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Comparison of virtual reality rehabilitation and conventional rehabilitation in Parkinson's disease: a randomised controlled trial

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Abstract

Objective To compare a 6-week virtual reality (VR) rehabilitation programme with a conventional rehabilitation programme in patients with Parkinson's disease.
Design Prospective, single-blinded, randomised controlled trial.
Setting Outpatients.
Participants Fifty-one patients with Parkinson's disease were assigned at random to a VR rehabilitation programme or a conventional rehabilitation programme.
Interventions Both programmes ran for 6 consecutive weeks, with a 40-minute session three times per week.
Main outcome measures The Balance Berg Scale (BBS) was used to measure balance. Secondary outcome measures were: Dynamic Gait Index (DGI) to evaluate ability to adapt gait to complex walking tasks; Disabilities of the Arm, Shoulder and Hand (DASH) scale to measure performance of the upper limb; and Short Form 36 (SF-36) to evaluate quality of life.
Results The VR rehabilitation programme led to an increase in BBS score {45.6 [standard deviation (SD) 7.9] vs 49.2 (SD 8.1), mean difference 3.6, 95% confidence interval (CI) 1.3 to 5.9; $P = 0.003$}, DGI score [18.7 (SD 4.7) vs 20.2 (SD 4.2), mean difference 1.6, 95% CI 0.6 to 2.5; $P = 0.003$] and SF-36 mental composite score [37.7 (SD 11.4) vs 43.5 (SD 9.2), mean difference 5.8, 95% CI 0.4 to 11.3; $P = 0.037$], and a decrease in DASH scale score [29.6 (SD 17.5) vs 21.6 (SD 15.1), mean difference −7.9, 95% CI −13.7 to −2.2; $P = 0.009$]. In contrast, the conventional rehabilitation programme only led to a decrease in DASH scale score [30.3 (SD 18.1) vs 25.1 (SD 15.8), mean difference −5.2, 95% CI −8.8 to −1.5; $P = 0.007$].
Conclusion These findings suggest that rehabilitation is useful in Parkinson's disease, and the VR rehabilitation programme was more effective in determining overall improvement than the conventional rehabilitation programme.
Clinical trial registration number : NCT02807740.

Keywords: Parkinson's disease; Rehabilitation; Virtual reality; Conventional therapy; Functional outcome

Introduction

Parkinson's disease (PD) is one of the most common neurodegenerative diseases, affecting one to two per 1000 population, and its prevalence increases with age [1]. The

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principal motor features are tremor at rest, rigidity, akinesia (bradykinesia) and postural instability [2]. PD is not only a motor disorder; it also presents a variety of non-motor symptoms (e.g. disturbance of mood, cognition and sleep) which reduce quality of life, often more than the motor symptoms [3,4].

The treatment goals of PD are to manage signs and symptoms and to improve quality of life. Treatment options include pharmacological therapy and surgery, usually with the aim of treating a specific manifestation of the disease. Despite pharmacological and surgical approaches, physiotherapy represents a key role in symptom management by maximising functional ability and minimising secondary complications through movement rehabilitation within a context of education and support [5].

Approaches to physiotherapeutic rehabilitation in PD can be conventional (e.g. aerobic exercise, treadmill, stretching and resistance exercises [6,7]) or non-conventional (e.g. dance, Tai Chi [8,9]). Virtual reality (VR) has been proposed as a new non-conventional rehabilitation tool, with potential added value over traditional physiotherapeutic approaches. It has the potential to optimise motor learning in a safe environment, and – by replicating real-life scenarios – could help improve functional activities of daily living [10].

VR is considered to be a useful rehabilitation approach because: (1) rehabilitation using repetitive task-specific training has been shown to be an effective approach in neurological rehabilitation; (2) a VR enriched environment allows the patient to perform cognitive and motor activities simultaneously [11,12]; (3) a VR programme simulates real-world activities, which provides enhanced ecological validity compared with more conventional therapy [13,14]; (4) risky activities that are unsafe to practice in therapy sessions can be practiced in a safe, regulated environment [10]; and (5) patients often practice for longer periods as VR programmes are considered to be more interesting and enjoyable than conventional programmes.

However, because of the scattered evidence of physical therapy in PD [15], there is insufficient evidence to prescribe a definite rehabilitation programme routinely, although there is increasing evidence of the effectiveness of paramedical therapies [16], and there is insufficient evidence to support or refute the effectiveness of one physiotherapeutic intervention over another [17].

The aim of this study was to compare the efficacy of a VR rehabilitation programme with a conventional programme in patients with PD.

Methods

This prospective, single-blinded, randomised controlled trial aimed to compare two different rehabilitation programmes in patients with PD. The total sample size was estimated through an a-priori power analysis. The analysis was carried out using G*Power V 3.1.3 (Franz Faul, Universität Kiel, Germany) assuming a multivariate approach for between effects, within effects and interactions.

The following parameters were used: effect size f = 0.33 (calculated from η^2p = 0.10 – medium effect), $\alpha = 0.05$, power = 0.80 and correlation between repeated measures r = 0.50.

Consecutive patients with PD, diagnosed according to the Gelb criteria [18], were enrolled in the study. Motor signs and symptoms were scored according to Unified Parkinson's Disease Rating Scale III [19]. Patients with secondary Parkinsonism or Parkinson's plus were excluded. The patients were enrolled at two centres which specialised in PD, and were informed prior to study entry that inclusion in a particular rehabilitation programme would be randomised. Patients signed informed consent forms to participate in the study, and the local ethics committee approved the study in accordance with the Declaration of Helsinki. The inclusion criteria were: (1) ability to perform the rehabilitation programme with a low risk of falling; (2) ability to perform motor rehabilitation independently; (3) absence of cognitive impairment (Mini-Mental State Examination score >25); and (4) no changes in drug therapy for PD during the rehabilitation programme. The exclusion criteria were: (1) severe hearing loss and/or visual deficit; and (2) serious comorbidities making it impossible to perform rehabilitation (e.g. postural hypotension, heart disease, stroke, severe shoulder–hip disease). Participants' data were collected on a case report form recording anamnestic data, dose of drug therapy for PD and other comorbidities. Patients were randomised using block randomisation: 26 patients underwent conventional rehabilitation and 25 patients underwent VR rehabilitation. Enrolment was performed by CP, II and DR, and randomisation was performed by ET. Enrolment started in June 2016 and ended in November 2016.

Patients were evaluated at baseline and at the end of the 6-week rehabilitation programme using the following measures.

Primary outcome measure

The Balance Berg Scale (BBS) was used to measure changes in functional standing balance over time [20].

Secondary outcome measures

The Dynamic Gait Index (DGI) was used to characterise mobility performance, specifically the ability to adapt gait to complex walking tasks associated with walking in community environments [21].

The Disabilities of the Arm, Shoulder and Hand (DASH) scale is a 30-item, self-report questionnaire designed to measure physical function and symptoms in people with musculoskeletal disorders of the upper limbs [22].

Short Form-36 is a self-administered questionnaire with eight specific categories of physical and emotional scores

Fig. 1. NIRVANA virtual reality rehabilitation scenarios. Patient is performing exercise 5 'to reach a mole'.

based on two main scores: physical composite score and mental composite score (MCS) [23].

Ad-hoc scales for liking the programme, difficulty of the programme and fatigue after physical therapy, according to the Likert scale [24], were used to acquire data at the end of the rehabilitation programmes.

Clinical evaluation was performed for each patient approximately 2 hours after drug intake, as this is when levodopa is expected to have its maximal effect (onset 20–40 minutes, duration of effect 2–4 hours after medication).

Electrocardiography and spirometry were performed at baseline in order to exclude heart or respiratory contraindications to performing physical therapy in both groups.

During the VR/conventional sessions, a diary was completed to note any changes in drug therapy for PD or other medical conditions, onset of acute illness, and data about liking the programme, difficulty of the programme and fatigue after physical therapy.

VR environment

Patients were tested in a VR rehabilitation scenario using equipment for motion analysis and NIRVANA (BTS Spa, Garbagnate Milanese, Milan, Italy). NIRVANA is a markerless system based on optoelectronic infra-red devices that allows patients to perform exercises in virtual settings with full audio-visual sensory immersion.

The tasks were conducted with the patient standing in front of the display screen and interacting simply through movement (Fig. 1).

The system was connected to a wall projector (brightness 4000 ANSI lumens, resolution 1024 × 768) and reproduced an interactive series of exercises involving coordination of the lower and upper limbs, as well as trunk control. An infrared video camera (fire wire data transmission technology with digital board camera, 400 Mbps 1394a, acquisition frequency 30 fps) detected patient movements. Activity was recorded simultaneously by a webcam to enable re-examination of the tasks. The details of all exercises performed by each patient were stored in the local database of the NIRVANA workstation and managed through a user-friendly interface.

Rehabilitation programmes

Patients underwent the conventional or VR rehabilitation programme for 6 consecutive weeks, involving a 40-minute session three times per week. The protocols are reported below.

Conventional rehabilitation programme

The conventional rehabilitation programme was performed according to the KNGF guidelines for physical therapy in patients with PD [25]. Each session involved three phases: (1) warm-up phase – passive mobilisation of main joints and muscular strengthening of lower limbs; (2) active phase (both standing and seated) – exercises of motor coordination with upper and lower limbs, balance training, start and stop exercises, and walking training; and (3) cool-down phase (with seated patient) – manipulation exercises, mobilisation exercises and respiratory exercises.

VR rehabilitation programme

Each VR session consisted of multiple exercises. Each exercise started with the patient in the centre of the room and asked to perform a task. Each exercise was performed by the patient for 4 minutes followed by 1 minute of rest.

- Exercise 1: to touch a moving trumpet displayed on the wall screen. When the trumpet was reached by the patient's arm, it disappeared and a sound was emitted.
- Exercise 2: to touch a rose projected on the wall screen as a hemiarc. In this exercise, the sequence of rose to touch, and therefore the distance between the target and the patient, was decided by the physical therapist.
- Exercise 3: to lead a dog to the four corners of the wall screen. Patients were free to move in the room.
- Exercise 4: to touch eggs projected on to the wall screen in a random order as quickly as possible. When an egg was reached by the patient's arm, it disappeared and a sound was emitted.
- Exercise 5: to reach a mole that came out from a hole. The patients did not know where the mole would emerge and they moved around the room. When the mole was reached by the patient's arm, it disappeared and a sound was emitted.
- Exercise 6: to perform a motor task as indicated by the physical therapist while maintaining balance between two lateral bars in order not to touch them and not make them emit a sound.
- Exercise 7: to clear all the leaves projected on to the wall screen as quickly as possible.

Table 1
Demographic data, clinical picture [Unified Parkinson's Disease Rating Scale Part III (UPDRS III)] and onset of disease of patients in the virtual reality rehabilitation programme and conventional rehabilitation programme groups at baseline.

	Virtual reality programme	Conventional programme
Male (*n*)	18	17
Female (*n*)	7	9
Age (years)	72 (7)	70 (10)
UPDRS III	23 (9)	25 (10)
Onset of disease (months)	89 (92)	57 (53)

Statistical analysis

The statistical analysis was performed by an examiner blinded to the randomisation. SPSS Version 20 (IBM Corp., Armonk, NY, USA) was used for the analysis. All data are expressed as mean [standard deviation (SD)]. The statistician was blinded to treatment assignment.

The Shapiro–Wilk test was applied, before analysis, to test the normal distribution of data. To verify differences in study variables between the conventional rehabilitation programme and the VR rehabilitation programme, a 2×2 multivariate analysis of variance for repeated measures was applied, considering time (i.e. pre and post intervention) as within factor, and rehabilitation programme group (i.e. conventional or VR) as between factor.

Further univariate analysis was considered if significant multivariate effects were detected. When significant interaction (i.e. condition for time) was observed, follow-up tests were conducted running separate repeated measures analysis of variance for programme (i.e. conventional or VR) to explore the different effects of the two protocols.

Due to the non-normal distribution of data for liking the programme, difficulty of the programme and fatigue after physical therapy, these data were examined using the Mann–Whitney *U*-test.

Variables were analysed to verify if any differences existed between the two groups at baseline.

Statistical significance was set at $P \leq 0.05$. Effect size was calculated according to the literature [26].

Results

In total, 51 patients were enrolled in the study [35 males, 16 females, mean age 71 (SD 8.5) years, mean disease duration 73.2 (SD 75.5) months].

Demographic data, clinical picture and onset of disease for both groups at baseline evaluation are reported in Table 1.

Mean (SD) values of the studied variables for both groups pre and post intervention are reported in Table 2.

Apart from liking the programme, difficulty of the programme and fatigue after physical therapy, all variables were found to have a normal distribution and no significant differences were identified between the two groups at baseline. Analysis showed a multivariate effect for time (pre to post) (Wilks' $\lambda = 0.581$, $P < 0.001$) and for interaction time by protocol (Wilks' $\lambda = 0.721$, $P = 0.020$).

Univariate tests indicated a significant main effect in pre–post treatment for BBS ($P = 0.005$; $\eta^2\text{p} = 0.149$) and DASH scale ($P < 0.001$; $\eta^2\text{p} = 0.249$), and a significant interaction (time*programme) was found for DGI ($P = 0.020$; $\eta^2\text{p} = 0.106$) and MCS ($P = 0.007$; $\eta^2\text{p} = 0.140$).

The VR rehabilitation programme led to an increase in BBS score [45.6 (SD 7.9) vs 49.2 (SD 8.1), mean difference 3.6, 95% confidence interval (CI) 1.3 to 5.9; $P = 0.003$], DGI score [18.7 (SD 4.7) vs 20.2 (SD 4.2), mean difference 1.6, 95% CI 0.6 to 2.5; $P = 0.003$] and SF-36 mental composite score [37.7 (SD 11.4) vs 43.5 (SD 9.2), mean difference 5.8, 95% CI 0.4 to 11.3; $P = 0.037$], and a decrease in DASH scale score [29.6 (SD 17.5) vs 21.6 (SD 15.1), mean difference −7.9, 95% CI −13.7 to −2.2; $P = 0.009$]. In contrast, the conventional rehabilitation programme only led to a decrease in DASH scale score [30.3 (SD 18.1) vs 25.1 (SD 15.8), mean difference −5.2, 95% CI −8.8 to −1.5; $P = 0.007$].

Between-group differences were found in liking the programme {VR, median 8 [interquartile range (IQR) = 1]; conventional, median (IQR = 2); $P = 0.011$} and fatigue after physical therapy [VR, median 4 (IQR = 4); conventional, median 2.5 (IQR = 3); $P = 0.004$], but no between-group difference was found for difficulty of the programme [VR, median 4 (IQR = 4); conventional, median 2 (IQR = 3)].

Data collected from diaries showed no changes in drugs taken over the 6-week period.

Discussion

These results showed that the participants who underwent VR rehabilitation had better outcomes for various functions compared with the participants who underwent conventional rehabilitation. In particular, the VR group showed a greater improvement in balance (BBS), walking (DGI), arm function (DASH scale) and the mental aspect of quality of life (MCS) compared with the conventional group.

In recent years, it has been recognised that the rehabilitation of patients with PD is not purely a motor task as other functions play a crucial role. For example, Iansek *et al.* [27] found that gait is strongly influenced by cognition, and as patients with PD can suffer from cognitive dysfunction, the capacity to normalise gait remains impaired. Moreover, correct execution of exercises performed during VR training can be confirmed by visual and/or acoustic feedback. A study by Carpinella *et al.* [28] that aimed to investigate the effect of biofeedback rehabilitation of balance and gait in patients with PD showed that the effect of feedback provided by the sensor was a powerful stimulus. In this context, rehabilitation in a VR setting could offer patients more stimuli, delivered visually and acoustically [29].

Table 2
Mean [standard deviation (SD)] values of variables in the study for the virtual reality and conventional rehabilitation groups pre and post intervention.

	Pre intervention Mean (SD)	Post intervention Mean (SD)	Mean difference (95% CI)	F statistic	*P*-value	η^2p
Berg Balance Scale						
Virtual reality	45.6 (7.9)	49.2 (8.1)[a]	3.6 (1.3 to 5.9)	F(1;24) = 10.689	0.003	0.308
Conventional	47.3 (7.6)	48.1 (7.2)	0.8 (−1.3 to 2.9)	–	0.441	–
Dynamic Gait Index						
Virtual reality	18.7 (4.7)	20.2 (4.2)[a]	1.6 (0.6 to 2.5)	F(1;24) = 11.218	0.003	0.319
Conventional	19.1 (2.9)	19 (3.9)	−0.2 (−1.3 to 0.9)	–	0.776	–
Disabilities of the Arm, Shoulder and Hand scale						
Virtual reality	29.6 (17.5)	21.6 (15.1)[a]	−7.9 (−13.7 to −2.2)	F(1;24) = 8.210	0.009	0.255
Conventional	30.3 (18.1)	25.1 (15.8)[a]	−5.2 (−8.8 to −1.5)	F(1;25) = 8.616	0.007	0.256
Physical composite score (SF-36)						
Virtual reality	35.9 (11.7)	36.8 (9.4)	0.9 (−3.9 to 5.8)	–	0.688	–
Conventional	43.8 (13.1)	46.7 (13.8)	−1.2 (−3.6 to 1.3)	–	0.343	–
Mental composite score (SF-36)						
Virtual reality	37.7 (11.4)	43.5 (9.2)[a]	5.8 (0.4 to 11.3)	F(1;24) = 4.889	0.037	0.169
Conventional	41.9 (12.8)	39.2 (12.6)	−2.6 (−5.6 to 0.4)	–	0.086	–

SF, Short Form 36; CI, confidence interval.
[a] Different from pre intervention ($P < 0.05$).

This study found that VR rehabilitation resulted in a greater improvement in walking and dynamic balance (according to DGI) than conventional rehabilitation; this is likely to be because VR rehabilitation is able to stimulate sensory-motor and cognitive functions (the whole body). A previous study [30] showed that motor signs of walking impairment, such as freezing, can be treated with cognitive intervention, and studies have shown that interventions that incorporate cognitive and motor tasks are able to improve physical and cognitive functions [31].

As balance is achieved and maintained by a complex set of sensory-motor control systems that include sensory inputs from vision (sight), proprioception (touch) and the vestibular system (motion, equilibrium, spatial orientation), all these sensory inputs are integrated together with motor output. Thus, VR rehabilitation may be able to improve balance as it is a global physical therapy that stimulates many physical functions such as those involved in balance, but also 'integrative' functions. The capability of VR to rehabilitate balance is of crucial importance as postural instability is one of the main problems faced by patients with PD as this can cause falls and consequent morbidity [30–34].

Although there are no specific outcome measures to investigate balance and ambulation in patients with PD, BBS and DGI fulfilled the criteria for 'recommended' measurements to be used in this disease [35].

The study results showed a significant improvement in arm function for both groups using the DASH scale. This result is very important as it shows that both rehabilitation programmes, although not focused on the upper limbs, are able to improve this important function which has an impact on performance of the activities of daily living. Concerning this last aspect, it would be very useful to collect information on how rehabilitation (both VR and conventional) could have improved performance of the activities of daily living. Unfortunately, this was not investigated in this study.

The VR rehabilitation programme led to an improvement in the mental aspect of quality of life. This result may be due, in part, to the fact that during the VR programme, the patient perceives him/herself as an active part of treatment, rather than playing a passive role as in the conventional programme. This improvement may also be due to the fact that patients with PD have usually experienced a long period of conventional rehabilitation, and a VR programme may be perceived as new and more interesting. VR programmes can be personalised according to the patient's attitude and premorbid life experiences, as it is known that these aspects can influence outcome [36].

Study limitations

This study had a few limitations. First, this was not a crossover study; this would have increased the strength of the results but would have required a long time to reverse people back to baseline. Second, follow-up data were not collected so the duration of improvement is not known. Third, the proposed set of virtual exercises did not represent daily activities, and devices to record possible modifications in real life were not used.

Conclusion

In conclusion, this study showed that the proposed rehabilitation programmes were useful to improve functional outcome in patients with PD. Comparison of the two programmes, based on physical exercises, showed that VR rehabilitation is more effective in determining overall improvement (gait, balance, upper limb function and mental aspect of quality of life) compared with conventional rehabilitation in a safe and stimulating setting. As such, the prescription of VR rehabilitation as a complementary treatment in patients with PD is encouraged. However, VR rehabilitation is not recommended for patients with cognitive or serious balance impairment.

More studies are needed to confirm these data in a wider sample of patients to evaluate the possible effects on activities of daily living and to evaluate if this improvement is maintained over time.

Ethical approval: Prot.n.5/2016/CE_FdG/SA.

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Conflict of interest: None declared.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.physio.2019.12.007.

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