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Study Protocol

Effects of Different Tonic, Isometric and Isometric/Vibratory Strength Training Programs on Motor Symptomatology in People with Parkinson's Disease: Study Protocol for a Randomized Trial

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Abstract: Background: The Chilean population has experienced increased longevity in recent decades, leading to an increased incidence of and mortality from neurodegenerative diseases such as Parkinson's disease (PD). PD is a chronic degenerative condition that affects the central nervous system. The main objective of this research is to evaluate the effect of 12-week programs of tonic, isometric, and isometric/vibratory muscular strength training while controlling the manipulation of the intensity variable on motor and non-motor symptomatology in PD patients. The secondary objective is to assess the levels of muscular strength in PD patients and their relationship with motor and non-motor symptomatology. Methods: A parallel-group, randomized trial will randomly assign (n = 34) people of both sexes with Parkinson's disease between stages I–III Hoehn and Yahr (H&Y), aged between 50 and 70 years to one of the experimental groups, in which they will undergo a total of 24 strength training sessions during 12 weeks. During the intervention period, the participants will be advised not to undertake additional exercise programs, to avoid substances that may disrupt metabolism and circadian cycles, and to maintain their medication regimen. The primary or motor evaluation of rest tremor will be performed with an accelerometer (Actigraphy), balance with the Mini-BESTest balance test, gait speed with the Ten Meters Walk Test, and non-motor symptomatology through anxiety, depression (MDS-UPDRS), and quality of life (PDQ-39) questionnaires. The Secondary evaluation of muscle strength will be performed with a functional electromechanical dynamometer. Discussion: Established as a hypothesis is that manipulating intensity variables in 12-week tonic, isometric, and isometric/vibratory muscle strength training programs has an effect on motor and non-motor symptomatology in people with Parkinson's disease. The research will establish the extent to which controlled muscular strength training has an effect on relevant factors related to motor and non-motor symptomatology.

Keywords: neurodegenerative disease; Parkinson Disease muscular strength; rehabilitation

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1. Introduction

In recent decades, the Chilean population has experienced an increase in longevity, which has translated into a higher prevalence of neurodegenerative diseases such as Parkinson's disease [1]. Reports indicate that, between 1990 and 2016, deaths attributed to Parkinson's disease (PD) increased by 16.5%, reaching a prevalence rate of 19.9%, making Chile the Latin American country with the highest increase in PD prevalence [2]. PD is a chronic degenerative [3], multisystem pathology that affects the central nervous system and is caused by the loss of dopaminergic neurons in the substantia nigra compacta of the basal ganglia in the midbrain [4], leading to a decrease in dopamine levels, neurovegetative disturbances [5], and motor control impairments [6]. Common symptoms experienced by individuals with PD include resting tremor [7], bradykinesia, joint stiffness, postural instability [8], gait disturbances [9], and reduced functional performance [10]. Non-motor symptoms associated with PD include sleep dysfunction, psychiatric disorders, gastrointestinal disturbances, and autonomic dysfunction [11], which have been defined as non-motor disorders associated with the disease [12]. There is sufficient evidence of the positive effects of physical activity and training programs in people with Parkinson's disease (PD), with reported improvements in overall health and a decrease in motor and non-motor symptomatology associated with the disease [13].

Muscular strength training is one of the strategies used to increase physical activity levels in PD patients [14–18]. The adaptations resulting from a strength training program significantly depend on the manipulation of variables such as the intervention program's duration, weekly frequency, volume (number of sets and repetitions), training duration, exercises performed, and intensity (load displaced, generally expressed relative to the subject's maximal force value) [19]. Recent studies have shown that, regardless of how strength training programs are structured, positive effects on motor symptomatology in PD patients occur [9,20–23]. However, the limited number of studies and high variability in the manipulation of strength training program variables, as well as the lack of control over performance variables and exercise intensity, do not allow for the determination of which performance variables associated with muscular strength training have the most significant impact on the changes induced due to this type of training in individuals with PD.

This hinders individualized exercise prescription to reduce motor and non-motor symptomatology. The main objective of this research is to analyze the effect of 12-week programs of tonic, isometric, and isometric/vibratory muscle strength training while controlling the manipulation of the intensity variable of motor and non-motor symptomatology with people with Parkinson's disease. The secondary objective is to assess the levels of muscular strength in PD patients and their relationship with motor and non-motor symptomatology.

Hypothesis: Manipulating intensity variables in 12-week tonic, isometric, and isometric/vibratory muscle strength training programs will affect motor and non-motor symptomatology in people with Parkinson's disease.

2. Materials and Methods

2.1. Design and Protocol Registration

A randomized, parallel-group trial was registered in the RBR-7p32sbb registry on 3 January 2024, before participant enrollment.

2.2. Eligibility Criteria

Participants eligible for the study must meet the following criteria at the time of randomization:

- Individuals of both sexes with a diagnosis of PD aged between 50 and 70 years, in stages I–III according to the Hoehn and Yahr classification.
- Authorized by their treating physician to participate in the intervention program.
- Medication-controlled.
- Capable of following verbal instructions and having motor autonomy.
- Mini-mental examination score greater than 24 points [4].

- Signed informed consent form to participate in the study.

2.3. Exclusion Criteria

- Participants with adherence below 80% to the different types of intervention sessions will not be included in the results analysis.
- People with orthopedic disabilities or other neurological conditions.

2.4. Sample Size

The total number of participants (n = 28) is based on a moderate effect size of 0.25, a significance level of 0.05, and a power of 0.80. With a dropout rate of 20% considered, the final sample size was calculated to be 34 subjects using the G* power 3.0 statistical software [23].

2.5. Randomization, Allocation, and Blinding

Subsequent to the initial evaluation, each of the participants will be randomly assigned to the tonic exercise group (GET), isometric exercise group (GEI), or isometric vibratory exercise group (GIV). Prior to participant recruitment, a blinded investigator will create a simple computer-generated randomization sequence to allocate participants to any group via the implementation of a publicly accessible official website designed for research randomization (https://www.randomizer.org, accessed on 1 June 2024). The muscle strength program assignments will be made individually in closed, numbered, dark, and consecutive envelopes. An external evaluator will open the envelopes in front of the participants to assign them to the experimental groups. Data analysts and primary outcome assessors will be blinded to participant allocation. Due to the nature of the intervention (supervised resistance exercise), the participants will be aware of the group to which they are assigned. The flowchart of the protocol is detailed in Figure 1.

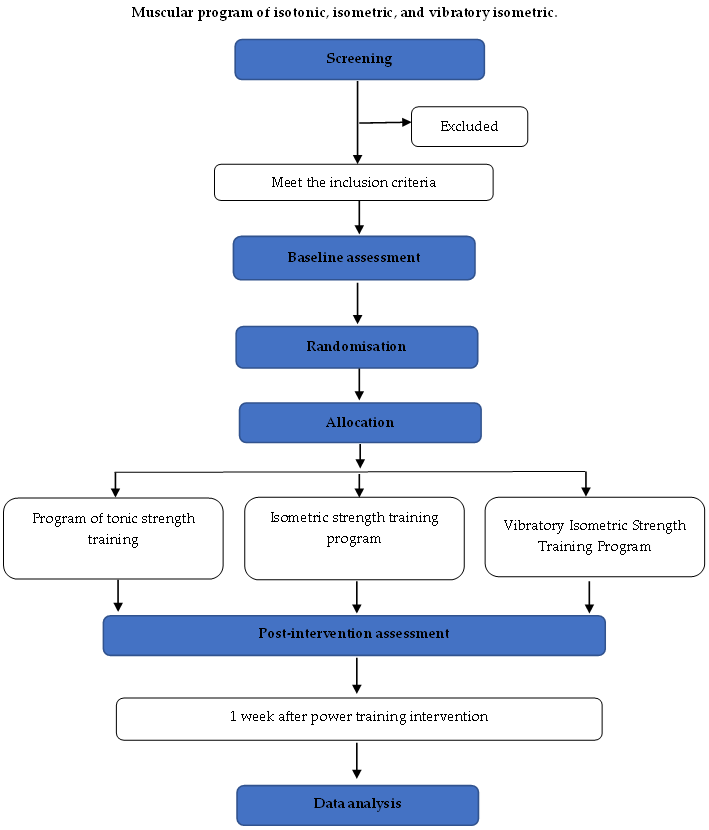

Figure 1. Flowchart of the study according to the Consolidated Standards of Reporting Trials (CONSORT) guidelines.

2.6. Intention to Treat

At the end of the study, the participants will be offered post-experiment treatment with the muscle training program that achieves the best effects on motor and non-motor symptoms.

2.7. Procedures

All patients who signed the consent form to participate in the study will be evaluated by a specialized medical team to establish their initial health and physical condition. To guarantee the confidentiality of patient information, all protocols will comply with Chile's Law 20.584 and the Helsinki guidelines [24] for human research.

2.8. Intervention

Throughout the intervention period, the participants will be advised to maintain their lifestyle habits, avoid engaging in additional exercise programs, avoid substances that may alter metabolism and circadian cycles, and maintain their medication in control during the training program.

2.9. Experimental Groups

All muscular strength training protocols will adhere to the guidelines established in the Consensus on Exercise Reporting Template (CERT). Participants assigned to the intervention groups will perform 24 strength training sessions, each lasting 45–60 min. The supervised training sessions will be led by physiotherapists specialized in strength exercises for individuals with Parkinson's disease. The training programs will be carried out in a gym equipped for muscular strength training. Each exercise session will consist of three phases: a warm-up phase, a development phase, and a cool-down or recovery phase. The warm-up phase will last 15–20 min and will include 5 min of low-intensity aerobic exercise (50–65% of heart rate reserve) on a stationary bike, 6 joint mobility exercises, and 2 core stability exercises. The intensity will be adjusted to values between 5 and 7 on the Rating of Perceived Exertion (RPE) scale [24]. In all programs, the same training volume will be maintained (series × repetitions), and the intensity for the intervention of the tonic and isometric vibration program will be progressive (50–70%) and isometric at 100%. The training load will be adjusted by adjusting series and repetitions. The strength development phase will include 2 upper limb pushing exercises, 2 upper limb pulling exercises, and 2 lower limb exercises, followed by a cool-down phase. The exercises described in the three phases are presented in Table 1.

Table 1. Muscular strength training program *.

		Exercises
Warm-Up Phase	Aerobic Part	5 min of low-intensity aerobic activity (50–65% HRR) on a stationary bike or elliptical machine
	Joint mobility sets and repetitions: 2 × 8	(performed in a seated position) Cervical rotation, acromio-humeral rotation, lumbar rotation, and flexion–extension coxofemoral rotation
Development Phase	Core stability exercises (4–5 RPE)	Pelvic tilt in a sitting position, abdominal bracing in a sitting position with a fitball, abdominal bracing with a band in the transversal plane, bird–dog, humeral rotation without abduction in a sitting position
	Resistance training (strength)	Bilateral seated bench, press unilateral isometric knee extension in closed, kinetic chain at 90°, unilateral open kinetic chain knee extension, bilateral seat row, biceps curl, triceps pushdown
Cool-Down	Dynamic/static stretching of major muscle groups, sets and repetitions: 1 × 12	Pectoralis major, dorsal width, quadriceps, hamstrings

HRR = heart rate reserve, RPE = Borg Rating of Perceived Exertion. * Note: Not all of these exercises will be performed in the same session; this represents the spectrum of exercises that will be used over the course of the training program.

Table 2 summarizes the periodization of the resistance training program during the development phase (12 weeks).

Table 2. Periodization of controlled resistance training programs with FEMD.

Muscle Strength Training Program: Tonic									
Weeks	1	-	4	5	-	8	9	-	12
Intensity (1RM%)		50%			60%			70%	
Sets		3			5			10	
Repetition		10			6			3	
Rest period (s)		60			36			18	
Muscle strength training program: Isometric									
Weeks	1	-	4	5	-	8	9	-	12
Intensity (1RM%)		100%			100%			100%	
Sets		7			5			3	
Repetition (s)		3			4.5			7	
Rest period (s)		60			36			18	
Muscle strength training program: Vibratory Isometric									
Weeks	1	-	4	5	-	8	9	-	12
Intensity (1RM%)		50%			60%			70%	
Sets		7			5			3	
Repetition (s)		3			4.5			7	
Rest period (s)		60			36			18	

s: seconds; 1RM%: percentage of 1 repetition maximum.

2.10. Data Collection

Baseline week 0 (from 29 August to 12 September 2024), follow-up week 6 (from 2 October to 6 October 2024), and final week 13 (from 24 October to 7 November 2024) assessments will be conducted at the Controlled Natural Movement Laboratory of the Universidad Católica de la Santísima Concepción. Prior to the intervention, as well as during and after the training programs (tonic, isometric, and isometric/vibratory), all participants will be evaluated for motor symptoms (resting tremor, bradykinesia, balance, and gait speed), non-motor symptoms (anxiety, depression, cognitive impairment, and quality of life), and levels of muscular strength.

2.10.1. Motor Symptomatology Assessment Protocol

As a primary outcome measure, motor and non-motor symptomatology will be evaluated. The primary outcome is considered clinically relevant (daily life) since it is essential for individuals to carry out daily activities such as work, household chores, and dressing, among many others.

Blinded researchers will assess the following motor symptomatology before and after the familiarization period:

(a) Resting tremor: Actigraphy accelerometer [25] in a 5-trial test of 20 s duration. The Fast Fourier Transform (FFT) will be calculated for the 15-s recording cutoff. The maximum power and initial maximum amplitude domain of the FFT will be reported within the limit of 1.5 to 9 Hz. From this signal, a quantity of the temblor will be extracted.

(b) Bradykinesia: A functional electromechanical dynamometer (FEMD) (Dynasystem Research, SYMOTECH, Granada, Spain) [26,27] will measure the displacement speed of the segment, with the seated biceps curl and unilateral leg extension at 30% of 1 RM.

(c) Balance: The Mini-BESTest balance test [22] will be used, which assesses static-dynamic balance. The scale measures balance primarily with closed eyes, sitting,

standing, performing a 360° turn, and a destabilizing stimulus, classifying the patient's behavior based on points.

(d) Gait speed: The fast speed of the Ten Meter Walk Test (TMW) [9] will be used, which measures the time in seconds that it takes a patient to run 10 m in a straight line. Sports clothing and shoes will be requested. Photocells (WITTY, Microgate® Bolzano, Italia) will be used to record speed, and a video camera will be used to record the step length and gait cadence.

2.10.2. Non-Motor Symptomatology Assessment Protocol

Blinded researchers will assess non-motor symptoms by completing a questionnaire in a personal interview after the familiarization period.

- Anxiety, depression, and cognitive impairment will be assessed using the MDS-UPDRS questionnaire [28].
- Quality of life will be measured using the Parkinson's Disease Questionnaire (PDQ-39) [29].

2.10.3. Anthropometry and Body Composition

Body weight (kg) and body composition (including percentage of body fat, lean body mass [kg], etc.) will be evaluated using a bioelectrical impedance device (InBody 120; InBody Co., Ltd., Seoul, Republic of Korea), and height will be measured using a digital stadiometer (Seca 202; Seca Ltd., Hamburg, Germany).

2.10.4. Muscle Strength Evaluation

Prior to, during, and after he strength intervention program, all participants will undergo two familiarization sessions with the use of the FEMD and the exercises of the three training programs. The activity will start with a standardized warm-up consisting of two parts. The first part will involve activation through 5 min of static biking or walking. The second part of the warm-up will consist of 4 sets of 10 repetitions with a load of 5–10% of the participants' body weight.

After the warm-up phase, the subjects will perform the maximum isometric strength evaluation in 3 sets of 5 s (s) with a 3-min pause between measurements until reaching the 1RM using the FEMD in 4 exercises: (a) a bilateral seated bench press with shoulder abduction at 90° and elbow flexion at 90°, (b) a bilateral seated row with shoulder abduction at 90° and elbow flexion at 90°, (c) a unilateral seated knee extension in an open kinetic chain at 90° knee flexion, and (d) a functional test of sitting and standing from a chair in 30 s, as presented in Figure 2. The evaluation will be performed in 2 sessions one week apart. Variables of maximum load, mean power, and strength will be recorded.

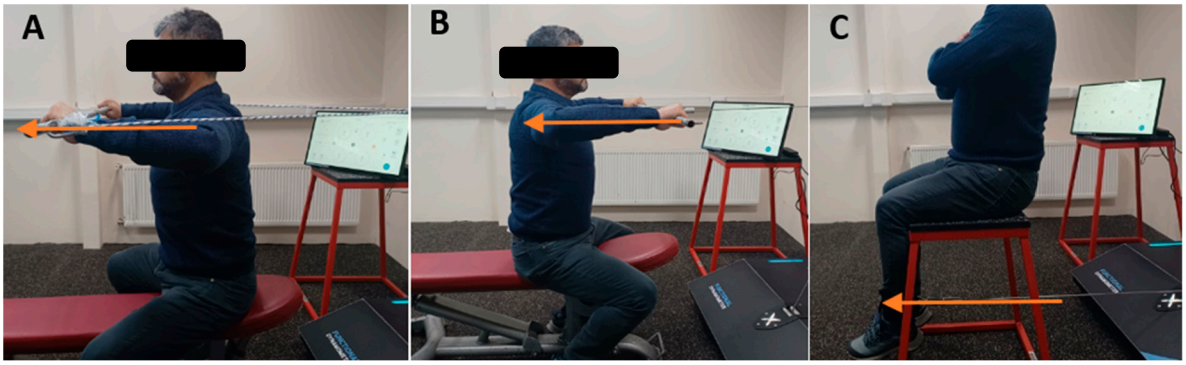

Figure 2. (**A**) bilateral isometric seated bench press, (**B**) bilateral isometric seated row, and (**C**) unilateral isometric knee extension in open kinetic chain.

2.11. Statistical Analysis

All data will be expressed as means and standard deviations. The distribution of the data will be evaluated using the Shapiro–Wilk normality test. Statistical models will be used, depending on the distribution of the data, to establish the differences between the pre-test, intermediate evaluation, and post-test for each group with an ANOVA statistical model of multiple comparisons if the distribution is parametric or the Friedman test if it is nonparametric. The comparison between groups will be evaluated with a parametric or non-parametric multivariate ANOVA model, as appropriate. In all calculations, a 95% confidence interval will be used for a p-value < 0.05. The JASP statistical package will be used in all cases.

3. Discussion

The purpose of this research is to evaluate the effect of 12-week muscular strength training programs (tonic, isometric, and isometric/vibratory) while controlling the manipulation of the intensity variable for motor and non-motor symptomatology in people with Parkinson's disease. The secondary objective is to assess changes in muscular strength induced via the three training methods and their relationship with symptom changes.

Previous studies have published published protocols for strength training in people with Parkinson's disease [30,31]. Some of them have used elastic bands, series, weights, self-loading, and strength machines; however, these protocols have presented great methodological variability in the assignment of the training load, which does not limit the reproducibility and control of the variables that condition muscle strength training, such as volume (set × repetitions), the rest time between series, the total training period, and the intensity of the muscular strength exercise. The manipulation of each of these variables must be adjusted independently, considering that the organization of each of them induces different responses in intramuscular and intermuscular coordination in microstructure, morphology, and neuromuscular metabolism [32]. This future research process will help overcome this important problem by providing a detailed training prescription via controlling the performance variables associated with the objectively controlled evaluation and manipulation of performance variables using an FEMD that is replicable and applicable in clinical settings. The research will establish the extent to which controlled muscle strength training has an effect on relevant factors related to motor and non-motor symptomatology in PPD.

Limitations

The limitations that may arise in this research are related to problems in controlling the participants' typical daily activity levels.

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Institutional Review Board Statement: The study will be carried out in accordance with the Declaration of Helsinki, and it was approved by the Scientific Ethics Committee of Universidad Católica de la Santísima Concepción (protocol code No. 22/2023 and 24 July approval date).

Informed Consent Statement: Not applicable.

Data Availability Statement: The dataset is available on request from the authors.

Conflicts of Interest: The authors declare no conflicts of interest.

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