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Review Article

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Review

Technology-Based Neurorehabilitation in Parkinson's Disease—A Narrative Review

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Abstract: This narrative review provides a brief overview of the current literature on technology-based interventions for the neurorehabilitation of persons with Parkinson's disease (PD). The role of brain–computer interfaces, exergaming/virtual-reality-based exercises, robot-assisted therapies and wearables is discussed. It is expected that technology-based neurorehabilitation will gain importance in the management of PD patients, although it is often not clear yet whether this approach is superior to conventional therapies. High-intensity technology-based neurorehabilitation may hold promise with respect to neuroprotective or neurorestorative actions in PD. Overall, more research is required in order to obtain more data on the feasibility, efficacy and safety of technology-based neurorehabilitation in persons with PD.

Keywords: brain–computer interface; exergaming; Parkinson's disease; robot-assisted therapies; virtual reality; wearables

1. Introduction

Novel technology plays an increasing role in neurorehabilitation. Most studies have focused so far on the possible roles of technology-based neurorehabilitation in neurological disorders with a relatively stable impairment, such as hemiplegia after a stroke. Parkinson's disease (PD) is a chronic neurological disorder featuring a slowly progressive disease course. While motor symptoms can usually be adequately controlled by pharmacological treatment in the early stages of the disease, most anti-parkinsonian drugs are associated with long-term complications such as motor fluctuations and dyskinesia. Besides, non-motor symptoms become more predominant during the course of the disease. Deep brain stimulation (DBS) has been established as an important treatment option in the moderate-to-severe stages of PD. However, many motor symptoms, such as hypokinetic gait disorder, freezing of gait (FOG), postural instability and/or camptocormia, are often refractory to pharmacological therapy or DBS. Furthermore, no disease-modifying treatment is currently available to halt or slow down the disease course.

Neurorehabilitation therefore plays an important role in the overall management of PD, and especially in the treatment of L-Dopa-unresponsive symptoms in the moderate-to-advanced stages of the disease. Furthermore, physical exercise may also have a neuroprotective or neurorestorative action in PD [1]. However, evidence-based data on this topic are scarce. Recently, the development of technology-aided treatment approaches has gained considerable interest in the rehabilitation of neurological patients. These approaches can be arbitrarily divided into brain–computer interface (BCI) technologies, exergaming

and/or virtual-reality (VR)-based exercises, robot-assisted therapies and wearables. This review attempts to provide a brief overview on the use of such innovative technology in the neurorehabilitation of persons with PD.

For the purpose of this review, the literature known to the authors and/or identified by a search of the PubMed database was used. The main key words were "brain-computer interface", "exergaming", "virtual reality", "robot-assisted", "exoskeleton" and "wearables", in conjunction with "Parkinson" or "Parkinson's disease". All publications were screened for elegibility for this narrative review and selected according to the investigators' opinion.

2. Brain–Computer Interface

Non-invasive electroencephalography (EEG)-based BCI technologies can be used to control a computer cursor or a limb orthosis, for word processing, accessing the internet and other functions, such as environmental control or entertainment [2]. In stroke patients, BCIs based on motor imagery (MI) can be used for closing the sensorimotor loop, e.g., by using functional electrostimulation [3]. It remains questionable whether MI-BCI could be useful to overcome the impairment in the cortico-basal ganglia-thalamo-cortical network in PD. Accordingly, a recent study demonstrated that persons with PD were capable of operating MI-BCI, but with low accuracy [4]. PD presents with pathological oscillations in the beta frequency band in recordings from this network. Beta power is correlated with the severity of parkinsonian symptoms and beta power reduction during the administration of levodopa or DBS is associated with symptom improvement. Accordingly, one study reported that neurofeedback can be used by bilaterally DBS-treated PD patients to down-regulate pathological beta oscillations in the subthalamic nucleus [5]. Similar data were found by other authors [6]. Future studies should further explore the potential of BCI using cortical activity as a target signal for neurofeedback or as a control signal for MI-BCI.

3. Exergaming/Virtual-Reality-Based Exercises

Exergaming has been originally defined as the activity of playing video games that involve physical exertion and are thought of as a form of exercise. VR is a technology that allows a user to act in and with an artificial environment. That environment is experienced through sensory stimuli provided by computer-controlled display and rendering technologies. The user's actions partially determine what happens in the environment. Similar technologies are augmented reality (AR) and mixed reality (MR). Exergaming makes increasing use of VR-, AR- or MR-based approaches. In 2011 treadmill training and VR were proposed to be viable in PD and to significantly improve physical performance, gait during complex challenging conditions and certain aspects of cognitive function [7]. Subsequently, the Park-in-Shape study addressed the question of whether high-intensity aerobic exercise combined with gaming elements provides symptomatic relief in PD [8,9]. The authors showed that such exercise can be performed at home by persons with PD with a mild disease severity [9]. In a proof-of-concept study, a balance training program with augmented visual feedback was not superior to conventional balance training [10]. However, balance-based exergaming training resulted in a greater improvement in postural stability compared with conventional balance training in another study [11]. The study V-TIME addressing the effects of treadmill training augmented with VR showed in a diverse group of older adults that this training led to reduced fall rates compared with treadmill training alone [12]. This effect was also statistically significant for a subgroup of 130 persons with PD. Besides, a Box and Blocks Test using VR has been evaluated for the measurement of manual dexterity in persons with PD [13].

Other studies addressed the efficacy and safety of commercially available systems such as Nintendo Wii^{TM} Fit, e.g., suggesting that a home-based balance program using Wii^{TM} Fit with a balance board can improve the static and dynamic balance, mobility and functional abilities of people affected by PD [2,14–16]. Computer-based rehabilitation games using Microsoft Kinect^{TM} were also reported to be safe and feasible for people with PD [17]. Microsoft Kinect^{TM} may be easier to use, since people do not have to stand on an

elevated platform. However, a recent review considered Nintendo Wii™ a better device for locomotion rehabilitation in people with PD than Xbox Kinect™ [18].

A Cochrane review found low-quality evidence of a positive effect of short-term VR exercise on step and stride length [19]. Accordingly, VR and physiotherapy may have similar effects on gait, balance and quality of life. A systematic review addressing the efficacy of VR-based approaches on gait, balance and mobility found a significant difference in favor of VR-based exercises for step and stride length, balance and general mobility as measured by the Timed Up and Go Test [20]. Other authors investigated 64 publications on exergaming in PD since 2014 and reported that in seven of nine RCT the intervention group provided better results than the control group regarding motor outcomes [21]. A recent review concludes that despite suggestions that VR can provide a more effective and less labor-intensive rehabilitation than non-VR rehabilitation, little evidence exists to date to support these claims [22]. These authors suggest the development of personalized assessments and rehabilitation using VR in order to adapt to individual changes over time and optimize motor learning.

4. Robot-Assisted Therapies

Robot-assisted gait training (RAGT) is probably the best examined kind of robot-assisted therapy in PD. Arguably, the best-known devices in Switzerland are the Lokomat® (Hocoma AG, Volketswil, Switzerland), Gait Trainer GT (Reha-Stim Medtec AG, Schlieren, Switzerland) and G-EO robot (Reha Technology AG, Olten, Switzerland). The robotic personal trainers Pro and ELITE (Dynamic Devices AG, Zurich), that employ artificial intelligence (AI), also focus on the lower extremities, but have not been investigated yet in persons with PD. Four persons with PD showed a reduction in FOG by RAGT using the Lokomat® [23]. Long-term robot-assisted treadmill walking using the Lokomat® has been suggested to reduce FOG in PD patients also in another study [24]. However, robotic gait training with the Lokomat® was not superior to treadmill training in improving gait performance in persons with PD [25]. Initial studies using the Gait Trainer GT suggested that RAGT may improve walking ability in PD patients and postural instability in persons with moderate-to-advanced PD, respectively [26,27]. However, RAGT with the Gait Trainer GT was not superior to equal-intensity treadmill training for improving walking ability in persons with mild-to-moderate PD [28]. RAGT with the Gait Trainer GT was also not superior to balance training for improving postural instability in this population [29]. However, robotic gait training using the Gait Trainer GT may be a useful strategy for the treatment of drug-refractory FOG [30]. A statistically significant improvement in a gait index was found in favor of RAGT using a G-EO robot in comparison to treadmill training [31]. Using the G-EO robot, the advantages were also greater with RAGT than treadmill training for individuals with a FOG-related disability [32]. The protocol of a controlled study that aims to investigate the effects of RAGT with the Walkbot-S™ (P&S Mechanics) on gait velocity in persons with PD has been published [33].

Robot-assisted arm training with the Bi-Manu-Track (Reha-Stim Medtec AG, Schlieren, Switzerland) may be a promising tool to improve the upper limb function, such as manual dexterity, in persons with PD [34].

Exoskeletons are wearable robots that are used in neurorehabilitation to augment a person's impaired physical ability. A known producer is Ekso Bionics, which markets the EksoNR, for the lower extremities, and the EksoUE, for the upper extremities. Myoswiss AG (Zurich) produces the MyoSuit, a soft and light-weight exoskeleton of the so-called next generation. To our knowledge, there are not any publications on the use of exoskeletons in PD. Altogether, the current evidence is not yet sufficient to support that robot-assisted therapies provide a more effective and less labor-intensive rehabilitation than traditional neurorehabilitation in PD patients.

5. Wearables

Wearables, that increasingly make use of AI, have so far mainly been used in PD for diagnosis or the monitoring of symptom severity [35]. It can be assumed that AI will also play a more prominent role in other areas of patient care, such as robot-assisted therapy and exergaming/VR-based exercises, allowing for the continuous adjustment of therapy parameters and, thus, personalized medicine.

The International Parkinson and Movement Disorders Society (MDS) Task Force on Technology has been entrusted by the MDS to promote the development of integrated measurement and closed-loop therapeutic systems with high patient adherence [36]. The goals are to (a) encourage the adoption of clinico-pathophysiologic phenotyping and early detection of disease milestones, (b) enhance the tailoring of symptomatic therapy, (c) improve the subgroup targeting of patients for future testing of disease-modifying treatments and (d) identify objective biomarkers to improve the longitudinal tracking of disease symptoms. A systematic review identified 73 technology-based devices for the measurement of motor symptoms [37]. Twenty-two were wearable, 38 were non-wearable and thirteen were hybrid devices. Nine devices were "recommended", 34 devices were "suggested" and 30 devices were classified as "listed". Within the wearable devices group, the Mobility Lab sensors from Ambulatory Parkinson's Disease Monitoring Inc. (Portland, OR, USA), Physilog® (Gait Up, Renens, Switzerland), StepWatch 3 (Cyma Corp., Mountlake Terrace, DC, USA), TriTrac RT3 triaxial accelerometer (Reining International, Madison, WI, USA), DynaPort (McRoberts B.V., The Hague, The Netherlands) and AX3 (Axivity Ltd., Newcastle, UK) were "recommended". Within the non-wearable devices group, the Nintendo Wii™ Balance Board and the GAITRite® gait analysis system (CIR Systems Inc., Franklin, VA, USA) were classified as "recommended". Within the hybrid devices group, only the Kinesia® system (Great Lakes Neurotechnologies, Cleveland, OH, USA) was "recommended". The reviewed devices focused on the measurement of gait, postural control and daily activity, with some of them also assessing bradykinesia, freezing, tremor or dyskinesia. The Parkinson's KinetiGraph (Global Kinetics, Victoria, Australia) and the Kinesia® system are FDA-approved [38]. The MDS Task Force on Technology published implementation guidelines to improve the assessment of persons with PD and tailor the symptomatic therapy, since based on PKG® measurements a significant proportion of persons with PD shows a sub-optimal motor symptom control [39,40]. A more recent review on the use of technology for measuring symptoms in the home environment has been published by Morgan et al. [41]. The most frequently investigated sensors for the monitoring of PD in this setting were inertial measurement units within wearable devices and/or smartphones. Smartphones can also be used for PD-specific apps such as the APDA symptom tracker or SwissParkinson, that allow for the documentation of disease symptoms by the patient and feature a variety of other functions. Wearables are currently not part of the routine care in PD, but will probably become increasingly important for the continuous monitoring of PD symptoms and may also, therefore, improve neurorehabilitation.

6. Limitations of this Review

Table 1 summarizes the key studies cited in this article. The main limitation of this manuscript is that it is not a systematic review of the present literature. Besides, there is no relevant literature on the topic of the degree to which technology-based neurorehabilitation may exert neuroprotective or neurorestorative actions in PD and, if so, whether they differ from the potential neuroprotective or neurorestorative actions possibly achieved by conventional therapy. Arguably, technology-based neurorehabilitation may be advantageous because it can usually be performed in a higher frequency and intensity than those of conventional therapy and can sometimes be made more easily available to patients with severe handicaps. However, an obstacle to the widespread use of technology-based neurorehabilitation in PD is the question of the degree to which the medical devices are user-friendly and readily usable at home in this population, suffering from motor impairment and often cognitive dysfunction. Besides, the sometimes heterogeneous results of the

cited studies may be due to the different settings in which the participating patients have been recruited. The majority of the medical devices discussed in this article have received a CE mark and can therefore be used in Switzerland. However, it is advisable to ascertain that the respective medical device is approved for the use in PD patients according to the specific regulations of the given country.

Table 1. Key articles on the use of technology-based neurorehabilitation in PD.

Study	Population	Sample Size	Intervention	Outcome(s)
He et al., 2019	STN-stimulated PD patients	$n = 3$	Neurofeedback	Downregulation of beta oscillations
Bichsel et al., 2021	STN-stimulated PD patients	$n = 10$	Neurofeedback	Regulation of beta oscillations
Mirelman et al., 2011	PD patients with gait disorder	$n = 20$	Treadmill training + VR	Gait and cognitive function
Mirelman et., 2016(V-TIME)	PD patients with falls	$n = 130$	Treadmill training + VR	Number of falls
Shih et al., 2016	PD patients (H&Y stage 1–3)	$n = 20$	Balance-based exergaming	Postural stability and functional balance
van der Kolk, 2019 (Park-in-Shape)	PD patients (H&Y stage 1–2)	$n = 130$	Home trainer + exergaming	MDS-UPDRS during Off
Esculier et al., 2012	Patients with moderate PD	$n = 10$	Balance training with Wii^{TM} Fit	Balance and mobility
Mhatre et al., 2013	PD patients (H&Y stage 2.5–3)	$n = 10$	Balance training with Wii^{TM} Fit	Balance and gait
Pompeu et al., 2014	PD patients (H&Y stage 2–3)	$n = 7$	Kinect Adventures!^{TM}	Game scores
Lo et al., 2010	PD patients with FOG	$n = 4$	RAGT (Lokomat$^{®}$)	FOG
Pilleri et al., 2015	PD patients with FOG	$n = 18$	RAGT (Gait Trainer GT)	FOG
Capecci et al., 2017	PD patients (H&Y stage $\geq$2)	$n = 96$	RAGT (G-EO robot)	FOG
Pahwa et al., 2020	PD patients	$n = 27.834$	Observational	Personal Kinetigraph$^{®}$ scores

The sample size refers to the total number of PD patients without healthy controls. STN—subthalamic nucleus, H&Y—Hoehn and Yahr, MDS-UPDRS—Movement-Disorders-Society-Sponsored Revision of the Unified Parkinson's Disease Rating Scale, FOG—Freezing of Gait.

7. Conclusions

Innovative technologies probably facilitate neurorehabilitation in PD. While BCI holds promise for the future, data are currently too scarce to draw any conclusions regarding its usefulness in the management of PD. Exergaming and VR-based exercises have already been successfully implemented in the neurorehabilitation of PD, but there are not many data on its efficacy in comparison to conventional therapies. In any case, exergaming and VR-based exercises may increase motivation and promote the access to therapies for persons with motor disabilities, which is of outstanding importance in the time of a pandemic such as COVID-19. Robot-assisted therapies are widely used, e.g., for stroke patients, but have so far mainly shown a moderate efficacy for the treatment of FOG in persons with PD. Wearables may play an increasing role in the monitoring of disease severity and, therefore, support neurorehabilitation in PD. So far, it has not been investigated whether technology-based neurorehabilitation may exert neuroprotective or neurorestorative effects in PD by increasing the intensity of physical exercise in persons with PD.

Conflicts of Interest: J.C.M. and D.Z. declare no conflict of interest. R.R. holds shares and receives royalties from Myoswiss AG.

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