WEARABLE DEVICES AND SMARTPHONES FOR PARKINSON'S DISEASE DIAGNOSIS

Sevasti Bostantjopoulou, Zoe Katsarou, Ioannis Dagklis
3rd Department of Neurology, Aristotle University of Thessaloniki

Abstract
Parkinson's disease(PD) is a common neurodegenerative disorder with a prevalence that is expected to increase in the next decades. The implementation of digital health technology (wearable devices and smartphones) in PD is promising. Wearable devices can capture subtle motor symptoms (voice ,facial expression, fine finger movements) and non-motor symptoms (REM sleep behavior disorder, gastric motility)thus improving early diagnosis, identifying prodromal PD and enabling population screening for PD. Furthermore sensors are useful for accurately and objectively evaluate and monitor in real life the motor (bradykinesia, tremor, gait parameters, freezing of gait, balance) and the non-motor symptoms of the disease as well as the treatment response and the fluctuations. Touch technology with keystrokes dynamics during typing a computer offers another opportunity for studying motor symptoms in PD. However there are limitations, barriers and risks on the use of digital technology. Further studies involving patients and caregivers will help implement technology in PD.

Key words: wearables, smartwatch, smartphone, Parkinson disease, digital technology

ΦΟΡΗΤΕΣ ΣΥΣΚΕΥΕΣ ΚΑΙ ΕΞΥΠΝΑ ΤΗΛΕΦΩΝΑ ΣΤΗΝ ΔΙΑΓΝΩΣΗ ΤΗΣ ΝΟΣΟΥ ΠΑΡΚΙΝΣΟΝ

Σεβαστή Μποσταντζοπούλου ,Ζωή Κατσαρού ,Ιωάννης Δαγκλής
Γ΄ Νευρολογική Κλινική ,Αριστοτέλειο Πανεπιστήμιο Θεσσαλονίκης

Περίληψη
Η νόσος του Parkinson (NP) είναι μία συχνή νευροεκφυλιστική διαταραχή της οποίας η συχνότητα αναμένεται να αυξηθεί τις επόμενες δεκαετίες. Η εφαρμογή της ψηφιακής τεχνολογίας (φορητοί αισθητήρες/συσκευές και έξυπνα τηλέφωνα) στην NP είναι πολλά υποσχόμενη. Οι φορητοί αισθητήρες/συσκευές και τα έξυπνα τηλέφωνα μπορούν να ανιχνεύσουν ελαφρά κινητικά συμπτώματα (μεταβολή της φωνής, της έκφρασης του προσώπου, των λεπτών κινήσεων των δαχτύλων) και μη κινητικά συμπτώματα (διαταραχή συμπεριφοράς στον ύπνο REM,μεταβολή της γαστρικής κινητικότητας). Μας δίνουν έτσι την δυνατότητα να βελτιώσουμε την πρώιμη διάγνωση της νόσου, να προσδιορίσουμε την πρόδρομη φάση και να ελέγξουμε τον πληθυσμό για την παρουσία της νόσου. Επιπλέον βοηθούν στην ακριβή και αντικειμενική αξιολόγηση και παρακολούθηση στην καθημερινή ζωή των κινητικών (βραδυκινησία τρόμος, παράμετροι βάδισης, πάγωμα στην βάδιση, ισορ-ροπία) και μη κινητικών συμπτωμάτων, της απάντησης στην θεραπεία και των διακυμάνσεων της θεραπείας. Επίσης η τεχνολογία επαφής με την καταγραφή των δυναμικών των πλήκτρων καθώς γράφει ο ασθενής στο υπολογιστή αποτελεί μία άλλη ευκαιρία μελέτης των κινητικών συμπτωμάτων. Υπάρχουν βέβαια περιορισμοί και προβληματισμοί στην χρήση της τεχνολογίας. Περισσότερες μελέτες με την συμμετοχή ασθενών και φροντιστών θα βοηθήσουν στη ευρεία εφαρμογή της τεχνολογίας στην νόσο.

Λέξεις κλειδιά: φορητές συσκευές, έξυπνα κινητά ,έξυπνα τηλέφωνα, νόσος Πάρκινσον, ψηφιακή τεχνολογία

Introduction

Parkinson's disease (PD) is a common neurodegenerative disorder affecting 6.2 million people worldwide and this number is expected to reach 12 million by 2040[1]. PD is a multisystem disorder and although motor symptoms are the hallmarks of the disease, PD is associated with a variety of non-motor symptoms [2,3].PD is very heterogeneous regarding the age of onset, the motor symptoms, the non-motor symptoms, the rate of progression and the genetic background[3,4]. Furthermore, the natural history of PD has a prediagnostic phase (preclinical and prodromal) and a manifested phase (early stage and late stage)[3-5]. The prodromal phase is characterized by a range of non-motor symptoms

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(constipation, REM sleep behavior disorder, smell loss e.t.c.) and a subtle motor signs (voice changes, decreased facial expression e.t.c.)[3-5]. This complexity of the disease make the implementation of precision medicine quite difficult.

Technology/wearables and Parkinson's disease

New technologies such as artificial intelligence, wearable sensors, smartphones, virtual reality ,machine learning e.t.c. that have been developed intend to generate accurate measurement of motor function[6-10]. The most widely used are inertial measurement units. These units have a triaxal accelerometer that measure inertia acceleration of a body, a triaxal gyroscope that measure angular accelerations , a global positioning technology and a magnetometer[8,11]. These inertial units have been embedded in wearable devices that can be attached to almost any part of the body (wrist, finger, trunk, foot). So, wearable sensors can record orientation, amplitude, frequency and speed of movements[11]. These sensors can also evaluate gait and give specific gait parameters. The wearable sensors are worn by the patient in the clinic and for remote monitoring in home setting, thus giving the opportunity for a continuous home monitoring during the activities of daily living[12,13]. The implementation of sensor based and wearable technologies is useful for the objectively evaluation and monitor patients with manifested PD, for the improvement of disease management and also for early disease diagnosis.

Evaluation of patients with manifested PD

The assessment of a patient with PD is challenging. Although clinical examination and MDS-UPDRS are the standards for PD evaluation there are some drawbacks. MDS-UPDRS and other scales are prone to subjectivity and they reflect the patient status at the in-person/clinic visit, that is in a precise moment. It is very important to be informed about the patient's symptoms (tremor, bradykinesia, gait disturbance, falls) and on/off states all day long during his daily routine. Therefore, wearable devices give the opportunity to continuously evaluate the patients' motor function in real time and thus objectively better manage PD symptoms and improve patients' quality of life.

Various digital technologies have been developed for the assessment of various aspects of motor function in PD, such as tremor, bradykinesia, gait disturbance, freezing of gait, falls and dyskinesias [6-15].In 2023 the UK National Institute for Health and Care Excellence (NICE) published their recommendations for the use of devices for remote monitoring of Parkinson's disease[16]. According to the Committee five wearable devices are conditionally recommended as options for remote monitoring of PD to inform treatment if further evidence is generated and cost impact is managed.These devices are: 1)***Kinesia360:*** the device has two sensors worn on the patient's wrist and ankle, a tablet and a charge pad. It measures tremor, bradykinesia, dyskinesia, body position and steps all day long (16 hours battery life) during daily activities, 2)***KinesiaU***: has a smartwatch and a smartphone for continuous recording or for recording specific active tasks. The device rates tremor, bradykinesia and dyskinesias (good, mild, moderate, severe),3)***PDMonitor***: the device comprises 5 sensors worn on both wrists, both ankles and waist, a SmartBox and a PDMonitor mobile application. PDMonitor measures arm/leg/body tremor, arm/leg/body bradykinesia, dyskinesia, off time, gait impairment as well as number of steps and gait analysis, freezing of gait and postural instability,4)***Personal KinetiGraph (PKG):***it consists of a PKG watch and a PKG report. The watch is worn on the wrist of the most affected side for continuous monitoring for 6-10 days. It measures tremor, bradykinesia, dyskinesias and motor fluctuations, and final 5)***STAT-ON:*** the wearable device worn on the patient's waist analyzes inertial signals with advanced machine learning algorithms and contains a communication unit that transfer the motor assessment to an external mobile device. STAT-ON measures gait parameters, freezing of gait, falls, posture, motor fluctuations, and dyskinesias but it does not measure tremor. Many other wearable devices/systems have reached a Technology Readiness Level (TRL) of 8-9 and have the FDA approval such as: Mobility Lab -APMD,DynaPort7-McRoberts and FeetMe Monitor Insoles[7,10]. Recently a new smartwatch based monitoring system- the Rune Labs Kinematics System- has been granted with FDA clearance [17]. This device uses an Apple smartwatch and special algorithms for detecting tremor and dyskinesias.

Non-motor symptoms in PD are common, they can precede the onset of motor symptoms and affect the patients' quality of life. Relatively few studies with digital health technology focus on non-motor symptoms of PD. Van Wamelen et al [18] identified eight studies using triaxial wrist-worn devices to monitor sleep quality and quantity in PD. The results of the devices correlated with the PD Sleep Scale, the patient's sleep diaries and the polysomnography measures.

Technology for Parkinson's disease diagnosis

The diagnosis of Parkinson's disease is challenging and according to Adler et al [19] there is only 26% accuracy for clinical diagnosis of PD in untreated patients and 53% accuracy in early PD patients responded to medication. So, multiple studies investigated the implementation of algorithms and digital technology for the early diagnosis of PD. Most studies focus on the discrimination between patients with PD and healthy controls. However a lot of effort has been put for the implementation of digital technologies for diagnosis of prodromal PD. Both ***Prince and de Vos***[20] using algorithms for alternate finger tapping test data collected on smartphones and ***Mehrang et al*** [21] analysing 20-step walking by built in sensors of smartphones reported feasibility to discriminate PD from non PD subjects. ***Lipsmeier et al*** [22] evaluated phonation, rest tremor, finger tapping, balance and gait with a smartphone during active tasks and passive monitoring at home for 6 months. They found that the wearable devices can accurately discriminate patients with PD and healthy controls. In the study of ***Di Lazzaro et al*** [23] PD patients and healthy controls performed the MDS-UPDRS part III wearing inertial sensors. They distinguished patients from controls with an accuracy of 97%. ***Adams et al*** [24] in the WATCH-PD study evaluated patients and controls wearing smartwatch and smartphone in the clinic performing standard assessment and at home wearing the smartwatch for seven days after each clinic visit. Also at home patients completed motor, speech and cognitive tasks on the smartphone every other week. Parameters that differ between early PD patients and healthy subjects were arm swing, the proportion of time with tremor and finger tapping. ***Del Din et al*** [25]studied 14 gait characteristics with a wearable sensor placed on the lower back in healthy controls longitudinally four times at 2-year intervals. They found that gait variability and asymmetry of all gait characteristics were the best predictors for prodromal PD approximately 4 years before clinical diagnosis.

Touch technology with keystrokes dynamics during typing a computer offers another opportunity for studying motor symptoms in PD. Subjects type their computer at home and data collection from key strokes events as the participants press and release the keys (hold time, release latency, interkey latencies, flight time, alternating finger tapping)were stored in a platform and analyzed by a computational algorithm. All studies found that computer keyboard interaction discriminate patients with early PD from controls[26-29].

Subtle motor signs in the prodromal phase of PD are reduced facial expression (hypomimia) and voice changes (hypophonia).Different speech tasks have been tried for detection of speech abnormalities such as vowel phonation(«aaa»),syllable and sentence repetition and reading[30]. Smartphones used for capturing speech abnormalities (frequency variability, duration of pause intervals and rate of speech timing) succeeded to separate early PD patients from controls [30,31]. ***Singh and Xu*** after analysing 1000 voice samples (the subject said «aaah» for 10-s audio using a smartphone) propose a method that reaches 99% accuracy for predicting PD[32]. Furthermore ***Arora et al*** [33] found that voice was a discriminator factor for separating participants with idiopathic REM sleep behavior disorder from PD participants. For evaluation of facial expression computer vision and machine learning were used to measure the variance of facial movements (key eye and mouth related features) when the participants perform six basic emotions or when reading[30,34,35]. Especially ***Pegolo et al***[35] implemented a face tracking algorithm based on the Facial Action Coding System (56 landmarks describing the eyes ,the nose, the mouth, the cheeks).The studies concluded that quantitative evaluation of facial expression can assist in quantifying the degree of impairment in PD, identifying early PD patients from normal controls and classified emotions.

The iPROGNOSIS project supported by a European Horizon 2020 grant (coordinated by Aristotle University of Thessaloniki-Department of Electrical and Computer Engineering with the collaboration of the 3rd University Department of Neurology and the participation of different countries-U.K., Germany, Portugal, Sweden and Belgium) aimed to recognize patterns of motor and non-motor symptoms of PD for the early PD detection. Participants interact with their smartphones during all day activities. The parameters that recorded were: speech, movements by analysing the typing patterns on smartphone keyboards, facial expression in selfies and emotional content in text messages. Furthermore a smartwatch analysed sleep pattern and a smart belt was used for the assessment of real life eating difficulties. ***Iakovakis et al*** [36] evaluating PD patients and controls (interacting with touchscreen smartphones during natural typing) explored the combined discriminative potential of enriched keystroke variables (both timing and pressure) and achieved an AUC =0.92 and 0.82/0.81 sensitivity/specificity. Moreover, ***Iakovakis et al*** [37] in an analysis of validation dataset of 36.000 typing sessions (PD patients and controls) achieved AUC 0.89 with sensitivity/specificity:0.90/0.83. The estimations correlated significantly with the items 22/23/24 of the UPDRS. Further validation analysis on de novo PD patients resulted in AUC of 0.97 0.93/0.90 sensitivity/specificity. ***Papadopoulos et al*** [38] used a deep learning framework that analyses data captured during natural user-smart phone interaction to predict tremor and fine motor movements and achieved 0.86/0.93 sensitivity/specificity. In order to evaluate speech voice features from running speech signals were extracted from passively-captured recordings over voice calls [39]. ***Laganas et al*** [39] reported an AUC 0.68 for the classification of PD patients versus controls. Using a smartwatch triaxial accelerometry computed sleep metrics (sleep

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efficiency index, total time sleep, sleep fragmentation index, sleep onset latency) used to discriminate between PD patients and controls [40].The univariate analysis achieved up to 0.77 AUC in early PD patients versus controls and a statistically significant association with the PD SleepScale 2 counterpart items. The iPROGNOSIS hypomimia (selfies) analysis module attempts to detect and quantify the decrease of variability of facial expressions in early PD patients[41]. Promising results (early PD patients versus controls) emerged from the study of ***Grammaticopoulou et al*** (sensitivity/specificity 0.79/0.82 for Hypomimia Severity Index)[41].For the assessment of real life eating difficulties ***Kyritsis et al*** [42] introduced the Plate -to-Mouth, an indicator that relates with the time spent by the hand operating the utensil to transfer food from the plate into the mouth. Wearable inertial measurement unit sensor data were collected in the clinics and in free living. The results reveal an AUC of 0.748 for the clinical dataset and 0.775/1.000 for the in-the-wild datasets towards the classification of in-meal eating behavior profiles to the PD and healthy control groups[42].The non-invasive evaluation of gastric motility –electrogastrography - in patients and controls was recorded by a special device(a smart belt).Analysis of electrogastrography signals captured after a 30-minute long electroga-strography (after 6 hours fasting) found differences between patients and controls primary for the post-prandial period[43].

Conclusions

The implementation of digital health technology will revolutionize PD diagnosis and treatment .Wearable devices will improve early diagnosis and identification of prodromal PD. Furthermore monitoring motor and non-motor symptoms in real life as well as response to treatment and motor fluctuations will drive us to a better precision medicine. Although the results of the studies are promising, there are several limitations on the use of wearable sensors such as small sample sizes of subjects in most studies, different number of sensors used, lack of consensus on the type and scope measures and the more appropriate approach for data captures, technical issued should be tackled and users should become familiar with technology [9, 44-46]. Future studies will help to adopt a widespread use of digital health technology.

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Main points:

The implementation of wearable devices and smartphones in Parkinson's disease is promising for:

a) early Parkinson's disease detection, even in the prodromal phase

b) objectively monitoring motor and non-motor symptoms and response to treatment

Useable points:

The implementation of wearable devices and smartphones in Parkinson's disease will improve:

a) medication adjustments

b) precision in treatment

c) clinical trial data