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Technological support for people with Parkinson's disease: a narrative review

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Background. Parkinson's disease resulting from the degeneration of specific areas of the brain, can cause severely disabling symptoms, such as freezing of gait. Freezing of gait increases the risk of falls through worsening of physical mobility, muscle stiffening, slow uncoordinated movements and often leads to hospitalization with significant worsening of quality of life for such patients. Indeed, older patients are at a significantly higher risk of negative outcomes related to PD.

Objective. This work focuses on the most recent findings regarding non-invasive intervention and monitoring strategies to counteract the effects of freezing of gait. In addition, several devices can also provide support for diagnosis, treatment, and quality of daily life, especially in older patients with PD.

Methods. This narrative review describes the current state of the art of devices based on cueing, monitoring and rehabilitation systems. Fifty-seven studies were selected.

Results. Overall findings demonstrates that these smart devices can act as a valid aid tools able to: i) learn patient motor habits in order to intervene during a freezing of gait episode, ii) monitor daily conditions, iii) send and store data on disease progression, iv) provide useful information for rehabilitation programs in a clinical or home care environment.

Conclusions. These technologies hold excellent prospects for patient treatment tailoring, especially in older patients in home care.

Key words: cueing, freezing of gait, Parkinson's disease, wearable device, stimulation

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INTRODUCTION

Parkinson's disease (PD) is the second neurodegenerative disease for incidence and the fastest growing in terms of disability and deaths [1,2]. This disease is characterized by a progressive decline of motor and non-motor abilities which leads to movement difficulties and a reduction of the quality of life (QoL) [3]. The main effects of PD are caused by a degeneration of the neuronal cells that produce dopamine, responsible for the activation of circuits that control movements and balance [4]. PD alters the function of the brain circuits that facilitate neuronal synchronization resulting in typical PD motor disorders (e.g. bradykinesia, stiffness of the limbs, rest tremor and postural instability) and non-motor disorders (e.g. speech impediments, olfactory dysfunctions, autonomic dysfunctions, sleep disturbances, fatigue) [5]. One of the most debilitating symptoms is freezing of gait (FoG), which often occurs in advanced stages of PD. Stride length and speed reduction with short episodes of involuntary absence of locomotion are some of the first indicators of FoG [6]. Commonly these motor blocks affect the lower limbs during walking, but other parts of the body may also be involved [7] (for example, patients may also experience upper limb frostbite [8]). This risk is greater in subjects with cognitive impairment and low self-awareness of their limitations. Patients who frequently experience episodes of motor block may develop a refusal to walk, thereby reducing their level of activity and social interaction [9]. Commonly, persons with PD are very vulnerable to mood changes [10]. However, patients who manage to regain control over their daily life activities can avoid negative psychological consequences, thus reducing states of anxiety and depression [11]. It is essential to effectively analyze patient QoL and habits to provide a targeted intervention plan [12] to improve autonomy and safety in everyday life [13]. Unfortunately, pharmacological treatments can often be ineffective or cause side-effects, such as drug addiction. Surgical procedures may also improve mobility difficulties, however these procedures remain expensive and invasive. Recently, the need to identify alternative techniques to improve PD symptoms is constantly growing in the scientific community. Non-pharmacological methods such as cueing systems [14], assume relevant importance in PD management, in particular when FoG episodes cannot be treated by drugs or surgery. Cueing systems exploit compensatory strategies able to improve patients' movement skills, such as length, cadence and gait speed [15]. The occurrence of FoG episodes can be reduced thanks to these strategies that bypass the deficit in generating internal stimuli through external signals or inputs (temporal and spatial) [16]. Technological advancement provides significant advantages for PD support through the development of new sensors, devices and treatments to reduce the effects of FoG [17]. Indeed, sensors and wearable devices are at the center of several PD studies in the literature. A widespread use of these devices has been mainly described in medical environments which limits data on their use in daily patient life activities. In addition, high costs, difficulty in use and discomfort in wearing them are also limiting factors in daily care [18]. To date, thanks to constant technological progress, smarter, more sophisticated wearable solutions are emerging [19,20]. Devices directly connected to smartphone functioning hold an important role on data collection for correct diagnosis, symptom control and therapy adjustments of fluctuating motor disorders [21]. Together with the emerging sciences, such as the Internet of Things (IoT) and Machine Learning (ML), the collection of this data can be converted into scientific and clinical databases of extreme importance. In the literature, different cueing strategies such as, continuous stimulation devices during movement [22] or activated only when needed, through autonomous real-time sensing algorithms to start stimulation [23-26] have shown to be efficacy. Moreover, devices have shown to predict disease course by rest tremor (RT) monitoring thanks to the study of upper limbs movements [27], identify problems related to food intake [28], detect problems through handwriting and digitography analysis [29,30]. Other studies [31-35] have focused on the definition of high-tech miniaturized and portable devices made of fabrics and materials that conform to the body. Recently, virtual reality (VR) has been showed to be a promising tool for rehabilitation, able to provide stimulation through cues with a patient in a safely controlled virtual environment [36,37]. This review will describe different solutions identified in the literature regarding devices based on detection, intervention through main cues systems (visual, acoustic, somatosensory), monitoring and rehabilitation that have been demonstrated to positively influence PD related motor skills.

METHODS

The research work produced a collection of technological proposals to provide support for patients with PD. All publications selected were identified in the period from January 2018 to December 2021. PubMed, Scopus and Web of Science databases were explored to select research works with a combination of the following keywords: Cueing AND freezing of gait AND Parkinson's disease AND wearable device AND stimulation. Eligibility criteria involved works that included information on the devices ability to extract motion data, manage motor blocks, and give remote support in PD. More specifically, the work aimed to highlight the positive influence of implementing these systems on patient gait and how they may offer opportunities for better care and better disease self-management. The devices were validated on patients at early or advanced states of the disease and in some cases healthy controls were involved. Different types of interventions were included. Some studies have evaluated the immediate effect of cues on reducing the occurrence of FoG episodes in limited sessions. Instead, others have focused on the long-term effects, proposing weekly programs consisting of several practice sessions in which the patient is trained to respond to the sensorial stimulation in everyday life scenarios. Several solutions have been proposed, with the use of different technologies and body area of application, as showed in Figure 1.

RESULTS

In this work, a total of fifty-seven studies were selected. All identified articles included data regarding:

- function (monitoring, detection, intervention, rehabilitation/training);
- cues (visual, auditory and somatosensory);
- signal delivery mode (on demand or continuous).

In the following section, we provide a description of wearable devices based on non-invasive sensory cues. The devices listed below exploit both continuously and/or on demand cueing function for monitoring gait information which is essential for intervention. Some devices have shown to act as home environment tele-rehabilitation tools and recreate everyday life scenarios in which patients can follow training programs safely. These wearable systems are made up of actuators and sensors, accelerometers and gyroscopes that capture gait information and events in order to activate appropriate stimulus actions on patients. Sensors are characterized by the ability to study movements and body position. Actuators deliver preventive actions through cues, giving the user support in dangerous situations such as FoG episodes. Tracking the patients' movement is the key function of these devices, not only because of the ability to predict and detect motor blocks, but also because it can provide a wide dataset of motor habits to help physicians make diagnoses and monitor disease course. Both existing cueing systems and established monitoring solutions will be described. A further section will present the latest studies on the implementation of virtual reality (VR) based solutions for physical and cognitive home training.

MONITORING AND DETECTING DEVICES

In a 2021 study by Borzi et al. [3] showed that an integrated wearable system with inertial sensors and ML was used to detect and predict the occurrence of FoG episodes. The walking activity data of eleven patients with PD was collected. The devices were placed on both legs of the patients while they carried out a Timed Up and Go (TUG) test, replicated domestic environments (i.e. passage from a spacious environment to a narrow and furnished corridor) in order to increase the risk of FoG episodes. These activities were aimed at validating the use of ML algorithms to detect the typical deterioration of the gait pattern prior to FoG episodes. Their results showed an excellent performance of ML models in predicting FoG events. In another study [39], the same authors monitored motor fluctuations in PD patients (n = 38) during daily life activities, through data processing on an IoT module (named SensorTile). The system components involved the use of a smartphone, IMU sensors and an electronic diary of motor fluctuations, posture and dyskinesia. In the same year, Bikias et al. [40] introduced DeepFOG, a non-invasive device that incorporated the data of an inertial measurement unit into a commercial smartwatch to reduce patients' risk of falling. This study was carried out in participants undergoing continuous walking activities using a wrist positioned device to acquire data on FoG episodes. Based on the collected data, the device demonstrated a promising performance and, moreover, has the potential to be implemented with stimulation functions through auditory, rhythmic or somatosensory cues. DeepFOG has valid characteristics as an important telemedicine tool to inform doctors about the frequency of FoG events of their patients. In a further publication by Diep et al. [41] used a FoG predicting technique in ten PD patients through the acquisition of kinematic data, measured by wearable shank-positioned Inertial measurement unit (IMU) sensors. Patient movements were analyzed during a stepping in place (SIP) test. Findings underlined an important reliability in FoG detection during the SIP test as well as, general and specific participants' gait parameters. Marcante et al. [42] focused on the development of a device made up of a pair of pressure insoles, equipped with a 3D accelerometer to detect FoG episodes. Twenty participants with PD took part in video recording sessions, to record information on carrying out activities based on daily actions commonly performed a home environment (i.e. opening a door, getting out of bed, walking, using tools). The device detected motor block episodes, thus proving to be an excellent tool in patient daily life. In a study by Pardoel et al. [43] an insoles system equipped with an accelerometer, a gyroscope and plantar pressure sensors was used. This work was aimed at collecting data on

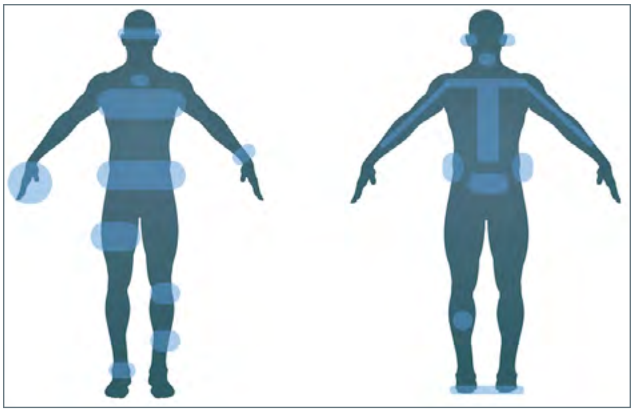

Figure 1. Different body areas where devices and sensors have been positioned (head, chest, wrist, hand, waist, lips, knee, shin, ankle, feet). Some devices have the possibility of applying sensors to multiple parts of the body and have been defined as "multi-body area".

walking characteristics in eleven PD participants during a walking test. Participants were asked to carry out additional activities simultaneously with the walking activity along a predefined path, in order to increase the risk of FoG. The device was able to detect and report motor blocks. Shalin et al. [44] also used a pressure-sensitive insole to collect enrolled participants' data through sensors to predict FoG episodes. Participants, wearing the insoles, had to face a path that had the aim of triggering FoG episodes through a double-task test (e.g. turning in a narrow hallway while holding a tray with a cup). By a comparison between data collected on participants who experienced FoG episodes and those who did not, the device showed high reliability in detecting and predicting block states. Moreover, Prado et al. [45] presented the DeepSole system on predicting FoG episodes. The device consists of a printed circuit with a microcontroller and IMU, and an instrumented base with pressure sensors and vibration motors. The system was tested on 10 PD participants suffering from frequent FoG episodes. The subjects had to practice walking for 6 minutes, during which data relating to motor habits were recorded. Users had described the system as soft, flexible and fitting snugly into any standard footwear. Findings showed that the device successfully identified FoG episodes with only a number of false predictions. In 2020, Orozco-Arroyave et al. [46] adopted a smartphone application as an useful information collector for PD motor assessment and monitoring. Apkinson is an application based on algorithms that evaluates different motor features such as language production, arms, hands and legs movements, and other parameters such as finger beating. Thanks to this application, patients can carry out tests in which they must juggle speaking, walking and moving their hands. Test results are provided in real time and can offer essential information about the disease course. In a 2020 study, Aich et al. [47] used a knee-positioned wearable device based on a triaxial accelerometer system for detecting FoG episodes in PD subjects. The device can learn patient's movements in all directions without causing any discomfort. Participants performed a walking test in a room equipped with a 3D motion capturing system. The ability to perceive acceleration variations of the wearable system monitored all movement activities and recognized FoG episodes. The use of this device holds a specific assessment in the home environment during daily activities. Findings showed that this device could be a great support to the patient during daily living activities in a real-life scenario. Moreover, Reches et al. [48] focused on wearable sensors effectiveness for motor learning tools. Sensors were placed on the lower back and on each ankle. In the FoG triggering test, patients had to undertake walking activities and be involved in cognitive, motor and emotional challenges. The goal was to provoke conditions that triggered FoG episodes in patients to study the motor changing. This automated ML method may be considered as a valid FoG assessment tool and an aid in personalizing treatment. Demrozi et al. [49] presented a wearable device based on tri-axial accelerometer sensors that also used ML algorithms to explore walking habits of PD patients and classify trigger movements typical of pre-FoG, FoG and no-FoG behaviors. The sensors were placed on the back, hip and ankle, respectively. Results demonstrated that the device was able to predict FoG by identifying pre-FoG events. The authors suggested a potential role of mobile device implementation and the administration of rhythmic cues from a wearable device may assist patients during FoG states. In 2019 Pierleoni et al. [50] developed a set of wearable devices equipped with a triaxial accelerometer, a triaxial gyroscope and a triaxial magnetometer to monitor patients' RT and FoG episodes in home monitoring. The devices operate via Bluetooth and offer a real-time processing of the acquired data. This characteristic is fundamental and together with daily PD symptoms provides essential information for the dosage and the effective tailoring of drug therapy. To validate this system, a series of tests were carried out. The devices were positioned on both the chest and wrists. PD and healthy subjects underwent two tests to increase RT severity and invoke FoG episodes. The RT test engaged the patient in cognitive activity (i.e., counting from 0 to 100). In order to evoke FoG episodes, patients were subjected to tests including: TUG, passing through a narrow passage, and passing through a door that ends up sitting on a chair positioned on the other side. Findings showed important accuracy in both RT classification and FoG events detection. Therefore, this proposed system can be used to create a personalized rehabilitation program and provide patient support.

Since FoG is not limited to lower extremities, it can also be experienced as upper limb motor blocks. Some studies have focused on collecting data on arm movements to identify effective compensatory strategies to relieve FoG states. In 2021, Kyritsis et al. [51] used a smartwatch to monitor the temporal evolution of eating behavior, Plate-to-Mouth (PTM). The PTM is an indicator that evaluates the time to transfer a quantity of food from the plate to the mouth during the meal. Indeed, eating behavior is a factor that is often overlooked, but it can be very important in controlling the effectiveness of treatments. It was possible to create a profile of eating habits for PD subjects using the distribution of bites during food intake activity and thus recognize behavioral variations. PTM was the first work that integrated the use of sensors to introduce an indicator of eating behavior for PD using commercial smartwatches. In a similar paper by Fagerberg et al. [52] eating behaviors in PD were investigated since problems caused by motor dysfunctions might have a negative influence on changes in energy intake. The purpose of this study was to evaluate the difference in energy intake between healthy control patients and PD patients at an early and advanced stage during a food intake activity. The results showed that energy intake is lower in subjects with advanced disease and could be a marker of disease progression. Another study by Iakovakis et al. [53] in 2019, proposed a PD detection digital solution, working on users' interaction with their daily technological devices. An App that processes keystroke data from subjects' typing activities on smartphone screens. The study aimed to identify the raw information related to the motor impairment caused by PD and in particular, to the stiffness and slowness of movements which can alter behavioral habits. Other works have focused research on RT monitoring and tracking. RT is a severe consequence of PD, often defined as a rhythmic and involuntary oscillatory movement of a part of the body [54]. There is an ongoing and substantial interest on identifying a system to track and quantitatively measure RT. In 2021 and 2020, Milano et al. [55] and Ferrigno et al. [56] proposed a tracking system based on magnetic measurements to track the movement of a robotic arm. The work validated a system able to obtain a rapid and real-time diagnosis of PD symptoms. The device exploits the measurements of translational and vibrational movements in a limited cubic domain to obtain information on motor symptoms. For the validation of the device, they proposed tests that could emulate different types of RTs and trajectories. The system correctly recognized them emitting information on the time position in a 3D domain and on the vibrational frequencies associated with the movement itself. These tests demonstrated the system's ability to track information on mild symptoms associated with PD. This device may be implemented in the early stages of PD diagnosis. Following, Mahadevan et al. [57] monitored motor fluctuations related to RT on PD through data using a wrist accelerometer. Participants performed a series of walking activity tests in which data on symptom fluctuations were collected. The system has been proven to be able to discriminate treatment-related changes in motor states. In 2020, Dai et al. [58] evaluated inertial sensing-based wearable devices (ISWD) for the quantification of parkinsonian tremor and bradykinesia. A total of forty-five PD patients and thirty healthy subjects were enrolled for the study. Sensors were placed on the fingertips of the participants to detect the movements performed. Participants performed tremor and finger tapping tests which were tracked simultaneously by the ISWD system and a 6-axis high-precision electromagnetic tracking system (EMTS). In another work, Marino et al. [59] used a low-cost device capable of quantifying the frequency and amplitude of RT and the stressful condition. The device can provide a real-time analysis of tremor data recorded on fingers, collecting parameters regarding frequency and amplitude. Tremor symptoms of forty-one PD patients were evaluated. Findings showed that it was possible to identify the presence of tremor influenced by emotional stress and during muscular effort. This device proved to be a useful tool in the differential diagnosis and therapeutic management of PD. In a further study by Hssayeni et al. [60], an algorithm was developed to monitor the severity of PD tremor during free-body activity based on the data acquired by a wearable sensor positioned on the wrist and ankle. The authors hypothesized that this system, combined with wearable sensors, could provide a reliable approach to estimate tremor severity for treatment options.

On demand cueing devices

In 2021 Zoetewei et al. [61] presented on-demand cueing tools consisting of a smartphone, IMU sensors and headphones for the delivery of auditory cues. This work aimed at verify the effectiveness of the DeFOG system over four weeks in PD patients (n = 62) subjected to triggering FoG tests in order to collect data moments before these episodes. Subsequently, they performed walking tests on simple paths and on more challenging paths with greater cognitive commitment. Results showed that treatment using this cueing system reduced FoG episodes. In the same year, Imbesi et al. [62] studied the use of multisensory wearable devices as a support tool for PD patients. They integrated a smartphone-based CuPiD-system with Vuzix Blade SG smart glasses, able to project two-dimensional images on the lenses. The device can deliver visual (smart glasses), auditory (wireless earphones) and somatosensory (vibration on the right and left temples) cues. Following Li et al. [63] proposed a FoG monitoring device capable of monitoring and intervening on FoG episodes. This home environment device consists of plantar pressure sensitive insole which, due to inertial sensors (IMU) can learn movements and identify characteristics of gait predicting real-time FoG episodes. The wearing of the insoles starts monitoring, thus the device does not to be activated. In case of a FoG episode warning, visual cues are sent through a laser transmitter that projects a beam on the floor helping the patient out of the motor block state. Furthermore, the device works remotely collecting and sending patient data to their physician, proving to be an important telemedicine tool. Next, Stuart et al. [64] examined a wearable vibrotactile signaling device, the UpRight Go. This device is comprised IMU sensors positioned on the neck, trunk and lower back. The goal of this study was to verify the effectiveness of the device in improving postural alignment. The subjects involved were evaluated in sitting, standing and walking activities. Tests were carried out in both laboratory and at home, one hour per session. Results showed that stimulation via somatosensory signals reduced neck flexion, improving postural alignment, but no changes were found in trunk and lower back posture. These improvements were found in both laboratory and home testing environments in sitting and standing positions only, not while walking. In Kishi et al. [65] work, a wearable robot device for gait assistance was presented. This work aimed at assessing arms stimulation effects on walking activity. The robot's function was to send rhythmic stimuli on the patient's upper limbs. During the walk, the rhythmic stimuli were synchronized with the swinging movement of the arms. Participants performed a 30 m walk on a flat floor, under various conditions such as, using or not using the robot and with or without stimulation. The arm swing amplitude, stride length and speed increased with robot rhythmic assistance. Dvorani et al. [66] introduced a wireless wearable device working through Bluetooth, Mobil4Park. This device is equipped with two IMU sensors positioned on instep at shoe and shank, an electric tactile stimulator positioned on the hip and an intelligent device adjusting the stimulation intensity. Although this device has not been tested in PD, one may hypothesize that it may monitor PD motor habits and provide non-invasive electrical stimulation to prevent FoG episodes. In 2019, Marsh et al. [67] presented a device able to learn kinematic patterns and detect the conditions that preceded FoG episodes. The device consists of integrated accelerometers and gyroscopes that can perform a gait analysis and intervene when motor disruptions are detected. The system used visual cues, specifically a red laser light that turns off when the motor block is overcome. Participants performed two walking activities: the 2-minute walk test (2MWT) and the obstacle course. The results showed improvements in 2MWT and no effects in the obstacle course. In the following study by Punin et al. [68] a low-cost, compact, affordable and easy-to-use device-based wireless wearable system was presented. This device showed to be capable of tracking gait movements and delivering vibratory stimuli when FoG episodes occured. The device aimed to reduce the duration of the FoG episodes by allowing a prompt resumption of gait to prevent serious injuries (n = 8). Two devices were positioned on both lower limbs, (one to monitor the movements and to provided stimulation, while the other was used only for stimulation purposes). To validate the device, they performed gait tests such as: walking straight, turning back, going up steps. During tests, a great variability was noted in walking attitude after motor blocks. Indeed, when subjects returned to normal walking activity, they presented sudden and accelerated movements. Nonetheless, it has been observed that this device supports real-time monitoring of motor abilities and carrying out daily activities. In a further study, Sweeney et al. [69] investigated the ability of double-tap gestural interactions to facilitate the automatic activation of somatosensory cues in PD. A waist positioned device connected to lower limbs positioned electrode collected information on touch gesture signal analysis during programmed walking activities. Findings showed that, once the gestures parameters were acquired, the device was able to recognize those that preceded FoG episodes and to intervene by sending electrical stimulations. In 2019, Mikos et al. [70] presented a FoG detection system able to send auditory and somatosensory cues. The device, ankle positioned, acquired and elaborated motor data to detect FoG episodes and provided biofeedback. Auditory cues are delivered via Bluetooth earphones, while somatosensory vibration cues are provided via a belt. The small device was considered comfortable and showed good accuracy in the classification and detection of FoG episodes. In the same year, Serio et al. [71] and Volpe et al. [72] conducted their research on a device that uses nanotechnology that converts human body thermal energy into mechanical energy. The device, named Equistasi, is a patch-like apparatus that provides focal mechanical vibratory stimulation on the muscle areas, interacting with mechano-receptors, Golgi tendon organs and neuromuscular spindles. The device is small and can be reused multiple times in different body areas. It is composed exclusively of applied nanotechnology fibers, does not contain any pharmacological element and offers support in rehabilitation therapy. The vibratory stimulation of the device allows for greater postural stability and facilitation of movements. It has been suggested a potential role on the central system with cognitive and psychological improvements. The vibration produced is deep and imperceptible and improves balance, thus reducing the risk of falls. Findings showed that combined physiotherapy, training and stimulation programs were superior to rehabilitation alone on improvin balance. Equistasi was showed to be a useful aid in the treatment of medium-advanced PD by improving gait, posture and stability as well as, in addition to physiotherapy and drug therapy. Equistasi was also used in cases of ataxia in adults [73]. Bartels et al. [74] presented a wearable device with a real-time feedback function to improve gait. StepPlus is a wireless operating shoe positioned device that estimates real-time step length and provides auditory and somatosensory stimuli when necessary, through a smartphone app. The function of this device could be essential for monitoring the progression of the disease by gait disorder. Early findings have underlined that this device accurately measured stride length in relation to different users with different motor habits, thus providing evidence for potential use in both clinical and home activities.

Continuous cueing devices

In 2021, Pasker et al. [75] proposed a prototype of a wearable device that provides continuous auditory and somatosensorial cues, with a Bluetooth function, PARKIBIP. This device is placed on the patient's ankles, and it is made up of an accelerometer, a gyroscope, a magnetometer and a vibratory unit. The device can analyze and identify motor habits as well as create a clinical record. The primary goal of the authors was to integrate the use of the device in domestic environments. In the same year, Tan et al. [76] showed improvements in mobility by a vibrotactile stimulation device in PD patients suffering from FoG episodes. They proposed CUE1, a device positioned on the sternum that provides rhythmic somatosensory stimulation during walking. Their study was based on two PD patients with FoG episodes that did not respond adequately to drug treatment. The subjects carried out TUG tests with the device set both on and off. The use of this device successfully reduced FoG episodes in both patients and significantly improved their mobility. Due to the low number of participants additional research is needed. In a following report by Gondo et al. [77], a portable gait rhythmogram device (PGR) was presented. Nineteen PD patients underwent movement parameter analysis by the device during walking activity. Music therapy sessions with a gradually implemented rhythm were carried out. The results showed that auditory cues improve gait parameters by evoking gait-related internal rhythm information in PD participants. In 2020, Cakmak et al. [78] focused on the efficacy of intrinsic stimulation of the ear muscle area (IAMZS). Study participants underwent three test sessions structured as follows: only drug; only stimulation; combined use drug and stimulation (n = 10). They found that the use of the drug alone was ineffective on improving the length and speed of the stride as well as, turning speed. Continuous rhythmic acoustic stimulus was associated with improved gait parameter. The same positive results were also found in combined drug and stimulation session. Consequently, this device may provide support during drug withdrawal periods and postpone long-term side effects of high-dose pharmacological treatment. Rossi et al. [79] proposed tactile anklets devices to improve walking quality and overcome FoG states. The tactile anklets work as walking pacemakers delivering somatosensorial cues to correct gait defects. The report was performed in PD patients (n = 15). Sensory stimulation was delivered in a rhythmic and alternating manner, decreasing the FoG episodes without risks for the patients. Motor parameters showed a significant improvement in pace speed and stability using a motion capture system. In an earlier 2019 study, Wilkinson et al. [80] concentrated on the effect of stimulation on the ear muscle area. ThermoNeuroModulation, a non-invasive wearable portable device for home use, was designed to provide caloric vestibular treatment in PD patients by thermal waveforms using aluminum ear probes mounted on a wearable headset twice a day. The study lasted... weeks and at every follow up changes in motor and non-motor symptoms as well as changes in everyday activities were assessed. The vestibular treatment showed a high user satisfaction providing motor and non-motor benefits. In a paper by Cao et al. [81], the effects of a wearable device on visual cues were studied. PD participants were divided into two groups: i) FoG episodes (n = 15), ii) No FoG episodes (n = 20). All participants underwent walking tests in three different conditions: no stimulation; stimulation of wearable laser lights; transverse stripes on the floor. In the last two conditions, parameters related to stride length were improved. Therefore, the use of these visual cues could be an effective strategy for FoG rehabilitation. Following, Lee et al. [82] studied the impact of using GoogleGlass (GG) on PD. Ten subjects, in different walking activity scenarios with and without GG, tested two personalized auditory-visual modalities, "Walk With Me" (WWM) and "Unfreeze Me" (UM). In WWM modality, walking activity was synchronized with auditory stimulus played by the device, acting as a metronome with a user's set pace of the walk. In UM, PD patients were asked to replicate the same rhythmic movements they saw on GG device lens while wearing the device. Mobile smart glass technology such as, GG may benefit patients with FoG, although this work described mixed results. In fact, in the WWM mode, all walking activities assessed improvements, except for walk. While in the UM mode, all walking activities worsened except walking double task, contrary to what the authors had expected. In 2020 Sweeney et al. [83] designed a FoG device to test the efficacy of auditory, visual and somatosensorial cues on a PD subject. This system was made up of a smartphone that via wireless headphones sent rhythmic auditory cues to which patients had to synchronize step time, a system of laser lights positioned on shoes (PathFinder) that provided projected obstacles on the floor to climb and one electrical stimulator positioned on the quadricipital muscle via skin surface electrode (PALS-Axelgaard). Participants had to perform different tasks along a path characterized by turning movements, passages through doors, rooms and corridors. Although the findings are limited by the small number of subjects tested, these devices demonstrated a positive effect of cueing in terms of reduction of percentage of time in FoG and number of FoG episodes occurring.

Virtual reality devices

In recent years, the concept of virtual reality (VR) has achieved considerable popularity in the field of PD rehabilitation together with traditional approaches. VR improves motor learning in safety, reproduces everyday life scenarios in virtual environments in PD [84]. VR has the potential to be used as a cue-based system to learn how to overcome motor blocks [85] , and it has also several advantageous features for patient management, as they can easily be followed remotely [86]. These devices allow patients with PD to remain active both physically and mentally even when forced to remain at home [87]. In fact, especially in the elderly, a worsening QoL can be the result of physical inactivity and together with other risk factors, such as high blood pressure, depression and anxiety, can lead to worse outcomes [88]. In several studies, it has been shown that VR systems are often composed of physiological and motion acquisition sensors. These technologies can be extended to detection and intervention on FoG episodes [89]. In 2021, Chen et al. [90] studied the effects of a week training with VR device. Participants performed walking test-based on a virtual path made up of visual obstacles using C-Mill, a treadmill equipped with a screen and a belt that acted as a projector. The purpose was to use this training to improve the quality of functional abilities of subjects, since VR is a useful tool to help people to refine their perceptions, motor and cognitive skills, to boost motor control and to reduce the risk of fall. Initial findings showed an improvement in all walking activities. Following Mota et al. [91] presented a VR wearable device based on SixthSense technology, capable of providing an extrasensorial perception. This work aimed at integrating the ability of the device to perceive information from the surrounding environment, process and transmit such information into the rehabilitation activities of PD patients. The device, positioned on the sternum, works through a camera that collects environmental information and detects the movements of the user's hands through sensors. The system recognizes surrounding images and based on the information collected, visual responses are generated via a projector. This study focused on delivering specific movement programs from both daily activities and physical activity in form of interactive games. In this way, the PD patients can interact with the projected image in therapy sessions for motor rehabilitation. In the same year, Finley et al. [92] evaluated the usability of Wordplay VR, using a set of devices to implement immersive virtual reality using headsets, hand controllers and HTC Vive sensors. The device monitored real-time body movements which allowed to practice skills such as, turning, avoiding obstacles, solving problems while walking and navigating in unpredictable environments. The use of the virtual environment did not lead to adverse effects. In 2021 and in 2019, Impellizzeri et al. [93] and Calabrò et al. [94], respectively carried out a study on a VR device aimed at the PD clinical rehabilitation. CAREN is a sensory room made of a safety structure with a user's harness, a screen positioned in front of an oscillating platform, a treadmill and two infrared cameras. The system provides rehabilitation through activities that require both motor and cognitive abilities. In both studies, CAREN-based rehabilitation was shown to be safely effective by significantly improving gait speed and dynamic-static balance. In a further follow-on publication, Cikajlo et al. [95] conducted a study on the Exergames system as a telemedical approach integrating cognitive and physical training. Exergame are a category of videogames that combine physical exercise with entertainment, but at the same time are useful tools to improve and control health status. Twenty-eight patients were enrolled in the study trained on the same game and were divided into a home group and a clinical group. Exergames use showed an improvement in motor skills underlining an effective and safe telemedical system in both groups In 2020, Janssen et al. [96] evaluated the effects of using VR HoloLens holographic viewer in PD. HoloLens is a wireless wearable device based on a HD-3D optical display, a spatial sound scanning system and a holographic interface for patients to interact by gaze, voice or hand gestures. The authors included 16 participants who performed 180° revolutions around their axes within a square. Testing activities were performed under different conditions: with visual cues displayed through the lenses and control conditions with a metronome beat played at a defined frequency or without any external input. They found that visual cues alone did not lead to improvements during FoG episodes. A worsening of the axial kinematics parameters, turn scaling and timing were observed. They highlighted that a goal-directed stimulation might not be sufficient. In 2020 Schuch et al. [97] evaluated the feasibility, safety, and efficacy of a 5-week VR training program. Twenty-three PD patients were enrolled in different tests: TUG; ten-meter walking (10MWT) and various cognitive functions. Their results suggested that 10-20 minutes of VR training is a feasible and safe rehabilitation activity, although they did not find improvements in mobility and cognitive performance. The authors highlighted the need for a combination of specific training in virtual and physical environments for functional mobility

Table I. Monitoring and detecting devices.

Year/author	Device	Placement	Function	Subjects
Borzi et al., 2021 [38]	IMU sensors	Shins	Detection	11
Borzi et al., 2021 [39]	SensorTile	Waist	Monitoring	38
Bikias et al., 2021 [40]	DeepFoG	Wrist	Detection	11
Diep et al., 2021 [41]	IMU sensors	Ankles	Detection	10
Marcante et al., 2021 [42]	Insoles	Feet	Detection	20
Pardoel et al., 2021 [43]	Insoles	Feet	Detection	11
Shalin et al. , 2021 [44]	Insoles	Feet	Prediction/detection	11
Prado et al., 2021 [45]	DeepSole	Feet	Detection	10
Orozco-Arroyave et al., 2020 [46]	Apkinson	Multi body areas	Monitoring	17
Aich et al., 2020 [47]	Fit.Meter Fit.Life	Knees	Detection	40
Reches et al., 2020 [48]	IMU sensors	Lower back Ankle	Detection	71
Demrozi et al., 2020 [49]	IMU sensors	Back/Hip/Ankle	Detection	10
Pierleoni et al., 2020 [50]	MARG	Wrist/chest	Monitoring	10
2021 Kyritsis et al., 2021 [51]	Plate-to-mouth	Hand/Head	Monitoring	28
Fagerberg et al., 2020 [52]	Smartwatch	Wrist	Monitoring	64
Iakovakis et al., 2019 [53]	Smartphone	Hand	Monitoring	33
Milano et al., 2021 [55]	Tremor device	Hand	Monitoring/detection	-
Ferrigno et al., 2020 [56]	Tremor device	Hand	Detection	-
Mahadevan, 2020 [57]	Tremor device	Wrist	Monitoring	81
Dai et al., 2020 [58]	ISWD	Hand	Monitoring	85
Marino et al., 2019 [59]	Tremor device	Hand	Monitoring	41
Hssayeni et al., 2019 [60]	Tremor device	Wrist/Ankle	Monitoring	24

improvements. Following, in study by Bekkers et al. [98], a type of intervention based on VR treadmill training was identified, with the aim of preventing FoG episodes and to overcome mobility difficulties. Participants underwent a 6-week training activity 3 times a week. The training was based on exercises to be performed while walking on the treadmill. The VR intervention was used to impose a cognitive load on patients to deal with the risk of falling, stimulating cognitive abilities and visual processing through visual and adjusted according to training responses. Participants showed a significant improvement in balance with a lower risk of falling. FoG episodes increased in months following the end of treatment. The results obtained during treatment are encouraging, but highlight the need for tailored and constant rehabilitation to counteract FoG-related effects. In another work, Ona et al. [99] developed a VR device able to evaluate clinical manual skills (the Box and Blocks) through an immersive experience. The system was based on a set of Leap Motion Controller to capture the movement of the user's hand and the Oculus Rift headset for a full immersion. The device has high spatial and temporal reading parameters; thus, it could be used as tool for monitoring the course of the disease. In a further study, Pazzaglia et al. [100] used the NIRVANA VR system to compare VR rehabilitation program to a conventional rehabilitation program over a 6-week period in PD patients. The NIRVANA system allowed patients to immerse themselves in different interactive scenarios, with stimulating rehabilitation paths. During activities, the system was able to measure and provide data relating to patient progress. In this study, both rehabilitations achieved encouraging results, but VR rehabilitation was shown to be more effective. In 2019, Janeh et al. [101] used the GAITRite system to perform gait analyzes in 15 PD patients. GAITRite is based on a gangway and a VR viewer that places patients in a virtual environment. This VR system study aimed to test for strategies on improving gait symmetry and stride length using visual and proprioceptive cues. Compared to natural gait, VR manipulation activities significantly increased stride width and oscillation time variability for both sides of the body.

CONCLUSIONS

This paper has described several recent wearable system solutions proposed for PD diagnosis, rehabilitation, monitoring and support (Tabs. I-IV). Thanks to

Table II. On demand cueing devices.

Year/author	Device	Placement	CUE	Subjects
Zoetewei et al., 2021 [61]	DeFog System	Ears/Chest/Feet	Auditory	62
Imbesi et al., 2021 [62]	Smart Glasses (Vuzix Blade)	Head	Multisensory	-
Li et al., 2021 [63]	Insoles	Feet	Visual	-
Stuart et al., 2021 [64]	UpRight Go	Neck/trunk/lower back	Somatosensorial	25
Kishi et al., 2020 [65]	Gait Assistance Robot	Upper limbs	Somatosensorial	30
Dvorani et al., 2020 [66]	Mobil4Park	Instep/Shank/Hip	Somatosensorial	-
Marsh et al., 2019 [67]	Belt	Waist	Visual	20
Punin et al., 2019 [68]	Anklet	Ankles/Shins	Somatosensorial	8
Sweeney et al., 2019 [69]	Double-tap gesture Belt	Waist	Somatosensorial	29
Mikos et al., 2019 [70]	Ankle-worn system	Ankles	Auditory Somatosensorial	63
Serio et al., 2019 [71]	Equistasi	Multi body areas	Somatosensorial	55
Volpe et al., 2019 [72]	Equistasi	Multi body areas	Somatosensorial	40
Bartels et al., 2018 [74]	StepPlus	Feet	Auditory	7

Table III. Continuous cueing devices.

Year/author	Device	Placement	Cues	Subjects
Pasker et al., 2021 [75]	PARKIBIP	Ankle	Multisensory	-
Tan et al., 2021 [76]	CUE1	Sternum	Somatosensorial	2
Gondo et al., 2021 [77]	Portable gait rhythmogram (PGR)	Waists	Auditory	19
Cakmak et al., 2020 [78]	Intrinsic Auricular Muscle Zone Stimulation (IAMZS)	Ears	Auditory	10
Rossi et al., 2020 [79]	WEARHAP-PD (Haptic anklets)	Ankle	Somatosensorial	15
Wilkinson et al., 2019 [80]	ThermoNeuroModulation	Head	Somatosensorial	33
Cao et al., 2020 [81]	Wearable laser lights	Waist/wrist/feet	Visual	35
Lee et al., 2020 [82]	Google glass	Head	Auditory/lisual/ somatosensorial	10
Sweeney et al., 2020 [83]	FoG devices set	Ear/quadricep/feet	Auditory/visual/ somatosensorial	12

technological advances achieved in sensors field, wearable computing and ML, the use of wearable devices is rapidly growing. These analytical systems are based on connectivity and communication with users. An important advantage is that these technologies do not require any invasive integration with the human body, but only device wearability by users to capture motor data which in turn allows for patient interaction in a natural, adaptive and predictive way. We have highlighted the importance of QoL when a late PD diagnosis occurs, or in the case of advanced state PD, there remains an urgent need to find smart solutions for regaining patient autonomy and self-confidence. In this review, we have aimed at underlining various solutions and potential real-life applications. Advanced technologies in sensor fields can offer support in different fields:

- monitoring and assessment of symptoms, to improve knowledge of disease course and provide target assistance and therapies;
- overcoming FoG episodes, one of the most debilitating symptoms of PD;
- improving physician/patient interaction on potential rehabilitation opportunities through VR technologies.

The latter point has proven to be an essential factor due to pandemic impact. Indeed, since PD population is mainly characterized by elderly subjects, these devices can play a fundamental role as valid tools in older patients at risk of infection in clinical environments. Indeed, limited activity in older patients generates the fear of social isolation. Thus, the need for recovery is detrimental for older PD patients to remain active physically and mentally. This review highlighted the ability of state-of-art technologies to monitor motor symptoms and assist patients in overcoming motor blocks. Many reports demonstrated an improvement in motor parameters with accurate cue stimulation methods. Another important pivotal role is that many of these devices can be used independently and in home environments by the patients. At the moment, clinical medical advances together with advanced technology may offer a valid support to help patients improve motor abilities and self-confidence.

Table IV. VR devices.

Year/author	Device	Placement	Subject
Chen et al., 2021 [90]	C-Mill	Waist	53
Mota et al., 2021 [91]	SixthSense	Sternum	-
Finley et al., 2021 [92]	Wordplay VR	Head	9
Impellizzeri et al., 2021 [93]	CAREN	Sensory room	30
Calabrò et al. 2019 [94]	CAREN	Sensory room	22
Cikajlo et al. 2021 [95]	Exergaming	Video Simulation	28
Janssen et al., 2020 [96]	HoloLens	Head	16
Schuch et al., 2020 [97]	VR Box	Head	23
Bekkers et al., 2020 [98]	VR treadmill	Sensory room	121
Ona et al., 2020 [99]	VR headset	Head	20
Pazzaglia et al., 2020 [100]	Nirvana	Sensory room	51
Janeh et al., 2019 [101]	GAITRite	Sensory room	15

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