Parkinsonism and Related Disorders 109 (2023) 105345

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

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

Wearable sensors for assessing disease severity and progression in Progressive Supranuclear Palsy

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ARTICLE INFO

Keywords:
Progressive supranuclear palsy
Wearable sensors
PSP rating scale
Gait

ABSTRACT

Introduction: Progressive supranuclear palsy (PSP) is an atypical parkinsonism characterized by prominent gait and postural impairment. The PSP rating scale (PSPrs) is a clinician-administered tool to evaluate disease severity and progression. More recently, digital technologies have been used to investigate gait parameters. Therefore, object of this study was to implement a protocol using wearable sensors evaluating disease severity and progression in PSP.

Methods: Patients were evaluated with the PSPrs as well as with three wearable sensors located on the feet and lumbar area. Spearman coefficient was used to assess the relationship between PSPrs and quantitative measurements. Furthermore, sensor parameters were included in a multiple linear regression model to assess their ability in predicting the PSPrs total score and sub-scores. Finally, differences between baseline and three-month follow-up were calculated for PSPrs and each quantitative variable. The significance level in all analyses was set at ≤ 0.05.

Results: Fifty-eight evaluations from thirty-five patients were analyzed. Quantitative measurements showed multiple significant correlations with the PSPrs scores (r between 0.3 and 0.7; $p < 0.05$). Linear regression models confirmed the relationships. After three months ~~visit~~, significant worsening from baseline was observed for cadence, cycle duration and PSPrs item 25, while PSPrs item 10 showed a significant improvement.

Conclusion: We propose wearable sensors can provide an objective, sensitive quantitative evaluation and immediate notification of gait changes in PSP. Our protocol can be easily introduced in outpatient and research settings as a complementary tool to clinical measures as well as an informative tool on disease severity and progression in PSP.

1. Introduction

Progressive supranuclear palsy (PSP) is an atypical parkinsonism characterized by four core clinical domains: ocular motor dysfunction, postural instability, akinesia and cognitive dysfunction [1]. Based on the differential involvement of the core domains, a number of phenotypes of the disease have been described [1]. A profound alteration of the gait pattern presents early in the course of the disease and is spanned across all phenotypes [2,3].

Currently, the gold standard to assess disease severity is the PSP rating scale (PSPrs), a clinician-administered tool specifically designed for PSP [4]. The PSPrs has been validated in large cohorts of patients and used as the primary end-point in several clinical trials aimed at testing disease-modifying treatments [5–7]. Although it has shown good sensitivity in detecting disease progression over follow-up, the PSPrs is a clinician-dependent assessment and does also have some limitations especially in the early stages of the disease [8]. Moreover, a specific training is needed to administer the PSPrs in order to reduce the

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https://doi.org/10.1016/j.parkreldis.2023.105345
Received 9 November 2022; Received in revised form 20 February 2023; Accepted 23 February 2023
Available online 24 February 2023

inter-rater variability, as for any other clinician-administered tools.

Recently, new technologies have been developed to gather objective and more sensitive measures of gait dysfunction in a variety of movement disorders [2,3,9]. Indeed, wearable sensors represent one of the most promising systems, displaying a satisfactory compromise between device complexity and the amount of acquired data [9]. Being portable and wireless and requiring a low-grade training, wearable sensors are easy to use in an outpatient setting. High quality standardized informative data on gait and stance dysfunction can be acquired in a short time [9]. However, to date, there is no standardized gait protocol using wearable sensors specifically designed to evaluate disease severity and progression in PSP.

Herein, we intend to propose a simple and informative protocol to gather objective measures of gait and balance in PSP with wearable sensors, feasible in both clinical and research settings. By applying statistical models, we aim at correlating spatio-temporal objective parameters of gait with the PSPrs total scores (PSPrs-TOT) and sub-scores to assess if wearable sensors can provide a reliable measure of disease severity and progression in PSP.

2. Methods

2.1. Patients and clinical evaluation

PSP patients were enrolled from the Center for Neurodegenerative diseases (CEMAND) of the University of Salerno, Italy, between January 2021 and May 2022 and diagnosed with the Movement Disorders Society (MDS) clinical criteria [1]. All patients qualified for either probable or possible PSP [1]. Exclusion criteria for the present study included: gait requiring bilateral assistance; dementia according to the DSM-V criteria; significant comorbidities possibly impacting on gait, including other neurologic disorders, orthopedic diseases, or cardiovascular/respiratory diseases and/or brain surgery. Patients requiring unilateral assistance for walking (as a cane or a helper holding one upper limb) were included in the present study.

A subgroup of patients underwent two evaluations, at both baseline and after three months.

PSPrs was administered to all patients by expert clinicians (FA and MFT). The scale is composed by 28 items, distributed into six domains: history, mentation, bulbar, ocular motor, limb motor, gait/midline. The total score ranges from 0 to 100, where 100 represent the worst possible outcome.

2.2. Wearable sensor procotol

All patients performed a gait and balance assessment with the APDM wearable sensors (Opal™, APDM, Portland, USA) and their parent company software (Mobility Lab™, APDM). Each sensor features two accelerometers, one gyroscope and one magnetometer recording on three axes (vertical, mediolateral, anteroposterior) with a sample rate of 20–128 Hz.

Three wearable sensors were used and placed with the provided straps as follows: one on each foot and one on the back in the lumbar area. Placement was carried out following APDM instructions [10].

The protocol included:

[1] A 2-min walking test for the evaluation of gait on a linear, 10-m-long surface with no obstacles along the way. The patients were asked to walk at their best, without resting during the registration time.

[2] A 30-s sway test to evaluate stance balance. The simplest form of this test was selected for our patients (i.e.: firm surface with open eyes and feet apart).

[3] A 360°turning test where the patients have been asked to spin around with a complete turning in place both on the right and on the left side.

Overall, the protocol required about 10 min for the complete administration (5 min for the set-up and creation of patient's profile in the sensor software and 5 min for the selected motor tasks).

Recorded measurements for each task are enlisted in Supplementary Table 1.

2.3. Statistical analysis

Spearman's correlation was performed to verify the relationship between parameters from the wearable sensors and the PSPrs-TOT and sub-scores. Correlations were deemed moderate with r between 0.3 and 0.59 and strong with $r \geq 0.6$. Upon verification of methodologic assumptions (Supplemental material), multiple linear regression models were built using the PSPrs-TOT and sub-scores as dependent variables and parameters from wearable sensors as independent variables.

The difference between baseline and a three-month follow-up for both PSPrs and wearable sensor variables was calculated using paired sample *t*-test or paired sample Wilcoxon test as needed. Subsequently, the percentage of change over time was calculated from baseline for both PSPrs and wearable sensor variables.

An additional analysis was conducted with either independent sample *t*-test or Wilcoxon to detect clinical and digital differences in clinical and digital measures between patients able to walk on their own and patients needing assistance.

The statistical analysis was conducted using the Statistical Package for Social Science (SPSS, version 25). Alpha significance level was set to $p \leq 0.05$ for all statistical analysis.

3. Results

Fifty-eight evaluations from thirty-five patients were analyzed, with twenty-three patients being tested twice. Ten patients (29%) required unilateral support to perform at least one of the wearable sensor-based tasks. Demographic and clinical data are shown in Table 1 and 2.

Spearman's correlation showed a significant relationship between a variety of quantitative parameters from wearable sensors and the PSPrs-TOT and sub-scores. The heatmap in Fig. 1 shows the direction as well as the level of each correlation. Fig. 2 shows a graphic representation of a few significant correlations.

As for PSPrs-TOT, moderate inverse correlations were notably found with gait speed ($r = -0.434$; $p < 0.001$), and with stride length, swing and turning velocity, 360° angle and 360° turning velocity and moderate direct correlations with gait double support, stance and turning duration.

As for PSPrs sub-scores, gait/midline subscore presented a strong inverse correlation with gait turning velocity, moderate inverse correlations with gait speed, stride length, swing, 360° angle, 360° duration and 360° turning velocity and moderate direct correlations with gait

Table 1
Demographic and clinical data of the enrolled cohort.

	PSP patients (N = 35)
Age	68.14 ± 5.45 (59–79)
Gender (men/women), n (%)	27/8 (77/23)
Age at onset	64.49 ± 5.81 (56–76)
Disease duration	4.23 ± 2.53 (1–14)
Phenotype (PSP-RS/P/PGF), n (%)	28/5/2 (80/14/6)
PSPrs-TOT	42.47 ± 9.18 (25–69)
Hoehn and Yahr	3 ± 0.39 (2–4)
Patients requiring assistance	10 (29%)

Values are shown in median ± standard deviation (range).
PSP: progressive supranuclear palsy.
PSPrs-TOT: PSP rating scale total score.
PSP-RS: PSP with Richardson's syndrome.
PSP-P: PSP with Predominant Parkinsonism.
PSP-PGF: PSP with progressive gait freezing.

double support time and stance. The limb sub-score disclosed a strong inverse correlation with gait turning velocity, a moderate inverse correlation with 360°angle and 360° turning velocity and a moderate direct correlation with gait turning duration and sway mean velocity. The ocular motor sub-score presented a moderate inverse correlation with gait cadence and moderate direct correlations with gait cycle duration, forward APA peak and sway mean velocity. The mentation sub-score disclosed a moderate inverse correlation with first step duration. Finally, the history sub-score showed moderate inverse correlations with gait stride length and turning velocity and 360° angle (Fig. 1).

Table 2 shows the regression coefficients and statistical significance obtained for each linear regression model. For each sub-score of the PSPrs the R^2 score was greater than 0.70. In particular, for the bulbar, ocular motor, limb sub-scores and PSPrs-TOT the R^2 reached values greater than 0.9 indicating an excellent fitting between the model and the data. Moreover, each PSPrs sub-score was easily predicted by no more than three independent variables extracted from our protocol. It is worth noting that 9 out of 15 variables included in the models came out from the gait task while only 3 were extracted from the 360° turning test and the sway. In detail, the PSPrs-TOT was best predicted by gait turning velocity and stance ($R^2 = 0.976$; $p = 0.002$ and $p < 0.001$ respectively).

As for the PSPrs sub-scores, the history sub-score was predicted by first step duration and 360° turning test angle; the mentation sub-score was predicted by sway centroidal frequency and 360° turning test duration; the bulbar sub-score was predicted by first step and turning duration; the ocular motor sub-score was predicted by a combination of gait cadence, forward APA peak and sway mean velocity; the limb sub-score was predicted by gait turning duration and sway mean velocity; gait/midline sub-score was predicted by gait speed and 360° turning test angle ($R^2 = 0.791$; $p < 0.001$ and $p = 0.049$ respectively).

Supplementary Table 2 shows the differences between data acquired at baseline and after three months for the subgroup of 23 patients. Among wearable sensor measurements, only cadence and cycle duration from the 2-min walking test presented a significant increase over time (by 3.69% and 3.94% respectively). As for the PSPrs, the total score did not show a significant change over the follow-up (0.78% increase), but significant differences were detected for the "emotional lability" item (36.54% decrease) and the "arising from chair" item (16.31% increase).

Supplementary Table 3 shows differences in PSPrs and wearable sensor variables between patients still able to walk on their own and patients needing assistance. As expected, patients needing assistance during walking performed worse in several PSPrs items as well as digital measures.

4. Discussion

Herein, we propose a simple, feasible and informative protocol to gather quantitative measures of gait and balance from wearable sensors in PSP. Several parameters extracted from our protocol showed a significant correlation with the PSPrs-TOT and sub-scores suggesting

Wearable sensor parameters	History	Mentation	Bulbar	Ocular Motor	Limb	Gait/ midline	PSPrs-TOT
Two-minute walking test							
Cadence (mean)	0,099	-0,038	-0,239	**-0,398****	-0,265	-0,232	-0,287
Speed (mean)	-0,279	-0,070	-0,066	-0,177	-0,321	**-0,446****	**-0,434****
Double support (mean)	0,214	-0,036	0,034	0,054	0,269	**0,395****	**0,306***
Stance (mean)	0,210	-0,041	0,053	0,045	0,265	**0,408****	**0,306***
Stride length (mean)	**-0,356***	-0,010	-0,055	-0,06	-0,266	**-0,45**	**-0,401**
Cycle duration (mean)	-0,092	0,016	0,243	**0,410****	0,281	0,247	0,296
Swing (mean)	-0,212	0,041	-0,054	-0,045	-0,268	**-0,412****	**-0,309***
Turning duration	0,308	0,149	0,278	0,126	**0,401****	0,241	**0,411****
Turning velocity	**-0,443****	-0,015	-0,271	-0,057	**-0,604****	**-0,637****	**-0,579****
Steps in turn	0,082	-0,040	-0,003	0,023	-0,038	-0,080	-0,012
APA duration	-0,114	0,007	0,173	0,235	0,159	-0,034	0,044
First step duration	-0,233	**-0,413***	0,258	0,392	0,094	0,006	-0,076
Forward APA peak	-0,079	-0,103	0,170	**0,519****	0,342	0,312	0,282
Lateral APA peak	-0,336	-0,047	-0,184	0,103	-0,103	0,113	-0,136
Sway							
Sway area	0,004	0,096	-0,051	0,097	0,096	0,014	0,104
SMS sway	0,051	0,051	-0,131	0,149	0,070	0,035	0,118
RMS sway coronal	-0,118	0,097	0,026	0,085	0,052	-0,049	0,020
RMS sway sagittal	0,07	0,039	-0,136	0,152	0,070	0,075	0,135
Centroidal frequency	-0,033	0,262	0,105	0,145	0,041	-0,051	0,095
Frequency dispersion	-0,259	-0,132	0,12	0,261	0,129	-0,111	-0,022
Jerk	0,089	0,124	-0,116	0,151	0,159	0,171	0,186
Jerk coronal	-0,013	0,142	-0,015	0,251	0,154	0,092	0,133
Jerk sagittal	0,089	0,12	-0,145	0,139	0,159	0,161	0,177
Mean velocity	0,040	-0,069	0,039	**0,375***	**0,312***	0,287	0,264
Mean velocity coronal	-0,086	0,147	0,070	0,279	**0,309***	0,158	0,189
Mean velocity sagittal	0,045	-0,147	0,055	**0,337***	**0,332***	0,291	0,255
360° turning test							
Angle	**-0,408****	0,165	-0,150	0,082	**-0,386***	**-0,518***	**-0,407***
Duration	-0,257	0,304	-0,166	0,138	-0,226	**-0,338***	-0,182
Turning velocity	-0,312	0,181	-0,210	-0,001	**-0,365***	**-0,482***	**-0,369***

Label
Direct correlation
Not correlated
Inverse correlation

Fig. 1. Title: Heatmap showing direction and degree of correlations between wearable sensors parameters and the PSP rating scale total score and sub-scores.
Fig. 1 legend: The degree of correlations is highlighted by the color tones, with lighter shades indicating weaker correlations and darker shades indicating stronger correlations.
Significant results are highlighted in bold.
**Significance level at 0.01.
*Significance level at 0.05.
APA: anticipatory postural adjustment.
RMS: root mean square.
PSPrs-TOT: Progressive Supranuclear Palsy rating scale total score.

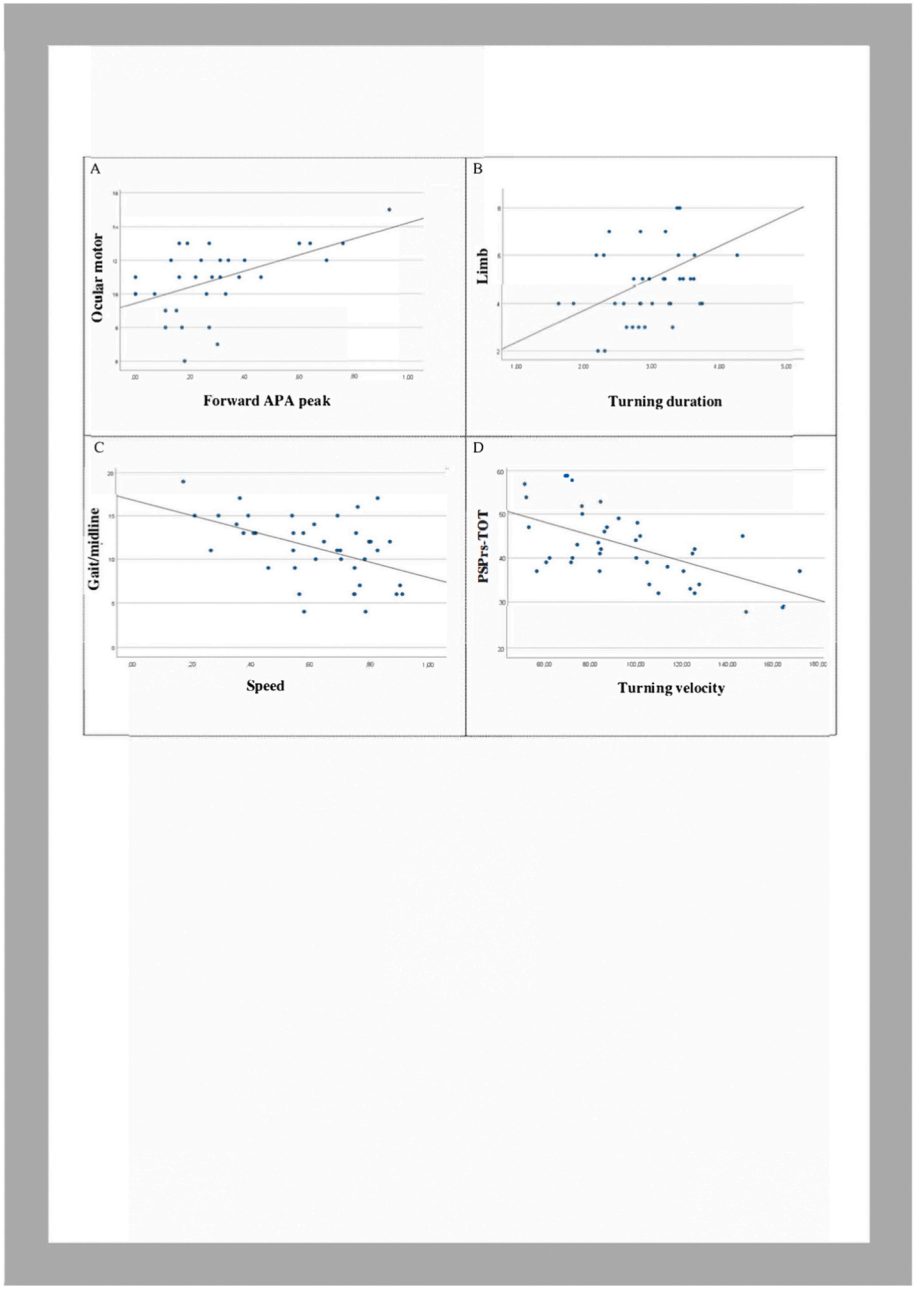

Fig. 2. Title: Spearman's Correlation analysis. Fig. 2 caption: A) Ocular Motor with APA forward peak, B) Limb with turn duration, C) Gait/midline with gait speed, D) PSP tot with turn velocity.
APA: anticipatory postural adjustment.
PSPrs-TOT: progressive supranuclear palsy rating scale total score.

wearable sensors could be a marker of disease severity in PSP.

In detail, the PSPrs-TOT showed several correlations with objective parameters from both the walking and the 360° turning tests, while no relationship was detected with any parameter from the sway test. Multiple linear regression analysis e the PSPrs-TOT is strongly associated with walking parameters.

In community-dwelling older adults, gait parameters have been linked with both global cognitive function and impairment in specific cognitive domain [11]. In movement disorders as Parkinson's disease and in different types of dementia, gait impairment has been associated with worst quality of life, increasing mortality and morbidity [12,13]. These findings suggest objective gait parameters may represent valid proxy of disease severity and reflect measures of activities of daily living (ADL) [14]. In PSP, gait and balance impairment represent cardinal features of the disease since the earliest stages. Moreover, both greater gait impairment at clinical evaluation and higher PSPrs-TOT have been associated with shorter survival [5]. In line with such evidence, our data would suggest objective gait parameters captured with wearable sensors could represent valid markers of disease severity in PSP.

A variety of objective gait and balance parameters correlated with specific PSPrs sub-scores. Unsurprisingly, the gait/midline sub-score presented the most robust correlations with several parameters from the walking and turning tests. The relationship with gait speed is of particular interest given that it is easily acquired. Moreover, being aware of the informative weight of such a simple parameter could be riveting for the clinician. The PSPrs gait/midline sub-score includes scoring of axial impairment which represents a core features of PSP and has also been linked to poorer quality of life [15]. Therefore, such data further reinforce the relationship between objective measures extracted from wearable sensors and severity of disease in PSP.

As for other PSPrs sub-scores, the limb sub-score includes scoring of rigidity, dystonia, bradykinesia and apraxia. Thus, it is not surprising that patients with greater severity of such features take longer to turn during walking and 360°turning test. Complementary, a reduced

Table 2
Multiple Linear Regression analysis.

Sub-scores	Variables	R^2	β	p-value
History	First step duration (G)	0.748	0.511	**0.005**
	Angle (T)		0.395	**0.025**
Mentation	Duration (T)	0.789	0.437	**0.018**
	Centroidal frequency (S)		0.474	**0.011**
Bulbar	First step duration (G)	0.913	0.27	**0.033**
	Turning duration (G)		0.706	< **0.001**
Ocular Motor	Cadence (G)	0.964	0.677	< **0.001**
	Forward APA peak (G)		0.173	**0.027**
	Mean velocity (S)		0.183	**0.003**
Limb	Turning duration (G)	0.915	0.788	< **0.001**
	Mean velocity (S)		0.188	0.056
Gait/midline	Speed (G)	0.791	1.241	< **0.001**
	Angle (T)		−0.396	**0.049**
PSPrs-TOT	Turning velocity (G)	0.976	−0.252	**0.002**
	Stance (G)		1.222	< **0.001**

Significant results are highlighted in bold, R^2 coefficient of determination, β coefficient of equation.
PSPrs-TOT: progressive supranuclear palsy rating scale total score; APA: anticipatory postural adjustment; G: 2-min walking test for gait evaluation; S: sway; T: 360° turning test.

turning velocity associated with a greater limb burden may reflect the presence of freezing of gait, another cardinal feature of PSP [1]. However, since the PSPrs lacks of a specific item on freezing of gait, such consideration remains speculative.

As for the PSPrs ocular motor sub-score, our results support the hypothesis that ocular and gait impairments in PSP may have a common pathophysiology, being both linked to midbrain atrophy and dysfunction [16,17]. Of note, the saccadic slowing and limited oculomotor range may independently contribute to worse gait and balance performances.

A few other correlations were shown between the PSPrs history and mentation sub-scores and sensor measurements. Indeed, it is widely recognized that cognitive and functional status, risk of falls and insomnia (all aspects evaluated with such sub-scores) may be related to gait parameters in the general population and particularly in PSP patients [2,13,18].

Surprisingly, no significant relationship was found between the PSPrs bulbar sub-score and wearable sensor parameters. However, the PSPrs bulbar sub-score includes two items only evaluating dysarthria and dysphagia, which can present different degree of severity irrespective of motor impairment in PSP. Dysarthria and speech disorders can be a prominent manifestation of early PSP, not necessarily accompanied by early balance and gait impairment [1].

Overall, the protocol designed for the present study is easy to be applied and does not require any specific training or certification. Our data demonstrates that three sensors only (two on the feet and one on the lumbar area) can provide informative data on disease severity in PSP avoiding more expensive and time-consuming sensor combinations. This is in line with previous studies using sets of six inertial sensors in Parkinson's disease, with the most significant variables extracted from those on both feet and lumbar area [20,21]. The remaining inertial sensors are usually located on the upper extremities assessing arm swing. Since it is known that in PSP the axial impairment outweighs the appendicular one [1], it is not surprising that our protocol is able to evaluate disease severity in PSP with only three sensors compared to a previous study using six sensors [22]. Moreover, the use of only three sensors located on lower limbs enabled us to include patients in need of unilateral assistance for walking. In fact, a walking aid would have compromised the arm parameters but may have a marginal impact on measurements extracted from back and feet sensors. In this regard, when comparing patients still able to walk on their own with patients needing assistance, the two groups only differed in PSPrs motor-related items (i.e. falls, tapping, gait), and walking and turning tasks from the wearable sensor protocol, but not in the PSPrs postural stability item and in sway-derived parameters. Such findings prompt us to hypothesize that the two populations mostly diverge on dynamic rather than static parameters in both clinician-related and digital measures. However, this observation needs to be verified in larger samples and with more sophisticated analyses.

As for the evaluation of disease progression over the three-month follow-up, cadence and cycle duration from the walking test showed a significant deterioration over time. As for the PSPrs, the item 25 (i.e. arising from chair) presented a significant worsening ($p = 0.039$), while the item 10 (i.e. emotional lability) showed a significant improvement ($p = 0.046$). Arising from chair is a motor task likely related to the axial motor impairment. Future studies should add such motor task within the wearable sensor motor protocol and confirm its sensitivity to detect disease progression. However, based on our preliminary findings, we could hypothesize that over short-term follow-ups digital measures are more sensitive than PSPrs to detect gait deterioration in PSP patients. As for the item 10 (i.e. emotional lability) different factors can account for its improvement. First, correcting for multiple comparison would have abolished the significance of such finding. Then, item 10 score is strongly dependent on both patient's status at the time of the visit and caregiver's report and may not merely represent severity of the disease (also due to the Hawthorne effect) [4]. Finally, we cannot exclude that emotional incontinence may get reduced with progression of the disease and/or modified by pharmacological treatment [23].

Similarly to a recent study [22], we failed to show any correlation between the sway test and the PSPrs-TOT. Since the majority of correlations involved dynamic gait parameters (ie, stance, double support time), we hypothesize dynamic instability contribution to the PSPrs outweighs static instability contribution in the early phase of the disease. Notwithstanding, the implementation of a wearable sensor protocol for the evaluation of balance may increase clinician awareness on this core aspect of the disease which is seldom explored by movement disorder specialists with specific clinician-administered scales (ie, Performance-Oriented Mobility Assessment [24], Berg Balance Scale [25]).

Implementing the use of wearable sensors in PSP is of great importance. Indeed, clinicians may acquire a detailed and objective evaluation of gait and stance by gathering data and information on a variety of parameters. Such approach has been demonstrated to be useful in hospital-based gait labs using motion analysis instruments, as the optoelectronic systems and force platforms, considered the gold standard for capturing gait characteristics. As a matter of fact, wearable sensors can provide similar data as hospital-based gait analysis labs but without their costs and specific, expensive settings. Additionally, they present a lower complexity of both the experimental setup and the data processing procedures. They also provide a high level of portability [26], suitable for remote-monitoring of patients' daily activities in their environment. As such, different wearable sensors are being tested in a variety of neurodegenerative diseases [27].

The protocol proposed in the present study is suitable for research settings, to monitor both disease severity and progression and to assess the efficacy of potential disease-modifying treatments. In fact, the application of the present protocol is time-effective. In about 10 min objective wearable sensor parameters can be obtained using the output section of the sensor software. Data can be arranged in either a report showing deviation from normal values or downloaded as they are. The report is reader-friendly and in case of multiple assessments the percentage of change in respect to baseline is shown. After a reasonable practice, administration of such protocol requires the same amount of time as the administration of the PSPrs (which requires a training as well). As for all other assessments, patients with cognitive decline may need more time and support to complete the protocol. Applicability of such protocol in demented patients needs to be verified as a diagnosis of dementia was considered an exclusion criterion for the present study.

Another possible use is for telehealth consultancies, especially for

patients who can't access the clinic at all follow-up visits. All these potential applications of wearable sensor technology make of utmost importance the implementation and standardization of protocols in different disease populations and settings, particularly when it comes to rare diseases such as PSP. In fact, we also intend this study to be a starter point for the validation of standardized protocol in home-monitoring, in order to evaluate patients all day long, accounting for the complex variability of their symptoms.

Compared to a recent study by Sotirakis et al. [22], we evaluated a larger cohort of PSP patients (35 versus 17) with three sensors only on the lumbar region and both feet. Furthermore, we performed a systematic evaluation of the relationship between wearable sensor variables and the PSPrs-TOT and subscores in order to obtain a validation of our protocol in comparison with the actual gold standard in terms of clinical evaluation of the disease. We foresee that, as for other neurodegenerative diseases, technology-based data will be increasingly used in the future as a reliable outcome in clinical trials testing disease-modifying drugs. In this perspective, a solid body of evidence is of utmost importance. Thus, both these studies could be the first contributors to the literature on wearable sensors in the PSP population.

We recognize that this study has some limitations. First of all, our wearable sensor protocol was only applied to patients still able to walk, thus excluding a large part of PSP patients with severe gait and balance impairment. However, advanced PSP patients represent a major challenge for the application of any research protocol including the present one. The sample size is small; nonetheless, this is an exploratory study regarding a rare disease in which the number of enrolled patients is still greater than other similar studies. Also, although the proposed protocol is easy to apply, it still needs an appropriate setting to register standardized data (i.e. a long, linear surface) and to make the patients feel comfortable and confident in performing the requested tasks. Regarding testing for repeatability, for the present research we relied on previous published data [28] but we are aware future studies should check for test-retest validity also in PSP population. Finally, we acknowledge the lack of correction for multiple comparisons in our analysis may have increased the number of significant correlations between wearable sensor variables and clinical scores. However, our study was exploratory in nature and our results need to be confirmed. More studies and longer follow-ups are needed to strengthen the validity of our wearable protocol in PSP patients and further expand on clinical significance of sensor parameters that have revealed most sensitive to change.

5. Conclusions

In spite of the wide availability of modern digital technology and the growing amount of literature being collected, digital measures are far to be considered endpoints in clinical trials neither in movement disorders or dementia. However, there is a strong need to fasten clinical research and therapeutic development for patients affected by neurodegenerative diseases. Delay in the implementation of digital measures in clinical trials is due to several barriers including limited attention to aligning with patient-centered outcomes and lack of data standards and harmonization [29]. Herein, we propose a standardized protocol to evaluate gait and balance in PSP with digital sensors proven to correlate with the PSPrs-TOT and sub-scores, the current gold standard for the evaluation of disease severity. The strongest relationships were found among PSPrs scores and gait parameters, as measured with only three wearable sensors. Furthermore, we demonstrated the change of objective gait parameters over a short-term follow-up. Another advantage of our protocol is that it can be used with patients in need of unilateral support. Thus, we suggest our wearable sensor protocol may be complementary to other clinical measures for an objective evaluation of disease severity and progression in early and middle stages PSP in both clinical and research settings.

Ethical compliance statement

The study has received ethical approval and has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki (Code of Ethics of the World Medical Association) and its later amendments. The patient signed written informed consent. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

Funding sources

This work was supported by the University of Salerno FARB2019.

The funding source had no involvement in research conduction, preparation of the article, study design and collection, analysis and interpretation of data.

Authors' roles

F.A.: Research project: Execution, Data analysis: interpretation of results, Manuscript Preparation: Writing the first draft, Review and Critique; M.R.: Data analysis: statistical analysis, interpretation of results, Manuscript Preparation: Review and Critique; C.R.: Data analysis: statistical analysis, interpretation of results, Manuscript Preparation: Review and Critique; M.F.T.: Research project: Execution, Manuscript Preparation: Review and Critique; M.R.: Manuscript Preparation: Review and Critique; R.E.: Manuscript Preparation: Review and Critique: Manuscript Preparation: Review and Critique; M.A.: Manuscript Preparation: Review and Critique; M.T.P.: Manuscript Preparation: Review and Critique; P.B.: Manuscript Preparation: Review and Critique; M.P.: Research project: Conception, Organization, Execution, Data analysis: interpretation of results, Manuscript Preparation: Review and Critique.

Financial disclosures for the previous 12 months

Disclosures from the past year: Dr Marina Picillo is supported by the Michael J Fox Foundation for Parkinson's research; Prof Paolo Barone received consultancies as a member of the advisory board for Zambon, Lundbeck, UCB, Chiesi, Abbvie and Acorda; the other authors report no financial diclosures.

Declarations of competing interest

None.

Acknowledgments

We thank all patients who took part in this study.

Appendix ASupplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.parkreldis.2023.105345.

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