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Immersive Virtual Reality High-Intensity Aerobic Training to Slow Parkinson's Disease: The ReViPark Program

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Abstract: Intense exercise can be neuromodulatory and neuroprotective against Parkinson's disease (PD). Indoor cycling is a good and safe option for this population, but some barriers (monotonous and repetitive environment, lack of monitoring, and an inability to compete with others) could limit its use. Immersive virtual reality (IVR) could be a possible solution to some of these drawbacks, increasing patient motivation and thus adherence to forced exercise programs using cycloergometers. A double-blind, randomized, controlled clinical trial was conducted to explore the feasibility and effects of the ReViPark program (high-intensity pedaling + IVR for 3 months with two sessions per week) on PD progression. In all, 52 people with PD were allocated to the ReViPark group (n = 30; 70.87 ± 6.67 years) and smart cycloergometer group (n = 22; 70.59 ± 6.67 years). This program was feasible, with no adverse effects (no significant Simulator Sickness Questionnaire symptoms and a low negative experience rating for the Game Experience Questionnaire (0.04/4)), no dropouts, high adherence, and good usability (System Usability Scale score of 82.90%). The ReViPark group showed significant improvements in functionality, quality of life, and disease progression as measured by their balance, gait and risk of falling (Timed Up and Go $p = 0.028$; Tinetti test $p = 0.046$), PDQ-39 scores ($p = 0.035$), and MDS-UPDRS scores ($p = 0.001$). This program is feasible and could lead to improvements in the functional parameters, quality of life, and symptomatology of the participants.

Keywords: rehabilitation; exercise; virtual reality exposure therapy; Parkinson's disease; wearable technology; physiotherapy; physical activity; cycling

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Citation: Rodríguez-Fuentes, G.; Campo-Prieto, P.; Cancela-Carral, J.M. Immersive Virtual Reality High-Intensity Aerobic Training to Slow Parkinson's Disease: The ReViPark Program. *Appl. Sci.* **2024**, *14*, 4708. https://doi.org/10.3390/app14114708

Academic Editors: Andoni Carrasco-Uribarren, Lucia Billeci, Xavier Marimon, Portela Alejandro and Oliver Millan

Received: 7 May 2024
Revised: 21 May 2024
Accepted: 27 May 2024
Published: 30 May 2024

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1. Introduction

Parkinson's disease (PD) is a degenerative disorder of the central nervous system. It is the second most common neurodegenerative disease after Alzheimer-type dementia [1]. PD is characterized by the loss of dopaminergic neurons in the compact part of the *substantia nigra* of the basal ganglia. This explains the symptomatology that characterizes PD patients in both motor (rigidity, tremors, bradykinesia, and postural reflex and gait disorders) and non-motor ways (disorders of the neuropsychiatric sphere and cognitive impairment or sleep impairment, among others) [2,3].

The degeneration suffered by patients with PD leads to their personal, family, and social spheres being affected, which increases their social isolation. Although the basis of PD treatment is medical-surgical and pharmacological (particularly for levodopa), owing to these patients' functional impairment, which deteriorates over time, exercise therapy has been shown to prevent functional disability and also improve both some physical abilities and their quality of life [2,4–11], thus limiting the negative influence of symptomatology and slowing the progression of the disease [10,12]. Furthermore, it appears that high-speed, complex, and repetitive movements result in activity-dependent neuroplasticity [13–18], or

as De Laat et al. [19] pointed out in their recent study, intense exercise improves the functionality of dopaminergic neurons, which become neuromodulatory and neuroprotective against PD.

Among the various methods of carrying out high-speed or intense physical activity, we came across some studies that analyzed the potential benefits of high-cadence cycling or forced exercise cycling [11,13,15,18,20–24]. Miner et al. [11] pointed out that this method of cycling is more than just a passive increase in cadence; rather, it is a technique by which the patient is forced to be active and is assisted by the machine in acquiring the desired speed, which is higher than that which he or she would achieve on his or her own.

Other benefits of this type of exercise in PD patients are aspects such as improved joint mobility ranges [21], improved gait [22,24,25], increased hand coordination [18,22,24], an increase in brain activity similar to that produced by medication [13,15,20,26], a reduction in motor symptomatology such as rigidity, tremors, and bradykinesia [13,18,23–25,27], improved muscular endurance and cardiovascular fitness [18,28], improved sequential coordination of movements during gait transfers [29], and finally not presenting side effects from any medication. Moreover, these benefits have longer lasting effects over time (for at least 48 h, according to Ridgel and Ault) [24].

Despite all their positive aspects, most of these studies are short interventions of only a few sessions or even one standalone session delivered indoors [13,20,21,23,24,27]. Also, as Miner et al. [11] pointed out, cycling interventions have some drawbacks, such as the need for someone to assist the patient with his or her exercise, the difficulty in getting on and off the bike (in the case of tandem cycling), the monotony of the environment (indoors), the possible decrease in motivation and lack of adherence to the protocols when carried out alone (in the case of cycloergometers), and finally the cost (in both cases but especially for cycloergometers).

Immersive virtual reality (IVR) is a possible solution to some of these drawbacks, as it could increase patient motivation and thus adherence to forced exercise programs using cycloergometers. IVR, via a head-mounted display (HMD), immerses patients into a virtual world where they can experience different environments and carry out tasks in first-person scenarios, which are comparable to real situations [30]. This technology has previously been used with PD patients and has achieved promising therapeutic results [5,6], although not in combining high-intensity forced cycling and IVR interventions. Benefits include the potential individualization of the sessions, by adapting them to each patient, as well as being motivating and safe. To the best of our knowledge, no studies have been conducted that incorporate IVR into forced cycling programs aimed at people with PD.

Our hypothesis is based on the theory that the addition of IVR to a high-intensity aerobic exercise program carried out by PD patients on a smart cycloergometer may be able to obtain better therapeutic results than exercise regimes carried out without it. The greatest novelty of this research lies in testing whether exposure to virtual scenarios can amplify the benefits of forced pedaling.

Therefore, the objective of this study is to determine the differential effects of carrying out high-intensity aerobic physical exercise on smart cycloergometers in immersive virtual reality environments versus the same exercise undertaken in real closed environments by people diagnosed with Parkinson's disease.

2. Materials and Methods

2.1. Study Design

A double-blind, randomized, controlled clinical trial was performed, where the patients did not know to which research group they belonged to and the evaluators were external and did not know to which group the patients belonged.

2.2. Participants

A total of 52 people with PD belonging to the Parkinson's associations of Vigo (Vigo, Pontevedra, Spain) and Baixo-Miño (Tui, Pontevedra, Spain) participated in the clinical trial. Of the 52, 30 were men, and 22 were women (42.31%), with a mean age of 70.79 ± 6.59 years.

Participation was voluntary and was offered to all the members of the associations who met the following inclusion criteria: (1) having been diagnosed with idiopathic PD by a neurologist; (2) presenting a stage of disease progression between 1 and 3 on the Hoehn and Yahr scale; (3) being able to move without assistance; and (4) not presenting dementia (MoCA > 26).

The following were defined as the exclusion criteria: (1) presenting comorbidities that would make the practice of physical exercise or performance of the different scheduled assessments inadvisable and (2) presenting severe visual or auditory disturbances, vertigo, psychosis, or uncontrolled epilepsy that would prevent the sessions from being carried out.

The calculation of the sample size necessary to carry out this research took into account the effects of a high-intensity aerobic program [31] on motor symptomatology in people with Parkinson's disease (MDS-UPDRS III; effect size of d: 0.79). G*Power software (3.1.9.3 version for Mac) [32] was used, accounting for 10% loss, a confidence level (1-α) of 95% and a statistical power (1-β) of 0.80. A total of at least 44 participants was deemed necessary to successfully complete the study.

In order to optimize resources, a random distribution by cluster was carried out, where the experimental group (EG) was randomly assigned to the Vigo Parkinson's Association group while the control group (CG) was formed with the members of the Baixo-Miño Parkinson's Association. The study began with 30 participants in the EG and 22 in the CG.

The study was carried out while following the ethical principles for medical research on human subjects according to the Declaration of Helsinki [33], and it was in compliance with all the provisions established in Organic Law 3/2018 concerning Personal Data Protection and Guarantee of Digital Rights (Organic Law 3/2018 on May 25), according to which strict confidentiality of the data, as well as the results of the tests performed, must be maintained. In addition, the study was submitted to the Research Ethics Committee of the Galician Health Service (SERGAS), which approved it and issued registration code 2023/286. All participants signed the corresponding informed consent form, and they as well as their relatives and guardians were all informed in detail about the study, its aims, and its benefits.

2.3. Evaluation Tools

The evaluation of the different parameters under investigation in this project was carried out twice (pre- and post-intervention assessment). In addition, additional control evaluations were conducted on the parameters indicated by the smart cycloergometer for both groups (baseline, after 15 days, and final) and also at the end of the intervention only with the EG regarding the usability, tolerability, and applicability of IVR.

2.3.1. Pre- and Post-Intervention Assessment

Assessments were carried out before the start of the intervention program and at its completion, and they were performed in both groups. The following values were assessed:

- For the sociodemographic and pharmacological characteristics of the sample, an ad hoc questionnaire was conducted where the following variables were collected: age, sex, years since Parkinson's diagnosis, first symptom of the disease, as well as any antiparkinsonian pharmacological treatment being received.
- Regarding functional aspects, the following variables were analyzed:
    1. For dynamic balance, we used the Timed Up and Go (TUG) test [34]. This test evaluates basic functional mobility of the subject, in addition to dynamic and static balance and the risk of falling [35]. As well as the basic version of the test, it was also performed with the addition of a simultaneous double task. (The participants performed mathematical operations.)

2. Lower extremity strength with Five Sit-to-Stand Test (FSTST) [36,37].
3. The gait and balance were measured using the Tinetti Mobility Test [38,39]. This test also helps with identifying people at risk of falling.

- For quality of life, the Parkinson's Disease Questionnaire (PDQ-39) [40,41] was used to assess this aspect. The PDQ-39 scale assesses 8 different domains: mobility (10 items), activities of daily living (6 items), emotional well-being (6 items), stigma (4 items), social support (3 items), cognitive status (4 items), communication (3 items), and bodily discomfort (3 items).
- With regard to symptomatology and follow-ups, the Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) [42] was used for this purpose. It is made up of four parts: Part I (non-motor experiences of daily living), Part II (motor experiences of daily living), Part III (motor exploration), and Part IV (motor complications).

2.3.2. Specific Evaluation of the EG

This assessment was carried out at the end of the intervention, with the aim of evaluating the safety, usability, and personal impressions of the IVR and assessing the following:

- For the safety of the immersive experience, the Simulator Sickness Questionnaire (SSQ) was used [43–45], which consists of 16 items grouped into 3 subscales according to symptomatology: (1) oculomotor symptoms; (2) disorientation; and (3) nausea.
- System usability was evaluated using the System Usability Scale (SUS) [46,47].
- Personal impressions were evaluated with the post-game module of the Game Experience Questionnaire (GEQ-post game) [48]. The GEQ-post game questionnaire assesses four components: positive experiences, negative experiences, fatigue, and return to reality. In the absence of a validated version of the questionnaire in Spanish, and for ease of understanding, the questionnaire was translated by the authors and has been used in previous research [49,50].

The study design and all the process are summarized in Figure 1. The specific scales used to evaluate the characteristics of exposure to IVR were previously employed in other studies [50,51]. In addition to the different questionnaires and scales indicated above, the patients were also followed up with by means of an attendance register (an ad hoc record sheet of adherence to the program), with monitoring and recording of heart rate data performed by means of a heart rate monitor, in which individualized workload limits were established for each patient (70–80% of maximum heart rate (MHR)). At the end of each session, each patient also recorded the rate of perceived exertion (RPE) that the session entailed, and these data were recorded using the modified Borg scale [52].

2.4. Intervention Program

The intervention program was carried out over a period of 3 months, with 2 sessions per week. The program for the CG consisted of static cycling using smart cycloergometers (MOTOmed® loop p.la, RECK MOTOmed, Betzenweiler, Germany). The patients had to pedal continuously for 25 min (a 5 min warm-up, 15 min for the main part, and 5 min to return to calm). The cycling program consisted of seven phases, combining increasing and decreasing passive and active pedaling in both the warm-up and cool-down phases and active pedaling in the main part, during which the participants had to pedal at a cadence of 80–90 rpm, aiming for an intensity of between 70 and 80% of their maximum heart rate and a perceived exertion rate of 8–9/10 on the modified Borg scale [52], based in previous studies in rodent and human models [53,54]. These smart cycloergometers were chosen because they have a specific program for PD, and it can assist with movement in case the participant cannot reach a certain level (and even detect and resolve unilateral spasms).

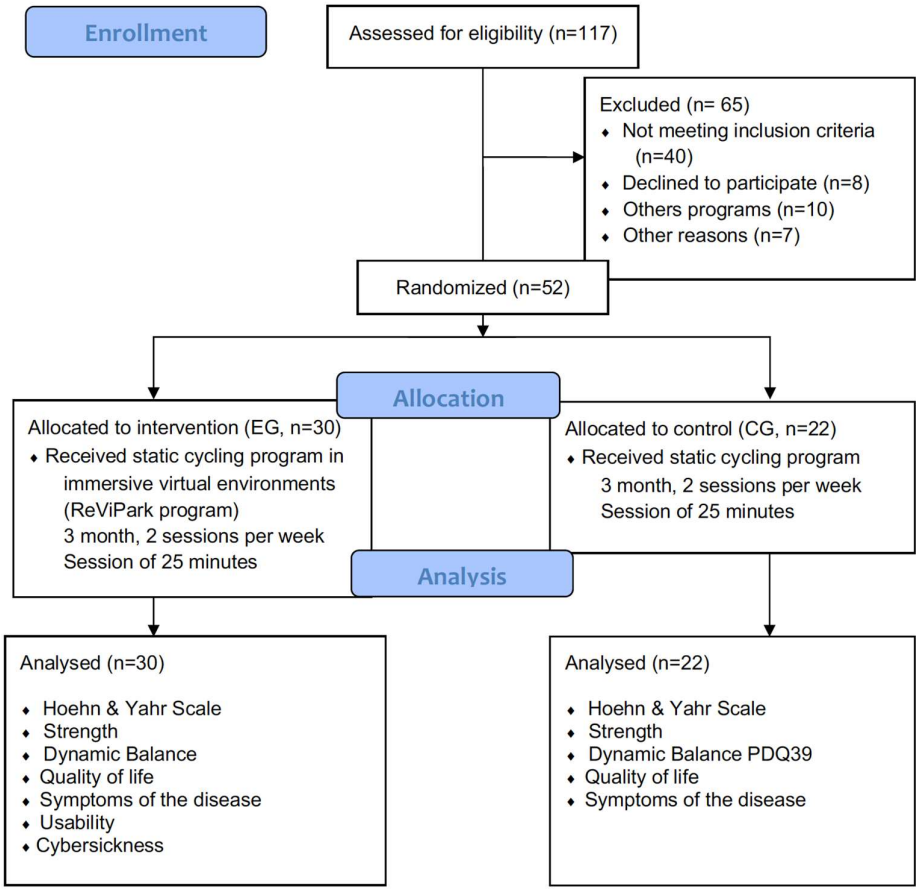

Figure 1. Study design: CONSORT 2010 flow diagram. Static cycling program in immersive virtual environments (ReViPark program) versus static cycling program in patients diagnosed with Parkinson's.

The EG program (ReViPark program), on the other hand, combined the same pedaling protocol of the program as that established for the CG with the incorporation of an IVR program through the Meta Quest II hardware and HoloFit software (available in the library at www.oculus.com, accessed on 10 December 2023), which when synchronized with the smart cycloergometer allowed the patient to pedal through virtual environments, such as different European cities (London, Paris, Venice, etc.), natural landscapes, or sports competitions, while simultaneously performing small cognitive tasks (see Figure 2).

Finally, it should also be noted that both groups continued with their usual therapeutic programs during the intervention period, which consisted of physiotherapy sessions, cognitive exercises (focused on memory, attention, and language), psychology (focused on developing strategies to manage stress, anxiety, or depression), and occupational therapy.

2.5. Data Analysis

The normality of the variables under study was tested using the Shapiro–Wilk test. Assuming normality of the variables, the homogeneity and homoscedasticity of the randomly formed groups (CG and EG) were tested by applying a Student's *t*-test for the independent data and Levene's test. A descriptive analysis of the groups was performed by calculating the measures of central tendency (mean and standard deviation) of the quantitative variables and the percentages of the qualitative variables. The effect of the ReViPark program compared with the cycling program without virtual reality was evaluated by applying parametric tests (intragroup Student's *t*-test and 2 × 2 intergroup ANOVA (Anova Applied Electronics, Inc., San Francisco, CA, USA)). All analyses were performed globally and by stratifying the sample by gender. The data obtained were processed with IBM-SPSS statistical software v.25. The value of statistical significance was set at $p < 0.05$.



Figure 2. An example of a virtual scenario and user pedaling on a smart cycloergometer.

3. Results

A total of 52 patients with PD participated in the study, and no patients were discharged for the duration. Table 1 shows the main characteristics of the sample. As is shown, both groups were homogeneous, with no statistically significant differences.

Table 1. General characteristics of the EG and CG (first reading).

Variables	All (n = 52)	EG (MOTOmed® + IVR) (n = 30)	CG (MOTOmed®) (n = 22)	Student's t and Chi-Squared Test Results
Age (years)	70.79 ± 6.59	70.87 ± 6.67	70.59 ± 6.67	t = 0.127; p = 0.899
Sex (% of women)	42.31	36.67	50	
Time diagnosed (years)	6.40 ± 4.77	5.60 ± 4.06	8.23 ± 5.88	t = 1.470; p = 0.080
Hoehn and Yahr scale	1.82 ± 0.87	1.71 ± 0.90	2.08 ± 0.76	t = −1.287; p = 0.103
Stage 1 (%)	37.30	51.60	23.10	
Stage 2 (%)	39.23	32.30	46.15	Chi = 5.613; p = 0.132
Stage 3 (%)	23.47	16.20	30.75	
First symptom				
Tremors (%)	40.80	38.70	42.90	
Rigidity (%)	20.75	12.90	28.60	Chi = 4.729; p = 0.193
Bradikinesia (%)	17.15	12.90	21.40	
Other (%)	21.30	35.50	7.10	
Pharmacology Equivalent dose of levodopa LEDD (mg)	532.33 ± 229.75	538.94 ± 161.92	526.33 ± 297.53	t = 1.001; p = 0.129

Regarding the characteristics of the high-intensity aerobic exercise program carried out, it should be noted that the patients as a whole completed an average of 42 sessions during the 6 months of intervention (range: 40–48). Furthermore, taking into account the seven phases that each session consisted of, we should also highlight that of the 25 min each session lasted, on average, 626.62 ± 259.72 s (range: 300–1148 s) of exercise were carried out actively while 893.91 ± 341.80 s (range: 419–1215 s) were performed passively, and the average distances covered per session were 4400.14 ± 1945.84 m actively (range: 1000.15–7966.18 m) and 5496.18 ± 2545.53 m passively (range: 2039.75–8001.7 m).

In the Supplementary Material (Table S1), the details of the intervention program carried out for both the EG and CG are presented. The following variables were analyzed: duration of the program, distance covered, pedaling symmetry, resistance tolerated, average speeds of the active and passive phases, energy consumed, work performed, muscle tone, any identified spasms, and each participant's perception of effort. The comparative study between both groups indicated no significant differences between the control group and the experimental group. Therefore, the program carried out on the smart cycloergometer was similar for both groups. The use of an IVR headset did not modify the execution parameters of the program undertaken in any of the phases of analysis carried out.

Table 2 shows in detail the differential study of the effects of the intervention program in both groups with respect to the functional parameters. These data show that the use of an IVR headset in the EG led to statistically significant improvements when compared with the CG in terms of dynamic balance, gait, and risk of falling, all of which are parameters of vital importance in the population diagnosed with PD.

Table 2. Analysis of the effects of intervention programs (MOTOmed® + IVR; MOTOmed®) on functional parameters.

	Variable	EG (MOTOmed® + IVR) (n = 30) Average ± SD	CG (MOTOmed®) (n = 22) Average ± SD	Student's t Test Results
Pre-intervention	Strength of lower train			
	Five sit to stand (s)	14.30 ± 5.42	13.08 ± 3.00	t = 0.901; p = 0.186
	Dynamic balance			
	Time up and go (s)	14.08 ± 18.28	12.46 ± 9.19	t = 0.359; p = 0.361
	Time up and go + cognitive task (s)	17.64 ± 26.02	14.51 ± 11.95	t = 0.495; p = 0.312
	Tinetti scale			
	Balance (pts)	12.89 ± 3.54	14.80 ± 1.77	t = −2.143; p = 0.019
	Gait (pts)	9.47 ± 1.87	10.20 ± 2.55	t = −1.011; p = 0.159
	Total (pts)	22.37 ± 4.88	25.00 ± 3.87	t = −1.872; p = 0.035
Post-intervention	Strength of lower train			
	Five sit to stand (s)	13.81 ± 6.68	13.18 ± 4.54	t = 0.336; p = 0.369
	Dynamic balance			
	Time up and go (s)	10.16 ± 6.42	13.70 ± 4.51	t = −1.589; p = 0.040
	Time up and go + cognitive task (s)	11.59 ± 9.27	14.57 ± 12.52	t = −1.828; p = 0.206
	Tinetti scale			
	Balance (pts)	15.00 ± 2.53	15.33 ± 1.59	t = −0.465; p = 0.322
	Gait (pts)	11.37 ± 1.40	9.75 ± 2.93	t = 2.540; p = 0.007
	Total (pts)	26.37 ± 3.54	25.53 ± 3.64	t = 0.736; p = 0.233

Table 3 shows the comparative study between the two groups in terms of the quality-of-life parameters and disease symptomatology pre-intervention and post-intervention. The results show that the use of an IVR headset generated significant differences between the groups in favor of the EG in the following domains: stigma, cognition, body discomfort, and total score for the PDQ-39 questionnaire (University of Oxford, Oxford, UK). Furthermore,

the analysis of symptomatology also showed that the use of an IVR headset (Meta Quest II (Oculus VR, Menlo Park, CA, USA)) led to significant improvements in all of the dimensions composing the MDS-UPDRS scale.

Table 3. Analysis of the effects of the intervention programs (MOTOmed® + IVR and MOTOmed®) on the parameters of quality of life and disease symptomatology.

	Variable	EG (MOTOmed® + IVR) (n = 30) Average ± SD	CG (MOTOmed®) (n = 22) Average ± SD	Student's t Test Results
Pre-intervention	PDQ-39			
	Mobility	19.19 ± 23.02	29.25 ± 28.78	t = −1.380; p = 0.087
	Activities of daily living	16.67 ± 19.75	22.92 ± 21.48	t = −1.066; p = 0.146
	Emotional well-being	20.16 ± 15.92	32.24 ± 24.80	t = −2.101; p = 0.020
	Stigma	0.01 ± 0.01	0.01 ± 0.02	t = −1.001; p = 0.161
	Social support	0.01 ± 0.01	0.01 ± 0.02	t = −1.603; p = 0.058
	Cognition	0.03 ± 0.02	0.05 ± 0.03	t = −2.804; p = 0.004
	Communication	0.02 ± 0.03	0.03 ± 0.04	t = −0.949; p = 0.174
	Physical discomfort	0.04 ± 0.03	0.06 ± 0.04	t = −1.887; p = 0.033
	Total score	7.01 ± 5.55	10.79 ± 7.53	t = −2.037; p = 0.024
	MDS_UPDRS			
	Part IA: Non-motor experiences of daily living	10.42 ± 12.70	22.50 ± 19.75	t = −2.691; p = 0.005
	Part IB: Non-motor experiences of daily living	15.92 ± 12.41	25.47 ± 17.12	t = −2.329; p = 0.012
	Part II: Motor experiences of daily living	15.81 ± 16.51	19.90 ± 14.61	t = −0.909; p = 0.184
	Part III: Motor evaluation	11.79 ± 12.72	20.19 ± 16.91	t = −2.039; p = 0.023
	Part IV: Motor complications	2.99 ± 8.99	23.12 ± 31.83	t = −3.385; p = 0.001
	Total score	21.86 ± 18.82	42.70 ± 31.33	t = −3.003; p = 0.002
Post-intervention	PDQ-39			
	Mobility	14.08 ± 19.61	24.53 ± 22.46	t = −1.636; p = 0.054
	Activities of daily living	14.78 ± 19.92	22.14 ± 19.53	t = −1.207; p = 0.117
	Emotional well-being	22.58 ± 17.24	30.47 ± 26.95	t = −1.221; p = 0.114
	Stigma	0.00 ± 0.01	0.02 ± 0.03	t = −3.548; p = 0.001
	Social support	0.01 ± 0.03	0.01 ± 0.02	t = −0.188; p = 0.426
	Cognition	0.02 ± 0.02	0.06 ± 0.04	t = −3.699; p = 0.001
	Communication	0.02 ± 0.03	0.02 ± 0.02	t = 0.776; p = 0.221
	Physical discomfort	0.03 ± 0.03	0.05 ± 0.03	t = −2.379; p = 0.011
	Total score	6.41 ± 4.90	9.70 ± 6.46	t = −1.858; p = 0.035
	MDS_UPDRS			
	Part IA: Non-motor experiences of daily living	9.44 ± 10.94	22.66 ± 20.97	t = −2.822; p = 0.004
	Part IB: Non-motor experiences of daily living	12.19 ± 7.63	25.20 ± 17.58	t = −3.505; p = 0.001
	Part II: Motor experiences of daily living	10.64 ± 10.32	18.51 ± 16.06	t = −2.021; p = 0.025
	Part III: Motor evaluation	5.40 ± 6.69	18.47 ± 15.81	t = −3.939 p = 0.001
	Part IV: Motor complications	1.67 ± 4.46	5.73 ± 12.06	t = −1.657; p = 0.052
	Total score	15.11 ± 9.80	34.77 ± 23.36	t = −4.023; p = 0.001

Table 4 shows the 2 × 2 analysis (moment; program) in relation to the functional parameters, quality of life, and disease symptomatology. Significant differences are shown in several functional parameters (dynamic balance, balance, and gait), in the stigma dimension of quality of life (PDQ-39), and in parts III (motor) and IV (motor complications) of the Parkinson's symptomatology scale (MDS-UPDRS). Finally, Figure 3 shows indicators

of disease progression with the scores (pre- and post-intervention) for all parts of the MDS-UPDRS.

Table 4. Analysis of the effects of the program, with moments (initial and final), group (experimental and control), and time × group (EG and CG).

		Difference between Final and Initial	95% Confidence Interval (Lower; Upper)	ANOVA 2 × 2 Time (Pre and Post) × Group (EG and CG) (F, *p*, η^2)
Strength of lower train				
Five sit to stand (s)	GE	0.488	−2.847; −3.824	$F_{1.91} = 0.066$; $p = 0.798$; $\eta^2 = 0.01$
	GC	−0.103	−2.665; −2.45	
Dynamic balance				
Time up and go (s)	GE	3.919	−3.262; 11.100	$F_{1.91} = 1.302$; $p = 0.028$; $\eta^2 = 0.12$
	GC	−2.116	−9.803; 5.570	
Time up and go + cognitive task (s)	GE	6.048	−4.295; 16.291	$F_{1.91} = 2.577$; $p = 0.015$; $\eta^2 = 0.16$
	GC	0.813	−5.181; 6.808	
Tinetti scale				
Balance (pts)	GE	−2.105	−3.851; −0.359	$F_{1.91} = 1.927$; $p = 0.016$; $\eta^2 = 0.18$
	GC	−0.533	−1.693; 0.626	
Gait (pts)	GE	−1.892	−2.834; −0.951	$F_{1.91} = 6.024$; $p = 0.016$; $\eta^2 = 0.07$
	GC	0.450	−1.445; 2.345	
Total (pts)	GE	−3.998	−6.421: −1.574	$F_{1.91} = 3.753$; $p = 0.046$; $\eta^2 = 0.05$
	GC	−0.533	−0.3137; 2.071	
PDQ-39				
Mobility	GE	5.110	−5.862; 16.082 [G]	$F_{1.96} = 0.002$; $p = 0.968$; $\eta^2 = 0.001$
	GC	4.718	−13.126; 22.075	
Activities of daily living	GE	1.881	−8.195; 11.959	$F_{1.96} = 0.017$; $p = 0.897$; $\eta^2 = 0.001$
	GC	0.7812	−13.288; 14.851	
Emotional well-being	GE	−2.419	−10.851; 6.013 [G]	$F_{1.96} = 0.236$; $p = 0.628$; $\eta^2 = 0.003$
	GC	1.768	−16.041; 19.577	
Stigma	GE	0.003	−0.002; 0.008 [G]	$F_{1.96} = 3.929$; $p = 0.049$; $\eta^2 = 0.04$
	GC	−0.010	−0.025; 0.005	
Social support	GE	−0.004	−0.155; 0.006	$F_{1.96} = 0.418$; $p = 0.519$; $\eta^2 = 0.004$
	GC	0.001	−0.012; 0.015	
Cognition	GE	0.002	−0.008; 0.013	$F_{1.95} = 1.496$; $p = 0.224$; $\eta^2 = 0.016$
	GC	−0.118	−0.334; 0.102	
Commuication	GE	0.001	−0.013; 0.014	$F_{1.96} = 1.467$; $p = 0.229$; $\eta^2 = 0.016$
	GC	0.155	−0.006; 0.037	
Physical discomfort	GE	0.006	0.007; −0.008 [G]	$F_{1.97} = 0.044$; $p = 0.835$; $\eta^2 = 0.001$
	GC	0.004	−0.021; 0.029	
Score total	GE	1.384	−2.170; 3.378 [G]	$F_{1.96} = 0.035$; $p = 0.852$; $\eta^2 = 0.001$
	GC	1.091	−3.889; 6.072	
MDS_UPDRS				
Part IA: Non-motor experiences of daily living	GE	0.972	−5.067; 7.012 [G]	$F_{1.96} = 0.030$; $p = 0.863$; $\eta^2 = 0.001$
	GC	−0.156	−13.990; 13.678	
Part IB: Non-motor experiences of daily living	GE	3.730	−1.543; 9.004 [G]	$F_{1.96} = 0.381$; $p = 0.539$; $\eta^2 = 0.004$
	GC	0.273	−11.603; 12.085	
Part II: Motor experiences of daily living	GE	5.164	−1.886; 12.214	$F_{1.96} = 0.388$; $p = 0.035$; $\eta^2 = 0.004$
	GC	1.394	−9.010;11.799	
Part III: Motor evaluation	GE	6.385	1.171; 11.600 [G]	$F_{1.96} = 0.745$; $p = 0.390$; $\eta^2 = 0.008$
	GC	1.723	−9.478; 12.924	
Part IV: Motor complications	GE	1.328	2.267; 4.923	$F_{1.96} = 5.589$; $p = 0.020$; $\eta^2 = 0.06$
	GC	17.395	1.487; 33.304	
Total score	GE	6.751	−0.948; 14.450 [M]	$F_{1.96} = 0.018$; $p = 0.894$; $\eta^2 = 0.001$
	GC	7.922	−11.227; 26.460	

[G] Significant differences between groups. [M] Significant differences between moments.

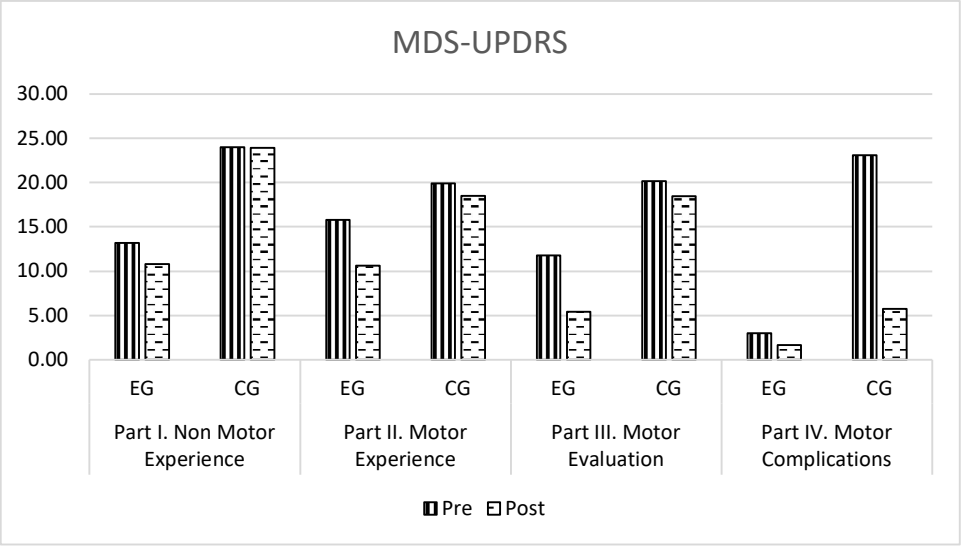

Figure 3. Pre- and post-intervention scores of MDS-UPDRS (parts I, II, III, and IV).

As far as the specific results for the IVR component are concerned, it should be noted that there were no adverse effects related to cybersickness generated by the immersive application. The majority of the participants reported a total absence of the main symptoms of cybersickness, and those who did experience some symptoms described them as being mild. By size, 7% of the sample reported feeling mild symptomatology related to nausea, 2.93% experienced mild symptomatology related to oculomotor symptoms, and 6.29% reported symptoms related to disorientation. Post-game experiences evaluated with the GEQ highlighted the predominance of positive experiences (2.92/4) over negative experiences (0.04/4), fatigue (0.23/4), and return to reality (0.15/4) with residual values. Finally, the hardware and software usability were considered to be quite good (SUS scores: 82.90/100).

4. Discussion

The present study hypothesized that the addition of IVR to a high-intensity aerobic exercise program carried out by patients with PD on a smart cycloergometer could result in better therapeutic results than those obtained through just the use of a cycloergometer on its own. This hypothesis arose from the studies carried out by Carels et al. [55] and Williams et al. [56], which indicated that when people obtain pleasure from an exercise session, they are more likely to adhere to it long term, and thus identifying ways to manipulate the exercise experience to induce a "pleasure" response in people who do not exercise regularly is an important scientific challenge for overcoming levels of physical inactivity. Exergames (gamification of exercise) may be associated with greater interest, greater pleasure, and greater enjoyment than traditional physical activity. Since exercise becomes part of a virtual experience [57], effort is attenuated perceived, which maximizes the enjoyment of exercise while increasing motivation during training [58–60]. Previous studies carried out in a healthy young population [61–63] showed that training with IVR in contrast to the same method but without IVR generates a higher heart rate (188 bpm; 12.9 METs per session), while the perception of effort is lower. Gomez et al. [62] indicated that the use of exergames causes intense myoelectric activity along with resistance training, which does not occur during traditional resistance training. On the other hand, Mologne et al. [63] developed resistance training with IVR and traditionally with the same volume, observing much more favorable adaptations in the IVR group in terms of body composition, cardiometabolic parameters, and muscular endurance strength. The data collected seem to confirm this hypothesis, as this high-intensity exercise program using a cycloergometer with the additional support of IVR HMDs produced significant improvements in dynamic balance and gait when these were measured with the TUG test, the TUG dual-task test, and the Tinetti scale, suggesting a decreased risk of falls, an important issue in patients with

PD. Additionally, a significant improvement was observed in PD symptomatology when measured with the MDS-UPDRS, as well as the patients' quality of life when measured with the PDQ-39 scale. Finally, it should be noted that, although not significant, an improvement was also observed in lower limb strength as measured with the FTSST, while in the CG, there was a slight deterioration. These data are in line with previous research on the therapeutic benefits of high-intensity aerobic exercise in PD patients [11,64,65].

Although there are no previous studies combining a smart cycloergometer and IVR to carry out high-intensity aerobic exercise in patients with PD, there are also some studies that explored the use of forced pedaling with IVR [66] or the use of active video games in populations of healthy young adults [67] and how exposure to virtual and immersive scenarios influences the subject's perception of effort. According to Runswick et al. [66], virtual scenarios can reduce the perception of effort, and according to Stewart et al. [67], the type of activity performed can have the same effect. Our study confirms this fact, as the group that did the pedaling work with IVR presented lower RPE values while having traveled a greater distance (1400 m) than the group that exercised without IVR.

On the other hand, while there are no previous studies like ours proposed for patients with PD, there is research where this type of high-intensity forced cycling work has been performed without the use of the IVR component, which also generated significant improvements across the variables considered in our study. In relation to improvements in balance, Ridgel et al. [23] found reductions in time of 2.1 s in the TUG test after the performance of three 40 min sessions of forced cycling at 75–85 rpm and at 50–80% of the reserve heart rate. In our case, we obtained in the group that used IVR an average reduction of 3.92 s, a difference greater than 3.5 s, which is considered the minimum clinically important difference in cases of PD [68]. For its part, the pedaling group without IVR, although there was post-intervention improvement in the dual-task TUG test, did not reach the minimum clinically important difference, as in the study by Ridgel et al. [23].

In relation to gait improvements, this study's results are in line with the findings of previous research. After one 40 min session of forced cycling at 80 rpm and at 60–70% of the reserve heart rate, Corbett et al. [21] observed an improvement in the hip's range of motion. Gait improvement was also seen in other research, both in studies of only a few sessions [24] and in interventions of several weeks [22,25].

We also found significant improvements in motor function and a reduction in PD symptomatology when these were assessed with the MDS-UPDRS, both in Part III (motor assessment) and Part IV (motor complications). These findings are also in line with those of previous studies, including not only those using the timed motor test battery [22] but also those using the MDS-UPDRS [13,18,20,23,24,27] or functional MRI [13,20]. However, although Stuckenschneider et al. [25] observed improvements in subjects' gaits and tremor reduction (measured with a Kinesia device containing accelerometers and gyroscopes), they did not achieve significant improvements in the MDS-UPDRS (Part III). Thus, the group that performed pedaling with IVR showed improvements of 6.38 points in subscale III and 6.75 points in the total score, which represent a moderate and minimal clinically important difference, respectively [69]. There was also a minimal clinically important difference in parts IB and II, reaching more than 2.64 points and 3.05 points, respectively [70]. These clinically relevant scores for patients were also observed in the CG (Part IV and total score of the MDS-UPDRS), showing the benefits that high-intensity aerobic exercise had in the sample using a smart cycloergometer and improving the motor function and the symptoms generated by PD.

Likewise, quality of life was assessed in our study via the PDQ-39 scale. After the intervention, the SG achieved significant improvements when compared with the CG in the domains of stigma, cognition, physical discomfort, and total score. These findings contrast with those of Cruise et al. [8], who after the study group carried out a cardiovascular exercise program at 60–85% of the maximum heart rate (stationary bike, rowing, or treadmill) and strength for 12 weeks (2 sessions/week) found no significant improvements in the quality of life of the PD patients. This may have been due to a lower cardiovascular exercise

intensity requirement than that which was utilized in our study. This could be an aspect to keep in mind during future research.

Finally, the results of the specific variables related to IVR show that its application is safe and tolerable. Although IVR and cybersickness are sometimes linked in the literature, in the present study, the adverse symptomatology related to virtual exposure was residual, being in line with other studies that used IVR for PD [51,71,72], and in our case, the number of sessions was significantly higher than those of the comparative studies. Even so, this possibility should never be ruled out, since virtual scenarios with movement or accelerations and the variability of each participant can trigger cybersickness more easily. The usability of the equipment was also high (>82%). Even though they were older people, which could lead to some reluctance to use new technologies, the EG felt comfortable with the intervention carried out. Furthermore, based on our experience in research and clinical practice, the HoloFit software allowed users to completely dispense with the hand controllers altogether and control their actions in the IVR scenarios via movements of the HMD. In our opinion, this could represent a breakthrough and reduce the limitations of previous studies, where tremors limited the participation of users with PD in IVR [71]. It would be interesting to know if other exergames based on other sports modalities can achieve similar benefits without compromising the safety of the intervention and if this therapy will be incorporated into regular clinical practice to be able to quantify the weight of possible technical failures, such as a Wi-Fi network failure, the stability of online software, or battery life.

Limitations

The results obtained are promising. However, there are some limitations. Firstly, there was no follow-up to objectively assess the possible durability of the effects. Secondly, there was no third comparative group who did *not* perform high-intensity exercise so as to determine the possible benefits of this mode of intervention compared with exercise at other intensities. Finally, having established as inclusion criteria only patients with mild-to-moderate PD (Hoehn and Yahr scale: I–III), the segment of patients with more severe symptomatology (Hoehn and Yahr scale: IV) was left out, even though the study was concerned with analyzing results in relation to the disease stage.

Therefore, future research should take these aspects into account to provide greater robustness to the preliminary findings shown in this study.

5. Conclusions

The preliminary results of this study show that patients diagnosed with mild-to-moderate Parkinson's disease (stages I–III) can carry out a high-intensity pedaling-based physical exercise protocol and, moreover, accomplish this in an immersive virtual environment. Furthermore, the IVR software (www.oculus.com, accessed on 10 December 2023) and hardware proposed, when employed in combination with smart cycloergometers for the performance of multi-sensory stimulation therapies, are safe, tolerable, and easy to use for people with PD.

Moreover, the effects of the ReViPark program (high-intensity pedaling + IVR over a period of 3 months) led to improvements in several disease domains. In particular, functional parameters such as strength of the lower train, dynamic balance, and gait are crucial aspects for avoiding falls in PD and ensuring functionality, quality of life, and the symptomatology of the participants as indicators of disease progression in terms of motor and non-motor aspects.

However, future studies incorporating longer interventions and follow-up assessments are needed to corroborate these findings.

Finally, this study opens the door to future research opportunities, such as additional aspects of using mixed reality (virtual reality or augmented reality) and the possibility of expanding the program to other pathologies (such as dementia or other neurological conditions) and other methods of virtual rehabilitation (cognitive or mental health-focused therapies).

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/app14114708/s1, Table S1. Analysis of the physical parameters of the intervention program, taking into account the three evaluation times of the program and the EG and CG studied.

Author Contributions: Conceptualization, methodology, and formal analysis, P.C.-P., G.R.-F. and J.M.C.-C. (all authors); software, validation, data curation, and visualization, P.C.-P.; resources, G.R.-F. and J.M.C.-C.; writing—original draft preparation, review, and editing, P.C.-P., G.R.-F. and J.M.C.-C. (all authors); supervision, project administration, and funding acquisition, P.C.-P. and J.M.C.-C. All authors have read and agreed to the published version of the manuscript.

Funding: Intramural Call for Biomedical Research Projects 2022, from the Galicia Sur Health Research Institute (IISGS). Code: CI22-B-03.

Institutional Review Board Statement: This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Servizo Galego de Saúde (protocol code 2023/286; date of approval: 14 December 2023).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The raw data supporting the conclusions of this article will be made available by the authors on request.

Acknowledgments: We are grateful for the collaboration of the therapy staff of the Parkinson's Association of Vigo and the Baixo-Miño Parkinson's Association, as well as all their members, for making this project possible.

Conflicts of Interest: The authors declare no conflicts of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

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