Handbook of Research on Trends in the Diagnosis and Treatment of Chronic Conditions

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Chapter 23
Trends and New Advances on Wearable and Mobile Technologies for Parkinson's Disease Monitoring and Assessment of Motor Symptoms:
How New Technologies Can Support Parkinson's Disease

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ABSTRACT

The aim of this work is to analyze the trends and new advances carried out in the last decades in the field of Parkinson's disease monitoring and management and more specifically regarding wearable and mobile technologies. The challenges of such technologies is to monitor, to assess and to manage the full range of PD symptoms through monitoring and testing routines while not hampering the patient's daily activities, identifying the correlation between the different dimensions affecting the severity of symptoms and the evolution of the disease and enabling the clinician to manage more efficiently the patient by providing timely indications on the effectiveness of the therapy and suggestions on therapy changes.

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INTRODUCTION

Parkinson's disease (PD) is a degenerative neurologic disease. Degenerative means "declining in quality"; thus, it increases in severity over time and neurologic refers to the nervous system. Therefore, PD is a disease of the nervous system that gets worse over time. It is also a chronic, progressive neurologic disease. Chronic means "of long duration" and progressive means "proceeding in steps" or "advancing". PD does not go away and it gradually gets worse (Weiner, Shulman, & Lang, 2013). Although it is possible that it starts earlier, PD is extremely linked with age and the average onset age is after 60 years old. For this reason, due to the current trends of population ageing, PD is getting more and more significant in several countries. To many people, the term Parkinson's disease is synonymous to having a tremor. However Parkinson's disease is much more than suffering a tremor (Perkin, 1998; Tugwell, 2008), though this is indeed one feature of the disease that occurs in the majority of patients. Equally, there are many causes for having a tremor apart from Parkinson's disease. The cardinal features of PD are resting tremor, rigidity, bradykinesia (or slowness) and gait disturbance with disequilibrium (Obeso, Olanow, & Nutt, 2000). PD is an age-related illness primarily affecting the elderly population and often resulting in a marked decline in the quality of life of both patients and caregivers (Cubo et al., 2005). Parkinson's disease is a progressive neurodegenerative condition characterized and diagnosed by the presence of motor and non-motor symptoms (Lebouvier et al., 2010). Symptoms tend to appear gradually, normally in just one side of the body at first, although both sides will be affected as Parkinson's progresses. PD follows a slowly chronic progressive course, and the motor cardinal symptoms of the disease appear only when the degenerative process has progressed for a long time (Lebouvier et al., 2010), in most cases probably for more than 10 years (Hawkes, Del Tredici, & Braak, 2007). Currently, diagnosis and progression of PD is based mainly on clinical criteria. Diagnosis of PD relies on the presence of two out of three of major motor signs, namely tremor, bradykinesia, and hypertonia, implying that the diagnosis is made only many years after the real onset of the neurodegenerative process (Hughes, Daniel, Ben-Shlomo, & Lees, 2002).

BACKGROUND

The concept of monitoring individuals in the home and community settings was introduced more than 50 years ago, when Holter monitoring was proposed (in the late 1940s) and later adopted (in the 1960s) as a clinical tool. However, technologies to fully enable such vision were lacking and only sporadic and rather obtrusive monitoring techniques were available for several decades (Paolo Bonato, 2010). Recent advances in mobile and wearable technology have provided means to supplement the information gathered using tools based on patient's direct observation as well as interviews and questionnaires. The growth of mobile technologies has been raising in the last decades for general purpose, and consequently a new generation of wearable sensors and systems has recently become available thus providing clinical personnel with a "window of observation" in the home and community settings. These tools allow one to capture patients' activity level and exercise compliance, facilitate titration of medications in chronic patients, and provide means to assess the ability of patients to perform specific motor activities (Paolo Bonato, 2009). Wireless Body Area Networks (WBANs) of intelligent sensors represent an emerging technology for system integration with great potentials for unobtrusive ambulatory health monitoring during extended periods of time (E. Jovanov, 2005).

PARKINSON'S DISEASE MONITORING, ASSESSMENT AND MANAGEMENT

In Europe, each neurologist or general practitioner (GP) normally cares for 50 to 800 patients with PD. The range in workload is a result of diversity both in national health systems and in the availability of clinical resources across Europe. Even at 50 patients per clinician, this represents a serious challenge to homecare monitoring for specialized conditions. PD patients normally visit their specialized clinician or GP every 4-6 months. As a result, any changes in the patient's conditions may not be recognized for several months, unless the patients themselves make contact (Greenlaw et al., 2009; Pastor-Sanz, Pansera, Cancela, Pastorino, & Waldmeyer, n.d.). Commonly in clinical practice, apart from the visits to the hospital, patients are asked to self-report their health status, for example, by asking patients to recall the number of On and Off hours (motor fluctuations). This kind of self–report is subject to perceptual bias (e.g. patients often have difficulty distinguishing dyskinesia from other symptoms) and recall bias. Another approach is the use of patient diaries, which can improve reliability by recording symptoms as they occur, but does not capture many of the features useful in clinical decision making (Group, 2001; Pastor-Sanz et al., n.d.). On the other hand, during the short office visit in his neurologist the patient may appear very well and he misses to report symptoms of wearing off. As a result, treatment modifications are not undertaken in time (Pastor-Sanz et al., n.d.). Moreover, understanding the process is not an easy task, motor performance throughout the day mainly depends on the intermittent dopaminergic drug intake, even in influence by timing and quantity of each individual dose of levodopa, as well as, other phenomena, such as delayed response or no-response depends also on stress, food intake and many other factors. Patients will greatly benefit from a quantitative objective assessment tool of their motor status in daily life in relation to the dosing schedule (Pastor-Sanz et al., n.d.). This scenario manifests several weaknesses in the treatment and management of PD patients but also, it reveals the deficiencies in the management of PD from the health care systems, either from the clinical practice as well as from the health care providers. This situation contrasts with other chronic conditions such as diabetes and cardiovascular diseases where available low-cost monitoring tools for years (glucometers and portable Holters) allowing the clinicians to know much better the progression of the disease on their patients. Telemedicine brings healthcare delivery to the home environment by connecting the patient with medical professionals. It is not intended to replace health professional care or visits, but rather to enhance the level of care (Polisena, Coyle, Coyle, & McGill, 2009). Telemedicine programs can reduce healthcare utilization through early detection of a worsening condition, timely treatment, and the avoided need for further tests (Jorge Cancela, Arredondo, & Hurtado, 2013).

RELATED RESEARCH WORKS

Inertial Sensors

An Inertial Measuremen.t Unit (IMU) works by detecting the current rate of acceleration using one or more accelerometers, and detects changes in rotational attributes along the reference axis through one or more gyroscopes. It is important to understand that even the gyroscopic information is liked with the orientation of the device in the space (pitch, roll and yaw using) this information is not directly provided by the gyroscopes themselves, instead this kind of sensors provide the angular velocity respect to the different rotation axis. For this reason, some IMUs also include a magnetometer, mostly to assist calibrate against orientation drift. Since PD major symptoms are related to motor performance, inertial sensors have been used as monitor tool during the last years.

The use of IMU has been explored as feasible solution to monitor and assess the different motor symptoms of PD, with special emphasis on the cardinal motor symptoms. (Russmann et al., 2004; A Salarian, Russmann, Vingerhoets, Burkhard, & Aminian, 2007; A Salarian, Russmann, Vingerhoets, Burkhard, Aminian, et al., 2007; A Salarian, Russmann, Wider, et al., 2007; Arash Salarian et al., 2004) at the École Polytechnique Fédérale de Lausanne, Switzerland, developed and validated a comprehensive system for PD motion monitoring based on a portable data-logger with body-fixed inertial sensors. This equipment was used to the ambulatory monitoring of physical activities in Parkinson's disease patients, the long term assessment of gait, tremor, dyskinesias, On-Off fluctuations and bradykinesia. (Griffiths et al., 2012) worked in an objective, continuous and automatic assessment of bradykinesia and dyskinesias using inertial sensors. The output of the algorithm calculates dyskinesia and bradykinesia scores every two minutes. (Lo, Suresh, Stocco, González-Valenzuela, & Leung, 2011) have been working also in the automatic detection of dyskinesias, using three pairs of wireless inertial sensors, aimed at efficiently timing the self-administration of prescription drugs in PD patients. (Zwartjes, Heida, van Vugt, Geelen, & Veltink, 2010) built an ambulatory monitoring system that provides a complete motor assessment by simultaneously analyzing current motor activity of the patient (e.g., sitting, walking, etc.) and the severity of tremor, bradykinesia, and hypokinesia using a set of four inertial sensors.

The gait kinematics and the assessment of the human walking pattern in PD is a recurrent use of IMU sensors. (Barth et al., 2011) built a mobile, lightweight and easy applicable sensor system to measure gait patterns in PD and to distinguish mild and severe impairment of gait. Subjects performed standardized gait tests while wearing sport shoes equipped with inertial sensors. Signals were recorded wirelessly and features were extracted in a computer. This method was able to classify patients and controls as well as to distinguish mild from severe gait impairment. (Baston, Mancini, Schoneburg, Horak, & Rocchi, 2014) introduced an instrumented method to characterize postural movement strategies to maintain balance during stance (ankle and hip strategy), by means of inertial sensors, positioned on the legs and on the trunk.

Very linked to the gait assessment, many works focus their aim in the identification of the Freezing of Gait (FoG) episodes, especially due to their impact on the daily life of the patients. Steven T. Moore and colleagues at the Mount Sinai Hospital in New York, US have developed and validated a system for long-term monitoring of gait in PD. The characteristics of every stride were taken over 10-h epochs were acquired using a lightweight ankle-mounted sensor (accelerometer and gyroscope) array that transmitted data wirelessly to a small pocket PC at a rate of 100 Hz. A global threshold detected 78% of FoG events and 20% of stand events were incorrectly labeled as FOG. Individual calibration of the freeze threshold improved accuracy and sensitivity of the device to 89% for detection of FOG with 10% false positives. This system was also used to quantify the dynamic response of locomotion to the first oral levodopa administration of the day in patients with fluctuating PD. The small, variable stride length characteristic of Parkinsonian gait, and fluctuations of efficacy associated with levodopa therapy, such as delayed onset, wearing off, and the On-Off effect, could reliably be detected from long-term changes in stride length using this system (Moore, Dilda, Hakim, & Macdougall, 2011; Moore, MacDougall, Gracies, Cohen, & Ondo, 2007; Moore, MacDougall, Gracies, & Ondo, 2008; Moore, MacDougall, & Ondo, 2008). (Sama, Pardo-Ayala, Cabestany, & Rodríguez-Molinero, 2010) worked in the automatic estimation of spatio-temporal gait properties from signals provided by inertial body sensors. The approach is based on time series analysis. The human gait is represented as a dynamical system (DS), which internal states are hidden. Daily living activities are detected and spatiotemporal parameters of human gait are estimated using methods sharing a common structure based on feature extraction and kernel methods (Samà, Angulo, Pardo, Català, & Cabestany, 2011).

Eventually, inertial sensors are combined with other kind of sensors or data inputs to enhance the characterization of PD abnormalities. (Kimura et al., 2007) combined 3 inertial sensors and 8 dry-type EMG surface differential electrodes to study the perturbation occurrence during walking and (Sanders, Devergnas, Wichmann, & Clements, 2013) investigated how EEG readings can be used together with inertial movement measurements.

Also, IMUs can be part of more complex systems, for example, the detection of FoG events can be combined with the use of auditory cues helping the patient to "unfreeze" when a FoG event is detected. (Mazilu, Blanke, Hardegger, Troster, et al., 2014; Mazilu, Blanke, Hardegger, Tröster, et al., 2014) presented a real-time auditory system for cueing after the onset of freezing episodes. It detects freezing episodes from ankle-mounted motion sensors, which stream data via a mobile phone. Their final system was able to detect FoG events with an average sensitivity and specificity of more than 95%, and mean detection latency of 0.34s in user-dependent settings (Mazilu et al., 2012). Jovanov et al. (2005, 2009) built a wearable, unobtrusive system for real-time gait monitoring, which consists of an inertial wearable sensor and wireless headset for the delivery of acoustic cues. The system recognizes FOG episodes with minimum latency and delivers acoustic cues to unfreeze the gait (E Jovanov, Wang, Verhagen, Fredrickson, & Fratangelo, 2009; Emil Jovanov, Milenkovic, Otto, & De Groen, 2005). Another example of application is the IMU integration on games, (Tous et al., 2014) integrated a network of on-body inertial measurement units with a platform that allows patients to perform rehabilitation exercises through a variety of videogames and interaction methods.

Some works involving inertial sensors are related to the automatic identification of daily activities by PD patients such as (Zhang, Markovic, Sapir, Wagenaar, & Little, 2011) and (Martín et al., 2013).

(Giuffrida, Riley, Maddux, & Heldman, 2009) and (Heldman et al., 2011) designed, built and assessed Kinesia™ for automated assessment of PD tremor using the accelerometers and gyroscopes in a compact patient-worn unit to capture kinematic movement disorder features. In this study, PD subjects performed the tremor subset of the UPDRS motor section while wearing Kinesia™. Quantitative kinematic features were processed and highly correlated to clinician scores for rest tremor ($R2 = 0.89$), postural tremor ($R2 = 0.90$), and kinetic tremor ($R2 = 0.69$). The quantitative features were used to develop a mathematical model that predicted tremor severity scores for new data with low errors. Kinesia™ has been also employed for automated tremor and bradykinesia severity score assessments at home. By completing motor exams 3–6 times per day over 3–6 days (Mera, Heldman, Espay, Payne, & Giuffrida, 2011).

(Tsipouras et al., 2012) (Tsipouras et al., 2010) proposed an automated levodopa-induced dyskinesia (LID) assessment based on the analysis of signals recorded from several accelerometers and gyroscopes. The analysis was performed related to the number and topology of sensors used; several different experimental settings were evaluated while a 10-fold stratified cross validation technique was employed in all cases. Moreover, several different classification techniques were examined. The ability of the methodology to be generalized was also evaluated using leave-one-patient-out cross validation. The obtained results indicate high classification ability (93.73% classification accuracy).

Accelerometers

Even whether the inertial sensors have been proved to be an outstanding tool for the detection and quantification of the motor symptoms in PD, some research works are focus on using exclusively the accelerometers for PD monitoring, in spite of the initial limitation, using only accelerometers brings the direct benefit of simplifying the hardware platform of the sensors and cost reduction. An accelerometer is a device that measures proper acceleration ("g-force"). Proper acceleration is not the same as coordinate acceleration or linear acceleration (rate of change of velocity). For example, an accelerometer at rest on the surface of the Earth will measure an acceleration g = 9.81 m/s2 straight upwards. In the same way that with the inertial sensors, different combinations of Body Area Networks (BAN) have been tested in combination with diverse kinds of algorithms in order to achieve the PD assessment of motor symptoms.

(Van Emmerik & Wagenaar, 1996) performed one of the first studies using accelerometer data to assess the dynamics of movement coordination and tremor during gait in PD. Parkinson's disease patients showed overall less adaptations in relative phase than the control group, especially those involving the upper extremities. In The Netherlands, Keijsers et al. carried out several research works using four pairs of triaxial accelerometers mounted on the wrist, upper arm, trunk, and leg on the most affected side in combination with neural networks to detect and quantify the dyskinesia and LID as well as to study the motor fluctuations in PD patients (Keijsers, Horstink, Van Hilten, Hoff, & Gielen, 2000; Keijsers, Horstink, & Gielen, 2003a, 2003b, 2006).

Based on a preliminary work on data mining and artificial intelligence systems carried out by (P Bonato, Sherrill, Standaert, Salles, & Akay, 2005), (Sherrill et al., 2005), (S Patel et al., 2006, 2007; Shyamal Patel et al., 2009; Shyamal Patel, Hester, et al., 2008; Shyamal Patel, Hughes, et al., 2008) and (Lorincz et al., 2007) continued using wearable sensors to predict the severity of symptoms and motor complications in Parkinson's disease. Within these works they determined the optimal window length to extract features from the sensor data, the optimal parameters for the SVM's and also analyzed how well individual tasks performed by patients captured the severity of various symptoms and motor complications. A significant decrease in the prediction error (for tremor, bradykinesia, and dyskinesia) was seeing when increasing the window length from 1 second to 4 second, whereas prediction error values appear to plateau with a window of 5 second or longer. Average prediction errors for a window of 5 second were below the 5% target set when simulations were performed for all the symptoms and motor complications. They tested also the performance of these algorithms by using different SVM's kernels. No major differences were observed in prediction error values across the three kernels. Interestingly, differences were noted when the misclassification cost parameter "C" that led to minimum prediction error values for each of the kernels was taken into consideration. In general, a decrease in prediction error values was observed for all kernels when they increased the misclassification cost parameter "C" from 0.1 to 1000. No significant decrease in prediction error values was observed for the results derived using the polynomial kernel for "C"-values greater than 10, whereas a significant decrease in prediction error values for the exponential and the radial basis kernels was observed when the "C"-value was further increased to 100. Later, they studied the impact on the estimation error of utilizing different combinations of the feature types. Results indicated that it is possible to reliably estimate clinical scores on the basis of three feature types that are compatible with implementation on the SHIMMER platform: the RMS value, the data range value, and two frequency-based features (i.e., the dominant frequency and the ratio of energy of the dominant frequency component to the total energy). They achieved average estimation error values of 3.4% for tremor, 2.2% for bradykinesia, and 3.2% for dyskinesia. Later, in 2011, they validated a longitudinal tracking of severity of motor symptom m in PD using wearable sensors is feasible. Showing that they were able to track UPDRS scores for two tasks by using a regression Random Forest to within 0.5 points on a scale of 0-4. They observed that the estimation of scores for alternating hand movement task (AHL/AHR) was more accurate than leg agility task (LAL/LAR) (Shyamal Patel et al., 2011). Finally, (B. Chen et al., 2010; B.-R. Chen et al., 2011; Shyamal Patel et al., 2010) built and validated the integration of these wearable technologies with a web-based application. It is aimed to the development of a home-monitoring system used to objective longitudinal monitoring of symptoms patients with Parkinson's disease who experience severe motor fluctuations.

(LeMoyne, Mastroianni, Cozza, Coroian, & Grundfest, 2010) initial testing and evaluation of the iPhone wireless accelerometer application for quantifying Parkinson's disease tremor. Moreover, they proposed a device with a wireless and potentially wearable 3D MEMS accelerometer mounted on the dorsum of the hand to track the Parkinson's disease for quantifying Parkinson's disease hand tremor using accelerometer nodes and gloves (LeMoyne, Coroian, & Mastroianni, 2009; LeMoyne, Mastroianni, & Grundfest, 2013).

Lord et al. (2008) validated an ambulatory monitoring device that uses accelerometer signals to assess the quality and quantity of walking and mobility related activities in home and community. They measured gait speed, step length and step frequency during a test of functional gait that included single, dual and multiple task components (Lord, Rochester, Baker, & Nieuwboer, 2008).

(Barroso et al., 2011; Gil, Nunes, Silva, Faria, & Melo, 2010; Júnior et al., 2011) examined the effect of PD on the complexity of the tremor time series of PD patients using the Approximate Entropy method (ApEn) from accelerometers signals. ApEn differenced physiological tremor from tremor in PD patients with high accuracy. (Pansera et al., 2009) studied also the variation of Sample Entropy in the acceleration signals as indicator of the gait performance. Results show considerable differences between the patients and the subjects, both for sample entropy (in 3 of the 5 sensors) and in the gait asymmetry index (left vs. right limbs). (Dijkstra, Kamsma, & Zijlstra, 2010; Dijkstra, Zijlstra, Scherder, & Kamsma, 2008) worked on the detection of the walking periods and postures using a single small body-fixed accelerometer in patients with mild to moderate Parkinson's disease. They worked also in the development of algorithms for the detection of the step length, step frequency and other gait features based only on the fluctuations of an accelerometer in the patient trunk. The algorithm is known as the inverted pendulum model and its variations.

(Palmerini, Rocchi, Mellone, Valzania, & Chiari, 2011) carried out a study to assess the feasibility of using accelerometers to characterize the postural behavior of early mild PD subjects. A total of 175 measures were computed from the signals to quantify tremor, acceleration, and displacement of body sway. Feature selection was implemented to identify the subsets of measures that better characterize the distinctive behavior of PD and control subjects. It was based on different classifiers and on a nested cross validation, to maximize robustness of selection with respect to changes in the training set. Several subsets of three features achieved misclassification rates as low as 5%. Many of them included a tremor-related measure, a postural measure in the frequency domain, and a postural displacement measure. Results suggest that quantitative posture analysis using a single accelerometer and a simple test protocol may provide useful information to characterize early PD subjects as well as the disease's progression. Additionally, (Palmerini, Mellone, Avanzolini, Valzania, & Chiari, 2013b) studied the feasibility of deploy an instrumented Timed Up and Go Test (TUG) for PD subjects.

A single accelerometer, worn at the lower back, was used to record the acceleration signals during the test and acceleration-derived measures were extracted from the recorded signals. A subset of three features (two from Turning, one from the Sit-to-Walk component), combined with an easily-interpretable classifier (Linear Discriminant Analysis), and was found to have the best accuracy in discriminating between healthy and early-mild PD subjects. Also, (Palmerini, Mellone, Avanzolini, Valzania, & Chiari, 2013a) assessed the feasibility of using accelerometers to classify early PD subjects (two evaluations over a 1-year follow-up), satisfactory accuracies were obtained in the classification of PD subjects by using an ad hoc wrapper feature selection technique. (George Rigas, Tzallas, Tsalikakis, Konitsiotis, & Fotiadis, 2009) built a system able to perform a real-time quantification of resting tremor in the PD. The behavior of the subjects is measured using tri-axial accelerometers, which are placed at four different positions on the body. Frequency-domain features, strongly correlated with the RT activity, are extracted from the accelerometer data. The classification of RT severity based on those features, provided accuracy 76%. Then, they extended the system to automatically detect both resting and action/postural tremor. The estimation of tremor type (resting/action postural) and severity is based on features extracted from the acquired signals and hidden Markov models. The obtained results verified that the proposed method successfully: 1) quantifies tremor severity with 87% accuracy, 2) discriminates resting from postural tremor, and 3) discriminates tremor from other Parkinsonian motor symptoms during daily activities (G Rigas et al., 2012). (Exarchos et al., 2012) presented a method based on partial decision trees and association rules for the prediction of PD symptoms. The proposed method is part of the PERFORM system. PERFORM is used for the treatment of PD patients and even advocate specific combinations of medications (Tzallas et al., 2014). The accuracy of the symptoms' prediction ranges from 57.1 to 77.4%, depending on the symptom. (J Cancela et al., 2010) and (Pastorino et al., 2011) described a methodology to automatically detect the severity of bradykinesia in motor disease patients using wireless, wearable accelerometers. This methodology was tested with cross validation through a sample of 20 Parkinson's disease patients. The assessment of methodology was carried out through some daily living activities which were detected using an activity recognition algorithm. The Unified Parkinson's Disease Rating Scale (UPDRS) severity classification of the algorithm coincides between 70 and 86% from that of a trained neurologist depending on the classifier used. These severities were calculated for 5 second segments of the signal with 50% of overlap. (Louter et al., 2014) explored the use of a triaxial accelerometer as a tool to identify the risk of developing PD by quantifying nocturnal. Outcome measurements included mean acceleration, and qualitative axial movement parameters, such as duration and speed. Compared with controls, patients with PD had an overall decreased mean acceleration, as well as smaller and shorter nocturnal axial movements. (Bachlin et al., 2010; Bächlin et al., 2009; Marc Bächlin et al., 2009) developed a real-time wearable FoG detection system that automatically provides a cueing sound when FOG is detected and which stays until the subject resumes walking. This wearable system uses on-body acceleration sensors to measure the patients' movements. It automatically detects FOG by analyzing frequency components inherent in these movements. When FOG is detected, the assistant provides a rhythmic auditory signal that stimulates the patient to resume walking. The device detected the FOG events online with a sensitivity of 73.1% and a specificity of 81.6% on a 0.5 sec frame-based evaluation (M Bächlin et al., 2010).

Voice

Voice and speech is also affected in Parkinson's disease and the assessment of alterations on such aspects can be also relevant to evaluate the status and evolution of PD patients. (Rusz, Cmejla, Ruzickova, & Ruzicka, 2011) carried out a study to determine whether voice and speech disorder were present from early stages of PD. Within this work, it was found that measurement of the fundamental frequency variations applied to two selected tasks was the best method for separating healthy from PD subjects. It was demonstrated that 78% of early untreated PD subjects indicate some form of vocal impairment. The speech defects thus uncovered differ individually in various characteristics including phonation, articulation, and prosody. Khan et al. (2013, 2014) presented a method for assessing PD based on speech. A set of 13 features, including were used for training a Support Vector Machine (SVM) using n-fold cross validation. The classification accuracy of SVM was 85% in 3 levels of UPDRS-S scale and 92% in 2 levels with the average area under the Receiver Operating Characteristic (ROC) curves of around 91%. The strong classification ability of selected features and the SVM model supports suitability of this scheme to monitor speech symptoms in PD (Khan, Westin, & Dougherty, 2013, 2014)(M. A. Little, 2006; M. A. Little et al., 2007; M. A. Little, McSharry, Hunter, Spielman, & Ramig, 2009; M. Little, McSharry, Moroz, & Roberts, 2006; A Tsanas, Little, McSharry, & Ramig, 2011; A Tsanas, Little, McSharry, Spielman, & Ramig, 2012; Athanasios Tsanas, Little, McSharry, & Ramig, 2010) carried out an ambitious project aimed to collect 10.000 sustained phonations ("aaah" vocal sounds) through telephone-quality digital audio lines, under realistic, non-lab conditions, to test the hypothesis that it is possible to detect PD through these recordings. This follows up several previous studies in which they shown that this detection is possible with lab-quality digital audio recordings of sustained phonations, and that these results are not noticeably degraded when the audio is passed through simulated, low-bandwidth mobile telephone audio compression with channel distortion (A Tsanas, Little, McSharry, Spielman, & Ramig, n.d.). Furthermore, they were able to accurately predict the severity of PD symptoms using the UPDRS (A Tsanas et al., 2011). To detect Parkinson's from the voice, they extract a large number of dysphonia features (specifically 132 in previous studies (A Tsanas et al., n.d., 2012)) from digital audio signals of sustained phonations ("aaah" sounds). Then several feature selection algorithms (Lasso, mRMR, RELIEF, LLBFS (A Tsanas et al., 2012)) were applied, and passed the selected features to standard supervised classifier algorithms (random forests and SVMs). To address over fitting, cross-validation was used, both "leave audio samples out" and "leave subjects out" schemes, in order to approximate the true generalization performance on unknown cases (A Tsanas et al., 2011, n.d., 2012). Another approach followed was the use of multinomial logistic regression classifier with Haar wavelets transformation as projection filter that outperform logistic regression is used (Athanasios Tsanas et al., 2010).

They found that some of the recently proposed dysphonia measures complemented already existing algorithms in maximizing the ability of the classifiers to discriminate healthy controls from PD subjects reaching almost 99% overall classification accuracy using only ten dysphonia features (A Tsanas et al., 2012). In terms of detecting the disease, at best they achieved was 98.6% detection accuracy under lab conditions (A Tsanas et al., 2012). In terms of the severity of symptoms, the average prediction error is 3,5 points on the 176-point UPDRS scale (approx. 2% mean absolute, cross-validation error) under simulated mobile telephony conditions (A Tsanas et al., n.d.).

Shoe Sensors

As it was previously mentioned, PD disturbances have a huge impact on gait performance, for that reason the monitoring and assessment of the walking pattern subjects has been profoundly study. (Thalen, Marin-Perianu, Havinga, & others, 2007) integrated accelerometers into a shoe to study the gait performance in PD by using a low-power sensor node equipped with movement sensors. In addition, this system called SensorShoe, gives real-time feedback and therapy assistance to the patient, and provides the caregivers an effective remote monitoring and control tool. (Bae, Kong, Byl, & Tomizuka, 2011) developed a mobile gait monitoring system, based on a smart shoes, proposed for the diagnosis of abnormal gait and rehabilitation. It monitors PD patients' gait by observing the Ground Reaction Force (GRF) and the center of GRF, and analyzes the gait abnormality. (Mariani, Jimenez, Vingerhoets, & Aminian, 2013) also developed a wearable sensors on-shoe and processing algorithm, which provides outcome measures characterizing PD motor symptoms (accuracy ± precision of 2.8 ± 2.4 cm/s and 1.3 ± 3.0 cm for stride velocity and stride length estimation compared to optical motion capture). In addition, they use a novel spatio-temporal parameters, including turning, swing width, path length, and their intercycle variability, was also validated and showed interesting tendencies for discriminating patients in On-Off states and control subjects. (Morris & Paradiso, 2002) built a wireless wearable system that was developed to provide quantitative gait analysis outside the confines of the traditional motion laboratory. It includes three orthogonal accelerometers, three orthogonal gyroscopes, four force sensors, two bidirectional bend sensors, two dynamic pressure sensors, as well as electric field height sensors. The GaitShoe was used to study healthy and Parkinsonian gait (Bamberg, Benbasat, Scarborough, Krebs, & Paradiso, 2008) showing significant variations on stride length, stride time and the percentage of the stride spent in stance between healthy and PD subjects. (Jamthe, Chakraborty, Ghosh, & Agrawal, 2013) proposed a wireless monitoring of PD patients for fall detection based on an embedding force sensor into the subject's shoe. They also proposed a non-invasive, wireless technique that could detect multiple occurrences of Freezing of Gait (FoG).

(Heldman et al., 2012) developed and evaluated the algorithms for quantifying gait and lower extremity bradykinesia in patients with Parkinson's disease using kinematic data recorded on a heel-worn motion sensor unit. Multiple linear regression models were developed based on the recorded kinematic data and clinician scores and produced outputs highly correlated to clinician scores with an average correlation coefficient of 0.86. (Grandez, Bustamante, Solas, Gurutzeaga, & Garcia-Alonso, 2009) proposed a novel system for the monitorization of gait of patients affected by PD. Force Sensitive Resistors (FSR) are used, embedding them in an insole, which allows the capture and analysis of the gait over long periods of time and while the patient interacts with a natural (non-controlled) environments.

Telematic and Remote Visits

Following a different approach, ICT and new technologies have been used to connect patients and clinicians in order to allow physicians to carry out the examination through a telematic visit. Also, telerehabilitation has been employed. The telematic visit has the potential to deliver services in the home or local community via videoconferencing and through interactive computer-based therapy activities. This form of service delivery has the capacity to optimize functional outcomes by facilitating generalization of treatment effects within the person's everyday environment, and enable monitoring of communication and swallowing behaviors on a long-term basis.

Several works have been carried out to study the feasibility of using telematic services for remote assessment of Parkinson's disease patients, (Hubble, Pahwa, Michalek, Thomas, & Koller, 1993) tested the interactive video conference for the examination of PD patients, (Dobkin et al., 2011) examined the feasibility and effect of telephone-based cognitive–behavioral therapy for depression in PD, (Marzinzik et al., 2012) reviewed a telemedicine-based care model for drug optimization in PD, in this model patients send video recordings made in their homes to the treating team via the Internet. Also, for treatment optimization, (Fincher, Ward, Dawkins, Magee, & Willson, 2009) evaluated the usefulness and usability of follow-up telehealth medication counseling (both videophone and telephone. All these studies shown the feasibility of this kind of service delivery, some of the also conclude that it can benefit the therapy optimization (particular interest for patients with complex conditions who do not necessarily have to undergo hospital treatment), also videophone users were more satisfied with the equipment and counseling. Overall, videophone counseling sessions were significantly more useful than the telephone sessions. Nurses found visualization via videophone significantly more useful for medication and self-management interactions.

(Tindall, Huebner, Stemple, & Kleinert, 2008; Tindall & Huebner, 2009) from the Department of Veterans Affairs Medical Center, Lexington, Kentucky, USA have been working in the feasibility of delivery the Lee Silverman Voice Treatment (LSVT)® treatment through videophones placed in the homes of individuals with idiopathic PD offers an alternative and could improve accessibility of treatment. (Biglan et al., 2009; E. R. Dorsey et al., 2013; E. Dorsey et al., 2010; Rajan, Seidmann, Dorsey, Biglan, & Reminick, 2011) from Department of Neurology, University of Rochester Medical Center, Rochester, New York, USA conducted a randomized, controlled pilot trial to evaluate the feasibility, effectiveness, and economic benefits of using web-based videoconferencing to provide specialty care to patients with PD in their homes. Compared with usual care, those randomized to telemedicine had significant improvements in quality of life, motor performance and patient satisfaction. The visits resulted in improvements in motor and cognitive symptoms and suggest that telemedicine may be useful for delivering care to this population. Likewise, researchers at the University of Queensland in Brisbane in Australia have investigated the validity and feasibility of online delivery of the LSVT® as well as a telerehabilitation application for assessing the speech and voice disorder associated with PD such as dysphagia (a swallowing disorder), hypokinetic dysarthria, swallowing disorders. Online assessment of disordered speech and voice in Parkinson's disease appears to be valid and reliable (G. A. Constantinescu et al., 2010; G. Constantinescu et al., 2010, 2011; Sharma, Ward, Burns, Theodoros, & Russell, 2011, 2013; Theodoros, 2008; Theodoros et al., 2006).

Other

Apart of all the abovementioned systems, other alternatives have been proposed to assess efficiently PD patients by using a wide range of technologies and methods designed ad-hoc or based on commercial solutions already available in the market but not specifically designed fro PD assessment.

(Kupryjanow, Kunka, & Kostek, 2010) proposed a virtual-touchpad for the automatization of some UPDRS tests for the diagnosis of PD patients (Finger Taps test and the Rapid Alternating Movement of Hands test). (Aly, Playfer, Smith, & Halliday, 2007) assessed the suitability and clinical value of a low cost system for PD diagnosis, in particular the presence of tremor, by asking the patients to perform a shape-tracing task using a graphic tablet. (Smits et al., 2014) tried to assess whether standardized handwriting can provide quantitative measures to distinguish patients diagnosed with PD from age- and gender-matched healthy control participants. In this study, a pen tip trajectories were recorded during circle, spiral and line drawing and repeated character "elelelel" and sentence writing, performed by Parkinson patients and healthy control participants. The results of this work showed that PD patients were slower than healthy control participants. Westin et al. (2010, 2011) and Memedi et al. (2011) developed a test battery for assessing patient state in advanced PD, consisting of self-assessments and motor tests (tapping and spiral drawing tasks). Using statistical and machine learning methods, time series of raw data are summarized into scores for conceptual symptom dimensions and an "overall test score" providing a comprehensive profile of patient's health during a test period of about one week (Memedi, Westin, Nyholm, Dougherty, & Groth, 2011). The test battery could detect treatment effect both in self-assessments, tapping tests' results and Archimedes spirals scores (Westin, Dougherty, Nyholm, & Groth, 2010; Westin, Ghiamati, et al., 2010). Also, (Tucha et al., 2006) presented a study comparing kinematic aspects of handwriting movements both on their usual dopaminergic treatment and following withdrawal of dopaminergic medication

(Grandez, Solas, Bustamante, & Sedano, 2010), (Bustamante, Grandez, Solas, & Arrizabalaga, 2010) and (Bustamante et al., 2010) proposed a testing device for PD designed to carry out two of the most used tests for these patients: the finger-tapping test and the hand-grip strength test. It consists on a glove, equipped with Force sensitive Resistors (FSR), a tiny hardware device which gathers the data and a PC application, which presents the results to the doctors.

CONCLUSION AND FUTURE RESEARCH WORK

Parkinson's disease disturbs a wide range of the patients' capabilities especially those regarding the motor performance. For this reason most of the previous works are focused on the monitoring, assessment and management of the motor symptoms or signs. In many cases it has been shown that the analysis of motion features could lead to an objective and continuous monitoring of the PD patients. In a first approach, most of the works tried to detect and quantify the cardinal motor symptoms of PD as well as their gait performance. Then, the variation of the severity of the symptoms along the day can be certainly used for the identification of On-Off fluctuations. This information has an important clinical implication since it is an indicator that a medication adjustment is required.

Apart from these signals systems a wide amount of works related with telematic visit were found as well as the use of telematic services to facilitate the performance of several kinds of tests assesses the potential of computer games peripherals to measure the motor dysfunction in Parkinson's diseases is (with a particular interest in the quantification of bradykinesia). In some cases the outcome of the sensors are transmitted remotely to the hospital or to the research center, as well as the use of telematic services to facilitate the performance of motor tests remotely. Especially relevant is the case of all the sensors that can be used as wearable sensors, like the accelerometers or the inertial sensors, in this case, these sensors have been sometimes integrated with other sensors of the same kind conforming Body Area Networks (BAN) able to cover a wider range of symptoms or improving the accuracy in the detection and assessment of symptoms. Or even, they were integrated with other sensors conforming more complex systems such as closed-loop system (HELP project (Ahlrichs, Samà, Rovira Simón, Herrlich, & Rodríguez Molinero, 2013)), telehealth systems (PERFORM (Jorge Cancela, Pastorino, Arredondo, & Hurtado, 2013; Tsipouras et al., 2014; Tzallas et al., 2014)), platforms to deal with the FoG using cueing (CuPID (Casamassima et al., 2014; Casamassima, Ferrari, Milosevic, Rocchi, & Farella, 2013)) and also they have been integrated into a web-based applications enabling home monitoring of patients with (PD) using wearable sensors (Mercury (B. Chen et al., 2010; B.-R. Chen et al., 2011)).

A common problem faced in all cases is how to deal with the huge quantity of data generated by a continuous monitoring of patients and how to extract knowledge and clinically relevant information to help in the decision making process and in the end how to use the raw data collected in a smart way to help the clinicians, the patients and any other stakeholder involved in the process. For this reason, apart from the classic signal processing (data filtering, normalization, features extraction, etc…) a further analysis or processing is required. The employment of machine learning techniques such as classifiers or regressions has been a common practice improving the initial studies which were more focus on the simple signal and statistical analysis.

In any case, the growing number of mobile and wearable gadget represent a valuable opportunity also for the health sector. The familiarity, awareness and knowledge of the technology by the general users will promote the adoption of these technologies also for the healthcare routine. The use of WBAN or BAN merging data from the different sensors and/or tests carried out in a mobile app can cover a wider spectrum of symptoms or improve the characterization of the already known symptoms. Likewise, the combination of remote monitoring with telematic visits offers an interesting new approach.

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