Review

Automated Systems Based on Wearable Sensors for the Management of Parkinson's Disease at Home: A Systematic Review

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Abstract

Background: *Parkinson's disease is a common neurodegenerative pathology that significantly influences quality of life (QoL) of people affected. The increasing interest and development in telemedicine services and internet of things technologies aim to implement automated smart systems for remote assistance of patients. The wide variability of Parkinson's disease in the clinical expression, as well as in the symptom progression, seems to address the patients' care toward a personalized therapy.*

Objectives: *This review addresses automated systems based on wearable/portable devices for the remote treatment and management of Parkinson's disease. The idea is to obtain an overview of the telehealth and automated systems currently developed to address the impairments due to the pathology to allow clinicians to improve the quality of care for Parkinson's disease with benefits for patients in QoL.*

Data Sources: *The research was conducted within three databases: IEEE Xplore®, Web of Science®, and PubMed Central®, between January 2008 and September 2017.*

Study Eligibility Criteria: *Accurate exclusion criteria and selection strategy were applied to screen the 173 articles found.*

Results: *Ultimately, 55 articles were fully evaluated and included in this review. Divided into three categories, they were automated systems actually tested at home, implemented mobile applications for Parkinson's disease assessment, or described a telehealth system architecture.*

Conclusion: *This review would provide an exhaustive overview of wearable systems for the remote management and automated assessment of Parkinson's disease, taking into account the reliability and acceptability of the implemented technologies.*

Keywords: *eHealth, IoT, m-Health, Parkinson's Disease, telemedicine, telemonitoring, wearable sensors*

Introduction

The increasing aging of population is resulting in a wide prevalence of chronic diseases such as neurodegenerative disorders, which require long-term high-cost treatments.[1] A plan to develop strategies able to reduce healthcare costs for age-related pathologies is an important challenge for the future.[2,3]

In this scenario, Parkinson's disease (PD) is a neurodegenerative illness that affects millions of people worldwide, and its incidence is growing.[4] PD is caused by a critical loss of dopamine in the forebrain, which results in typical cardinal motor symptoms such as tremor, postural instability, muscular rigidity, and bradykinesia/hypokinesia.[5] In addition, common nonmotor symptoms such as autonomic dysfunctions, sleep disturbances, and olfactory symptoms are critical factors that degrade the quality of life (QoL) of PD patients[6] and make the pathology severely disabling, both physically and socially.[7,8]

The long-term development of the disease, expression of symptomatic complications (e.g., motor fluctuations) during specific times of day, long waiting lists, and traveling costs (particularly for people who live in rural areas) are just a few reasons that support the need to move Parkinson's care into the home and to develop new care models.[9]

The wide variability in clinical expression, as well as in progression of somatic symptoms,[10] makes the pathology difficult to adequately identify and treat.[11] Particularly, as the pathology onset appears unilaterally, with specific impairments, and it develops differently among patients,[12] it makes sense that a personalized and adapted therapy should be administered based on the individual needs of PD patients.

This approach would enable optimal care and would treat the predominant symptoms.[13] The approach would also meet the principles of the novel precision medicine concept for healthcare systems,[14] which aim to provide the best available care for each subject. In particular, precision medicine is expected to integrate the best evidence-based knowledge in different fields, including molecular imaging, deep brain stimulation, and wearable sensors, to identify the optimal solution for the treatment and management of PD patients.[15] Personalized strategies are also important to support patients' engagement in their care path, making them active in their own health.[16]

Recently, advances in wearable sensors, information, and communication technologies, as well as data mining, are promoting the design and the implementation of e-Health systems that allow to provide novel therapeutic and monitoring solutions for PD patients.[17] These systems aim to maximize the efficiency of healthcare, enhancing its quality without increasing costs. This is accomplished through augmented contacts between patients and clinicians and sharing information between the different stakeholders. These systems also promote the empowerment of patients to actively manage their health and to adopt healthy behaviors.[18]

In the same vein, internet of things (IoT) systems for healthcare are emerging.[19] They can allow the collection of huge amounts of patients' data through wearable sensors that are connected to a medical database through mobile devices. These data are analyzed by intelligent algorithms to obtain useful information for discriminating relevant health conditions, adjusting therapy, monitoring disease progression, and supporting both clinicians and patients in decision-making.

This review article aims to provide a wide overview of the telehealth and automated systems currently developed to address the impairments caused by PD to allow the clinicians to improve the quality of care for the pathology and provide relative benefits for patients in QoL. In particular, this article provides a review of the typologies of smart systems that were investigated and implemented for PD management in the last decade and focuses both on the kind of technology used and the system performance. Such systems are organized into three different categories on the basis of their level of development. Indeed, some works presented technologies able to provide automatic assessment of one or more specific impairments in PD, and they were tested in the actual home environment.

Alternatively, other studies focused on the development of mobile health applications for remote automated PD management. Finally, several articles described the architecture of a telemedicine system for the provision of a remote healthcare service for PD patients. For each category, the existing systems that emerged from the review process were investigated, analyzed, and discussed.

Materials and Methods

DATA SOURCES

An electronic database search was performed on September 15, 2017 using IEEE Xplore®, Web of Science®, and PubMed Central® to identify articles concerning the use of wearable sensors for automated and remote management of Parkinson's disease. According to the PRISMA statement,[20] an additional manual search was performed (e.g., through citations of articles included in this review), but no further articles were relevant for inclusion in this review article.

SEARCH TERMS

Specifically, the terms and keywords used for the literature research were ("*Parkinson*") AND ("*wearable*" OR "*inertial*" OR "*accelerometer*" OR "*acceleration*" OR "*gyroscope*" OR "*EMG*" OR "*EEG*" OR "*ECG*" OR "*GSR*" OR "*clothes*") AND ("*Telemedicine*" OR "*Telehealth*" OR "*Telecare*" OR "*Telemonitoring*" OR "*mhealth*" OR "*ehealth*" OR "*M-Health*" Or "*E-Health*" OR "*Mobile Health*" OR "*Home Monitoring*" OR "*IoT*" OR "*Internet of Things*") located within title and/or abstract and/or keywords.

STUDY SELECTION PROCESS

Only original full-text articles published in English, between January 2008 and September 2017, which discussed the use of wearable/portable sensors for automated remote PD assessment and management, were included in this review. First, duplicated references were manually identified and excluded. Then, during the screening procedure, items were excluded if: (1) they were an abstract, a letter, a review article, or a chapter from a book or (2) they were not written in the English language.

Each author independently screened the articles that were excluded with reason if: (1) they did not use any type of wearable/portable sensors; (2) they did not manage Parkinson's disease; (3) they did not appear appropriate for this review after the reading of title and abstract; or (4) they were not full access. In addition, (5) if multiple articles written by the same author had similar content, articles published in journals were selected instead of articles presented at conferences. Furthermore, (6) if multiple articles written by the same author with similar content were presented at conferences, the most recent article was selected. Disagreements about the inclusion/exclusion and classification of the articles were solved through meetings and discussions among the authors.

Finally, the selected articles, fully evaluated and included in this review, were classified into three groups based on whether (1) they implemented devices for automatic assessment of PD symptoms or impairments (e.g., freezing of gait [FOG], tremor) and they were tested in the actual home environment; (2) they developed m-health applications on smartphone/tablet for PD; or (3) they designed a telemedicine service, describing its architecture.

DATA ABSTRACTION

Data were abstracted from each selected article, as reported in *Tables 1–3*. For the first 2 categories evidenced the technological solutions used, the experimental aspects, and the performed analysis. In particular, for the technology, the typology of the sensors, their placement over the body, and the sampling frequency were reported. About the experimental sessions, the designed protocol adopted and the subjects involved according to their pathology and their health status were described. Furthermore, the last three columns of the *Tables 1–3* synthetized the extracted features, the applied statistical methods, the implemented classifiers, and the main findings for each work. Differently, for the third category, the focus was on the technology used, the symptom addressed, the architecture and performance of the telehealth system, and the preventative measures adopted in terms of privacy and secure transmission of data.

Results

APPLICATION OVERVIEW

Obtained in the research were 173 articles: 62 references were retrieved from IEEE Xplore, 43 references were obtained from Web of Science, and 68 references were taken from PubMed Central. After removing the duplicated items, 106 references were fully assessed within the evaluation procedure. Finally, according to the eligibility criteria, 55 articles resulted, which were adequate for the present work and were included in the final review (*Fig. 1*).

ANALYSIS METHODS

The selected articles for this review were divided into three categories based on their level of development. The first category included works that implemented technological solutions for the automatic assessment of one or more specific symptoms of PD. The designed protocol for these studies demanded that experimental sessions be performed in the home environment. The automated evaluation of PD impairments represents the first step toward a telemedicine system and allows the patients to automatically monitor their health status; this application is particularly valuable for the most disabling symptoms.

The second category of articles encompassed studies in which a mobile application was developed for PD management. This category is a further step toward the fully automated assessment of the pathology at home, allowing the patients to use a highly common technological device (i.e., the smartphone) that could acquire data directly, process the data, and eventually provide timely feedback to the users.

Finally, the third category featured researches in which telehealth services were designed and/or implemented. This class can include works from other categories, such as wearable solutions tested in the home environment or mobile apps for PD. In addition, the class can provide the complete system architecture, which integrates wearable sensors, mobile/web-based applications, servers for the storage and elaboration of acquired data, and smart interfaces for communication between patients, caregivers, and medical staff (*Fig. 2*).

REPORTED RESULTS

More than half (52.7%) of the 55 fully evaluated articles were published during the past 3 years and 74.5% over the past 5-year period (*Fig. 3a*). This result confirmed the increasing interest for wearable systems in PD remote applications, as well as the need to improve telecare services for chronic patients. Thirty-one articles (56.4%) were published in journals, while the others were presented in international conferences. Regarding the application, 30 studies (54.4%) were tested in the home environment, 21 works (38.2%) implemented mobile applications, and 24 articles (43.6%) presented telehealth systems for PD. Nevertheless, only 4 articles (7.2%) concerned all three topics (*Fig. 3b*).

AUTOMATED SYSTEMS TESTED AT HOME

The possibility to have an automated evaluation of specific symptoms or disturbances can represent the first step toward a remote management of the disease. In particular, some impairments such as FOG,[21–23] risk of falls,[24] motor fluctuations, and dyskinesias[25–31] can mainly occur during specific times over the day. For this reason, it is not easy for the neurologist to evaluate the symptoms during a clinical examination at the hospital. The opportunity to measure and analyze motor performances at home can allow the patients to record their impairments precisely when they first appear, allowing the clinician to keep track of them over time.

Accelerometers (ACC) and gyroscopes (GYR) are the most used sensors for these measurements (*Table 1*) because they represent a valid trade-off between unobtrusiveness and accuracy for motion measures.[30,32–34] Furthermore, they can eventually be included in a smartphone,[22,35] a wristband,[29] or a smartwatch,[36,37] which are common technological tools, to increase the acceptability and usability of these systems.[35] These works aimed to address one or more symptoms, and their feasibility was typically measured by evaluating the ability of the system to discriminate PD patients from healthy subjects of controls (HC)[26,38–45] or to correlate well with UPDRS clinical scores.[26,30,40,41,46]

Machine learning approaches (e.g., Support Vector Machine, Decision Tree, Random Forest, and Neural Networks) were generally implemented to evaluate the accuracy of the system in assessing the investigated symptoms.[21–23,25,27,28,30,36,38,47] However, sometimes long-term studies involved a limited number of

Table 1. Studies Implementing Automated Systems for PD Assessment, Tested in Home Environment

REFERENCE	TECHNOLOGY	SENSOR PLACE	RECORD.FREQ	DESIGNED PROTOCOL	SUBJECTS	EXTRACTED FEATURES	ANALYSIS/ CLASSIFIERS	CLASSIFIER PERFORMANCE OR FINDINGS
21	ACC, GYR	Waist	200 Hz	Scripted activities and free ADL, including: (1) showing the researchers around their home; (2) Stand Up and Go test crossing through a doorway and then, turning back (up to 10 times); (3) going outdoors and taking a short walk; (4) dual task activity (20 min, both OFF/ON states)	21 PD	A set of features, including: skewness, kurtosis, higher harmonics, autoregression coefficients, mean, SD	SVM (generic model vs. personalized model), sensitivity (sens.), specificity (spec.), geometric mean (GM)	Enhancement in GM: 7.2% for the personalized model compared to the generic model; 11.2% for the novel generic method compared to the traditional MBFA generic model; 10% for the novel personalized model with respect to the MBFA personalized model.
22	*GaitAssist* app, smartphone	Ankles	32 Hz	Participants deployed and used the system on their own, without any clinical support, at their homes during three protocol sessions in 1 week. Exercises: gait initiations, additional dual tasking, turning exercises	9 PD	Power on locomotion band, Power on freeze band, Total Power, Freeze Index	C4.5 model	Real time hit rate 97% for FOG detection; detection delay of ≤0.5 s
23	ACC, GYR	Each limb, waist	62.5 Hz	Short-term recordings (15 min) in hospital: (1) lying on the bed; (2) rising from the bed and sitting on a chair located by the bed; (3) standing up from the chair and performing a series of tasks (walking, opening and closing a door, drinking, and random movements). Long-term recordings (8 h/day for 5 days) at home	Short term: 24 PD. Long term: 12 PD	Tremor: time and frequency domain features. LID: mean value, SD, entropy, energy in specific frequency sub-bands, and entropy of the frequency spectrum. Bradykinesia: approximate entropy, sample entropy, RMS value, cross correlation value, and range value. FOG: entropy	Hidden Markov Models (HMM), DT, SVM, RF	Classification accuracy: 87% for tremor, 85.4% for LID, 74.5% for bradykinesia, 79% for FOG. Mean absolute error: 0.088 for tremor, 0.31 for LID, 0.25 for bradykinesia, 0.79 for FOG
24	ACC, GYR, Kinect®	Wrist	Not reported	Daily activities at home: (1) walking between rooms (e.g., to collect something); (2) preparing drinks or cooking; (3) sorting, washing, and hanging out clothes; (4) ascending and descending stairs; (5) negotiating steps between rooms; (6) crossing open spaces in large rooms	5 PD at high risk of falling	Qualitative observations	Qualitative assessment	High risk of falling when people transferred between sitting and standing, walked, turned, negotiated steps, and tackled tasks while standing
25	ACC, GYR	Each limb and waist	62.5 Hz	1st: laboratory, to test technical performance; 2nd: hospital, to test clinical compliance; 3rd: home, to evaluate system prototype; 4th: to test system wearability	1st: 20 HC; 2nd: 36 PD, 3rd: 44 PD and 12 Parkinsonism; 4th: 24 users	Features to measure dyskinesia (dysk), bradykinesia, and tremor (e.g., step frequency, velocity, arm swing frequency, and entropy of gait signal)	DT, SVM	93.73% accuracy (acc.) for the classification of levodopa induced dysk (LID) severity. 86% acc. for bradykinesia severity and 87% acc. for tremor. Touch-screen PC was well accepted.
26	ACC, GYR	Ankles	Not reported	Everyday activities: making coffee, lying, sitting quietly, sitting and counting coins, dressing. 1st study: 6 h, laboratory-environment; 2nd study: 12 weeks in home-environment	1st: 23 PD (7 leg dysk), 13 HC; 2nd: 10 PD (7 dysk)	Ratio of the angular rate around the z-axis over the angular rates lying within the xy-plane	*Ad hoc* algorithm for dysk detection; correlation coefficient	85% sens., 98% spec.. 0.96 acc. for dysk detection in laboratory environment; perfect discrimination in home environment; 0.61 ($p<0.001$) correlation with UPDRS
27	ACC	Waist	200 Hz	1st: activities guided but execution free (e.g., indoor/outdoor walking, FOG provocation, dysk, false positive tests), (before/after medical intake, at home). 2nd: Laboratory activities (walking in a straight line, over an inclined plane, carrying a heavy object, setting a table, going upstairs and downstairs) and outside protocol (walking for >15 min)	1st: 92 PD. 2nd: 10 PD (mild to moderate with motor fluctuations)	Power spectrum in dyskinetic band (0.68–4 Hz), nondyskinetic band (8–20 Hz), and posture transitions (0–0.68 Hz)	SVM (leave-one-out-subject)	100% sens., 98% spec. for strong trunk dysk; 39% sens., 95% spec. for weak dysk on limbs; 93% sens., 95% spec. for all strong dysk or weak dysk on trunk
28	Trigno™ (Delsys Inc): ACC, EMG	Distal portion of each limb	Not reported	4 h continuously recorded during unscripted and unconstrained activities in a 100 m^2 laboratory that simulated a studio apartment	Training set: 11 PD. Test set: 4 HC, 8 PD	Low pass energy, High pass energy, Lag and Height of first peak in autocorrelation of ACC corrected signal	Dynamic NN (DNN)	>90% sensitivity (sens.), >90% specificity (spec.) for moderate and severe levels of tremor and dysk

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Table 1. Studies Implementing Automated Systems for PD Assessment, Tested in Home Environment *continued*

REFERENCE	TECHNOLOGY	SENSOR PLACE	RECORD.FREQ	DESIGNED PROTOCOL	SUBJECTS	EXTRACTED FEATURES	ANALYSIS/ CLASSIFIERS	CLASSIFIER PERFORMANCE OR FINDINGS
29	Kinesia™ (ACC, GYR)	Wrists and ankles	Not reported	6 ADL (2 h): (1) hygiene: brushing hair and teeth, (2) dressing: putting on/taking off a jacket and shoes, (3) eating: setting a table, eating a snack, and/or drinking a beverage, (4) desk work: writing on paper and using a computer, (5) entertainment: reading and/or watching television, and (6) laundry: folding towels and clothes from a basket	13 PD with LID history	Tremor, dyskinesia, and bradykinesia before and after medical intake	ROC, AUC, radar charts, True Positive Rate, False Positive Rate, Correlation coefficient, Wilcoxon signed rank test	Algorithm scores for tremor, bradykinesia, and dyskinesia agreed with clinician ratings of video recordings (ROC >0.8). Significant differences ($p<0.01$, $p<0.001$) in performances after and before medical intake.
30	ACC	Wrists	100 Hz	1st study: 4 h in laboratory performing MDS-UPDRS III items (4, 6, 10, 11, 15 e 17) for upper limb bradykinesia, tremor, and gait. 2nd study: 7 days at home performing ADL	34 patients	91 features, including: Fourier coefficients, empirical cumulative distribution function features, and statistical features	Artificial NN (ANN) leave-one-out. Correlation coefficients	Dysk assessment: 0.38 sens., 0.99 spec. in laboratory, 0.49 sens., 0.93 spec. at home; ON-OFF detection: 0.65 sens., 0.83 spec. in laboratory, 0.51 sens., 0.87 spec. at home; Correlations: UPDRS IV/dysk r = 0.52, $p=0.008$ (excellent diaries), r = 0.52, $p=0.004$ (good diaries); UPDRS IV/ON-OFF not significant; diaries/dysk r = 0.69, $p=0.001$ (excellent diaries), r = 0.65, $p=0.002$ (good diaries); diaries/ON-OFF: r = 0.63, $p<0.004$ (excellent diaries), r = 0.56, $p<0.01$ (good diaries)
31	ACC	Wrists, ankles, waist	40 Hz	4 days at home	2 PD	Mean, energy, high frequency energy content, correlation and frequency domain entropy, a 5 bin histogram representation of the spectral contents over all 3 axes	Algorithm based on axis parallel rectangle (APR) fitting in the feature space	The APR based multiple instance learning algorithm had the best accuracy compared to other classification algorithm
32	ACC	Wrists	100 Hz	1st study: 4 h in laboratory performing MDS-UPDRS III items (4, 6, 10, 11, 15 e 17) for upper limb bradykinesia, tremor, and gait. 2nd study: 7 days at home performing ADL	34 patients	Questionnaire responses, wearing time of sensors	Likert-style questionnaire, Wilcoxon rank-sum test	Long-term monitoring with wrist-worn sensors is acceptable to this cohort of PD patients
33	ACC, GYR	Each limb and waist	62.5 Hz	To wear the system at home and to move freely carrying out daily activities (5–7 days, running 2 sessions of 4 h/day)	11 PD	Entropy and classic gait parameters (e.g., step frequency, velocity, stride length)	Wearability assessment	All participants agreed that the provided solution did not obstruct them in everyday activities nor did it effectively limit their activities
34	ACC, GYR	Each limb and waist	62.5 Hz	Not specified (subjects tested the wearability of the system at home over time)	32 PD	Wearability in terms of: energy cost, comfort, and biomechanical (pain, discomfort)	Rapid Entire Body Assessment (REBA), Borg and CRS scales in combination with a body map	The acceptance of this system is satisfactory with all the levels of effect on each component scoring in the lowest ranges
35	IMU + smartphone + mobile app	Feet	Not reported	Gait training for 30 min, thrice per week for 6 weeks	11 PD	Average time and distance walked, steps taken, cadence, gait speed, and both praising and corrective messages delivered per session by the app	Likert scale for usability	System usability was satisfactory
36	Smartwatch (GENEActiv™)	Wrist	50 Hz	20 motor tasks divided into 5 groups (resting, gross upper limb movement, fine upper limb, periodic hand movement, and walking) repeated 6 times during 2 days of hospital visits, and 2 additional days of home monitoring.	19 PD	Relative energy features and mean relative energy for each of the wavelet scales	Wavelet, SVM (19-fold cross validation), ROC, AUC	AUC = 0.75 for rest dyskinesia; AUC = 0.92 for walking dyskinesia; AUC = 0.70 for bradykinesia
37	Smartwatch + *EchoWear*® app	Wrist	Not reported	Month-long in-home trial involving commonly used speech tasks; sustained vowel phonation, low and high pitch range	6 PD	Perceptual Loudness, zero-crossing rate, spectral centroid, short-time energy	Qualitative assessment	Configurability, computational intelligence, and interoperability of the interface for remote monitoring of speech treatments

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Table 1. Studies Implementing Automated Systems for PD Assessment, Tested in Home Environment *continued*

REFERENCE	TECHNOLOGY	SENSOR PLACE	RECORD.FREQ	DESIGNED PROTOCOL	SUBJECTS	EXTRACTED FEATURES	ANALYSIS/ CLASSIFIERS	CLASSIFIER PERFORMANCE OR FINDINGS
38	ACC, GYR, CASAS Smart home, smartphone	Upper dominant arm, ankle of dominant side	30 Hz	IADL: water plants, medication management, wash countertop, sweep and dust, cook, wash hands, TUG test, TUG test with name generation, Day Out task	1^{st}: 25 PD, 50 HC; 2^{nd}: 9 Mild Cognitive Impairment (MCI), 16 PDNOMCI, 9 PDMCI, 18 HC	Ambient sensor features, wearable sensor features, day out task features, participant features, activity features	DT, Naive Bayes, RF, SVM, Ada/DT, Ada/RF. ANOVA, ROC	0.74 AUC, 0.75 acc. (individual tasks), 0.70 AUC, 0.70 acc. (combined tasks) for PD/HC recognition with Ada/RF. 0.96 AUC, 0.85 acc. (individual tasks), 0.64 AUC, 0.32 acc. (combined tasks) for PDNOMCI/PDMCI/MCI/HC recognition with Ada/DT. Best performance using all sensors and all activities
39	Body worn monitor (BWM) with ACC	Waist	100 Hz	(1) Laboratory data: 4 intermittent straight line walking trials over a 10-m walkway at preferred speed. (2) Free-living gait data collected over 7 days	47 PD, 50 HC	14 gait characteristics (e.g., step velocity, step length, and swing time) representative of five domains (pace, variability, rhythm, asymmetry, and postural control)	Shapiro–Wilk test, t-tests or Mann–Whitney U, Wilcoxon signed-rank tests, Spearman rank-order correlations	The impact of environment was significant for all gait characteristics ($p<0.001$). Between-group differences in gait characteristics were exaggerated in free-living conditions. Free-living data showed low to moderate correlations ($r \leq 0.453$) with laboratory results for both groups. ABs ≤10 s did not discriminate between groups. Medium to long ABs highlighted between-group significant differences for pace, rhythm, and asymmetry
40	Opal inertial sensors (APDM, Inc., Portland, OR, USA)	Belt and feet	Not reported	10 h per day, 7 consecutive days during normal daily activities	13 PD, 8 HC	Mean and CV of: (1) number of turns per hour, (2) turn angle amplitude, (3) turn duration, (4) turn mean velocity, and (5) number of steps per turn	Shapiro–Wilk test, One-way Analysis of Variance, Pearson's correlation coefficients	PD showed impaired quality of turning compared to HC in turn mean velocity and mean number of steps. PD showed higher variability within the day and across days compared to HC. No differences between PD and HC in number of steps per day or% of the day walking during the 7 days. Statistically significant correlation between CV of turn velocity ($r=0.79$, $p=0.01$), the number of steps per turn ($r=0.61$ and $p=0.03$), and turn velocity ($r=0.61$, $p=0.03$) with the UPDRS motor score
41	Mobi8 TMSI (ACC), DynaPort Hybrid Monitor (ACC, GYR)	Lower back	256 Hz	Validation study: 1 min, straight-line walk at a self-selected comfortable pace inside a long hallway. Gait test: straight-line walk (∼25 m × 2). ADL simulation: 500 m walk at comfortable self-selected speed. Monitoring at home: 3 consecutive days	Validation: 22 PD, 17 HC. Monitoring: 1 PD, 1 HC	Stride time and stride time variability (validation study only). Dominant freq, amplitude, width (FD), and slope of the main freq of the power spectral density (PSD) in the 0.5- to 3.0-Hz band	*t* tests 2-tailed; paired *t* tests; Pearson coefficients	Width larger and amplitude and slope smaller in PD compared to HC (validation study and ADL simulation ($p<0.02$)). Width decreased and amplitude and slope increased with anti-Parkinsonian medications ($p<0.007$). Significant correlations ACC-derived measures/UPDRS-Gait5. Home data were similar to the clinic data.
42	Physilog® (ACC, GYR)	Shanks, wrists, sternum	200 Hz	iTUG test at home within 24 h before or after laboratory testing	6 PD, 8 HC	Stride length, stride velocity, cadence, peak arm swing velocity on the more affected side (MAS), and turning velocity	Repeated Measures ANOVA; *post-hoc* comparison Tukey–Kramer tests	Significant group effect for stride velocity ($p=0.03$), cadence ($p=0.001$), peak arm swing velocity MAS ($p=0.002$), and turning velocity ($p=0.003$). Significant interaction effect for stride velocity ($p=0.02$) and stride length ($p=0.002$). Significant location effect for turning velocity ($p=0.002$)
43	ACC, GYR	Wrists, ankles, trunk	Not reported	Subjects were continuously monitored at home over a 9-h period while performing their normal daily activities	10 HC, 6 PD	Tremor index: ratio of the power within frequency range of 4–8 Hz to the power of total rotation within frequency range of 0.1–8 Hz	Spectrogram	Significant differences were detected between PD/HC before and after medical intake
44	Opal inertial sensor (APDM, Inc., Portland, OR, USA) (ACC, GYR, MAG)	Pelvis	128 Hz	Laboratory: to walk on a path of a mixed route with short straight paths interspersed with 10 turns of 45°, 90°, 135°, and 180° in both directions, at 3 different speeds (12 times). Home: monitoring about 10 h/day for 7 days	Laboratory: 21 PD, 19 HC; Home: 12 PD, 18 HC	Bouts, hourly frequency of turning, duration of each turn, number of steps per turn, peak and average rotational turning rate, jerk, variability of these measures throughout the day and week	Sens. Spec.	Laboratory: 0.90 sens., 0.75 spec. compared to motion analysis; 0.76 sens., 0.65 spec. compared to video analysis. PD had a slower velocity and higher impairments compared to HC while turning. Home: significant differences between HC/PD in bout duration, active rate, turning duration, angle of turning, peak velocity of turning, number of steps for turning.

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Table 1. Studies Implementing Automated Systems for PD Assessment, Tested in Home Environment *continued*

REFERENCE	TECHNOLOGY	SENSOR PLACE	RECORD.FREQ	DESIGNED PROTOCOL	SUBJECTS	EXTRACTED FEATURES	ANALYSIS/ CLASSIFIERS	CLASSIFIER PERFORMANCE OR FINDINGS
45	ACC, GYR, smartphone + audiobiofeedback (*ABF-gait* app) and the instrumented cueing for *FOG*-training (*FOG-cue* app	100 Hz	Gait, FOG	Gait training for 30 min, 3 times per week for 6 weeks	20 PD, 18 HC	Gait speed, stride length, double support time	Kolmogorov Smirnov analysis and Levene's test, t-test. Fisher's LSD *post-hoc* analysis for effect size	$p<0.001$ for gait speed and stride length, $p<0.01$ for double support time both for PD and HC. PD improved more than HC both in comfort and dual task condition. Effect size: small for HC, moderate for PD.
46	(ACC)	Waist	Not reported	Walking free to show the home (>2 min); walk without assistance (10 m) (both in OFF/ON states)	75 PD	A single frequency feature consisting of the power spectra between 0 and 10 Hz	Spearman's correlation coefficient	Moderate correlation with UPDRS-III ($r=-0.56$; $p<0.001$). Good correlation with gait item ($r=-0.73$; $p<0.001$). Good correlation with Factor 1 (axial function, balance, and gait) ($r=-0.67$; $p<0.01$)
47	FAB system BioSyn® (ACC, GYR)	head, arm, forearm, trunk, pelvis, thigh, shank	100 Hz	Walking, walking turns of 180°, and fast walking (3 trials) at home	11 PD	Mean and peak amplitude values of each of 59 joint variables	Change space; Least Absolute Shrinkage Selection Operator (LASSO)	Correctly predicted 5 cases of improvement and 2 cases of worsening after medication
48	ACC, EMG sensors	Forearms, arms, thighs, shanks	Not reported	3 days, (2 days in clinical setting, 1 day in home setting). Longitudinal study. Heel tapping (30 s). forearm pronosupination (30 s)	5 PD	Intensity, modulation, frequency, periodicity, smoothness of movement, signal entropy	ReliefF and Davies–Bouldin (DB) cluster validity index; RF with 20 trees; Scatter Plot	Scatter plot visually showed a trend from a score of 1 to a score of 4. RMS ≈ 0.4 error in the estimation of the UPDRS score
49	ACC, GYR	Each limb, trunk, pelvis, head	100 Hz	1st: walking and turning, sitting and rising from a chair, figure 8 turns, reaching tasks. 2nd: free daily activity (1 h)	11 PD	Inter-trial variability, inter-subject variability; inter-task variability	Principal Component Analysis (PCA)	Very large variability among PD patients
50	3 IMU, (ACC, GYR) + Wii Balance Board® + smartphone + mobile app	Not reported	Gait, hypokinesia, dysk, tremor and sleep	ADL and sleep monitoring, balance, and cognitive tests 24/7 over 12 weeks (4 weeks without feedback and 8 weeks with feedback)	22 PD	MDS-UPDRS, H&Y, Montreal Cognitive Assessment (MoCA), MMSE, PDQ- 39, EQ-5D, Epworth Sleepiness Scale (ESS), Panic Disorder Severity Scale (PDSS), Nonmotor Symptom Scale (NMSS), Unified Dyskinesia Rating Scale (UdysRS), Clinical Global Impression - Severity Scale and Improvement Scale (CGI-S and CGI-I)	PSSUQ scale	Acceptance level of PD patients using the SENSE-PARK System as a home-based 24/7 assessment is very good

ACC, accelerometer; ADL, activities of daily living; EMG, electromyography; FOG, freezing of gait; GSM/GPRS, Global System for Mobile Communications/General Packet Radio Service; GYR, gyroscope; HC, healthy subjects of controls; IMU, inertial measurement unit; IR, infra-red; MAG, magnetometer; PD, Parkinson's disease; TUG, Time Up and Go.

Table 2. Studies Implementing Mobile Applications for PD

REFERENCE	TECHNOLOGY	RECORD. FREQ.	SYMPTOM/ IMPAIRMENT	DESIGNED PROTOCOL	SUBJECTS	EXTRACTED FEATURES	ANALYSIS/ CLASSIFIERS	CLASSIFIER PERFORMANCE OR FINDINGS
52	Smartphone (ACC,GYR) + *sTUG* app	100 Hz	Gait and posture	To perform the TUG test in the shortest amount of time (3 times)	3 PD, 4 HC	Total duration of: TUG, sit-to-stand transition, stand-to-sit transition. Subphase duration, maximum angular velocities, and upper trunk angles	N/A (mean and SD)	PD patients needed more time to complete the total test, as well as the individual phases of the test. HC had notably higher maximum angular velocity during the lift up phase. The duration of the stand-to-sit phase for HC was notably shorter than PD.
53	Smartphone (ACC) + mobile app	Not reported	Tremor	Resting task (10 s, 10 trials)	1 PD, 1 HC	Frequency (PSD) and spatiotemporal (mean averaged acceleration, SD, CV)	T-test	Statistical difference between PD/HC ($p<0.05$)
54	Smartphone (ACC) + mobile app	60 Hz	Tremor	Resting task, Postural task, Intention task, Kinetic task (bringing the phone to one's ear and back at a relatively slow velocity).	12 PD, 3 ET, 1 multiple sclerosis	Tremor amplitude, regularity, power distribution (3–7 Hz), median, peak of power freq, power dispersion, harmonic index.	Pearson coefficients	Tremor amplitude correlation to clinical scale: r = 0.76 for RT; r = 0.85 for PT; r = 0.88 for tremor amplitude for Intention tremor; r = 0.09 for KT. r = 0.7 for power distribution in KT.
55	Microsoft Band (ACC, GYR) + Android app for smartphone	62.5 Hz	Tremor	1st: simulated tremor and hand posture; 2nd: Resting task, Postural task, ADL; 3rd: several hours recording	1st: HC; 2nd: 11 PD; 3rd: 1 HC, 2 PD	Energy, energy ratios, principal components, tremor amplitude, tremor frequency	C4.5 DT 10-fold cross-validation; Pearson's coefficient	94% acc. for tremor detection; 85% acc. for RT/PT discrimination; r = 0.95 for UPDRS correlation of tremor amplitude, r = 0.97 for UPDRS correlation of tremor constancy
56	1-channel ECG wearable sensor + smartphone running on Android 6.0 "Marshmallow"® equipped with a gravity sensor, a magnetic sensor, and a step detector sensor + *DailyHeart* app	256 Hz	Cardiac activity	1st: to sit on a chair, stand up on command and walk forward for 5 m (5 times). 2nd: to sit on a chair for 3 min (adaption to current posture). ECG measurement started, the subjects had to remain seated for 1 min, stand up on command, and stand still for 1 min (3 times)	1st: 10 young HC. 2nd: 3 HC, 5 PD (not age matched)	1st: recognition rate of the algorithm, time difference between automated and manually labeled stand-up event. 2nd: Average and SD of RR intervals, average and SD of successive differences, root mean square of successive differences, number of successive differences ≥20 ms divided by all RR intervals	DT based on a leave-one-subject-out cross-validation	Recognition rate of 90.0% for the stand-up detection algorithm. 96.0% acc., 93.3% sens, 100% spec. for HC/PD classification. PD patients showed a considerably lower orthostatic reaction than HC
57	WiiFit, sensorized cane® (ACC), infrared temperature sensor, smartphone + mobile app	Not reported	Falls	Fingertip temperature measurement every 30 min, 5 times. The participant held the cane to walk a few steps then had a forward fall, backward fall, left fall, and finally a right fall. For the forward fall, each participant was asked to walk a few steps and then simulated the cane falling on a cushion	10 subjects	Signal vector magnitude and tilt angle	Fuzzy rules	81.67% acc. for fall detection. 2.88% average error in predicting fingertip temperature

ACC, accelerometer; GYR, gyroscope; HC, healthy subjects of controls; N/A, not available; PD, Parkinson's disease.

Table 3. Studies Designed/Implementing Telehealth Services for PD

REFERENCE	PORTABLE TECHNOLOGY	SYMPTOM/ IMPAIRMENT/TASKS	SYSTEM ARCHITECTURE	PRIVACY/DATA TRANSFER ISSUES	PILOT TESTS ON PD	FUNDING
22	GaitAssist with IMU on ankles, smartphone	FOG	IMU sensors, FOG-detection module, Motor-training exercise module, Preference module, Auditory feedback module, Telemedicine and logging module, patient UI, clinician UI	Logging module	Dataset: 9 PD. Results: see Table 1	EC under the FP7project CuPiD (288516)
23	ACC, GYR on each limb and waist	Tremor, LID, bradykinesia, FOG	Wearable Multi-Sensor Monitor Unit + Local Base Unit (Daily Monitoring Processor (composed of: Tremor Posture and Resting Recognizer, LID Recognizer, FOG Recognizers, Bradykinesia Recognizer, and Activity Recognizer) + Test Processor + Scheduler + Information Handler) + Centralized Hospital Unit (Alert Manager + Information Manager + Interoperability Manager)	Encrypted messages for transmission	Dataset: 24 PD in hospital, 12 PD at home. Results: see Table 1	EC under the FP7 project PERFORM (215952)
35	ACC, GYR, smartphone on the feet	Real-time gait analysis	IMU + smartphone + telemedicine service for remote data upload	Encrypted transmissions using the SSL protocol (https); authentication page for the login	Dataset: 11 PD. Results: System acceptability evaluation	EC under the FP7project CuPiD (288516)
37	Smartwatch®	Speech analysis	Smartwatch (EchoWear app), Fog Computing Platform (Intel Edison), Cloud	The Secure Copy Protocol (SCP) was used for transfer of files and directories between two hosts (local or remote).	Dataset: 6 PD. Results: qualitative (see *Table 1*)	Rhode Island Foundation Medical Research (20144261)
48	ACC, EMG sensors on forearms, arms, thighs, shanks	Heel tapping and forearm pronosupination	MercuryLive System, 3 tiers: (1) patient's host with wearable sensors and laptop, (2) clinician's host for patients' supervision and annotation tools, (3) central server coordinating data collection and videoconferencing services	Not reported	Dataset: 5 PD. Results: see *Table 1.*	Michael J. Fox Foundation
58	2 insoles (Moticon), smartphone in the pocket, wristband (Microsoft band)	Motor and nonmotor symptoms, including ON/OFF fluctuations	PD_manager platform: (1) clinicians' app (events for patients, therapy, communication with other health professional), (2) patients' app (recommendations for modifications in therapy and treatment), (3) caregiver's app (feedback symptoms and medical adherence)	Not reported	Dataset: 20 PD. Results: N/A	EC under the Horizon 2020 project PD_manager (643706)
59	Smartwatch, smartphone, fall detector, Philips Mobility Monitor® (ACC, barometer)	ADL	Smartwatch + smartphone (with *Fox Insight* app) + Cloud platform (Radboudumc data server, Amazon Web Services, ZenDesk software and servers)	Plan for: coding the data; storing the data on secure servers, separately from personal data; and restricting data use, by only allowing access to authorized researchers. When making information available to the wider research community, data will be anonymized and access will be granted only through a secure research database.	Dataset: 20 PD. Results: 88% streaming compliance for the sensor data	Michael J Fox Foundation, the Intel Corporation (Tel Aviv, Israel), Philips Research, Stichting Parkinson Fonds, and the Movement Disorders Society
60	SmartButton (ACC, GYR, MAGN) on the chest	Mobility: TUG and 30-s Chair Stand tests	3-tiered architecture: Tier 1 use a Smart Button - a wearable Bluetooth-enabled embedded computer with inertial sensors. The Smart Button is paired with a personal device at Tier 2 (smartphone, tablet, or PC). The personal device connects through the internet to an m-Health server at Tier 3.	Authentication and secure communication	N/A	U.S. National Science Foundation under grants CNS-1205439 and CNS-1217470.
61	Smartphone (ACC) on hand or ankle	Hand resting tremor and gait	Mobile app (*PD Dr*) on smartphone with (1) user log-in and account verification, (2) motor performance test module, (3) communication module with SMS and email, (4) test history management module + cloud service: data processing and decision-making	Privacy and data security are assured: In the mobile app, user log-in is required. All data stored are encrypted (Advanced Encryption Standard [AES]), any patient identity information are stored or displayed (according to Health Insurance Portability and Accountability Act (HIPAA) regulations). The data are deleted from the device after sending to the cloud server. At the transmission level, data are encrypted and transmitted through secure https. At the server level, data are stored in the database in encrypted format and only an authorized database administrator has access.	Dataset: 40 PD. Results: 0.77 sens., 0.82 acc for hand resting tremor, 0.89 sens., 0.81 acc for gait difficulty detection. The system is simple to use, user friendly, and economically affordable	Not reported

continued →

Table 3. Studies Designed/Implementing Telehealth Services for PD *continued*

REFERENCE	PORTABLE TECHNOLOGY	SYMPTOM/ IMPAIRMENT/TASKS	SYSTEM ARCHITECTURE	PRIVACY/DATA TRANSFER ISSUES	PILOT TESTS ON PD	FUNDING
62	ACC, GYR, compass on each limb and waist	Exercises from UPDRS	Sensor units, smartphone, application server, database server, and browser application	Specified communication systems (e.g., IEEE 11073 messages, HL7 Version 2 data exchange format)	N/A	Ministry of Science, Research and the Arts of Baden - Wuerttemberg
63	Smartphone and smartwatch (ACC)	Standard hand tremor tests, finger tapping tests, involuntary tapping and spiral-drawing tests	Android mobile phone, an external ACC/smartwatch, and a web server (Parse) that maintains mongo databases and uses a BSON Handler to communicate with the phone. Software architecture of the system consists of a data centered architecture built around the database and an object-oriented architecture (JAVA) for developing Android code, which by default uses call and return architecture.	Each user entity is also linked to an authorized session; sessions may expire when the user is idle or logs out.	Dataset: 11 subjects. Results: 95% acc. in PD identification	Not reported
64	Smartwatch (ACC), smartphone	Facial recording; Speech recording; Typical MDS-UPDRS III tasks	Three layers: Body sensor network + Multidimensional diagnostic monitoring + personalized tele-interventions	Not reported	Dataset: 5 HC. Results: qualitative evaluation of the usefulness	Not reported
65	Microsoft Band ®(ACC, GYR), sensor insoles, SimpleMed+ pillbox, smartphone	Gait, FOG, bradykinesia, dyskinesia, ON/OFF fluctuations	Mobile app for patients (modules: sensor monitoring, finger tapping, cognition battery, speech analysis, nutrition); mobile app for healthcare providers (modules: clinical record, patient assessment, calendar, nutrition, digital evaluation test, medication); notifications and alert systems (including DSS); educational gallery	All data are transferred using HTTP within a connection encrypted by transport layer security (TLS) or SSL. The TLS/SSL encryption is performed before any HTTP communication, so the whole interaction is protected. The client/users authentication interfaces are implemented following the OAuth 2.0 authorization framework specifications.	Dataset: 17 PD for gait, 11 PD for tremor, 13 PD for bradykinesia. Results: correct estimations: 69% for gait score, 91% for gait disturbance, 91% for FOG events, 94% acc. for tremor, 92% acc. for dysk, 82% acc. for bradykinesia	EC under the Horizon 2020 project PD_manager (643706)
66	ACC, GYR, smartphone on the feet	Real-time gait analysis	IMU + smartphone + telemedicine service for remote data upload	Data logging thread	Dataset: 12 HC, 16 PD. Results: 2.9% total RMS difference on step length estimation between this system and gold standard	EC under the FP7project CuPiD (288516)
67	Mercury Live with 9 ACC on forearms, arms, thighs, shanks, and waist	Monitoring	MercuryLive, System 3 tiers: (1) patient's host with wearable sensors and laptop, (2) clinician's host for patients' supervision and annotation tools, (3) central server coordinating data collection and videoconferencing services.	Securely encrypted services, including Secure Socket Layer (SSL), Secure Shell (SSH), and virtual private network (VPN). Using secure channels, both patients' and clinicians' software clients can access the database, web server, videoconferencing service, and a live data forwarding service to perform background data logging and live interactive sessions. Data transmission test resulted in: 80Kb/s of bandwidth available; 400 ms data latency; 200 ms video latency	Dataset: Not specified PD @home. Results: N/A	Michael J Fox Foundation
68	Gastrocnemius Expansion Measurement Unit (GEMU) based on a force-sensing resistor (FSR) CP0152 (Interlink, USA)	Step counting and dopaminergic therapy monitoring	FTP server Web based distributed authoring and versioning software	SSL encryption for authentication and data transfer	Dataset: 6 PD. Results: high degree of acceptance at a Health Technology Assessment study	Italian Ministry of Health under the project CASE
69	Smartphone (ACC, GYR) in custom-made glove case	Resting tremor, postural tremor	(1) An iPhone 4S with the latest iOS, with internet access enabled and screen orientation locked in vertical. (2) A web application to collect data from the smartphone's sensors. (3) A web server to host the site and store the signals, and (4) A MATLAB application for processing the signals received at the server	Plan for applying cryptography to all communications from the smartphone to servers (e.g., SSL encryption)	Dataset: 25 PD, 20 HC. Results: 82% sens. 90% spec. for PD/HC classification with ensemble of DT	Not reported
70	HELP system: intraoral device, subcutaneous pump, IMU on waist, blood pressure sensor on arm	Monitoring drug delivery	(1) A Body Sensor and Actuator Network (portable/wearable and home devices to monitor health parameters and body activity and to release controlled quantity of drugs in an automatic manner). (2) A remote Point-of-Care unit to supervise the patients under clinical specialist control	Not specified	N/A	EC through wearIT@work, CHRONIOUS, and Help-AAL

continued →

Table 3. Studies Designed/Implementing Telehealth Services for PD *continued*

REFERENCE	PORTABLE TECHNOLOGY	SYMPTOM/ IMPAIRMENT/TASKS	SYSTEM ARCHITECTURE	PRIVACY/DATA TRANSFER ISSUES	PILOT TESTS ON PD	FUNDING
71	Smartphone (ACC, GYR) to place on chest, waist, pocket, or ankle	FOG	Server and client applications: the client application (remote sensing) was installed in a smartphone. Other smartphone fixed to the patient's body was running server application (receive messages to start and stop measurement from the client program).	Socket communication between devices	Dataset: 15 PD. Results: 86% sens. with sensors on the waist using AdaBoost.M1 classifier	SNUH Research Fund (3420140050)
72	ACC on forearms, arms, thighs, shanks	MDS-UPDRS III tasks	MercuryLive, System 3 tiers: (1) patient's host with wearable sensors and laptop, (2) clinician's host for patients' supervision and annotation tools, and (3) central server coordinating data collection and videoconferencing services.	SSL and SSH for establishing secure channels for all data transfer	Dataset: late PD. Results: classification error 3.4% for tremor, 2.2% for bradykinesia, 3.2% for dyskinesia.	Michael J Fox Foundation
73	ACC on wrist + Personal Digital Assistant (PDA)	Tremor	Mobile unit with PDA (the server) + Hospital unit with central station PC (the client). TCP/IP communication and error handling protocols. The software contains three modules: (1) characteristics of the patient and results of the examination; (2) acquisition of signals during examinations; (3) receiving medical recommendations from the hospital unit.	Instrument access (username+password), data security. Bluetooth security procedures based on a L2CAP (Logical Link Control and Adaptation Protocol) implementing translation of data into secret code based on the SAFER (Secure And Fast Encryption Routine) and block cipher encryption algorithms. The identity of the devices is cryptographically authenticated previously to start communicating. Data interchange in the internet performed using International Mobile Telecommunications- 2000 (IMT-2000) standards (3G). Internet transmission tests were conducted in laboratory and in three private homes, and the observed velocities may be considered adequate for the desired application	Dataset: 10 PD, 10 HC. Results: 100% sens. 100% spec to detect adverse effects of disease with frequency features of tremor	Brazilian Council for Scientific and Technological Development and Rio de Janeiro State Research Supporting Foundation
74	Wristband (ACC, GSM/ GPRS)	Tremor	Patient mobile unit (sensors) + Hospital Unit (presentation, diagnostic, and storage)	Socket method to establish communication connection between request (client) and service provider (server)	N/A	Not reported
75	Nintendo Wii® Remote (NWR) with ACC in the hand and IR camera	Motor performances executing mini-games	WiiPD system: A motor assessment module, a nonmotor assessment module, a metric analyzer, and a visualization engine	Not reported	Dataset: 5 HC. Results: simulated symptom group is well recognized from the health group.	Department of Employment and Learning Higher Education Innovation Fund (Ulster University, North Ireland)

ACC, accelerometer; ADL, activities of daily living; FOG, freezing of gait; GYR, gyroscope; HC, healthy subjects of controls; N/A, not available; PD, Parkinson's disease; TUG, Time Up and Go.

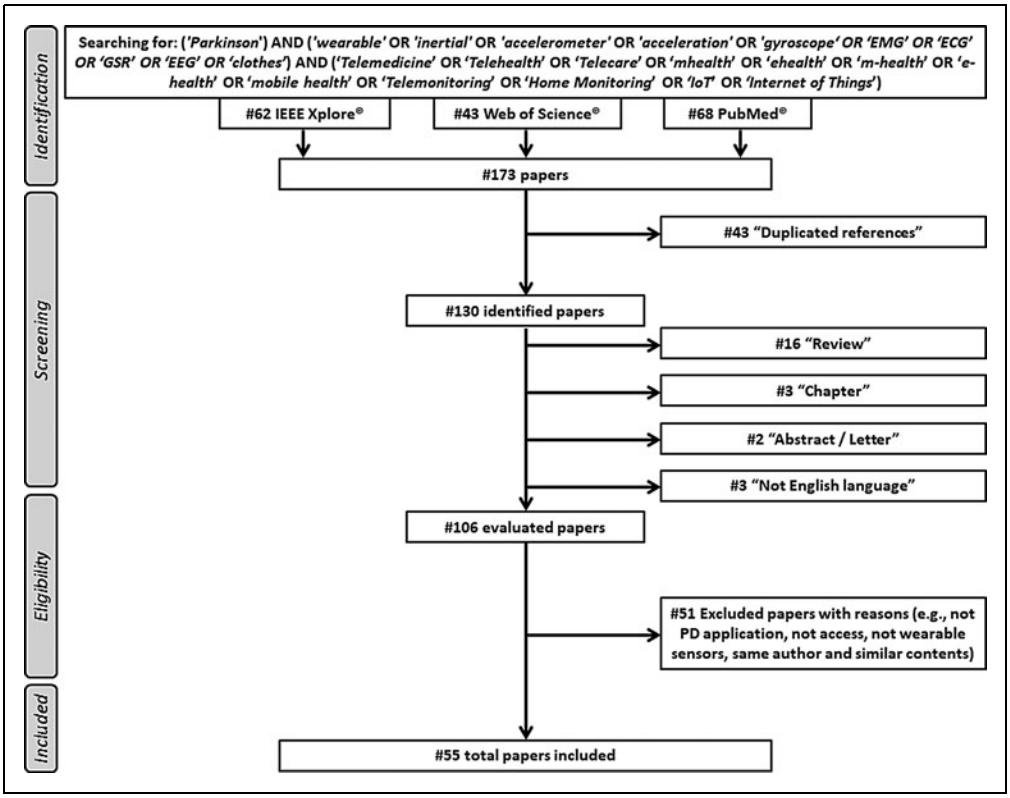

Fig. 1. Selection flowchart according to PRISMA statement.

subjects, so classification approaches were unreliable, and the statistical analysis was limited to significance and correlation of the features,[29,39–42,45,46] or it was conducted only visually[43,48,49] or qualitatively.[24,32–35,37,50] In *Table 1* are reported all the articles that performed tests at home (or simulated home[28,29]), including systems implementing also mobile apps,[45,50] a Web-based telemedicine system,[48] and the combination of all these topics.[22,23,35,37]

MOBILE APPS FOR PD

In agreement with the large use of smartphones in the population, mobile applications (m-apps) are commonly used in many fields (e.g., gaming and fitness). Healthcare, in particular, is one of the most typical fields for number of applications developed and downloaded.[51] The idea to design mobile apps for monitoring and assessing one or more symptoms in PD reflects the patients' needs to have an objective support for health monitoring during their daily activities without impact on them, both physically and socially.

In *Table 2* are reported only the works in which a mobile app was developed; m-apps tested at home are already reported in *Table 1*,[22,23,35,37,45,50] and articles that included m-apps in a complete telemedicine system are reported in *Table 3*. The mobile apps can be used directly on the patient's own smartphone or smartwatch, without additional devices, minimizing their obtrusiveness,[22,37,52–54] or they can be integrated with other sensors to improve the measurement capability.[23,35,55–57] They can

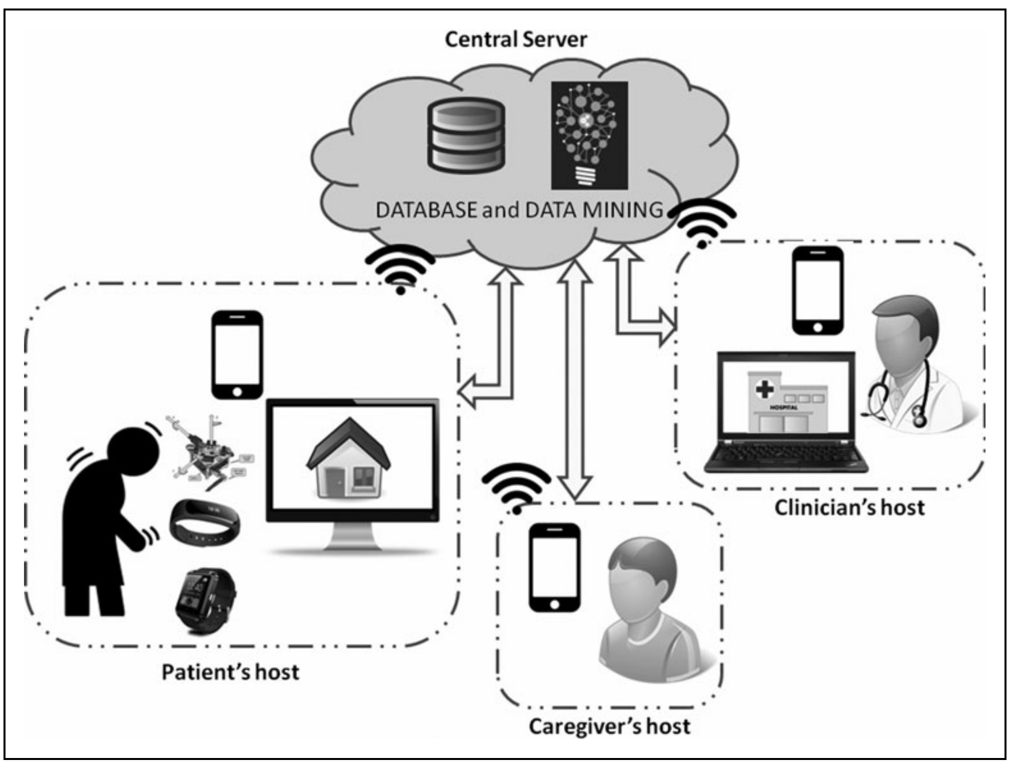

Fig. 2. The architecture of a general telehealth system.

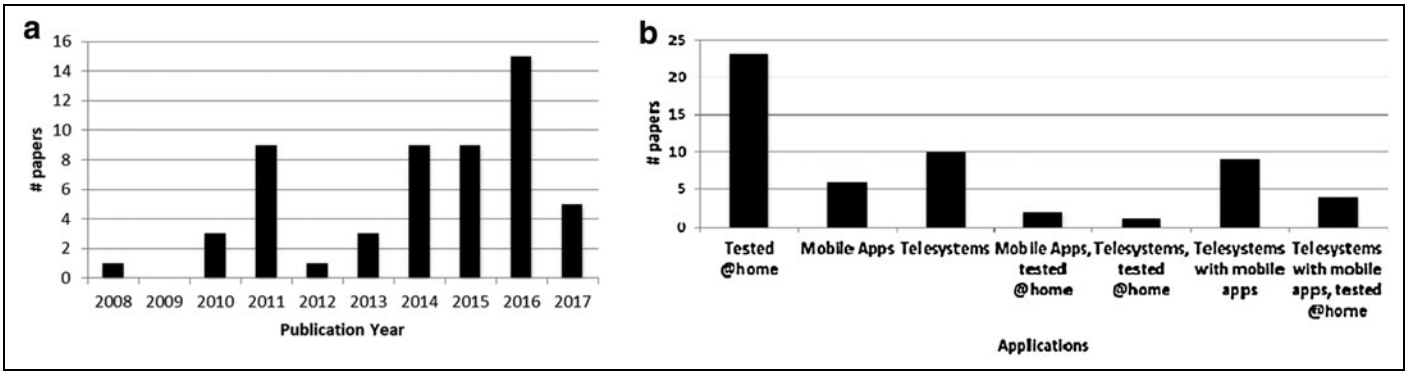

Fig. 3. Publication trend per year **(a)**; paper distribution per application **(b)**.

allow the recording of specific exercises (e.g., tremor analysis and TUG test),[52–54] as well as monitoring and recording of patients over several hours.[23,35,50,55] The apps can offer corrective feedback as well, encouraging the patients, for instance, to improve their physical activity or medical adherence.[35]

TELEHEALTH SYSTEMS

The implementation of e-Health or IoT systems is currently the final goal to have a valid solution for PD remote management (*Table 3*). Such systems included automated systems for the assessment and/or monitoring of specific symptoms,[22,23,35,37,48] and they developed also mobile[58–66] or Web-based[48,67–69] applications that allow both the patients and the clinicians to easily access the system through appropriate user interfaces. These systems would practically provide a modern telemedicine service using cloud platforms and server applications in which smart algorithms are implemented to analyze the acquired data (*Fig. 2*). Such systems allow a large amount of data to be transferred and managed, providing both the clinicians and the patients with useful information about disease progression and health conditions.

Long-term monitoring at home,[67] eventually during activities of daily living (ADL),[59] can be useful for the management of both early-mild patients by permitting the evaluation of the response to drug delivery[68,70] and for mid-advanced patients in which severe impairments such as ON-OFF motor fluctuation,[58,65] levodopa induced dyskinesias,[23] and FOG[22,71] often appear.

The motor analysis of standardized MDS-UPDRS III tasks (e.g., forearm pronosupination, heel tapping, gait, and tremor)[35,48,60–64,66,69,72–74] is another fundamental application that enables clinicians to have objective results about patients' motor performance over time, supporting remote differential diagnosis. Motor performance could also be assessed during ADL[59] or by executing virtual games.[75] Alternative systems involved speech analysis[37] and facial recognition[64] as well, which can add useful information about disease onset and progression, as described in MDS-UPDRS tasks 3.1, 3.2.

Since sensitive data are acquired, processed, and stored in the cloud, secure data transmission and privacy represent important issues to address by adopting preventative measures for data protection.[23,35,37,60,61,63,65,67,68,71–74]

Discussion

The increasing rate in age-related pathologies such as Parkinson's disease is causing an increase of chronic patients, with worsening in their QoL. These people need long-term treatments, therapy adjustments, and monitoring, but often, clinical examinations in hospitals are not sufficient for optimal management of the pathology due to long waiting lists, high traveling distance, working hours lost, etc.

The possibility to monitor the patients at home enables the evaluation of many aspects that are not always evident or are infeasible to assess during neurological examinations in clinic, including motor fluctuations and dyskinesias,[25–31] freezing events,[21,71] response to therapy adjustments before and after medical intakes,[29,43,47] and eventually correlated pathologies (e.g., cardiac activities).[56] Furthermore, the use of a monitoring system in the home environment could eliminate the "white coat effect," which is responsible for better performance in the hospital rather than during daily living activities.[44,56]

Acceptability,[32,34,68] usability,[35,50,62] and wearability[33] are all considerations that require particular attention to have an efficacious system that will actually be used by patients, without affecting their daily activities, both physically, avoiding impairments due to obtrusive heavy devices, and socially, avoiding devices that could be embarrassing and invasive for the users when they are in the community. For these reasons, the use of smartphones[52,56] or jewelry-like wearable sensors,[76,77] which are common technological tools, seems to be the best solution to have a portable inexpensive instrument, which is socially accepted and easy to use. Particularly, using internal sensors and algorithms of a smartphone prevents the need for additional hardware, almost for some kind of assessment.

Usability and acceptability from users' perspective are important issues for an operative and effective telemedicine system, as mentioned in several articles included in this review. Nevertheless, just few works reported quantitative results about them. In particular, Ferrari et al.[35] administered to the users a questionnaire based on a five-point Likert scale for the CUPID system usability and feasibility evaluation. They reported a satisfactory result, with a mean value of 4.5 out of 5. Similarly, Ginis et al.[45] also investigated usability for the CUPID system, obtaining very positive responses, as scores on user-friendliness were on average above 4 on a 5-point scale. Ferreira et al.,[50] also proposed to assess the usability of another system, the SENSE-PARK system, that achieved mean score of 2.67 out of 5 on the PSSUQ.

Another matter of debate is the optimal number of sensors to use, because preliminary results suggested that reducing them may lead to loss of potentially relevant information, especially for PD patients, who show a large variability in movements.[49] However, in accordance with literature, generally less than four sensor devices were used.[58] Anyway, energy harvesting approaches should be investigated because devices with long battery life are mandatory for long-term monitoring in unconstrained environments.[72,73]

The use of a tele-system for automated assessment of PD symptoms could support the neurologist in remote differential diagnosis, as well as through decision-making support systems.[58,65] While the test results are automatically uploaded into patient medical records, the system could provide instantaneous feedback to the users,[35,52,66] allowing the patients to obtain immediate results about their current condition without the direct involvement of any clinics.[63]

Since telehealth systems acquire and manage a wide amount of data, machine learning techniques are needed for their processing, analysis, and aggregation; thus, the results could be appropriately showed to patients and/or clinical staff, through smart user interfaces.[22,23] Technically, the management of a large amount of data requires attention to data loss and correct transmission of data.[25,67,73] Ethically, since sensitive data are acquired and processed, adequate measurements for data protection should be applied, including restricted and authenticated access to data,[22,60,63] secure encrypted data transmission (e.g., SSL, SSH, VPN, and TLS protocols),[65,67–69,72] and anonymized personal data.[59]

As limitation, most of the articles included in this review involve a limited number of subjects in the experimental sessions and have a lack of randomization, potential recall bias, and likely selection bias. Thus, the clinical validation of the proposed systems cannot be addressed,[73] and further investigations are required. In addition, sociocultural factors are usually not investigated in these works; therefore, there is a lack of information concerning the influence of relatives on telemedicine services and how gender, education, and working condition could affect their design and provision.

Finally, the development of telehealth systems is a step beyond the simple use of wearable sensors at home, because it means actively including patients and caregivers in the healthcare path,[25] promoting their empowerment in the management of their health status and disease progression through a conscious involvement.[58] The concept, indeed, is to transform the patients from end users to the main actors of the healthcare process, favoring the participation and cooperation of patients, caregivers, and clinical staff[25] to provide the best care available for each patient according to the precision medicine approach. Appropriate training sessions would be organized to enable people to correctly use the system. The possibility to have a more personalized therapy[31] seems also to increase the feeling of assurance of the patients regarding the appropriate healthcare path to follow.[65]

Generally, the adoption of telemedicine should be accompanied with the transformation of healthcare sector and overcome specific barriers. In terms of organization of the healthcare sector, reimbursement profiles should be defined considering which patients may benefit most and understanding the optimal frequency of telemedicine visits as replacement for in-person encounters.[78] Furthermore, a uniform regulation is missing in the domain of medical liability, at national and international level, thus hampering the development of telemedicine market in health services.[79] Telemedicine requires ubiquitous, adequate affordable broadband to support health information exchange to increase access to quality care for all individuals at the right place and the right time when it is needed.[78]

Conclusions

This review article provides an exhaustive overview of automated systems based on wearable and portable technologies for remote assessment and management of Parkinson's disease. The articles were divided into three categories according to the level of development of the implemented system, considering the automatic evaluation at home of PD symptoms and impairments, the development of mobile applications for PD assessment, and the design of e-Health systems for a complete remote healthcare service. Although they raised limitations, the use of such systems has the potentiality to enhance the PD management and treatment, supporting clinicians in remote monitoring and promoting the active engagement of the patients and their caregivers in the healthcare path. This aims to improve both patients' QoL and clinicians' quality of care toward an optimal personalized therapy.

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Authors' Contributions

ER was responsible for article structure and writing, synthesizing the information from the articles into text and tables. CM was the clinical supervisor, responsible for clinical aspects and contributing in introduction, methodology definition, and search strategies. FC was the scientific supervisor and contributed in methodology definition, article writing, discussion, and conclusion. All authors were involved in article screening and selection. All authors read, provided feedback, and approved the final article.

Disclosure Statement

No competing financial interests exist.

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