Can telerehabilitation games lead to functional improvement of upper extremities in individuals with Parkinson’s disease?

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Introduction

Parkinson’s disease (PD) is a progressive degenerative disorder that affects the nervous system. Nigrostriatal degeneration is the pathological hallmark of PD leading to the classical motor symptoms such as increased muscle tone (rigidity), slow movement (bradykinesia), resting tremor, and gait and postural impairment (Melnik, 1995). These symptoms are associated with nonmotor symptoms including cognitive, behavioral, autonomic, and sleep disturbances that adversely influence the patient’s quality of life (QoL). The motor signs of PD are mainly treated by L-DOPA and dopamine agonists, aiming to provide patients with independent functioning as long as possible. However, with disease progression, the patients often become less responsive to medication treatment and will develop motor (and nonmotor) fluctuations – dyskinesia (unintended, involuntary, and uncontrollable movements) after the first few years of disease. Therefore, physiotherapy has become increasingly more important in individuals with PD as they can retain more than three-fourth of all activities (Jankovic, 2008; Duncan and Earhart, 2011). Namely, motor rehabilitation ameliorates symptoms and improves movement functionalities and motor performance, and consequently increases the QoL (Angelucci et al., 2016) and is related to patients’ motivation for participation.

Physiotherapy increases participation and contributes toward the quality of movement, physical capacity, and manual activities, balance, walking, reaching, grasping, etc. However, studies to confirm the effectiveness are still in progress (Hindle et al., 2013). Recently, Clarke et al. (2016) reported a randomized clinical trial, stating that the physiotherapy and occupational therapy in mild to moderate PD did not contribute toward clinically...
meaningful improvements in daily living or QoL by validated instruments. They suggested that more structured and intensive therapy programs should be applied in all stages of PD. More intensive exercises with computer games (exercise + games = exergames) have been introduced for the motor rehabilitation of individuals with PD (Pompeu et al., 2014) and there have been several reports on functional progress and performance in balance (Dockx et al., 2016). Most of the reports used commercial games (Nintendo Wii or Kinect Xbox) requiring too fast responses that patients were not able to follow and were found to be too demanding (Barry et al., 2014). Commercially available games and applications also do not allow remote data management and control of the game difficulty on the basis of the functional performance outcomes (Susi et al., 2007). A feasibility study (Pompeu et al., 2014) on safety and functional outcomes (balance, dynamic gait, and QoL) reported on positive outcomes when using the commercial outfit of Kinect Adventures (Torres, 2008). Only a few studies have reported on the retention of intensive motor learning to improve daily tasks (Heremans et al., 2016) as suggested by Clarke et al. (2016), for example writing, moving small objects, etc. There were only a few short-term improvements in walking speed and balance (Tomlinson et al., 2013).

The objectives of the presented study were to assess the feasibility of delivery and the impact of the developed intensified exergaming with a gradual difficulty level control for individuals with PD beyond clinical programs, preferably at home. We hypothesized that the intervention can lead to functional improvements of upper extremities in patients with PD despite the progressing disease and without changing the medication plan.

Materials and methods
The requirements for intensified and target-based exercise therapy were a combination of variable difficulty level, physical exercise, cognitive, and coordinated movement capabilities (Farley and Koshland, 2005). Furthermore, for individuals with PD, the time for exercise therapy in the hospital is often limited. Continuation of exercise therapy at home could be an acceptable solution for the intensified exercising and prolonged period of training. A larger group of patients could perform the task according to a specific telerehabilitation protocol with less healthcare personnel at the same time as in the clinical settings. Primarily, we focused on the feasibility of home exercise therapy that requires simple, easy-to-operate, and nonobtrusive solutions with possible remote operation management, task scheduling, and data preview. An eye contact with the moving object and its manipulation (even virtual) may be a challenging task with enough physical exercise. We had checked whether the participants could set up, use, and follow the instructions on the screen without the assistance of the care person. Finally, we examined whether such an intervention could be clinically meaningful with an unchanged medication plan.

Participants
Forty-seven patients with PD were recruited at the University Rehabilitation Institute’s hospital. Among these, 28 patients (16 women, 12 men, 68 ± 7 years old, 172 ± 6 cm, 79 ± 10 kg, and duration of disease 6 ± 4 years) were eligible for the study (Fig. 1), and fulfilled the following inclusion criteria: (a) participants with levels 2–3 in the Hoehn and Yahr Scale (Goetz et al., 2004). (b) Mini-Mental Status Examination (Pachet et al., 2010) above 24. The physician, a neurologist, carried out the enrollment process. The details of the treatments and planned activities to determine the patients’ eligibility for participation in the study were unknown to the participants and the physician at the time of screening. They were also not aware of the participants’ technical skills.

Exergaming design
The ‘Fruit Picking’ computer game (Fig. 2) was developed with the Unity three-dimensional game engine (Unity Technologies, San Francisco, California, USA) and was designed as a target-based task (Paraskevopoulos et al., 2014). The three-dimensional infrared camera (Kinect V2; Microsoft Corporation, Redmond, Washington, USA; Kinect V2 SDK, 2016) tracked the motion of the body segments. The Kinect V2 raw data were filtered and translated to the coordinate systems attached to each body
segment, the arm, hand, trunk, and head of the participant. The game was designed for upper extremities; thus, the physical interaction zone was above shoulder height. This means that the camera sensor was focused on the trunk, arm and hands movements, and ignored the movements of the legs or the head.

The goal of the ‘Fruit Picking’ game was to collect virtual apples before falling off the virtual tree and place them in the basket in the lower part of the screen. The participant was instructed to raise the arm, open the hand, and try to grab the virtual apple by closing the hand. Opening the hand again would have resulted in the virtual apple falling to the ground and the participant would not receive points. The virtual hands were approximately the size of the real hands. When the participant grabbed the virtual apple successfully, and placed it in the basket, the computer added points to the score. The number of scored points depended on the game difficulty level, which escalated with the success of the participant. The participant proceeded to the next difficulty level when he or she successfully collected 15 apples three times in a row. Primary difficulty level was defined by the physiotherapist. The higher the difficulty level, the more widely the apples were distributed on the tree branches and ripened and fell faster from the tree. There were also limitations. Once the apple began to fall from the tree, it could no longer be grabbed. Each game session lasted exactly 2 min.

Telerehabilitation design
Our design targeted exergaming with serious games (Susi et al., 2007; Paraskevopoulos et al., 2014) for upper extremity exercises, such as reaching and grasping desirably outside the rehabilitation center or at home. Therefore, the gamification platform (Fig. 3) technically consisted of two parts: frontend and backend. Frontends were interfaces/applications interacting directly with the users during the exergaming (Wattanasoontorn et al., 2013). The users/patients exercised with the game and the system recorded and stored the data on a local computer. The backend part retrieved the stored data and enabled the medical professionals to review data remotely and plan/follow the exergame-based therapy. The system’s administrator could update the entire gamification platform, could add new medical professionals or handle their access privileges, and grant access to a physician to start monitoring the patients.

Technically, the server part (Linux operating system, Apache http server, MySQL relational database management system) was divided into three functional parts: storing data of the gamification platform, communication with the clients’ parts (gaming system), and administration over the web interface. The gamification platform comprised patients’ data, game schedule, game settings, game session results, and administrative data. The communication with clients’ parts consisted of web services providing game settings and synchronization of acquired data with the relational database. The administrative web interface enabled medical professionals to preview the patients’ data, add a new patient, modify game settings, or create a schedule. The saved data could be exported to other software tools (e.g. Microsoft Excel, Matlab; Mathworks Inc., Natick, Massachusetts, USA) for further analysis.
Study design and data analysis
Criteria for telerehabilitation

The exergaming (virtual reality supported exercise therapy) started during the rehabilitation program in the clinical settings where patients acquired the necessary skills to manage the equipment and took preliminary clinical tests. After that, the individuals continued with exergaming at home for additional 2–3 weeks, preferably in the morning 30–60 min after they took the medicine. The software was installed on a mini-PC Barebone (Gigabyte BRIX, i7, GIGA-BYTE Technology Co. Ltd., New Taipei City, Taiwan) and all connections were preset. The participant or the carer was only requested to connect it to the LCD TV (HDMI input) and establish a Wi-Fi internet connection at home.

The participants were seated in a comfortable chair in front of a 42″ LCD with Kinect V2 camera and started the upper extremity reaching and grasping exercise. The objective of the ‘Fruit picking’ game was to collect the apples falling from the tree (Fig. 2). The score depended on the number of apples collected and the difficulty level. The initial difficulty level was set to 1.

The participants took 10 exergaming trainings spanning over ~ 3 weeks. Each daily session lasted for a maximum of 30 min. Within the designated session, the participant had enough time to complete the ‘Fruit picking’ game at least five times. Short 2 min breaks were taken between the trials. No parameters were changed manually during the study. The final score for each session was defined by the number of apples collected and the difficulty level. The initial difficulty level was set to 1.

The telerehabilitation task was considered successful if the participants finished the exergaming sessions alone, without any functional assistance of the care person or therapist. However, we monitored whether the care person provided any technical assistance at setup and when beginning to use the application.

Functional status assessment
Clinical instruments for functional assessment [Unified Parkinson’s Disease Rating Scale (UPDRS) III (Movement Disorder Society Task Force on Rating Scales for Parkinson’s Disease, 2013), Box and Block Test (BBT), Nine-Hole Peg Hole Test (9HPT); Gammon et al., 2011], and daily functional tasks evaluation (Jebsen’s test; Jebsen et al., 1969) were used at patient admission and after the exergaming program. Jebsen’s test was carried out by the occupational therapist and the other tests were performed by the physiotherapist. The participating patients were also asked to fill the Parkinson’s Disease Questionnaire (PDQ-39) (Jenkinson et al., 1997) to estimate the health status over the last month.

Statistical analysis of the clinical tests’ outcomes was carried out using the Matlab Statistical Toolbox (MathWorks Inc.). Means, SDs, median values, SEMs, and confidence interval (95%) were computed for the 9HPT, BBT, UPDRS III, and all Jebsen’s subtests [writing a letter (WAL), card turning (CTURN), stacking checkers (STCHK), stimulated feeding (SFEED), moving light objects (MLO), moving heavy objects (MHO), small objects picking (SOP)] before and after the study. Both assessments were also tested statistically for mean differences using a paired-sample t-test ($P < 0.05$). Before analysis, data were checked for normality (histogram,
The success at the ‘Fruit picking’ exergame was also measured with the game score depending on the number of collected apples. The number of collected apples within the game decreased from the first session to the 10th session (mean: 35.26, SD: 13.92 to mean: 24.89, SD: 11.63) as the difficulty level increased from 1 to 10 (Fig. 4). However, the final game score ($P < 10^{-5}$, $d = 1.79$) increased significantly from the first to the last session (mean: 69.89, SD: 29.24 to mean: 237.76, SD: 129.08) (Fig. 4).

### Functional status assessment

The participants showed clinically meaningful outcomes according to the validated instruments. The categories of Jebsen’s test (Jebsen et al., 1969) showed faster accomplishment of tasks, but with a large variability. In addition, the normal-like distributed samples were rather asymmetrical (kurtosis/skewness: 0.29–2.24/0.96–1.76). After exergaming, all the participants needed less time to write a letter (mean: 24.03, SD: 15.52 s to mean: 20.64, SD: 13.4 s), picking of small objects (mean: 8.51, SD: 2.82 s to mean: 8.25, SD: 3.15 s), stacking checkers (mean: 6.30, SD: 1.91 s to mean: 5.54, SD: 1.45 s), stimulated feeding (mean: 9.44, SD: 3.81 s to mean: 8.49, SD: 2.12 s), moving light objects (mean: 4.44, SD: 1.19 s to mean: 3.94, SD: 0.99 s), and moving heavy objects (mean: 4.31, SD: 0.82 s to mean: 4.06, SD: 1.15 s), but more time for card turning (mean: 6.42, SD: 2.03 s to mean: 7.28, SD: 7.53 s) (Table 1). Improvements in WAL ($P = 0.003; C < 0.05, d = 0.23$) and NILO ($P = 0.006; P < 0.05, d = 0.46$) tests turned out to be statistically significant (Table 1, Fig. 5).

The data of the BBT (kurtosis/skewness: 0.51/0.1 before and $-0.32/0.59$ after intervention) and the UPDRS III (kurtosis/skewness $-0.32/-0.35$ before and $-0.11/0.09$ after intervention) had an almost normal, symmetrical distribution. The 9HPT had an almost normal, more peaked, and less symmetrical distribution (kurtosis/skewness: 0.76/0.3). The two functional clinical tests, the 9HPT (mean: 28.01, SD: 6.59 s to mean: 26.48, SD: 7.30 s) and the BBT (mean: 47.27, SD: 10.68 to mean: 51.65, SD: 11.26 cubes) and the motor part of the UPDRS III (Movement Disorder Society Task Force on Rating Scales for Parkinson’s Disease, 2013) (mean: 29.54, SD: 10.33 to mean: 27.29, SD: 10.38), showed improvements (Fig. 5). However, statistically significant improvements ($P < 0.05$) were found only in the BBT ($P = 0.002, d = 0.40$) and the UPDRS III ($P = 0.001, d = 0.22$). The UPDRS III showed a large discrepancy between the lowest (5) and the highest score (46 before or 50 after the exergaming). In addition, the range of the first quantile (25%) and the third quantile (75%) of the data and whiskers was 1.5 times the interquartile range (99.3% coverage) (Fig. 5). The outliers were data points beyond the whiskers.

The final game scores at the first session (before) and the 10th session (after), compared with the UPDRS III, showed that the higher final game score yielded a lower UPDRS III score and less WAL time and a higher BBT score. However, the regression coefficients were rather low: $R^2 = 0.0649$, 0.0509, and 0.007 for the BBT, the UPDRS III, and the WAL, respectively (Fig. 4).

The PDQ-39 (Jenkinson et al., 1997) showed that the participants’ major problems were related to mobility, body discomfort, and emotional well-being (Fig. 6), but...
less stigma or social support. On average, the participants could manage their day-to-day activities.

**Discussion**

**Criteria for telerehabilitation**

Our outcomes showed that the participating patients with PD were not technically skilled and mostly relied on their care person. Although the seven participants set up the system at home on their own, we did not observe any discrepancy between their data and the data of the other participants who were provided technical assistance. All results were stored regularly and no errors were recorded during the sessions. Similar findings on easy to use systems at home that can be controlled remotely over the internet were also reported by Pachoulakis et al. (2016).

All participants showed a significant improvement in their final game scores. Indeed, their score improved on a daily basis up to the fifth session, and then the score suddenly decreased because of the increased difficulty level. From then onward, the participants achieved the same or higher score as at the fifth session. The information on the game score can be useful when the participants perform the exergaming at home and these are the only available data because of the reduced number of outpatient clinical tests. The improvement in the final score was related to the improvement in the clinical tests (BBT, UPDRS III, and WAL). The BBT score increased with the final score and the other two clinical tests also showed an improvement as the final score was higher. However, none of these regressions could be statistically confirmed because of the outliers and small-scale changes in the clinical tests. Perhaps a population above the mid-stage of the PD would increase the statistical range, but severe motor problems at that stage can prevent successful participation in the exergaming.

**Functional status assessment**

Our findings showed that with the target-based task and the difficulty level control, we may achieve clinically meaningful results. The statistically and highly significant results of Jebsen’s tests (Jebsen et al., 1969), WAL, and MLO confirm that some functions of daily living had improved. In addition, improvements in the mean/median values were observed in the MHO, STCHK, and SFEED. These results, in combination with the significant changes in the BBT and the UPDRS III, may indicate a short-term increase in the QoL of the
participants. This might be in contrast to the findings of Clarke et al. (2016), but we need to consider that our study was limited to the upper extremities. However, motor functions in patients with PD rarely improve over time; therefore, the clinical outcomes presented as a result of the target-based exergaming are noteworthy. This is supported by the study on amplitude-based behavioral intervention (Farley and Koshland, 2005) reporting on reduced bradykinesia and hypokinesia because of targeted large range of motion. We believe that the improvements might be a consequence of higher motivation of the participants and we should have extended the exergaming period. However, more time spent on such games may not necessarily lead to additional improvements in motor functions (Miller et al., 2014). Apparently, the short-term improvement in motor functions (BBT, UPDRS III) and daily activities (Jebsen’s test) also led to an improvement in cognitive functions and consequently the quality of life of the participants with PD without changes in the regime of medications and lifestyle. A recent research review (Oertel and Schulz, 2016) reported that pharmacotherapy has also not been very successful in disease modification and emphasizes the importance of further research in the field of efficient treatment of motor symptoms. The outcomes of the self-reported questionnaire PDQ-39 (Jenkinson et al., 1997) showed that our participants had major problems with mobility, but fewer problems with the activities of daily living and emotional well-being. This may suggest that the specific changes were related to the exergaming rather than just recovery from a poor health condition.

Limitations of the study and future work
Apart from the technical assistance and errorless functionality of the system, it was very difficult to monitor the exact time when the patient took a medicine and what kind of activity they were engaged in alone and what kind of activity they performed with their carer. Here, we entirely relied on the patients’ reports. Preliminary instructions for use and testing with each participant should take place within the clinical settings to enable the patients to learn how to use the system at home independently. Nevertheless, we may encounter problems with the Wi-Fi connection (the software records the data locally and transfers the data when connection is available) and participants could regularly interrupt the exergame for various reasons. Our study does not cover users’ experiences or an intrinsic and extrinsic motivation survey that may provide additional information and reveal the weaknesses of the system in real-life applications. We estimated that 50 participants would yield enough sample power (>0.8) and effect sizes of around 0.4 for a pilot. To detect smaller effect sizes, a larger group (>100) would be required. However, the BBT and Jebsen’s MLO tests yielded moderate effect sizes and considerable improvement. If all 47 participants were
eligible, we would have had enough participants; with 26 participants, we would still have statistical power of around 0.7 for an effect size of 0.4. We also need to consider that subjective evaluations may affect the reliability of some clinical tests.

Home and telerehabilitation services are comparable with conventional therapy (Dhurjaty, 2004; Cikajlo et al., 2012), but can provide service to larger number of patients. Besides, require less travel and fewer healthcare personnel resulting in increased quality of life (Melnik, 1995). We found in a single group of participants that even with an unchanged medication plan and progress of the disease, there were improvements in motor functions in the upper extremities with exergaming. However, we did not find that such an intervention was better than a conventional approach. Future work shall include a follow-up and a multicentre trial in a larger group of participants to confirm the clinical value of the approach.

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Conflicts of interest
There are no conflicts of interest.

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