45	1.3	0.3	0.8	2.1			41	1.2	0.3	0.7	2.2		
	RO_RS	C	50	43.7	9.4	7.3	58.8	0.1	.6220	50	42.4	9.1	19.2	58.1	0.5	.0296*
		P	45	44.7	9.1	23.6	62.8			41	47.4	10.0	24.4	76.0		
Arms swinging (GTAH)	GT_Taps	C	49	12.5	2.0	4.5	18.0	0.6	.0130*	48	12.9	1.4	10.5	17.5	0.4	.1529
		P	48	14.6	4.6	7.0	36.5			47	13.9	3.6	7.0	29.0		
	GT_Exc	C	49	70.0	26.4	10.8	122.8	1.2[b]	<.00001*	48	68.2	26.1	28.2	135.0	0.8[b]	.0003*
		P	48	40.3	21.3	6.6	109.1			47	45.5	28.6	6.3	117.3		
	GT_wf	C	49	62.9	27.8	4.1	123.6	1.0[b]	<.00001*	48	75.3	25.6	32.7	129.4	0.9[b]	.00007*
		P	48	37.3	20.9	6.2	104.9			47	49.7	29.7	4.0	115.3		
	GT_IAV	C	49	131.5	17.6	93.4	177.5	0.6	.0115*	48	138.4	15.6	103.3	170.5	0.3	.1471
		P	48	144.8	28.3	102.2	228.5			47	147.9	37.4	108.9	332.7		

Note: Statistical significance between the two groups investigated (*p* adjusted) and discriminant capacity (effect size). C: control group; P: PD patients group; Effect size: Cohen *d*.

[a]Cohen $d > 0.8$ unilaterally.

[b]Cohen $d > 0.8$ bilaterally.

*$p < .05$.

Abbreviations: PD, Parkinson's disease; SD, standard deviation.

a much larger sample. Second, information on other clinical aspects of PD (e.g., speech, facial expressions, rigidity, freezing, postural instability) was lacking, for which other tools have already been developed or are being tested.[34–41]

In conclusion, the motor measures identified in this study are very reliable as they are highly discriminating (patients with PD vs. HC) and have high test–retest ICC values. In the near future, these parameters could be used for research purposes in telemonitoring tests for patients with PD.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare relevant to the content of this article. The Azienda USL Toscana Nord Ovest and Scuola Superiore Sant'Anna filed an Italian patent concerning SensHand.

DATA AVAILABILITY STATEMENT

The paper includes tables and supplementary material where the means, standard deviation, maximum and minimum values of motor measures are reported. Other specifications of the results and/or the datasets generated during and/or analyzed during the current study are available in aggregated from the corresponding author upon reasonable request.

PEER REVIEW

The peer review history for this article is available at https://publons.com/publon/10.1111/ane.13667.

ETHICS APPROVAL

The study (acronym CASANOVA, approved by the Ethical Committee of Tuscany Region, Area Vasta Nord Ovest, Italy, n°13,055/09.10.18, notified as n°1288/2019) was conducted in accordance with the International Conference of Harmonization Guideline for Good Clinical Practice and the declaration of Helsinki.

CODE AVAILABILITY

MATLAB R2018a (The MathWorks, Inc., Natick, MA, USA).

CONSENT TO PARTICIPATE

The participants signed the informed consent to participate in the study and to publish their data anonymously.

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