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Smartwatch for the analysis of rest tremor in patients with Parkinson's disease

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ABSTRACT

Wearable technology used in Parkinson's disease (PD) research has become an increasing focus of interest in this field. Our group assessed the feasibility, clinical correlation, reliability, and acceptance of smartwatches in order to quantify arm resting tremors in PD patients. An Android application on a smartwatch was used to obtain raw data from the smartwatch's gyroscopes. Twenty-two PD patients were consecutively recruited and followed for 1 year. Arm rest tremors were video filmed and scored by two independent raters using the motor subscale of the Unified Parkinson's Disease Rating Scale (UPDRS-III). The tremor intensity parameter was defined by the root mean square of the angular speed measured by the smartwatch at the wrist. Sixty-four smartwatch evaluations were completed. The Spearman coefficient among the mean of the resting tremor (UPDRS-III) scores and smartwatch measurements for tremor intensity was 0.81 ($p < .001$); smartwatch reliability to quantify tremors was checked by intraclass reliability coefficient with a resting tremor = 0.89, minimum detectable change = 59.03%. Good acceptance of the system was shown. Smartwatch use for PD tremor analysis is possible, reliable, well-correlated with clinical scores, and well-accepted by patients for clinical follow-up. The results from these experiments suggest that this commodity hardware has the potential to quantify PD patients' tremors objectively in a consulting-room.

1. Introduction

Parkinson's Disease (PD) is one of the most frequent movement disorders, and its presence is expected to increase in upcoming decades. Rest tremor, bradykinesia, and rigidity are the main motor symptoms in these patients [1]. Interval scales for tremor rating are valid clinical tools for the tremor examination [2,3]. Nevertheless, these tools are not exempt from bias. Consequently, the need for a system that measures this motor symptom in an objective, easy, and continuous way in PD patients is of great interest for movement disorders specialists [4–6].

New methods and technologies for the assessment of tremors and other motor symptoms in PD continue to be subject of intense research [7], but there is no clear consensus about the best technological solutions for this issue. Objective tremor quantification can be performed by analyzing data obtained from accelerometers or gyroscopes through different computational methods [8–12]. Some health industrial designs of wearable devices (such Kinesia TM, Perform system, Kinetigraph) integrate these kind of inertial sensors and can measure diverse

Abbreviations: PD, Parkinson's Disease; SW3, Smartwatch3; UPDRS, Unified Parkinson's Disease Rating Scale; ICC, Intraclass Correlation Coefficient; MDC, Minimum detectable change; CR, Coefficient of repeatability; SEM, Standard error of measurement; tLogICC, Intraclass Correlation Coefficient with log10 transformed data; tLogMDC, Minimum detectable change with log10 transformed data; tLogMDC%, tLogMDC percentage; tLogSEM, Standard error of measurement with log10 transformed data.

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motor signs in movement disorder patients [6,13,14]. Non-health related commercial devices such as the smartphone have been used to detect motor impairment in PD through analysis of keystroke dynamics during typing on smartphone touchscreens and keyboards [15–17]. There are some studies in which combinations of wrist sensors with smartphones to follow up on the cardinal signs of PD and other types of tremors are being tried [18,19]. Smartphone applications also have shown objective assessments in PD [20,21], but only a few studies have analyzed test-retest reliability of smart device tremor measures [21,22].

The goal of this study was to assess whether resting tremors in PD could be quantified by customizing non-health related commercial smartwatches in order to develop an instrument to objectively follow PD patients' rest tremors. Furthermore, the acceptance of the system was checked.

2. Material and methods

The Ethical Standards Committee on human experimentation at the Hospital Universitario “12 de Octubre” (Madrid) authorized all experiments. Signed informed consent was received from all participants.

2.1. Subjects

Twenty-two PD patients were consecutively enrolled from the Hospital Universitario “12 de Octubre” in Madrid (Spain) and followed for 1 year. None of the recruited patients had histories of head injuries, epilepsy, strokes, brain stimulators, or pacemakers. A total of four patients withdrew from the study before the last visit due to unrelated issues such as medical problems.

The mean age of the PD patients was 72 ± 7.6 years. Twenty-one patients (95%) were taking medication for their disease (dopamine agonist or levo-dopa). The main clinical features of the PD patients are shown in Table 1.

2.2. Instruments

The smartwatch system consists of a Smartwatch3 (SW3) Sony© worn at the wrist, wirelessly connected through a Bluetooth protocol with an Android Smartphone ASUS© inside of a belt-pouch (Kalenji®) placed at the waist [22]. A research smartphone Android Wear OS application designed by NetMD's consortium was designed to register raw data obtained from smartwatch's inertial sensors at a sampling frequency of 50 Hz. The smartphone saved a timestamp and the data of three dimensions from the gyroscopes. Fig. 1A depicts the smartwatch placement while the registry of the resting tremor graphically appears on the registry of inertial measurements when a tremor is present.

2.3. Approach

At baseline, a neurologist with expertise in movement disorders performed a detailed clinical history and neurological exam and applied the Unified Parkinson's Disease Rating Scale (UPDRS-III) to assign a total motor score (range = 0–68) [2]. PD diagnosis was assigned using the probable criteria for Parkinson's Disease by the Movement Disorder Society [1].

At recruitment, every enrolled PD patient was examined, and the resting tremors were video-filmed while a patient was sitting on a chair wearing the smartwatch system. They were re-evaluated in the next clinical visit after 3 to 6 months with the same tasks; 10 patients wore one smartwatch at one wrist, 12 patients kept a total of two smartwatches (one at each wrist), and four repeated the visit wearing two smartwatches. The PD patients kept on taking medication for their disease during the tests.

One neurologist examined the videos of each PD patient and scored the items related to arm rest tremor according to the UPDRS-III [2]. In addition, the videos were evaluated by a second trained, blinded rater in consonance with the same criteria. The mean of the scores was determined and used as the gold standard for the clinical tremor rating. In this way, the reliability of the clinical score is increased.

All of the patients were asked to answer a questionnaire, which was adapted from previous studies [13] in order to check the acceptance of the smartwatch system.

At last, in order to check the reliability of the system, 1 year after recruitment, new assessments were performed. Eighteen patients were reassessed with the same tasks twice consecutively, under similar conditions wearing one smartwatch at one wrist. Length of each task took 1 min approximately. Hence, test and retest were carried out consecutively in one examination protocol and patients kept wearing the watch during the repeated measurements.

Table 1
Demographic and clinical data of patients with PD (N = 22).

Age	
Mean ± SD	72.0 ± 7.6
Median [range]	71 [54–84]
Gender	
Female	9 (40.9%)
Male	13 (59.1%)
Disease duration (years)	
Mean ± SD	7.2 ± 7.3
Clinical scores at recruitment	
UPDRS III	19 ± 8.7
Hoehn & Yahr	1.9 ± 0.5
*Arm Rest tremor	0.95 +/− 0.98
*Clinical Score relative to limb wears the smartwatch	

2.4. Tremor analysis

Tremor quantification was performed through smartwatch gyroscope data analysis [9]. The gyroscope data (txt files) were processed on a 2.83 GHz Inter Core 2 Quad Q9500 machine operating Windows 7 Professional 32-bit. Segments of the three-dimensional gyroscope signals corresponding to the rest tremor clinical task were post-processed off-line using Matlab software (version 7.11.0 (R2010b); MathWorks, Natick, MA) off-line. A typical PD resting tremor consists of rhythmic movements at a frequency range of 4 to 6 Hz [23], but higher or lower frequencies have been described. To demonstrate the presence of a tremor, the angular speed of the three axes was analyzed separately. The inertial data were band-pass filtered using a 10th order Butterworth high-pass filter ($f_1 > 4$ Hz) and then by a 10th order Butterworth low-pass filter ($f_2 < 8$ Hz). The first filter withdrew the voluntary activities (< 3 Hz), and the last filter subtracted other high frequency tremors such as enhanced physiological tremor or orthostatic tremor (> 8 Hz) [22]. The tremor intensity was computed from the root mean square (RMS) of a 1-s moving window of the gyroscope signals. The chosen window size optimized the relationship among time resolution and accuracy. The parameter, “Mean intensity, *MI* (°/s)”, was the average value of the RMS in the three axes and determined the tremor intensity. The principal frequency of the tremor, *FT* (Hz), was calculated through the SPECTROGRAM function in Matlab with a window size of 1 s and a 90% of overlap.

2.5. Statistical analyses

The free software Version 1.0.136 – © 2009–2016 RStudio, Inc. was used. Corrupted videos or smartwatch data files were excluded, and only complete and valid assessments were computed. We obtained the weighted Cohen's kappa coefficients among raters for resting tremor scores. The mean of the clinical scores and tremor intensity results were analyzed using Shapiro-Wilk test of normality. Correlations between measures and scores were calculated using Spearman's rank correlation coefficient.

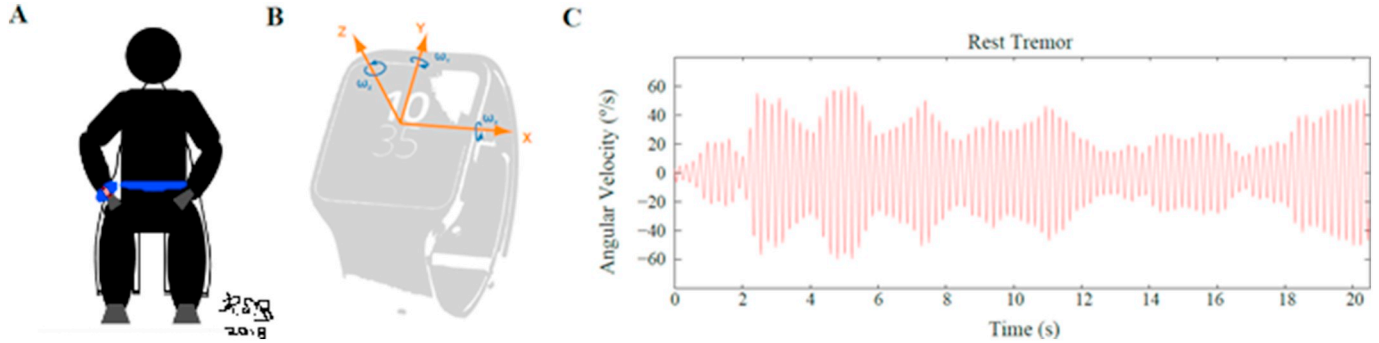

Fig. 1. A. Placement of the smartwatch at the wrist, smartphone in a belt-pouch; B. System of reference of the gyroscopes; C. Angular velocity (ω_x) measured during rest tremor while sitting on a chair.

The reliability of the smartwatch system was evaluated after examining additional registries of patients who concluded the one-year follow-up and re-tested the same task repeatedly twice during the same examination. This data was analyzed using Bland-Altman plots and determined intra-class correlation coefficients (ICC), minimum detectable change (MDC), standard error of measurement (SEM), and mean differences (bias) [24,25] with and without log10 transformation to normalize data. MDC was computed as follows = 2.77 * SEM; SEM: Standard error of measurement was calculated, SEM = standard deviation of patient population x (square root of (1-ICC)); Bias: Mean of differences [24,26]. Log10 transformed analyses included tLogICC Intraclass Correlation Coefficient, tLogMDC = 2.77 * tLogSEM, tLogMDC% = MDC of the log10 transformed data was expressed as a percentage of the baseline geometric mean, using the eq. [1-(10^(-MDC))]*100, tLogSEM = standard deviation of patient population of transformed data x (square root of (1-tLogICC)), tLogBias = Mean of differences of log10 transformed smartwatch data [25]. An estimation to clinical rating scale MDC% was performed from rating regression analysis following the Weber-Fechner law and the eq. [1-(10^(-MDC))]*100.

An outlier removal process was performed initially in a first step for calculation repeatability parameters when the value was higher than 3 standard deviation from the mean difference [27] and clinical change between ratings in UPDRS-III ≥1. By using the method, only one outlier was found and removed.

3. Results

Twenty-two PD patients were consecutively enrolled and requested to be followed up for 1 year. Sixty valid recordings for each task of a total of 64 assessments were obtained. Four corrupted videos or failed smartwatch data files were removed from the analysis. Afterwards, 18 patients completed a repeated assessment twice under similar conditions, yielding 36 additional tremor registries in order to check reliability.

The results of the measures are illustrated in Fig. 2. Spearman's correlation coefficients (ρ) between smartwatch measures and mean of clinical UPDRS-III scores for resting tremor intensity was 0.81 ($p < .001$). Also, Spearman's correlation coefficients for each rater were analyzed separately ρ1 = 0.84 ($p < .001$), ρ2 = 0.73 ($p < .001$) (Fig. 2). The test-retest reliability parameters are summarized in Table 2. Intraclass Correlation Coefficient with log10 transformed smartwatch data (tLogICC) was 0.89 ($p < .001$) and tLogMDC% was 59.03%. The clinical rating scale estimation of MDC% was 68%. The analyses were illustrated in Bland-Altman and box plots of successive measures as shown in Fig. 3. Global acceptance of the device was shown through the questionnaire. The average of satisfaction level was 8.3 over 10 (Table 3).

4. Discussion

The aims of this study were to check the feasibility and reliability of using a system based on smartwatches in order to register rest tremor in PD patients and to evaluate its clinical correlation as a monitoring tool of PD patients in a consulting-room over time. In addition to this, we were interested in exploring its level of acceptance.

Our findings showed that a Parkinsonian-related resting tremor was quantified satisfactorily using customized commodity hardware, showed a strong correlation with resting tremor score of UPDRS-III, and followed the Weber-Fechner law of psychophysics. Furthermore, the test-retest reliability of this system was good to excellent, and patients showed good acceptation of wearing a smartwatch to quantify their motor symptoms. Hence, this study put emphasis on the feasibility and reliability of adapting Android wearables as tremor transducers in a specialized clinical setting in order to quantify tremor intensity in an objective way. These results are in line with our previous work concerning smartwatch tremor analysis in essential tremor patients [22].

Previous assessments of tremor and motor function in PD (such as rigidity, bradykinesia) were tried with commercial systems such as the KinesiaTM [13,28] or the Wiimote® [29]. However, to the best of our knowledge, this is the first study with a customized smartwatch that permits the quantification of resting tremors in PD patients showing excellent test-retest reliability in a clinical setting. Along the same lines as our work, the research smartphone app tried by Lipsmeier et al. demonstrated moderate to excellent test-retest reliability in a phase 1 clinical trial [21]. Besides, this reliability expressed by ICC is similar to the rest tremor item of UPDRS-III subscale [30]. Reliability is crucial for any device aimed at monitoring tremors in a consulting room or even in daily life activities, but also the magnitude and measurement units of the MDC in tremor intensity that are able to reveal. Hence, the smartwatch MDC% for analyzing rest tremor was about 59% versus 68% of clinical rating scale MDC%. This percentage of change in smartwatch corresponds to 4 to 5° per second of angular speed which suggests that is difficult to perceive by human sight. This way we consider the effort of using smartwatches as transducers for tremor measuring is worth in order to gain objectivity in clinical assessment, with the potential to export wireless tremor intensity data along time to get clinical relevant information.

The customization of smart devices through research applications in order to register motion data from its integrated inertial measurement units permits clinicians and researchers to obtain relevant information about tremors and other movement disorders without the trade obstacles of a specific device. Hence, its ubiquity and versatility are the strongest points of using these devices in health research, and they can be adapted to open-source or open-hardware platforms. In this way, all of these technological advances applied to movement disorders field are opening new horizons in PD management [31].

Our study faced several limitations. First, the location of

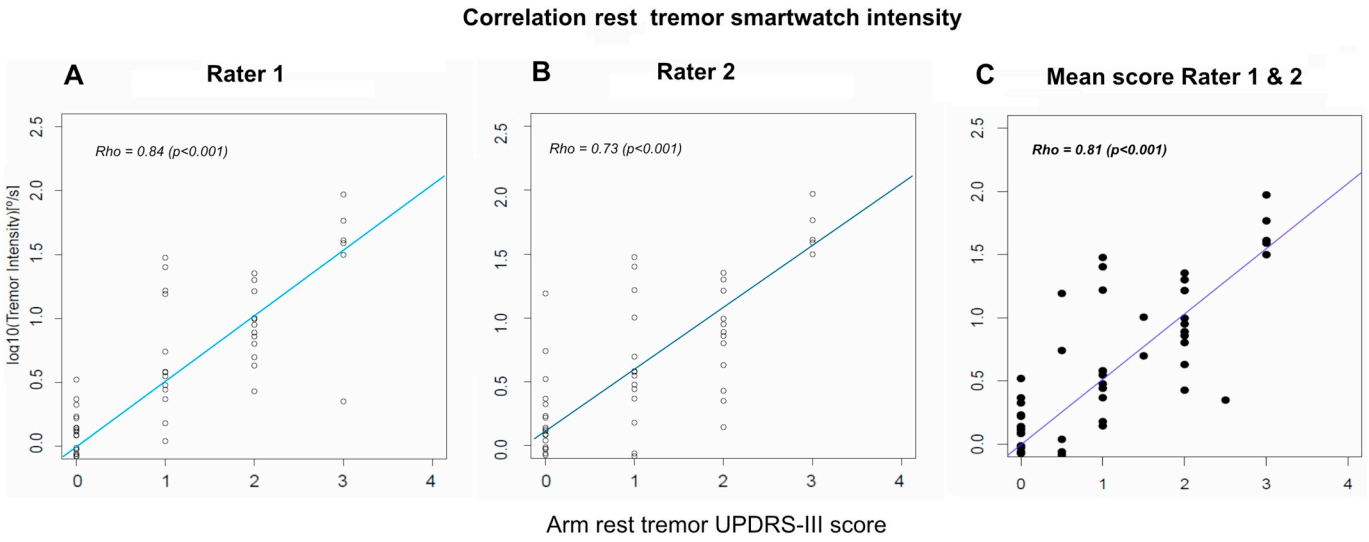

Fig. 2. The root mean square (RMS) of angular velocity [°/s] in a logarithm scale is shown to illustrate tremor intensity correlation with rest tremor item of UPDRSIII scale in: A. Rater 1, B. Rater 2, C. The mean score between raters. Tremor intensity follows the Weber-Fechner law of psychophysics which compare the log of gyroscopic data to the UPDRS-III (Giuffrida et al., 2009).

Table 2
Summary of clinical correlation and test-retest reliability parameters of smartwatch tremor measures.

Coefficient/Parameters for rest tremor		Statistical Test
Kappa	0.83	Z = 8.61 p-value = 0
Rho	0.81	S = 6812.1, *p*-value < .001
ICC	0.97	C.I. 95% [0.90–0.99]
*Median TI [°/s]	1.47	-
*IQR TI[°/s]	[1.16–3.27]	
MDC [°/s]	4.54	
SEM [°/s]	1.63	
Bias [°/s]	0.63	
tLogICC	0.89	C.I. 95% [0.728–0.958]
tLogMDC [°/s]	0.387	
tLogMDC [%]	59.03%	
tLogSEM [°/s]	0.139	
tLogBias [°/s]	0.067	

Kappa: Concordance between clinical raters (Linear weighted Kappa), Rho: Smartwatch measuring clinical correlation with Unified Parkinson's Disease Rating Scale (UPDRS-III). The reliability parameters ICC: Intraclass Correlation Coefficient, TI: tremor intensity, IQR TI: interquartile range tremor intensity, MDC: Minimum detectable change SEM: Standard error of measurement, Bias: Mean of differences, were calculated with and without log10 transformed data (tLogICC, tLogMDC, tLogSEM, tLogBias). These repeatability parameters were analyzed after removing outliers defined as parameters when the value was > 3 standard deviation from mean difference (Parrinello et al., 2016) and clinical change between ratings in UPDRS-III ≥1. *First assessment of test-retest substudy.

smartwatches at the wrist may miss distal finger tremors, which would be otherwise detected by visual inspection. All wrist-based systems share this disadvantage with respect to finger tremor monitoring. Development of finger devices could overcome this limitation. Second, low amplitude noise in signals measured by the gyroscopes was identified through the analysis; thus, this could affect the tremor estimation. The estimated magnitude of the gyroscope noise was about ± 1°/s but we were unable to determine if any other filter was implemented by the manufacturer as this information is confidential. Third, severe tremors are scarce in this study, partially explained by the fact that these patients are difficult to recruit due to a high disease burden. Next, the medications were kept stable for tremor measuring but some influence on tremor variability could have happened. However, these was minimum due to the measurements were performed in short periods of time and test-retest was inmediately consecutive. Finally, the functional impairment in the patients' daily life was not the scope of this study, so the clinically meaningful change of tremor intensity detected by this device remains unknown.

Further technical work will shorten and mechanize the process to non-experts clinicians. Furthermore, future studies should focus on automatic tremor intensity detection to not miss or misdiagnose tremor events, even in non-controlled settings. Daily activities interferences are one of the most important limitations to overcome.

However, designing algorithms that include context awareness could be useful [32]. This will be possible by implementing automatic classification systems that identify activities of the daily living [33]. Also, clinically meaningful changes in tremor intensity detected by these devices must be assessed in upcoming studies.

5. Conclusion

Objective quantification of rest tremor intensity with smartwatches in PD patients is feasible, reliable, and well-correlated with clinical scores. Further studies are required to check the validity of using smartwatches as transducers in PD clinical follow-up. Moreover, these devices are well-accepted by patients, so they could be a reasonable choice for quantify tremors objectively.

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Authors roles

Dr. López-Blanco (robretolb@gmail.com) collaborated in: 1) the conception, organization and execution of the research project; 2) the statistical analysis design; and, 3) performed clinical video-ratings, 4) and the writing of the manuscript first draft and the review and critique of the manuscript.

Dr. Velasco collaborated in: 1) the conception, organization and execution of the research project; 2) the statistical analysis design; and, 3) the review and critique of the manuscript.

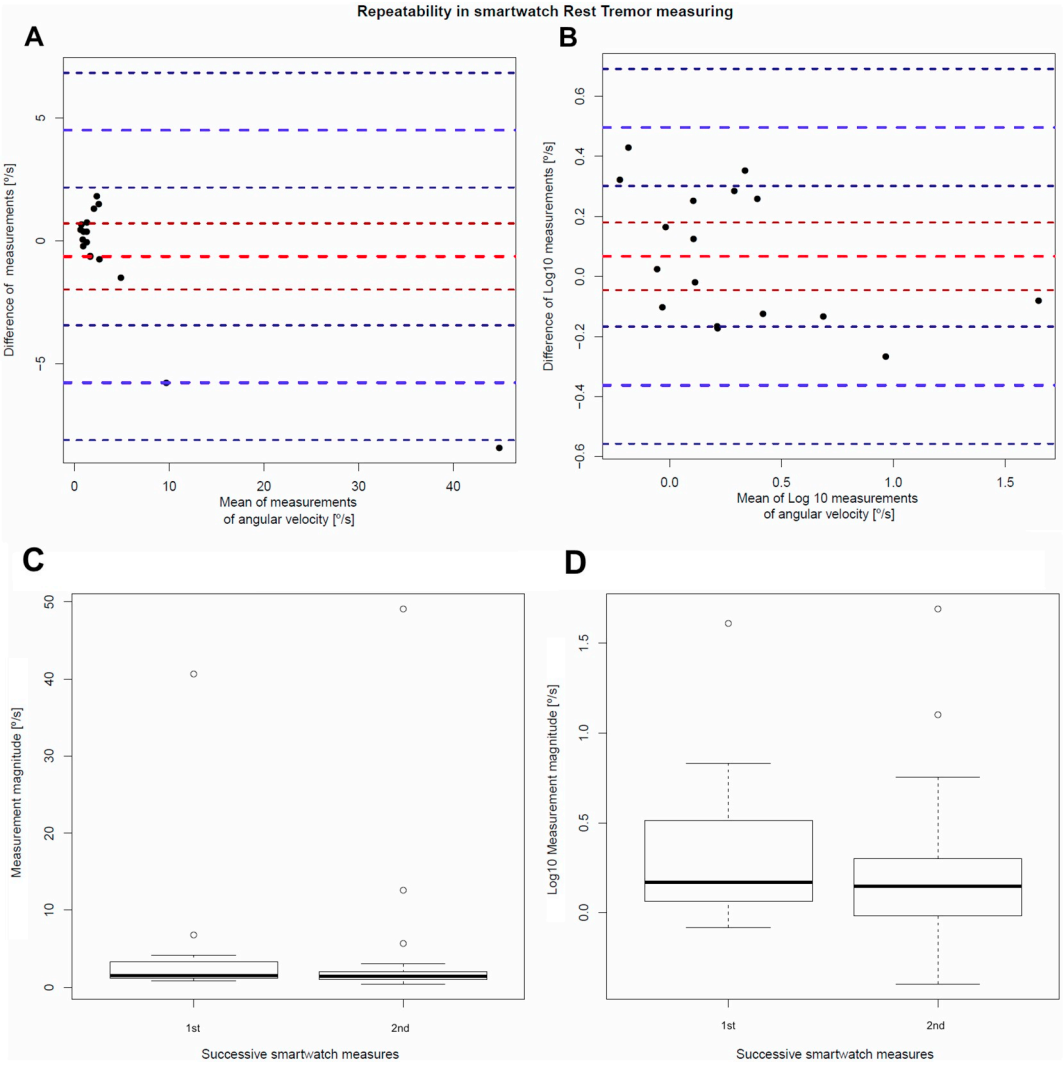

Fig. 3. AB. Bland-Altman plot of tremor measures without and with log10 transformed data obtained at rest respectively. Garnet dashed lines show the limits of the confident interval at 95% for mean of difference or "bias" (red dashed lines). Dark blue dashed lines correspond to upper and lower limits of the confident interval at 95% for measurement differences (blue dashed lines). CD. Box plots of successive smartwatch measures are shown without and with log10 transformed data. One outlier with > 3 standard deviation and clinical change between ratings in UPDRS ≥1 was removed from the plot. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 3
Smartwatch acceptance questionnaire. Acceptance questionnaire (adapted from Giuffrida et al).

Questionnaire of acceptance of the devices	Yes	No
1. Was the device comfortable to wear?	95.5%	4.5%
2. Did the device feel heavy?	0%	100%
3. Would you wear it in daily-life?	95.5%	4.5%
4. Did the device make difficult your arm movements?	0%	100%
5. Did the device make difficult your trunk movements (getting up, sitting down, or walking?	9.1%	90.9%
6. Would you find difficult the device placement at home?	18.2%	81.8%
7. Would you feel comfortable wearing the device in public?	86.4%	13.6%
8. In general, are you satisfied with the device?	95.5%	4.5%
9. How would you quantify your satisfaction with the device in general? From 0 (The most dissatisfaction) to 10 (the best satisfaction)	Mean = 8.3	

Dr. Méndez-Guerrero collaborated in: 1) the conception and execution of the research project; and, 2) performed clinical video-ratings, 3) the review and critique of the manuscript.

Dr. Romero collaborated in: 1) the conception, organization of the research project; and, 2) the review and critique of the manuscript.

Dr. del Castillo collaborated in: 1) the conception, organization of the research project; and, 2) the review and critique of the manuscript.

Dr. Serrano collaborated in: 1) the conception, organization of the research project; and, 2) the review and critique of the manuscript.

Dr. Rocon collaborated in: 1) the conception, organization of the research project; and, 2) the review and critique of the manuscript.

Dr. Benito-León collaborated in: 1) the conception, organization of the research project; and, 2) the review and critique of the manuscript.

Declarations of interest

None.
Dr. López-Blanco reports no disclosures.
Dr. Velasco reports no disclosures.
Dr. Méndez-Guerrero reports no disclosures.
Dr. Romero reports no disclosures.
Dr. del Castillo reports no disclosures.
Dr. Serrano reports no disclosures.
Dr. Rocon reports no disclosures.
Dr. Benito-León reports no disclosures.

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