Future Perspectives: Assessment Tools and Rehabilitation in the New Age

10

Greydon Gilmore and Mandar Jog

Abbreviations

BG	Basal ganglia
FOG	Freezing of gait
IRED	Infrared-emitting diode
LED	Light-emitting diode
MD	Movement disorder
PD	Parkinson's disease
UPDRS	Unified Parkinson's Disease Rating Scale
VR	Virtual reality

Introduction

The clinical study of movement disorders (MDs) remains a challenge, despite the advancement of technology, stemming partially from the difficulty of objectively studying the effect of the disease and its impact on the physical and mental state of the patient. Currently, validated methods for such assessments are entirely scale-based and hence face the issues of intra- and inter-rater reliability, correlation with the aspects of quality of life that actually affect the patient, and additionally, are not particularly sensitive to the therapeutic interventions that exist for these diseases.

G. Gilmore, M.Sc., B.Sc.
Physiology and Pharmacology, Western University,
London, ON, Canada N6A 3K7
e-mail: greydon.gilmore@gmail.com

M. Jog, M.D., F.R.C.P.C. (✉)
Clinical Neurological Sciences, London Health Sciences Centre,
London, ON, Canada N6A 5A5
e-mail: mandar.jog@lhsc.on.ca

H.F. Chien, O.G.P. Barsottini (eds.), *Movement Disorders Rehabilitation*,
DOI 10.1007/978-3-319-46062-8_10

The use of objective measurements for titration and adjustment of therapy is well accepted in disorders such as hypertension and diabetes. Medical management of these conditions is critically dependent on the measurement of the individual variables, namely blood pressure and blood sugar. At present, no such technique is being used in the clinical treatment of neurodegenerative disorders. Researchers have improved the reliability of disease assessment ratings through the increased use of objective and quantitative data collection tools over the past few years [1]. A recent review discussed current technology and the potential for these technologies to replace outdated clinical rating scales [1]. The advancement of successful and established (e.g., levodopa for Parkinson's disease) in addition to more complex interventions (e.g., deep brain stimulation, Duodopa pump treatment) has accentuated the need for improved assessment measures for many disorders. The question of "man versus machine," increasing the use of technology to counter subjectivity, has become more prevalent in the current literature looking to assess and quantify patient symptom profiles [1]. The primary goal of these attempts is to provide the clinician with a useful and noncumbersome yet reliable tool kit, especially for issues regarding mobility, to adjust therapy and thereby improve the patient's quality of life.

Parkinson's disease (PD) is a neurodegenerative MD presenting with several common hallmark motor symptoms such as: tremor, bradykinesia, dyskinesia, balance difficulty, falls, and gait impairment [5]. The primary pathophysiological cause of the PD motor symptomatology is the neurodegeneration of dopaminergic neurons in the substantia nigra pars compacta (SNc) within the basal ganglia (BG) [5]. One of the key features of the PD motor symptoms is that they manifest when there is a 60–80 % loss of dopaminergic neurons within the SNc [5]. PD is complicated further by frequently observed comorbid nonmotor symptoms, such as depression, cognitive deficits and sleep disturbances [5]. The nonmotor symptoms arise, in part, from neurodegeneration within other areas, including the cortex and locus ceruleus [5]. The important point here is that this spectrum of motor and nonmotor symptoms varies from person to person, and tends to become increasingly fluctuant as the disease progresses, requiring highly individualized therapy. In this chapter, PD is used as the signature disease to address the concepts of technology-based mobility assessment and individualized treatment optimization/rehabilitation.

To provide such individualized therapy, patients are currently required to meet with the physician in clinic every 6 months to a year, for a short period of time. The clinic visit provides a snapshot of the patient's condition, which often does not reflect the daily challenges that the patient may face and the assessment tools are not adequate to provide an insight into this issue. Given the lack of such measures (except for subjective quality of life scales), the clinician finds it virtually impossible to titrate management, medical, surgical or rehabilitative, to actually improve such function. Indeed, the adjustment of therapy is largely directed at the subjective reporting of the motor state and the observed motor state, but not during the performance of functional tasks. Furthermore, in clinical practice severity evaluation and adjustments in treatment rely too heavily on the clinicians' expertise, which lacks inter-rater reliability [1, 10]. The use of more objective and quantitative motor assessment methods, carried out while the patient is performing some standardized

activity of daily living tasks, which can then be used to optimize medical and rehabilitative management, is imperative in improving the quality of life for individuals diagnosed with PD. Although this approach is not likely to change the course of the disease, it may allow the patient with PD to continue to experience some control of their autonomy while dealing with increasing disease disability.

Clark [11] first proposed the concept of physical therapy as a treatment option for PD, even before the implementation of levodopa in the 1960s by Birkmayer [11]. Clark [11] described implementing specific exercises to help to improve the speed of extremities and to maintain these exercises to "prevent the deleterious effects of inactivity." Currently, rehabilitation is considered an effective adjunctive therapy to pharmaceutical and surgical treatments. Physical therapy rehabilitation allows for the maximization of functional abilities and improved quality of life. However, until recently, the underlying mechanism was unknown. The physical therapy rehabilitation techniques currently used are not suitable for individuals with PD owing to the symptomatic constraints of the disease. A recent meta-analysis examined current physical therapy techniques in individuals with PD and found that it provides only a transient improvement of motor symptoms [11]. Another randomized clinical trial explored the clinical effectiveness of individualized physiotherapy in a population of 762 individuals with PD [11]. It was found that physiotherapy was not associated with immediate clinically meaningful improvements in mild and moderate PD [11]. A successful rehabilitation technique for individuals with PD requires ecologically valid tasks that these individuals would normally perform every day. Furthermore, the area where the training occurs should be suitable for each patient as individuals may perform better in their own home or environments closer to home than in a clinic. Most importantly, rehabilitative techniques are often not available except at specialized centers requiring travel which is a difficult and unmanageable venture for most patients and caregivers. Hence, another way of bringing practical yet specialized rehabilitation techniques, i.e., those that are smart and portable, close to the patient, is a significant unmet need.

The assessment, treatment, and rehabilitation of PD are all interrelated and require integration in a potentially seamless manner to provide treatment optimization and thereby improve the quality of life for these individuals. This chapter explores the up and coming assessment, treatment, and rehabilitation techniques that are currently being explored for application in individuals with PD as one such scenario of a new frontier. Laboratory-based technologies in addition to portable and wearable systems for mobility assessment are discussed. Finally, a new methodology based on virtual reality (VR) for generating real-world scenarios within which patients can be assessed for medical management optimization and potentially for providing portable and targeted rehabilitation is explored.

In summary, the current needs of rehabilitation for PD are:

1. Subjective measures for recording physical/motor disability that are currently performed using clinical scales need to be replaced by objective instrument-based techniques. Such techniques would be portable, repeatable, and standardized.

2. Rehabilitative interventions are nonspecific and do not take into account the type of deficits that these patients face, namely strategy in performing activities of daily living. This needs to change.
3. An intelligent rehabilitation program would therefore be individualized to the disease, the stage of disease, and the patient's own perceived disability.
4. Assessment of the disability would be carried out within such an environment and based upon the detected performance difficulty, a rehabilitative strategy would be implemented.

Currently Used Scale-Based Assessment Techniques

The clinical assessment and monitoring of PD is challenging partly because of the complexity and heterogeneity of the disease. The methods used rely heavily on the clinicians' experience, which is inherently subjective and qualitative. There are a few commonly used assessment and monitoring techniques such as clinical rating scales, patient self-report, and patient diaries.

Clinical scales are used during the patient's visit and provide a quick overview of the current disease status. The most common clinical rating scale for PD is the Unified Parkinson's Disease Rating Scale (UPDRS). The UPDRS is the current gold standard for assessing and monitoring PD symptom severity. Part II is a subjective scale that assesses the impact of some of the activities of daily living. Part III of the UPDRS is a 31-item section used to rate motor symptom severity [15]. More specifically, the UPDRS contains an integer rating scale (0–4) to assess severity. A rating of 0 would be normal whereas a rating of 4 would indicate severe disability.

This assessment approach has several weaknesses that may hinder proper clinical care. The limited scoring range of the UPDRS decreases the sensitivity of the scale to detect smaller symptom changes. The UPDRS maintains intrinsic subjectivity and low inter-rater reliability, which limit its value as a measure in clinical diagnosis and research [10]. Individuals with PD who have more advanced disease tend to have fluctuations in their motor symptoms. The UPDRS, performed in the clinic, provides only a "snap-shot" of these fluctuations and may not reveal the true functional disability they experience while they are at home. In the context of this chapter, the main weakness of the scale is its inability to correlate Part II with Part III. That is, the functional impairment to the supposed activity of daily living due to the motor disability is not what is actually assessed during the motor examination. For example, the finger tapping task does not accurately reflect the ability to do up buttons, nor does the foot tapping task reflect leg mobility while standing or walking. In fact, the motor assessment is grossly incomplete and does not provide any resolution for important components such as balance, walking, and postural changes during goal-directed task performance. Therefore, how walking changes might affect a person going from a carpeted floor to tiles or the impact of turning in the kitchen during a cooking task, are not assessed. Indeed, the patient-driven part II and the clinician-performed part III do not give the clinician any reproducible way

to titrate medical or surgical treatment. It certainly does not help to design a rehabilitation program that would target the deficits that the patient has identified in part II of the UPDRS. The clinician then targets part III while the expectation is that somehow, directly or indirectly, an improvement in this rating would automatically translate to an improvement in some aspects of part II.

Patient self-report and writing diary cards take place outside of clinic, usually in the patient's own home. The benefits of these techniques are that they can be completed in an environment in which the patient is comfortable and provide a more detailed perspective of how they are functioning. However, these methods are subjective and rely on the patient's understanding of their own symptoms. Self-report relies heavily on the patient recalling all symptoms experienced from memory. Introducing diary cards greatly enhances self-report. The many limitations of using diary cards, especially in patients that have motor and possibly some degree of cognitive deficit are obvious. Patient compliance, recall bias, and fatigue from diary writing are just some of the issues facing this method of recording the impact of PD-related motor disability on daily function. However, the most important issue in home-based assessments by the patients themselves regarding their function is the lack of an objective motor state of the patient. Therefore, although these methods may be somewhat more realistic in their ability to generate data that indicate real-world deficits, it is not paired with the much-needed objective clinical assessment. The gap and disconnect therefore continues to exist.

In summary, the scale-based assessment techniques currently used:

1. Are short and often not reflective of the patient's real-world experience of functional impairment
2. Often differ from what patients may be like in their own home compared with in clinic assessments
3. Hold an inherent disconnect between the disability perceived by patients during the performance of the activities of daily living (including those such as crossing the street, putting clothes in the washing machine, etc.) and the motor rating made by the clinician in the clinic
4. Are poor in their accuracy and the ones that may be more accurate are not carried out with a simultaneous motor assessment such as PD diaries and self-report
5. Lead to a state where management decisions are being made based largely on inaccurate and often nonrepresentative data, which reduces functional therapeutic optimization.

Current Technology-Based Assessment Techniques

Objective and quantitative monitoring of PD motor symptoms has the potential to address the unmet needs identified with the current scale based tools. They can provide a measurable and quantitative set of information of the current disease state. These measurements can be accurately taken serially and allow the assessment of the effectiveness of various therapeutic interventions. Accuracy of symptom

measurement in individuals with PD is clinically imperative when deciding on treatment options and measuring their effect. Advancement in technology has provided the capability of monitoring human kinetics objectively and quantitatively. Various technology assessment tools have been developed and implemented for PD symptom monitoring. These assessment tools can either be laboratory-based or more portable for at-home use.

Laboratory-Based Methods

Vicon System

The Vicon™ system is an optical motion capture system that uses multiple cameras and body segment markers to capture body movements in 3D (Fig. 10.1a). Each Vicon camera is surrounded by a ring of light-emitting diodes (LEDs) that emit infra-red light (Fig. 10.1b). Infra-red reflective markers are attached to the individual on various body segments, the suggested number of markers to be used is 35–38 (Fig. 10.1c). As the participant walks in the capture zone the camera LEDs emit infra-red light that bounces off the body markers and is picked up by the Vicon

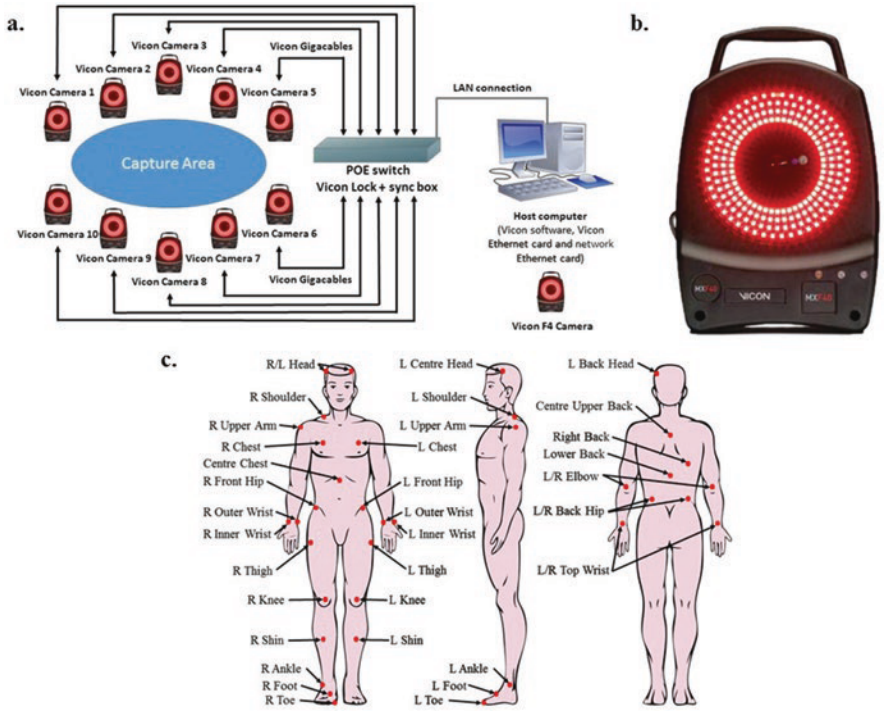

Fig. 10.1 (**a**) The measurement set up for the Vicon™ camera system. (**b**) The standard Vicon F40™ camera, reproduced with permission from MocapHouse [20]. (**c**) The standard infra-red reflective body marker positions required for accurate measurement [20]

Fig. 10.2 The Zeno™ walkway carpet system used to monitor gait performance in real time, image provided courtesy of Protokinetics

cameras. Each Vicon camera sends a 2D image to the MX Ultranet HD box every fraction of a second. The Ultranet box uses trigonometry to estimate the position of each marker in 3D; thus, each marker needs to be visible by at least two cameras at one time. The system is highly accurate and is able to detect movements within 1 mm at 250 frames per second [16, 17].

Das et al. [18] used the Vicon motion capture system in a population of individuals with PD and found a high correlation with the UPDRS. Many cardinal features of PD can be captured and analyzed using the proprietary software that is provided with this system. Such as tremor, bradykinesia, gait and postural stability [18]. Mirek et al. [18] explored the difference in gait parameter measures between PD and healthy control participants. It was found that the Vicon system was able to accurately detect a reduction in several gait measures in PD and control participants.

The main drawback to this system is the lack of portability. The system requires a large area for set-up and confines the individual to a round area where the cameras are able to record. If the individual moves outside the boundaries, the system will be unable to track their movements. The required number of body markers makes assessments with patients difficult because placing all the required markers is very time-consuming. The Vicon system is one of the more expensive motion capture technologies on the market, which limits the number of research laboratories that may be able to use it.

Gait Analysis Carpet System

Various gait assessment tools have been developed to quantify gait parameters while individuals walk across a pad with sensors. The Zeno walkway (Zenometrics™ LLC, Peekskill, NY, USA) is a 7-m-long carpet with embedded pressure sensors (Fig. 10.2). The sensors detect each footfall made by the participant while walking and relay the information to a computer for analysis. The software system captures each footfall on the Zeno walkway and provides accurate measurement of various spatial and temporal gait measures such as step length, stride velocity, single support time, double support time, and cadence, among many others [21, 22]. The sensor recording hardware is common to two main analysis software platforms,

GaitRite™ and PKMAS™. The validity and reliability of both software analysis systems has been shown in many studies to date [10, 23, 24]. Van Uden and Besser [24] examined the test–retest reliability of the Zeno walkway over a 1-week period. An intra-class correlation coefficient of over 0.90 was obtained for all spatial and temporal gait measures [24].

The Zeno walkway system allows the participant's gait performance to be quantified in an efficient manner, allowing post-hoc analysis to be conducted [4]. The ability to extract gait parameters during a patient's walk in real time has advanced the way in which treatment regimens are assessed. Obtaining these gait parameters can elucidate the characterization of disease [25, 26], the prediction of falls [27], and contribute to defining gait patterns in the progression of PD [28].

The main drawback to the Zeno walkway system is that it only provides 7 m of walking distance for analysis, which may not be a good representation of the general walking of the patient. Furthermore, a recent study examined the potential Hawthorne effect that arises while using the gait carpet [29]. It was found that patients walked significantly better when they knew they were being examined on the gait carpet [29]. The gait carpet system also needs to be used in a laboratory setting and is not a viable option for at-home monitoring.

In summary, laboratory based assessment techniques:

1. Are highly accurate and are able to record very reliably at a high resolution
2. Require the presence of a gait laboratory
3. Are not portable and need specialist expertise to be able to use
4. Are expensive and because of their very nature are primarily confined to academic institutions for gait and biomechanical research

Portable and Mobile Methods

Tele-monitoring is the remote monitoring of patients who are not at the same location as the health care provider. The ability of technology to provide a detailed objective and quantitative review of PD symptoms is making at-home monitoring a possibility. At-home assessment tools provide a method of observing patient symptoms on a continuous long-term basis. In this way, health care standards would improve and the cost would decrease. Patel et al. [30] developed a system that allowed tracking of PD motor fluctuations in the person's own home. The PD participants wore eight sensors that were connected to a web-based platform that sent data directly to the health care center. This system provided only details about motor fluctuations, but this method could be applied to other technologies to advance at-home monitoring of PD. Several of the systems currently available for home monitoring are reviewed briefly.

Kinect

The Kinect™ is a motion-sensing input device that provides full-body 3D motion capture (Fig. 10.3a). This system is used to directly control computer games through

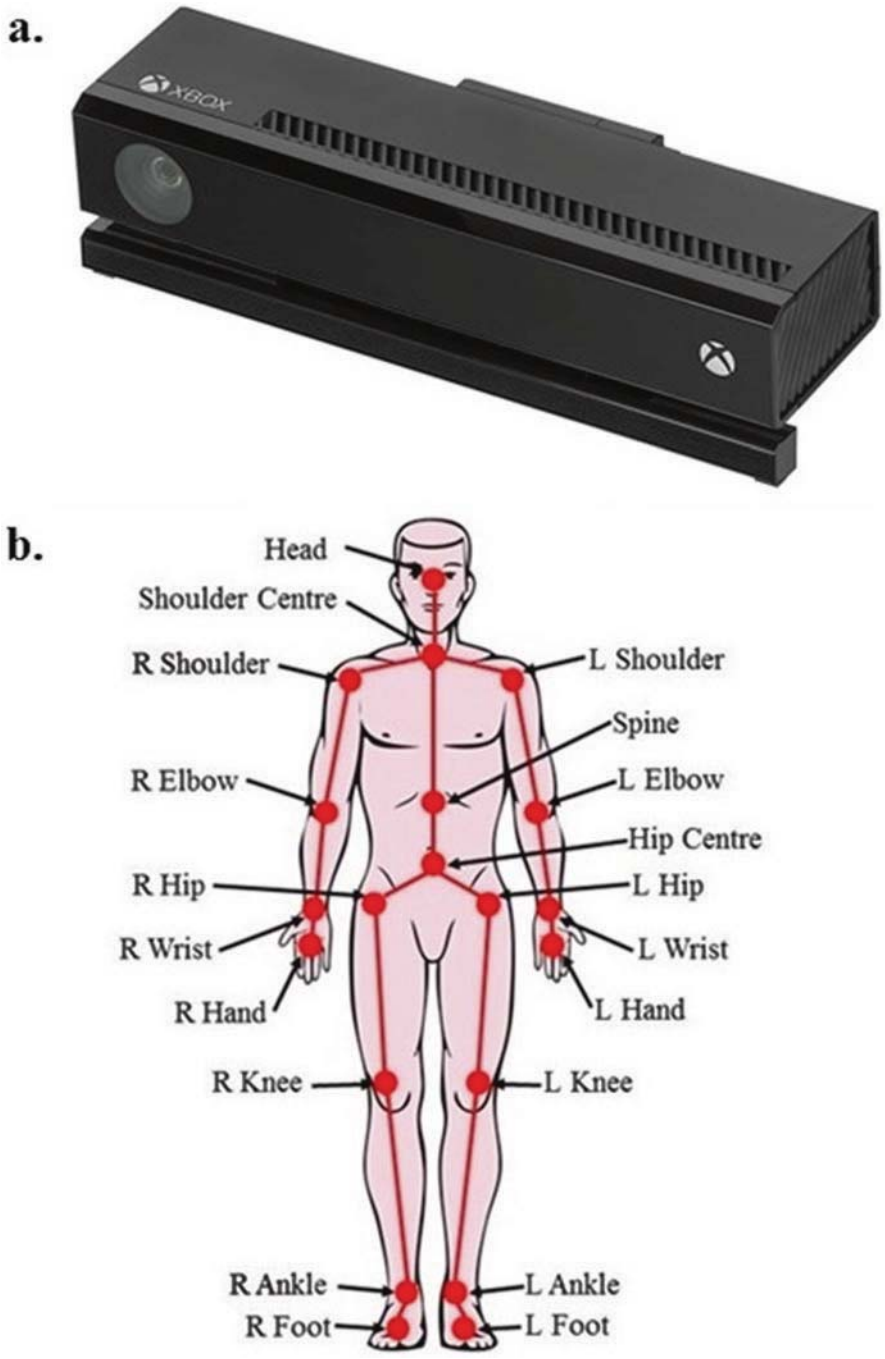

Fig. 10.3 (**a**) The standard Kinect™ system for Xbox One™ developed by Microsoft™, image from Wikimedia commons [32]. (**b**) The 20 key points that the Kinect sensor uses to generate a general skeleton for tracking users

body movement. One main strength of this system is that it is affordable and can be easily purchased. This system can be quickly set up anywhere and does not require markers to be placed on the body. Cancela et al. [31] developed a method for tracking gait performance in healthy subjects. They were able to track several features of the gait cycle with minimal error. Galna et al. [17] tested the Kinect system in 15 individuals diagnosed with PD. This group found that Kinect was able to track gross body segment movements very well, but fell short when attempting to track finer movements (such as toe tapping and tremor) [17]. Kinetic can currently be used to track bradykinesia quite well [17].

Currently, the system estimates the position of 20 anatomical landmarks (Fig. 10.3b). This estimation needs to be much more accurate and should have the capability to optimally adjust these landmarks for personalized use. The Kinect system is not portable, once it is set up the individual can only move a certain distance away and to the side of the sensor. However, this system is a viable option for at-home UPDRS assessment of patients. The patient can perform various motor assessment tasks in their own home while in front of the Kinect system.

Optotrak

Optotrak™ is a three-dimensional camera system used to track the motion of infrared emitting diode (IRED) markers (Fig. 10.4a). The IRED markers are placed on body segments of participants and the Optotrak camera tracks the movement of the markers in real time. The camera unit has a limited range within which participants have to stay for proper tracking (Fig. 10.4b). Optotrak has addressed this limitation and allows up to eight camera units to be used, which greatly expands the area of assessment. The Optotrak software provides kinematic data that are clinically relevant to individuals with PD, such as gait measures, tremor detection, and bradykinesia.

A recent study compared the gait measures extracted from the Optotrak system and the Kinect system. The agreement between the body measurements of the two systems was assessed using an intra-class correlation coefficient. It was found that gait parameters obtained from Kinect match well with the Optotrak system [31]. The Optotrak system is expensive, especially when acquiring more than one camera unit. The area of tracking for one camera unit is not sufficient for accurate body assessments and several units would need to be used for proper assessment. Although the Optotrak system has the advantage of being able to track finer movements, technology is quickly advancing and less expensive options may become available.

Wearable Inertial Sensors

Wearable inertial sensors are commonly used to measure motion and physical activity associated with daily living [34, 35]. The small size and ease of use make them ideal for placement on various body segments for real-time portable capture of multi-segmental body movements. The gaming and film industry has made use of these sensors in the design and development of their products. The clinical application of these sensors is still in its infancy but this application is quickly garnering attention.

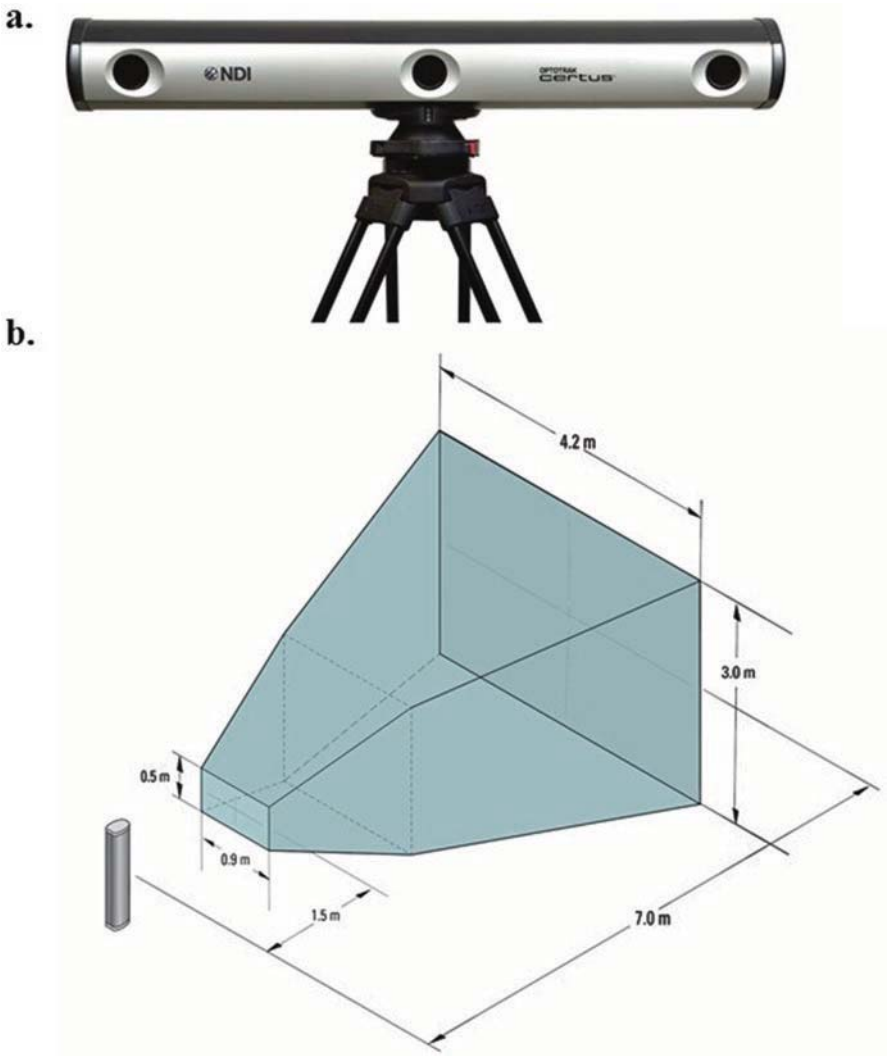

Fig. 10.4 The Optotrak™ system from Northern Digital allows real-time tracking of participants wearing infrared emitting diode markers. (**a**) The camera system used to track the markers, up to eight camera units can be used simultaneously, image provided courtesy of Northern Digital Inc. (**b**) The area of tracking for each camera unit, image provided courtesy of Northern Digital Inc.

There are three classes of inertial sensors. The combined signals of all three sensors have been used to accurately determine the temporal and spatial measures of body movement. The sensors are:

1. **Accelerometers**: measure the acceleration of linear motion. According to Newton's second law acceleration of linear motion is the force acting on a mass.

Accelerometers can be used to assess balance, gait and classification of movements.
2. **Gyroscopes**: measure the angular velocity giving information about orientation and rotation. These sensors allow recognition of movement within a 3D space.
3. **Magnetometers**: measure the precise movements of the body in the earth's magnetic field.

Wearable inertial sensors have been useful for application in assessing MDs [1, 36–38]. Chang et al. [39] developed a fall detection system by using three sensors (containing an accelerometer and gyroscope) placed on both feet and the waist. This study was able to accurately predict fall risk in various terrains including: motionless, walking, running, walking up an incline and climbing stairs [39].

Several studies have compared the UPDRS with the inertial sensors [40, 41]. Salarian et al. [41] found a high correlation between the total UPDRS and the data collected from three sensors in ten PD participants. This group was interested in monitoring ambulatory activity in a population of individuals with PD. PD often presents as an asymmetric disorder, one side of the body being more severely affected than the other. Sant'Anna et al. [40] assessed asymmetry of both lower and upper limbs during ambulation. The study used four sensors (both legs and wrists) to track asymmetry in 15 PD participants. They found a strong correlation (0.949) between the asymmetry scores of the UPDRS and the asymmetry values from the body sensors [40].

The inertial sensors are able to detect very fine movements, which patients and clinicians' do not notice. It is often argued that if patients do not notice the small changes in the parkinsonian state then employing these sensors is "overkill." However, this attribute could be beneficial for early diagnosis of PD by providing data that the clinical scales cannot detect [42]. Furthermore, the ability to detect such fine changes in the parkinsonian state may be beneficial in evaluating the efficacy of new treatments. These claims have to be validated in terms of making a difference in the diagnosis and treatment of patients. As such they remain predominantly in the research domain.

Kinesia

The Kinesia™ system (Cleveland Medical Devices Inc., Cleveland, OH, USA) is marketed as a clinical deployable technology that tracks tremor and bradykinesia in individuals with PD. This device is worn on a single finger, making the device very compact (Fig. 10.5). It has three accelerometers to track linear acceleration and three gyroscopes to measure angular velocity [43]. The device has shown test–retest reliability over clinic-based assessment techniques [44].

Motor symptoms of PD affect the entire body, which is a major concern with the Kinesia device. While it may be useful for detecting tremor and bradykinesia in the hand, it can provide limited detail about the symptom severity in the contralateral lower limb. Furthermore, PD motor symptoms are commonly asymmetric and affect one side more than the other [45, 46]. The motor symptoms may present bilaterally, but the severity of the symptoms may not be symmetrical [45]. The asymmetry of the disease represents another drawback for the Kinesia system.

Fig. 10.5 The Kinesia One™ sensor, which is placed on the fingertip and can monitor motor symptoms of PD, image provided courtesy of Kinesia

Motion Capture Suit

A full body sensor system is an appealing assessment technique that is gaining interest in the PD research field. Several motion capture suits have been used for research from animation companies such as Xsens™ and Synertial™ (Fig. 10.6a). These systems contain 16–19 inertial sensors that are located all over the body and provide information about all body segments (Fig. 10.6b). Research with the motion capture suit systems have shown reliability and validity at monitoring human movement [37, 47, 48]. These motion capture systems allow assessments to be completed outside of clinic and in the patients' own home environment.

Motion capture suit systems provide large quantities of data that need to be properly assessed for clinical impact. The main concern of these types of systems is the ability to extract relevant features. As previously mentioned, these sensors can detect small changes in body movements, but extracting these data for clinical application is not yet possible.

In summary, portable and mobile assessment methods:

1. Can be divided into those that are cheap and easy to implement but have lower resolution and those that provide very accurate information but large data sets.
2. Can be divided into sensor systems that utilize single or a small number of sensors for monitoring global body movements versus those that can monitor whole-body responses. To monitor single body parts (such as one limb) or to generate a global mobility score, single sensor systems may have some value. However, if a more detailed and whole-body measurement is required, then a multi-sensor system including body suit-type systems is more useful.
3. Are now becoming very affordable to buy, but lack the analysis software support to directly help clinicians to make management decisions.
4. Generally remain in the research domain, although vigorous efforts are on-going to make them clinically useful.

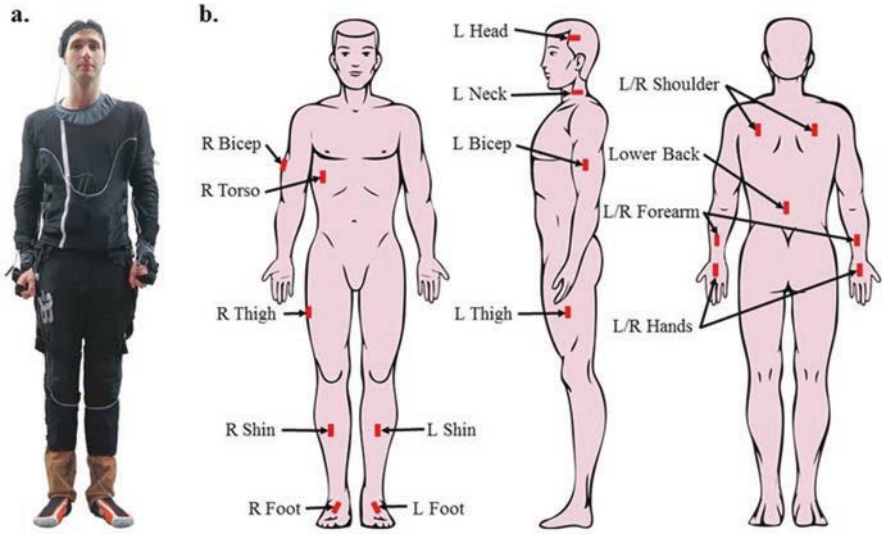

Fig. 10.6 The Synertial™ motion capture suit employs 17 sensors each containing a magnetometer, accelerometer, and gyroscope. The set-up time is minimal as the sensors are pre-placed onto the pants and top. (**a**) The Lycra motion capture, which houses 17 inertial sensors, reproduced with permission from LHSC [49]. (**b**) Diagram depicting the placement of the 17 inertial sensors on the body

Rehabilitation Approaches in Current Use

Despite optimal pharmacological treatment, the motor impairments in individuals with PD continue to deteriorate, leading to further impaired mobility [50]. The implementation of rehabilitation therapy is used as adjunctive treatment for troubling motor symptoms of PD. A multidisciplinary management plan for PD that incorporates both medical and rehabilitation therapy should be implemented to better manage the complex MD [51]. Medical management of PD is well understood. Additionally, several studies have shown supportive evidence for the implementation of rehabilitation techniques for PD management in combination [52]. Current rehabilitation techniques are discussed.

Rehabilitation Techniques for PD

Currently, physical therapy is the most widely used rehabilitation technique for the management of PD, focusing on improvements in gait, physical capacity (i.e., strength and endurance), posture, and balance [52]. Morris [53] was to our knowledge the first to describe a model of physical therapy management for individuals with PD. He proposed that the ability to move is not lost in PD; rather, it is an activation problem [53]. Morris suggested that the deficit in activation forces individuals

with PD to rely on cortical control mechanisms to initiate movement [53]. The model used task-specific strategies such as gait, sitting down, and turning in bed.

The model made use of external cues such as visual, auditory, and proprioceptive stimuli (rocking the body from side to side) [53]. In a healthy human brain, the BG are related to the triggering of internal cues for performing a desired motor function [54, 55]. In PD, such internal cued movements may be significantly affected because of the complex cortical–basal ganglionic dysfunction [54, 56, 57]. It is also possible that these cues are not used to select and modify the required motor response correctly. The results may be seen as a disruption of normal motor function in appendicular and axial systems, including gait. In this context of PD, the external cues used allow alternative brain circuits to be recruited, bypassing the defective BG circuitry [54]. Verschueren et al. [56] studied the influence of extern— cues on motor task performance In a population of PD participants, who were trained to perform a motor task that provided external feedback during the performance of the task. The PD participants were then asked to complete the motor task while blindfolded, eliminating the external feedback. It was found that performance was significantly reduced in PD participants when performing the task blindfolded [56]. It was concluded that providing the external feedback during the performance phase allowed PD participants to partially bypass the BG [54, 56]. A recent review of literature highlighted this fact that external cues access alternative neural pathways that remain intact in the PD brain, such as the cerebello-thalamo-cortical network [58].

The ability to put together a temporal order of task performance is thus very difficult for patients with PD, leading to task failure or "freezing." Such difficulties can be seen in all aspects of motor performance. To address this, the training model discussed above also used cognitive movement strategies, which break complex movements into separate components [53]. Individuals with PD are trained to perform each component separately and to pay conscious attention to their execution. Morris [59] provided some updates to the physical therapy model focusing on adjusting the rehabilitation strategy based on years of diagnosis. Morris suggests that the tasks used in newly diagnosed individuals should be different from individuals who have been diagnosed for more than 5 years. This is because of the progressive death of substantia nigra cells, despite optimal pharmacological intervention [59].

A recent meta-analysis, conducted by Tomlinson et al. [13], examined the effectiveness of physical therapy in 33 randomized clinical trials with over 1,500 PD participants. Tomlinson et al. [13] found that physiotherapy intervention provides a transient benefit in the treatment of PD, regardless of the physiotherapy intervention. However, in the long term, benefit from physiotherapy remains elusive [13]. This meta-analysis states that an issue with current studies focused on physical therapy for PD is that outcome measures are drastically different [13]. They suggest employing relevant, reliable, and sensitive outcome measures, which hints at both measurement of the physical improvement using reliable tools (such as the systems mentioned above), but also functional improvements in the tasks that actually matter to the patient. Indeed, an improvement in the endurance or strength in a PD population may not matter to the performance of a task such as doing the laundry or crossing the street.

Another issue with current physical therapy models for PD stems from the symptomatic constraints in PD such as rigidity, bradykinesia, freezing, and impaired

cognitive processing. Traditional rehabilitation techniques are not suitable for individuals with PD. King and Horak [60] developed an exercise program that was more suited to individuals with PD. However, the program was not adaptable to the various stages of the disease. A rehabilitation program, with functionally relevant tasks, that has direct applicability to the activities of daily living is a necessity. Providing a single space for rehabilitation for every patient is not ideal, as some patients may perform better in the contrived space [29]. Currently, PD patients are enrolled in standardized rehabilitation programs, in a contrived space, to carry out tasks that may not be applicable to their everyday life.

In summary, currently used rehabilitation techniques used for neurological diseases, especially PD:

1. Are nonspecific to the actual condition and stage of disease.
2. Are not targeted toward directly assessing and improving the functional impairments faced by the patient in daily life. Instead, nonspecific rehabilitation such as relaxation, stretching, cardiovascular fitness, and weight training are performed.
3. Could be more accurately assessed by using the sensor technologies discussed above to record out-of-laboratory mobility.
4. Are conducted in environments and contexts that are not yet individualized to the deficits of the disease.

Targeted, Disability-Based Rehabilitative Approaches to Parkinson's Disease

There are very few practical and useful devices available on the market for the specific treatment of PD symptoms. The two reviewed below are the only ones that have been adopted to some degree by patients and physicians. In the first instance, sensor technology is employed to measure a specific symptom, namely tremor, and a "made-to-measure" treatment is provided. In the second, a specific external cuing device is used to improve gait.

Active Cancellation of Tremor Device

The development of technologies that counter specific symptoms of PD, although not a cure, help to improve the quality of life of those affected. Tremor is one debilitating motor symptom of PD that affects daily activities. Tremor oscillates at a specific frequency range of 2–15 Hz, which can be measured using inertial sensors [61, 62]. The lower frequencies are indicative of a more severe tremor, whereas higher frequencies relate to mild tremor. The ability to measure the degree of tremor has led to the development of tremor cancellation devices. These devices measure the directionality of the tremor and move in the opposite direction to stabilize it.

Pathak et al. [62] designed a spoon that counteracts tremor in the hand, improving utensil accuracy for individuals with mild to moderate tremor (Fig. 10.7b). The

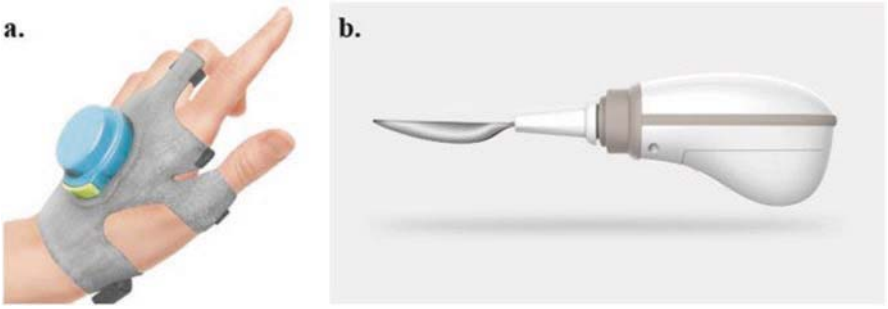

Fig. 10.7 Examples of assistive tremor cancelling devices. (**a**) The GyroGlove™ is worn to reduce hand tremor when the patient requires accurate hand movements, image provided courtesy of GyroGear. (**b**) LiftLabs™ tremor cancelling spoon, which improves accuracy by opposing tremor caused by disease, reproduced with permission from Kozovski [64]

study examined 15 participants diagnosed with essential tremor. The handheld device significantly reduced spoon tremor rated by the UPDRS and accelerometer data [62]. The main strength of this device is the non-invasive nature of the intervention; it is comfortable and easily adopted by its users. However, this device has not proven useful for individuals with severe tremor [62].

The GyroGlove™ is a new technology developed by Faii Ong that reduces tremor continuously (Fig. 10.7a) [63]. The glove is in development with a patent pending, but has the potential to reduce hand tremor in individuals with PD throughout the day. The glove makes use of gyroscopes that resist hand movement and thereby reduce tremors. However, tremor is often multijointed and involves the elbow and shoulder as well.

Laser Cane

Freezing of gait (FOG) is a common symptom in individuals with PD that shows little or no response to pharmacological and surgical interventions [65]. FOG has been estimated to affect 32% of all individuals diagnosed with PD [66]. Several auditory and visual cues have been used to counter FOG episodes in individuals with PD. Several studies have demonstrated that when PD participants walk across parallel lines on the floor there is an improvement in their FOG episodes [67–69].

The U-Step Laser Cane™ is a walking aid that projects a red laser line across the walking path, making use of the parallel line visual cue (Fig. 10.8). Donovan et al. [70] used the Laser Cane in a population of 26 individuals with PD and found a significant improvement in FOG after 1 month of usage. McCandless et al. [71] compared the Laser Cane with several other auditory and visual cueing interventions in a population of 20 individuals with PD. The Laser Cane was found to be the most effective cueing intervention for correcting FOG episodes [71].

In summary, disability-based rehabilitative approaches:

Fig. 10.8 The Laser Cane™ from U-Step™ is used to correct freezing of gait episodes by use of an external laser line cue, image provided courtesy of U-Step

1. Are able to provide patients with temporary relief of the specific motor symptoms that they may be experiencing.
2. Require continual battery replacements and may leave the patient without treatment if replacements are not kept ready.
3. Are adjunctive therapies to medical intervention and may not provide benefit to every patient.
4. Are affordable assistive devices, which makes the use of them possible in patients needing adjunctive symptom relief.

Future Technology-Based Rehabilitation of Parkinson's Disease

Technology will play an increasingly important role in the assessment and in the treatment of MDs. As discussed above, inertial sensors are currently providing real-time feedback on various PD symptoms, allowing treatment regimens to be individualized more efficiently. Physical therapy is also an important factor for the management of PD progression. Physical therapy techniques help to maintain mobility in addition to the treatment provided. As previously discussed, current

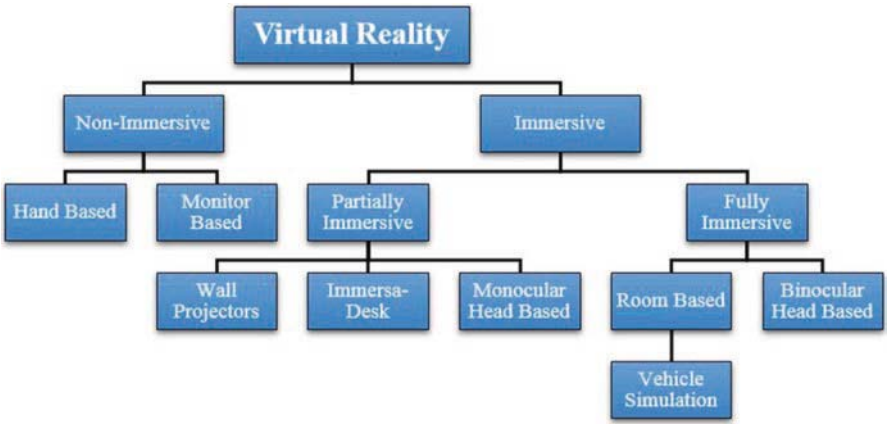

Fig. 10.9 A simplified taxonomy of virtual reality systems

physical therapy techniques are suitable for individuals not diagnosed with PD, use irrelevant tasks, and are performed in contrived spaces. These factors may contribute to the ineffectiveness of these programs in managing motor dysfunction in the PD population. Construction of ecologically valid situations is a necessity when attempting physical therapy for individuals with PD.

As discussed through the chapter, we have now reached a point where the ability to objectively assess the physical disability in the patient can now be supported using a variety of technologies. However, the questions that remain are:

1. How do we carry out these assessments in what would be termed "ecologically valid" environments?
2. How do we provide rehabilitation that then helps patients to optimize their performance within these and the many other environments that we face in our daily life?

Virtual Reality

Virtual reality (VR) may be an optimal tool for a more individualized rehabilitation strategy for individuals with PD. VR is the interaction of an individual in the real world with a virtual environment, which has been generated by a computer. VR can be non-immersive or immersive depending on the technology used (Fig. 10.9). VR makes use of visual, auditory, and haptic inputs, and the virtual environment provides feedback about performance. VR allows an individual to safely explore their environment independently. This technology would provide a flexible and scalable means of implementing realistic and functionally relevant tasks. VR is able to simulate realistic environments that would be too expensive and time-consuming to recreate in the real world for assessment and rehabilitation purposes. VR would address

the concern of current research studies that lack contextually relevant stimuli, making generalizability difficult.

1. **Non-immersive VR**: is generally screen-based and pointer-driven. This type of system requires the use of hand-held devices (cell phones, portable games consoles) and monitors (desktop computers).
2. **Partially-immersive VR**: provides the user with an augmentation of the real environment within a virtual environment.
3. **Fully-immersive VR**: provides users with three-dimensional virtual scenes.

Fully immersive VR allows natural interactive behaviors to take place while physiological measures are taken such as body segment movements or brain activity. This allows researchers to address several questions in a controlled environment while recreating real world situations. Furthermore, a fully immersive VR system would engage the sensorimotor system more fully than a simple stimulus, increasing the psychological and behavioral responses. For example, gait difficulty is a major concern in PD as it tends to worsen as the disease progresses. Fully immersive VR allows motor activation to occur during the simulated experience as these environments can allow patients to navigate and physically interact with virtual objects. Fully immersive VR allows the researcher to present multiple stimuli at one time that may not be present in a natural environment. Furthermore, changes can be made to these stimuli at short notice.

Nintendo Wii for Rehabilitation in PD

A recent study examined the use of the Nintendo Wii™ for non-immersive VR rehabilitation in a PD population. The Nintendo Wii is a force platform that provides information on force distribution and center of gravity (Fig. 10.10) [72]. Dos Santos Mendes et al. [72] recruited 16 individuals with PD and 11 controls for the 7-week study. Each participant completed ten training games at each visit. They found that the ability of PD participants to learn, retain, and transfer performance improvements depends on the demands, specifically cognitive demands [72]. It was noted that PD participants were able to transfer motor ability to similar untrained tasks [72].

Gonçalves et al. [73] tested the effectiveness of the Nintendo Wii for VR rehabilitation in 15 individuals with PD. Each training session lasted 40 min, occurring twice a week for 14 sessions. They found a significant improvement on the UPDRS, an increase in walking velocity, and a reduced number of steps during walking [73]. There was no follow-up with patients in the study; the assessments were conducted before training and immediately following training. Moreover, this study failed to demonstrate the appropriate retention of motor training, which is an important factor in physical rehabilitation techniques.

The use of the Nintendo Wii has demonstrated potential therapeutic advantage with rehabilitation in individuals diagnosed with PD. The Nintendo Wii is

Fig. 10.10 The Nintendo Wii™ balance platform used for rehabilitation in PD, image from Wikimedia commons [74]

cost-effective, easy to use, and extremely portable. The potential for at-home use is of great advantage with this non-immersive VR device. The drawback is that it is stationary and does not allow patients to be ambulatory during training. Gait training is an important aspect to physical therapy from which individuals with PD would benefit.

Immersive Virtual Reality for Rehabilitation in PD

Research into the implementation of immersive VR for rehabilitation in PD is limited, only appearing in a few published studies. Mirelman et al. [75] developed an immersive VR environment for gait training on a treadmill. Twenty individuals with PD were required and instructed to avoid obstacles in the VR environment while walking on the treadmill. The study lasted 6 weeks and the environment became more challenging as the study progressed to increase adaptability in the participants. Following the 6-week study it was noted that the participants had a significantly improved UPDRS score, gait speed, and stride length [75]. These improvement effects were maintained for up to 4 weeks post-training, and a few metrics continued to improve [75]. This study has several limitations that should be mentioned. The sample size and lack of a control group lower the impact of this study. The ability to compare the training with a control group would rule out any potential placebo or Hawthorne effect. Most importantly, improvement was observed and recorded while on the treadmill only, which lacks ecological validity. Participants must be able to ambulate and practice movement strategies in more realistic VR environments.

Arias et al. [76] tested the validity of using fully immersive VR and virtual environments for assessing PD motor symptoms in ten PD participants. Participants were trained to perform a finger-tapping task in the real environment followed by a virtual environment. An intra-class correlation and the mean difference between the real and virtual finger-tapping test showed high reliability [76]. Immersive VR is in its infancy and has limited implications for PD. Only a few studies have tested the

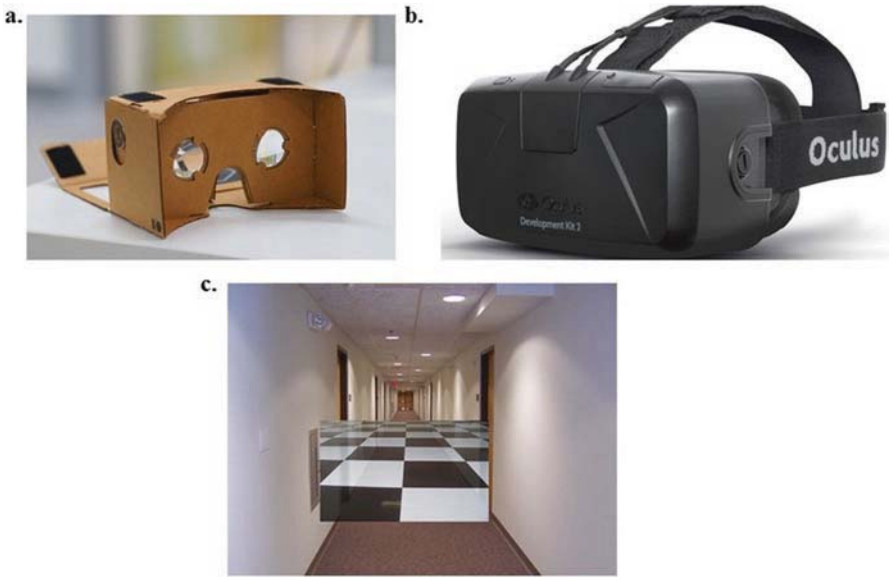

Fig. 10.11 Examples of virtual reality devices and a scenario. (**a**) The Google™ cardboard goggles provide an affordable alternative to virtual reality glasses using a smart phone, image from Wikimedia commons [78]. (**b**) Oculus Rift™ virtual reality headset, image from flickr creative commons [79]. (**c**) An augmented virtual reality scenario for freezing of gait in PD, reproduced with permission from Holmes [80]

application in a population of individuals with PD. Furthermore, the cost of these devices is currently fairly high, making personal use unfeasible. However, immersive VR is a promising rehabilitation technique that can provide a controlled, comfortable environment in which patients can complete ecologically valid tasks.

Augmented Immersive Virtual Reality Assessment and Treatment

Augmented immersive VR is the visual combination of the real-world environment with computer generated imagery (Fig. 10.11c) [77]. Instead of being immersed in a complete virtually simulated world, augmented reality allows the subject to experience a different location while staying connected with reality [77]. This form of VR allows for a more realistic virtual environment through which subjects can navigate. A recent augmented VR method has been established for individuals diagnosed with PD. Garcia et al. [77] proposed a method by which patients experience ecologically valid scenarios to navigate. The three scenarios that were established in augmented reality were watering plants, shopping in a grocery store, and crossing a busy street [77]. These scenarios were chosen as real-world situations in which individuals with PD would find themselves.

The preliminary work clearly shows that it is now possible to design and construct scenarios that allow the assessment of patients with disorders such as PD within

contextually relevant environments. This can be carried out using portable VR devices (Oculus Rift™, Google™ VR goggles, etc.) within a reasonable amount of space (Fig. 10.11a, b). Scenarios can be built to meet the major disability for the patient and implemented in their area of residence. Based upon the deficits elicited, a program can be designed, again in the same immersive environment, to provide rehabilitation to these patients with interesting, increasingly complex environments.

Conclusion

When discussing the future perspective of complete care for individuals with PD it is important to consider assessment methods, treatment techniques, and rehabilitation strategies. It is clear that technology will play an important role in the future of PD and other MDs in general. The ability to assess and monitor motor symptoms objectively and quantitatively with technology is reaching a state of maturity where portable, cost-effective methodologies are now becoming available. This will allow current treatments to be better targeted for each individual and more accurately test the efficacy of new treatments. Rehabilitation is a feasible adjunctive therapy for PD that maximizes the functional ability of each patient according to their disease state. Developing a program that employs ecologically valid scenarios in a comfortable environment for assessment will greatly enhance the effectiveness of the technique. When combined with objective measurement tools, the assessment of patient deficits in active scenario-based settings can provide a true picture of the real-world disabilities faced by patients in daily life. The same techniques can then be employed to generate a rehabilitative program that is individualized and targeted. The future of PD care relies on such individualized and optimized treatment and rehabilitation techniques that make use of advancing technology.

References

1. Yang K, Xiong WX, Liu FT, Sun YM, Luo S, Ding ZT, et al. Objective and quantitative assessment of motor function in Parkinson's disease from the perspective of practical applications [Internet]. Ann Transl Med. 2016;4(5):90. http://atm.amegroups.com/article/view/9420/10095.
2. Heldman DA, Giuffrida JP, Chen R, Payne M, Mazzella F, Duker AP, et al. The modified bradykinesia rating scale for Parkinson's disease: reliability and comparison with kinematic measures [Internet]. Mov Disord. 2011;26(10):1859–63. http://www.ncbi.nlm.nih.gov/pubmed/21538531.
3. Mera TO, Heldman DA, Espay AJ, Payne M, Giuffrida JP. Feasibility of home-based automated Parkinson's disease motor assessment [Internet]. J Neurosci Methods. 2012;203(1):152–6. http://www.ncbi.nlm.nih.gov/pubmed/21978487.
4. Egerton T, Thingstad P, Helbostad JL. Comparison of programs for determining temporal-spatial gait variables from instrumented walkway data: PKmas versus GAITRite [Internet]. BMC Res Notes. 2014;7(1):542. http://www.ncbi.nlm.nih.gov/pubmed/25134621.
5. Pahwa R, Lyons KE. Early diagnosis of Parkinson's disease: recommendations from diagnostic clinical guidelines [Internet]. Am J Manag Care. 2010;16(Suppl I):S94–9. http://www.ncbi.nlm.nih.gov/pubmed/20297872.
6. Burke RE, O'Malley K. Axon degeneration in Parkinson's disease [Internet]. Exp Neurol. 2013;246:72–83. doi:10.1016/j.expneurol.2012.01.011.

7. Gunn DG, Naismith SL, Lewis SJG. Sleep disturbances in Parkinson disease and their potential role in heterogeneity [Internet]. J Geriatr Psychiatry Neurol. 2010;23(2):131–7. http://www.ncbi.nlm.nih.gov/pubmed/20101072.
8. Lindgren HS, Dunnett SB. Cognitive dysfunction and depression in Parkinson's disease: what can be learned from rodent models? [Internet]. Eur J Neurosci. 2012;35(12):1894–907. doi:10.1111/j.1460-9568.2012.08162.x.
9. Bonnet AM, Jutras MF, Czernecki V, Corvol JC, Vidailhet M. Nonmotor symptoms in Parkinson's disease in 2012: relevant clinical aspects [Internet]. Parkinson's Dis. 2012;2012:198316. doi:10.1155/2012/198316.
10. Chien S-L, Lin S-Z, Liang C-C, Soong Y-S, Lin S-H, Hsin Y-L, et al. The efficacy of quantitative gait analysis by the GAITRite system in evaluation of parkinsonian bradykinesia [Internet]. Parkinsonism Relat Disord. 2006;12(7):438–42. http://www.ncbi.nlm.nih.gov/pubmed/16798053.
11. Clark EC, Clements BG, Erickson DJ, Maccarty CS, Mulder DW. Therapeutic exercises in management of paralysis agitans [Internet]. J Am Med Assoc. 1956;162(11):1041–3. http://www.ncbi.nlm.nih.gov/pubmed/13366704.
12. Birkmayer W, Hornykiewicz O. Der L-dioxyphenylalanin (=L-DOPA)-Effekt beim Parkinson-Syndrom des <enschen: zur Pathogenese und Behandlung der Parkinson-Akinese [Internet]. Arch Psychiat Nervenkr. 1962;203(5):560–74. doi:10.1007/BF00343235.
13. Tomlinson CL, Patel S, Meek C, Clarke CE, Stowe R, Shah L, et al. Physiotherapy versus placebo or no intervention in Parkinson's disease [Internet]. Cochrane Database Syst Rev. 2012;7(8), CD002817. http://www.ncbi.nlm.nih.gov/pubmed/22786482.
14. Clarke CE, Patel S, Ives N, Rick CE, Dowling F, Woolley R, et al. Physiotherapy and occupational therapy vs no therapy in mild to moderate Parkinson disease: a randomized clinical trial [Internet]. JAMA Neurol. 2016;73(3):291–9. http://www.ncbi.nlm.nih.gov/pubmed/26785394.
15. Goetz CG, Tilley BC, Shaftman SR, Stebbins GT, Fahn S, Martinez-Martin P, et al. Movement disorder society-sponsored revision of the unified Parkinson's disease rating scale (MDS-UPDRS): scale presentation and clinimetric testing results [Internet]. Mov Disord. 2008;23(15):2129–70. doi:10.1002/mds.22340.
16. Windolf M, Götzen N, Morlock M. Systematic accuracy and precision analysis of video motion capturing systems—exemplified on the Vicon-460 system [Internet]. J Biomech. 2008;41(12):2776–80. http://search.proquest.com/docview/1651859645?accountid=12347\n; http://sfx.scholarsportal.info/mcmaster?url_ver=Z39.88-2004&rft_val_fmt=info:ofi/fmt:kev:mtx:journal&genre=article&sid=ProQ:ProQ:ericshell&atitle=Classroom-Based+Narrative+and+Vocabulary+Inst.
17. Galna B, Barry G, Jackson D, Mhiripiri D, Olivier P, Rochester L. Accuracy of the Microsoft Kinect sensor for measuring movement in people with Parkinson's disease [Internet]. Gait Posture. 2014;39(4):1062–8. doi:10.1016/j.gaitpost.2014.01.008.
18. Das S, Trutoiu L, Murai A, Alcindor D, Oh M, De la Torre F, et al. Quantitative measurement of motor symptoms in Parkinson's disease: a study with full-body motion capture data [Internet]. Conf Proc IEEE Eng Med Biol Soc. 2011;2011:6789–92. http://www.ncbi.nlm.nih.gov/pubmed/22255897.
19. Mirek E, Rudzińska M, Szczudlik A. The assessment of gait disorders in patients with Parkinson's disease using the three-dimensional motion analysis system Vicon [Internet]. Neurol Neurochir Pol. 2007;41(2):128–33. http://www.ncbi.nlm.nih.gov/pubmed/17530574.
20. MocapHouse. Motion capture systems managed by IT backyard [Internet]. Introduction to Vicon F40 Camera; 2010. http://www.mocaphouse.com/"http://www.mocaphouse.com/, http://itbackyard.com/mocaphouse"http://itbackyard.com/mocaphouse
21. Bilney B, Morris M, Webster K. Concurrent related validity of the GAITRite walkway system for quantification of the spatial and temporal parameters of gait [Internet]. Gait Posture. 2003;17(1):68–74. http://linkinghub.elsevier.com/retrieve/pii/S096663620200053X.
22. Menz HB, Latt MD, Tiedemann A, Mun San Kwan M, Lord SR. Reliability of the GAITRite walkway system for the quantification of temporo-spatial parameters of gait in young and older people [Internet]. Gait Posture. 2004;20(1):20–5. http://www.ncbi.nlm.nih.gov/pubmed/15196515.

23. McDonough AL, Batavia M, Chen FC, Kwon S, Ziai J. The validity and reliability of the GAITRite system's measurements: a preliminary evaluation [Internet]. Arch Phys Med Rehabil. 2001;82(3):419–25. http://www.ncbi.nlm.nih.gov/pubmed/11245768.
24. van Uden CJT, Besser MP. Test-retest reliability of temporal and spatial gait characteristics measured with an instrumented walkway system (GAITRite) [Internet]. BMC Musculoskelet Disord. 2004;5(13):13. http://www.ncbi.nlm.nih.gov/pubmed/15147583.
25. Egerton T, Williams DR, Iansek R. Comparison of gait in progressive supranuclear palsy, Parkinson's disease and healthy older adults [Internet]. BMC Neurol. 2012;12(1):116. http://www.ncbi.nlm.nih.gov/pubmed/23031506.
26. Lord S, Galna B, Coleman S, Burn D, Rochester L. Mild depressive symptoms are associated with gait impairment in early Parkinson's disease [Internet]. Mov Disord. 2013;28(5):634–9. http://www.ncbi.nlm.nih.gov/pubmed/23390120.
27. Verghese J, Holtzer R, Lipton RB, Wang C. Quantitative gait markers and incident fall risk in older adults [Internet]. J Gerontol A Biol Sci Med Sci. 2009;64(8):896–901. doi:10.1093/gerona/glp033.
28. Hass CJ, Malczak P, Nocera J, Stegemöller EL, Shukala A, Malaty I, et al. Quantitative normative Gait data in a large cohort of ambulatory persons with Parkinson's disease [Internet]. PLoS One. 2012;7(8), e42337. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3411737/.
29. Robles-García V, Corral-Bergantiños Y, Espinosa N, Jácome MA, García-Sancho C, Cudeiro J, et al. Spatiotemporal gait patterns during overt and covert evaluation in patients with Parkinson's disease and healthy subjects: is there a Hawthorne effect? [Internet]. J Appl Biomech. 2015;31(3):189–94.
30. Patel S, Chen BR, Buckley T, Rednic R, McClure D, Tarsy D, et al. Home monitoring of patients with Parkinson's disease via wearable technology and a web-based application [Internet]. Conf Proc IEEE Eng Med Biol Soc. 2010;2010:4411–14. http://www.ncbi.nlm.nih.gov/pubmed/21096462.
31. Cancela J, Arredondo MT, Hurtado O. Proposal of a Kinect(TM)-based system for gait assessment and rehabilitation in Parkinson's disease [Internet]. Conf Proc IEEE Eng Med Biol Soc. 2014;2014:4519–22. http://www.ncbi.nlm.nih.gov/pubmed/25570996.
32. Wikimedia. Xbox Kinect Sensor [Internet]. 2014. p. Xbox-One-Kinect. https://commons.wikimedia.org/wiki/File:Xbox-One-Kinect.jpg.
33. Geerse DJ, Coolen BH, Roerdink M. Kinematic validation of a multi-kinect v2 instrumented 10-meter walkway for quantitative gait assessments [Internet]. PLoS One. 2015;10(10), e0139913. http://www.ncbi.nlm.nih.gov/pubmed/26461498.
34. Dobkin BH. Wearable motion sensors to continuously measure real-world physical activities [Internet]. Curr Opin Neurol. 2013;26(6):602–8. http://ec.europa.eu/public_opinion/archives/ebs/ebs_183_6_en.pdf.
35. Cuesta-Vargas AI, Galán-Mercant A, Williams JM. The use of inertial sensors system for human motion analysis [Internet]. Phys Ther Rev. 2010;15(6):462–73. doi:10.1179/1743288X11Y.0000000006.
36. Rahimi F, Duval C, Jog M, Bee C, South A, Jog M, et al. Capturing whole-body mobility of patients with Parkinson disease using inertial motion sensors: expected challenges and rewards [Internet]. Conf Proc IEEE Eng Med Biol Soc. 2011;2011:5833–8. http://www.ncbi.nlm.nih.gov/pubmed/22255666.
37. Rahimi F, Bee C, Duval C, Boissy P, Edwards R, Jog M, et al. Using ecological whole body kinematics to evaluate effects of medication adjustment in Parkinson disease [Internet]. J Parkinson's Dis. 2014;4(4):617–27. http://www.ncbi.nlm.nih.gov/pubmed/25055960.
38. Tao W, Liu T, Zheng R, Feng H. Gait analysis using wearable sensors [Internet]. Sensors. 2012;12(12):2255–83. http://www.mdpi.com/1424-8220/12/2/2255/.
39. Chang SY, Lai CF, Chao HCJ, Park JH, Huang YM. An environmental-adaptive fall detection system on mobile device [Internet]. J Med Syst. 2011;35(5):1299–312. http://www.ncbi.nlm.nih.gov/pubmed/21424848.

40. Sant'Anna A, Salarian A, Wickström N. A new measure of movement symmetry in early Parkinson's disease patients using symbolic processing of inertial sensor data [Internet]. IEEE Trans Biomed Eng. 2011;58(7):2127–35. http://www.ncbi.nlm.nih.gov/pubmed/21536527.
41. Salarian A, Russmann H, Vingerhoets FJG, Burkhard PR, Aminian K. Ambulatory monitoring of physical activities in patients with Parkinson's disease [Internet]. IEEE Trans Biomed Eng. 2007;54(12):2296–9. http://ieeexplore.ieee.org/stamp/stamp.jsp?arnumber=04359998.
42. Ahlskog JE, Uitti RJ. Rasagiline, Parkinson neuroprotection, and delayed-start trials: still no satisfaction? [Internet]. Neurology. 2010;74(14):1143–8. http://www.ncbi.nlm.nih.gov/pubmed/20368634.
43. Giuffrida JP, Riley DE, Maddux BN, Heldman DA. Clinically deployable Kinesia™ technology for automated tremor assessment [Internet]. Mov Disord. 2009;24(5):723–30. http://resolver.scholarsportal.info/resolve/08853185/v24i0005/723_cdktfata.
44. Heldman DA, Espay AJ, LeWitt PA, Giuffrida JP. Clinician versus machine: reliability and responsiveness of motor endpoints in Parkinson's disease [Internet]. Parkinsonism Relat Disord. 2014;20(6):590–5. http://www.ncbi.nlm.nih.gov/pubmed/24661464.
45. Marinus J, van Hilten JJ. The significance of motor (a)symmetry in Parkinson's disease [Internet]. Mov Disord. 2015;30(3):379–85. http://www.ncbi.nlm.nih.gov/pubmed/25546239.
46. Hoehn MM, Yahr MD. Parkinsonism: onset, progression and mortality [Internet]. Neurology. 1967;17(5):427–42. http://www.ncbi.nlm.nih.gov/pubmed/6067254.
47. Cutti AG, Giovanardi A, Rocchi L, Davalli A. A simple test to assess the static and dynamic accuracy of an inertial sensors system for human movement analysis [Internet]. Conf Proc IEEE Eng Med Biol Soc. 2006;1:5912–15. http://www.ncbi.nlm.nih.gov/pubmed/17946728.
48. Nguyen HP, Ayachi F, Lavigne-Pelletier C, Blamoutier M, Rahimi F, Boissy P, et al. Auto detection and segmentation of physical activities during a Timed-Up-and-Go (TUG) task in healthy older adults using multiple inertial sensors [Internet]. J Neuroeng Rehabil. 2015;12:36. http://www.ncbi.nlm.nih.gov/pubmed/25885438.
49. LHSC. LHSC Inside Magazine [Internet]. London, Canada. 2015. p. The Movement Towards Better Treatment of Parkinson. http://inside.lhsc.on.ca/article/summer-2015/movement-towards-better-treatment-parkinsons.
50. Nijkrake MJ, Keus SHJ, Kalf JG, Sturkenboom IHWM, Munneke M, Kappellea C, et al. Allied health care interventions and complementary therapies in Parkinson's disease [Internet]. Parkinsonism Relat Disord. 2007;13 Suppl 3:S488–94. http://www.ncbi.nlm.nih.gov/pubmed/18267288.
51. Rubenis J. A rehabilitational approach to the management of Parkinson's disease [Internet]. Parkinsonism Relat Disord. 2007;13 Suppl 3:S495–7. http://www.ncbi.nlm.nih.gov/pubmed/18267289.
52. Keus SHJ, Munneke M, Nijkrake MJ, Kwakkel G, Bloem BR. Physical therapy in Parkinson's disease: evolution and future challenges [Internet]. Mov Disord. 2009;24(1):1–14. http://www.ncbi.nlm.nih.gov/pubmed/18946880.
53. Morris ME. Movement disorders in people with Parkinson disease: a model for physical therapy [Internet]. Phys Ther. 2000;80(6):578–97. http://www.ncbi.nlm.nih.gov/pubmed/10842411.
54. Debaere F, Wenderoth N, Sunaert S, Van Hecke P, Swinnen SP. Internal vs external generation of movements: differential neural pathways involved in bimanual coordination performed in the presence or absence of augmented visual feedback [Internet]. Neuroimage. 2003;19(3):764–76. http://www.ncbi.nlm.nih.gov/pubmed/12880805.
55. Goldberg G. Supplementary motor area structure and function: review and hypotheses [Internet]. Behav Brain Sci. 1985;8(04):567. http://www.journals.cambridge.org/abstract_S0140525X00045167.
56. Verschueren SM, Swinnen SPP, Dom R, De Weerdt W. Interlimb coordination in patients with Parkinson's disease: motor learning deficits and the importance of augmented information feedback [Internet]. Exp Brain Res. 1997;113(3):497–508. http://www.ncbi.nlm.nih.gov/pubmed/9108216.
57. Samuel M, Ceballos-Baumann AO, Blin J, Uema T, Boecker H, Passingham RE, et al. Evidence for lateral premotor and parietal overactivity in Parkinson's disease during sequential

and bimanual movements. A PET study [Internet]. Brain. 1997;120(Pt 6):963–76. http://www.ncbi.nlm.nih.gov/pubmed/9217681.
58. Hackney ME, Lee HL, Battisto J, Crosson B, McGregor KM. Context-dependent neural activation: internally and externally guided rhythmic lower limb movement in individuals with and without neurodegenerative disease [Internet]. Front Neurol. 2015;6(6):251. doi:10.3389/fneur.2015.00251.
59. Morris ME. Locomotor training in people with Parkinson disease [Internet]. Phys Ther. 2006;86(10):1426–35. http://www.ncbi.nlm.nih.gov/pubmed/17012646.
60. King LA, Horak FB. Delaying mobility disability in people with Parkinson disease using a sensorimotor agility exercise program [Internet]. Phys Ther. 2009;89(4):384–93. http://www.ncbi.nlm.nih.gov/pubmed/19228832.
61. Calzetti S, Baratti M, Gresty M, Findley L. Frequency/amplitude characteristics of postural tremor of the hands in a population of patients with bilateral essential tremor: implications for the classification and mechanism of essential tremor [Internet]. J Neurol Neurosurg Psychiatry. 1987;50(5):561–7. http://www.ncbi.nlm.nih.gov/pubmed/3585381.
62. Pathak A, Redmond JA, Allen M, Chou KL. A noninvasive handheld assistive device to accommodate essential tremor: a pilot study [Internet]. Mov Disord. 2014;29(6):838–42. http://www.ncbi.nlm.nih.gov/pubmed/24375570.
63. Parkin S. MIT Technology Review [Internet]. 2016. p. Hope in a Glove for Parkinson's Patients. https://www.technologyreview.com/s/545456/hope-in-a-glove-for-parkinsons-patients/.
64. Kozovski A. RateMDs: Doctors Reviews and Ratings [Internet]. 2016. p. This Smart Spoon AidsParkinson'sPatientsinFeed.https://www.ratemds.com/blog/this-smart-spoon-aids-parkinsons-patients-in-feeding-themselves/.
65. Nonnekes J, Snijders AH, Nutt JG, Deuschl G, Giladi N, Bloem BR. Freezing of gait: a practical approach to management [Internet]. Lancet Neurol. 2015;14(7):768–78. http://www.ncbi.nlm.nih.gov/pubmed/26018593.
66. Giladi N, McMahon D, Przedborski S, Flaster E, Guillory S, Kostic V, et al. Motor blocks in Parkinson's disease [Internet]. Neurology. 1992;42(2):333–9. http://www.ncbi.nlm.nih.gov/pubmed/1736161.
67. Azulay JP, Mesure S, Amblard B, Blin O, Sangla I, Pouget J. Visual control of locomotion in Parkinson's disease [Internet]. Brain. 1999;122(Pt 1):111–20. http://www.ncbi.nlm.nih.gov/pubmed/10050899.
68. Suteerawattananon M, Morris GS, Etnyre BR, Jankovic J, Protas EJ. Effects of visual and auditory cues on gait in individuals with Parkinson's disease [Internet]. J Neurol Sci. 2004;219(1–2):63–9. http://www.ncbi.nlm.nih.gov/pubmed/15050439.
69. Jiang Y, Norman KE. Effects of visual and auditory cues on gait initiation in people with Parkinson's disease [Internet]. Clin Rehabil. 2006;20(1):36–45. http://www.ncbi.nlm.nih.gov/pubmed/16502748.
70. Donovan S, Lim C, Diaz N, Browner N, Rose P, Sudarsky LR, et al. Laserlight cues for gait freezing in Parkinson's disease: an open-label study [Internet]. Parkinsonism Relat Disord. 2011;17(4):240–5. doi:10.1016/j.parkreldis.2010.08.010.
71. McCandless PJ, Evans BJ, Janssen J, Selfe J, Churchill A, Richards J. Effect of three cueing devices for people with Parkinson's disease with gait initiation difficulties [Internet]. Gait Posture. 2016;44:7–11. http://www.sciencedirect.com/science/article/pii/S096663621500942X.
72. dos Santos Mendes FA, Pompeu JE, Modenesi Lobo A, Guedes da Silva K, Oliveira T de P, Peterson Zomignani A, et al. Motor learning, retention and transfer after virtual-reality-based training in Parkinson's disease--effect of motor and cognitive demands of games: a longitudinal, controlled clinical study [Internet]. Physiotherapy. 2012;98(3):217–23. doi:10.1016/j.physio.2012.06.001.
73. Gonçalves GB, Leite MAA, Orsini M, Pereira JS. Effects of using the Nintendo wii fit plus platform in the sensorimotor training of gait disorders in Parkinson's disease [Internet]. Neurol Int. 2014;6(1):5048. http://www.ncbi.nlm.nih.gov/pubmed/24744845.
74. Wikimedia. Wii Balance Board [Internet]. 2011. p. Wii Balance Board for Nintendi Wii. https://commons.wikimedia.org/wiki/File:Wii_Balance_Board_transparent.png.

75. Mirelman A, Maidan I, Herman T, Deutsch JE, Giladi N, Hausdorff JM. Virtual reality for gait training: can it induce motor learning to enhance complex walking and reduce fall risk in patients with Parkinson's disease? [Internet]. J Gerontol A Biol Sci Med Sci. 2011;66(2):234–40. http://www.ncbi.nlm.nih.gov/pubmed/21106702.
76. Arias P, Robles-García V, Sanmartín G, Flores J, Cudeiro J. Virtual reality as a tool for evaluation of repetitive rhythmic movements in the elderly and Parkinson's disease patients [Internet]. PLoS One. 2012;7(1), e30021. http://www.ncbi.nlm.nih.gov/pubmed/22279559.
77. Garcia A, Andre N, Bell Boucher D, Roberts-South A, Jog M, Katchabaw M. Immersive augmented reality for Parkinson disease rehabilitation. In: Intelligent systems reference library [Internet]. Berlin: Springer; 2014. p. 445–69. http://www.scopus.com/inward/record.url?eid=2-s2.0-84927509975&partnerID=tZOtx3y1.
78. Wikimedia. Google cardboard VR mount [Internet]. 2014. p. Assembled Google cardboard VRmount. https://commons.wikimedia.org/wiki/File:Assembled_Google_Cardboard_VR_mount.jpg.
79. DiCarlo, Eleni. Oculus Rift [Internet]. 2014. Flikr. New Oculus Rift Now Available for Developers. https://www.flickr.com/photos/bagogames/13300603614.
80. Holmes A. Online Press Release Distribution Service [Internet]. Palm Springs. 2010. p. Parkinson's Gait Dramatically Improves with High Tech Visual Feedback Device. http://ww1.prweb.com/prfiles/2010/04/11/689374/GaitAidsuperimp.jpg.