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Review Article

Artigo de Revisão

Impacts of High-Intensity Aerobic and Resistance Training on Functional Capacity of Patients with Parkinson's Disease: A Systematic Review

Impactos do treinamento aeróbico e resistido de alta intensidade na capacidade funcional de pacientes com doença de Parkinson: uma revisão sistemática

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Abstract

Introduction: Parkinson's disease (PD) is a neurodegenerative pathology that presents clinical manifestations, including involuntary tremors, joint stiffness and decline in muscle strength. PD is commonly associated with the death of dopaminergic neurons in the region of the basal ganglia, which are responsible for controlling motor activities. Treatment consists of medications, however, non-pharmacological tools such as supervised physical exercise are widely recommended.

Objective: To summarize the impacts of high-intensity aerobic and resistance training protocols on the functional capacity of PD patients.

Methods: Four databases [PubMed, Scopus, Embase, and Science Direct. After applying the eligibility criteria, the articles were independently selected by peer reviewers.

Results and Discussion: A total of 4,745 studies were identified by searching the databases, but only 17 met the eligibility criteria. Finally, 17 studies were included in this systematic review. Information was extracted about the study (author and year), characteristics of the sample (age, gender, sample size), information about the type of physical exercise, duration of the protocol, description of the exercise: warm-up; frequency; volume, in addition to extracting outcomes related to functional capacity (motor and non-motor aspects). Both training modalities (HIA and HIRT) can improve functional capacity variables in PD patients. We emphasize that those training modalities can act synergistically in the promotion of a better quality of life/health of these patients.

Key Points
- Exercise promotes brain benefits to motor functions
- Both training modalities (HIA and HIRT) can improve functional capacity variables in PD patients
- Distinct training modalities can act synergistically in the promotion of a better quality of life/health of these patients.

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Conclusion: Therefore, both modalities were able to improve non-motor and motor components (muscle strength, power, balance) related to functional capacity in PD patients.

Keywords: exercise, physical activity, physical training, neuroscience, Parkinson's disease.

Pontos Chave
- Exercise promotes brain benefits to motor functions
- Ambos os protocolos de alta intensidade promovem melhora nos componentes neuromotores/não neuromotores da capacidade funcional em pacientes com PD.
- Distinct training modalities can act synergistically in the promotion of a better quality of life/health of these patients.

Resumo

Introdução: A doença de Parkinson (DP) é uma patologia neurodegenerativa que apresenta manifestações clínicas, incluindo tremores involuntários, rigidez articular e declínio da força muscular. A DP é comumente associada à morte de neurônios dopaminérgicos na região dos gânglios da base, responsáveis pelo controle das atividades motoras. O tratamento consiste em medicamentos, no entanto, ferramentas não farmacológicas, como o exercício físico supervisionado, são amplamente recomendadas.
Objetivo: Resumir os impactos de protocolos de treinamento aeróbio e resistido de alta intensidade sobre a capacidade funcional de pacientes com DP.
Métodos: Quatro bases de dados [PubMed, Scopus, Embase e Science Direct. Após a aplicação dos critérios de elegibilidade, os artigos foram selecionados de forma independente por pares.
Resultados e Discussão: Foram identificados 4.745 estudos por meio de busca nas bases de dados, mas apenas 17 atenderam aos critérios de elegibilidade. Finalmente, 17 estudos foram incluídos nesta revisão sistemática. Foram extraídas informações sobre o estudo (autor e ano), características da amostra (idade, sexo, tamanho da amostra), informações sobre o tipo de exercício físico, duração do protocolo, descrição do exercício: aquecimento; frequência; volume, além de extrair resultados relacionados à capacidade funcional (aspectos motores e não motores). Ambas as modalidades de treinamento (HIA e HIRT) podem melhorar as variáveis da capacidade funcional em pacientes com DP. Ressalta-se que essas modalidades de treinamento podem atuar sinergicamente na promoção de uma melhor qualidade de vida/saúde desses pacientes.
Conclusão: Portanto, ambas as modalidades foram capazes de melhorar os componentes não motores e motores (força, potência, equilíbrio) relacionados à capacidade funcional em pacientes com DP.

Palavras-chave: exercício, atividade física, treinamento físico, neurociência, doença de Parkinson.

Impacts of High-Intensity Aerobic and Resistance Training on Functional Capacity of Patients with Parkinson's Disease: A Systematic Review

Introduction

Parkinson's disease (PD) is a neurodegenerative pathology that presents several clinical manifestations, including involuntary tremors, bradykinesia, disequilibrium, joint stiffness, the decline in muscle strength, postural instability, and mask-like facial expression(1). The mechanisms associated with the development of PD includes the death of dopaminergic neurons in the basal ganglia region, which is responsible to produce dopamine and the control of motor activities, is frequently described(2,3).

Evidence shows that significant reductions in the neuronal supply of dopamine can cause focal lesions in the cerebral and nigrostriatal cortex(4), leading to a decline in postural reflexes, slowness, flexed posture, shorter steps, and shuffling followed by a decrease in elevation of foot when walking(5), factors affects the equilibrium leading to increase the risk of falls, due to balance disorder(6). Additionally, patients with PD may also have deficits in cognitive functions (working memory, visuospatial skills, executive functions, and attention), impairing the performance of basic daily tasks and the life quality(7). The general treatments involve dopamine-related drugs, however the application of lifestyle tools, including regular physical activity and supervised physical exercise (PE) programs are widely recommended(8,9). In early PD patients' regular physical activity were significantly associated with slower deterioration of postural and gait stability(10). Furthermore, in PD patients, supervised PE can improve gait ability, joint mobility, and functional capacity(11). Thus, the number of studies relating PE and PD have grown substantially, however, there is still information that needs to be clarified in relation to which type, volume (time spent and/or work done in the exercise), intensity (low, moderate, vigorous), frequency and duration (acute or chronic), should be recommended for patients with PD(1).In addition, different types of PE (aerobic and resistance) can act as an adjunct method in relieving symptoms, and even neuroprotection(12). Recently, it has been demonstrated that regular exercise improves dopaminergic neurotransmission in the basal ganglia and the substantia nigra(13).

In that context, a specific exercise program has arisen out, due to its short-time session duration and diversity of health benefits: the high-intensity exercise (HIE), which is characterized by short and intermittent periods of vigorous exercise, followed by predefined recovery periods(14). The execution of this PE modality can promote cardiovascular and metabolic benefits including reduction of blood pressure and resting heart rate(15) and, in animal model, promoted lipogenesis(16). In the nervous system, high-intensity protocols may potentiate neuroplasticity(17,18) and cognitive abilities in healthy and pathological populations, including patients with PD(19). However, the impacts of different modalities and high-intensity protocols on non-neuromotor and neuromotor components in patients with Parkinson's disease are still unclear. Therefore, understanding the impacts of high-intensity protocols on individuals with PD is extremely important. Thus, the objective of this systematic review was to summarize the impacts of high-intensity protocols (aerobic and resistance/strength) on functional capacity in patients with PD.

Abbreviations
- ***1RM***: One-Repetition Maximum
- ***HIAT***: High-Intensity Aerobic Training
- ***HIE**: High-Intensity Exercise*
- ***HIRT***: High-Intensity Resistance Training
- ***NIH***: National Institutes of Health
- ***PD***: Parkinson's Disease
- ***PICOS***: Population / Intervention / Control / Outcomes/ Study
- ***PRISMA***: Preferred Reporting Items for Systematic Reviews and Meta-Analysis
- ***ROM**: Range of Motion*
- ***UPDRS***: Unified *Parkinson's* Motor Rating Scale

Methods

The present review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines.

Eligibility criteria

Eligibility criteria were previously selected to minimize the risk of bias. The inclusion and exclusion criteria followed the PICOS (Population / Intervention/ Control/ Outcomes/ Study) (Quadro 1). There were no restrictions on language or publication date. Studies that did not meet the eligibility criteria, as well as review publications, letter, duplicates, and presence of data used in different studies were excluded.

	Inclusion Criteria	**Exclusion Criteria**
Population	Patients with Parkinson's Disease	Non-Parkinson's Disease Patients
Intervention	High-Intensity Aerobic Training (HIAT), High- Intensity Resistance Training (HIRT)	No HIAT or HIRT
Control	No HIAT or HIRT	Patients with Parkinson's disease exposed to any other type of PE protocol or nutritional intervention
Outcomes	Functional Capacity (Non-Neuromotor and Neuromotor outcomes)	Outcomes not related to functional capacity (motor and non-motor aspects)
Study	Clinical Trial	Reviews; Case report; Letter to editor; comments, etc.

Frame 1 – PICOS strategy.

Information sources and Search strategy

The search strategy was conducted during the period from May to June 2022. The databases used were PubMed (Medline), Scopus, Science Direct and Embase. The search strategies used were: ((((*High-Intensity Interval Training*) OR (*High Intensity Interval Training*)) OR (*High Intensity Interval Trainings*)) OR (*High Intensity Training*)) AND ((*Parkinson Disease*) OR (*Parkinson's Disease*)). Filters were also used in the databases: [Humans and type of publication].

Selection and Data collection process

The screening of studies was performed by reading the title, abstract and full text. Two independent researchers performed the selection of studies (MSSF and GCJS). A third rater resolved discrepancies. Data were extracted through two independent researchers. A third rater resolved discrepancies (TRL).

Data items

Data were extracted about the study (Author and year), sample characteristics (age, sex, sample size), information about the type of PE (High Intensity Aerobic Training – HIAT) and High Intensity Resistance Training – HIRT), duration of protocol (weeks), description of HIE: warming up; frequency; volume (weight; number of sets and reps; intensity; resting). Data were collected according to the following characteristics: non-neuromotor functional capacity; neuromotor functional capacity; and methodological quality assessment.

Non-Neuromotor Functional Capacity

2-minute Test (number of steps); 6 Minute Walk (meters); 8-Foot-Up-and-Go (seconds); Tinetti Balance; Cadence (steps/minute); Velocity (m/s); Ankle ROM (degrees); Gait speed (meters); Step length (meters); Sit-to-Stand; Stride length (meters); Cadence (Rotations per minute); Functional Mobility; Velocity (degrees/seconds); Total time (seconds); Gait departure (seconds); Gait Return (seconds); Stand-Sit-duration; Total step count; 10 meters comfortable; 10 meters fast pace; 50-foot fast pace; Stair ascent and descent (seconds); 10 meters walk (meters/seconds); Time up and Go (seconds); 2.45 up and go (seconds).

Neuromotor Functional Capacity

Knee flexor and peak muscle activation; relative peak muscle activation; Knee extensor activation; Muscle strength leg press and extension; Muscle volume (cm3); Average torque (newtons. meters); Peak muscle force (newtons); Motor unit activation; Single Leg Balance Test (seconds); Peak power (Watts); Arm-Curls; Sit-to-stand; Lower Body flexibility; Upper Body flexibility; Motor Learning Sequence; Unified Parkinson's Motor Rating Scale (UPDRS) III motor; UPDRS motor score; Workload (Watts); Hip Range of Motion (degrees); Knee Range of Motion (degrees); Power (Watts).

Methodological Quality Assessment

Assessment of methodological quality and risk of bias were assessed from the National Institutes of Health (NIH) Quality of Controlled Intervention Studies. The Quality Assessment tool has a checklist of 14 questions designed to assess the internal validity (Described as randomized, Treatment allocation–two interrelated pieces, Blinding, Similarity of groups at baseline, Dropout, Adherence, avoid other interventions, Outcome measures assessment, Power calculation, Prespecified outcomes and Intention-to-treat analysis) of studies of intervention. All criteria were answered as "yes", "no" or "not applicable". Each included study was rated as good, fair, or poor quality based on the quality rating guidance document provided along with the assessment instrument.

Results and Discussion

A total of 4,745 studies were identified in databases searches . PubMed/Medline (n=71); Scopus (n=95); Science Direct (n=4351); Embase (n=228). After the removal of duplicates (n=228) through Endnote X20 software, 4,517 articles were screened for the inclusion process. Then, 4,490 publications were excluded after observing the title/abstract, remaining 27 studies were selected for reading the full text. Finally, 17 studies were included in the present systematic review. The process of search, selection, and inclusion of studies was summarized in the flow diagram of the PRISMA statement (Figure 1). The present study included articles published between 2006 and 2020 (Table 1).

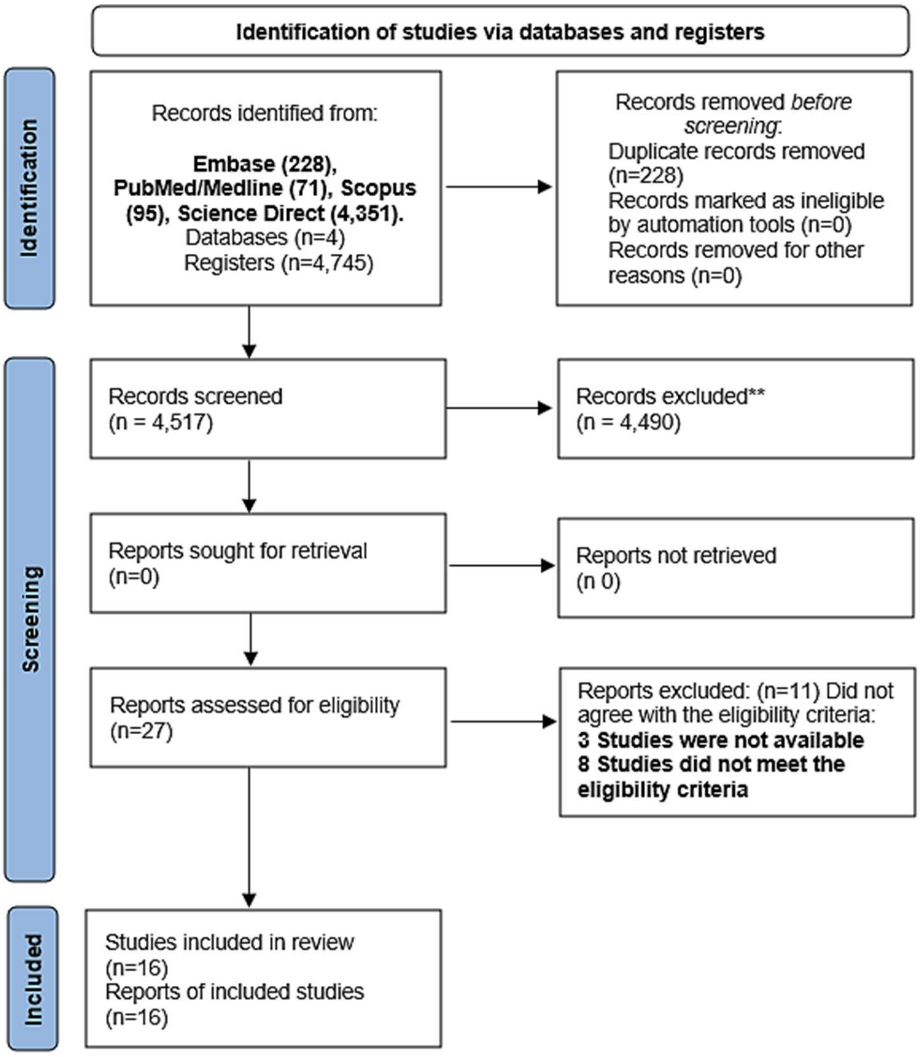

Figure 1 – PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only.

Table 1 – Sample and exercise protocols description

Author	**Average age (y)**	**Sex**	***n***	**Type**	**Duration**	**Description of High-Intensity Exercise Regime**
Cancela et al.(20)	68.33	F/M	24	HIAT	8 weeks	Duration of session: 15-25 min: Weeks 1-2: 3 sets x 2 min; Weeks 3-4: 4 sets x 2 min; Weeks 5-6: 5 sets x 2 min; Weeks: 7-8: 6 sets x 2 min.
Dibble et al.(21)	64.30	UF	19	HIRT	12 weeks	Duration of each session 45-60 min, Intensity: Uninformed; 3 days/week.
Dibble et al.(22)	64.30	UF	20	HIRT	12 weeks	Duration of each session 45-60 min, Intensity: Uninformed; 3 days per week.
Duchesne et al.(23)	59.00	F/M	44	HIAT	12 weeks	3 times per week, 1 hour session duration. Started at 20 min and 60% intensity per session, then increased in steps of 5 min and 5% intensity each week until they reached 40 min of protocol at 80% intensity. To reach a high intensity level, the bike's cadence was kept at 60 rpm.
Fiorelli et al.(2)	66.50	F/M	12	HIAT	1 week	21 min of HII of 1 min alternated with MIIE of 2 min totaling 25 min.
Fisher et al.(24)	64.00	F/M	10	HIAT	8 weeks	24 sessions. The protocol was set at 10% of each participant's body weight. Each session had a MET greater than 3.0 MET's and/or 75% of an age-appropriate maximal HR. Treadmill continuously for 45 min within the above MET level.
Harvey et al(3)	68-69	F/M	20	HIAT	12 weeks	Participants completed 4 repetitions of 4-minute HIE, each interspersed with 3.5 min of recovery. The repetitions consisted of a combination of 4 of the exercises, each performed for 45 sec.
Reed et al.(25)	61.00	F/M	43	HIAT	12 weeks	4 sets × 4-min of HIE work periods at 85%–95% peak HR.
Kelly et al.(26)	66.50	F/M	15	HIRT	16 weeks	3 days per week. 5 exercises (leg press, knee extension, bench press, overhead, pull down), each for 3 sets x 8-12 repetitions until voluntary fatigue. Training loads were based on ~70% of the 1RM.

Author	Average age (y)	Sex	*n*	Type	Duration	Description of High-Intensity Exercise Regime
Rosenfeldt et al.(27)	63.23	F/M	31	HIAT	8 weeks	A stationary bike was used with control that increased cadence by 30%. This cadence was set to a rate that was approximately 30% greater than the subject's self-selected pace. Each exercise session consisted of 5 min of warm-up, 40 min of main exercise.
Morberg et al.(28)	61.33	F/M	12	HIRT	32 weeks	4-6 basic free weight exercises. The intensity of the resistance training started at a 15 RM, ending at a 6 RM.
O'Callaghan et al.(4)	UF	F/M	13	HIAT	12 weeks	4 repetitions of 4-min HIE, each interspersed with 3.5 min of recovery. The repetitions consisted of a combination of 4 of the exercises, each performed for 45 sec.
Rose et al.(29)	63.00	M	13	HIAT	8 weeks	3 sessions of 1 h/week on a positive pressure antigravity treadmill for lower limbs.
Rose et al.(5)	63.38	UF	13	HIAT	8 weeks	3 sessions of 60-min training sessions/week; The program consists of 3 blocks: First block (5 to 15 sec sprints at 50% BW), Second block (5 to 10 min of steady-state continuous walking or running at 50% BW (70% and 80% of estimated HR capacity), and the Third block (5 sets of 60 sec of running separated by a 30-sec pause).
Schenkman et al.(6)	64.00	F/M	43	HIAT	24 weeks	4 days a week with 3 days a week adherence. 30 min of treadmill exercise at target HR.
Shulman et al.(30)	66.10	F/M	23	HIAT	12 weeks	Started with a duration of 15 min and a HR of 40% to 50% of maximum reserve. Intensity and duration were increased by 5 min, 0.2 km/h and 1% of slope every 2 weeks as tolerated to achieve 30 min at 70% to 80% heart rate reserve.

BW: Body Weight; **HR**: Heart Rate; **HIE**: high-intensity exercise **HIAT**: high-intensity aerobic training; **HIRT**: high-intensity resistance training; **F**: female; **M**: male; **MET**: metabolic equivalent of task; **min**: minutes; **sec**: seconds; **MIIE**: moderate interval intensity exercise; **rpm**: rotations per minute; **RM**: repetition on maximum weight; **UF**: uninformed.

The participant patients in the studies were aged between 59-69 years and a major part of the samples were of both sexes. Twelve studies conducted intervention with High Intensity Aerobic Training (HIAT) and four used High Intensity Resistance Training (HIRT). Training protocols were heterogeneous on duration, , ranging from 1-24 weeks. Regarding the structure of the high-intensity training duration of time sessions, it ranged from 15-60 minutes; intensity in aerobic protocols ranged from 40-95% of heart rate reserve. In HIRT the intensity varied from 50% of body weight to 70% of 1RM. The frequency for both PE protocols ranged from 3-4 days a week.

In the present systematic review, various tests to evaluate non-neuromotor components of functional capacity in patients with Parkinson's disease were observed, including: 1)2 minute step; 2)Tinetti Balance; 3)Six-Minute Walk; 4)8-Foot Up-and-Go; 5)Workload; 6)Velocity; 7)Sit-to-Stand; 8)CSP; 9)Mobility; 10)Total time; 11)Stand-Sit-duration; 12)Total step count; 13)10 m Comfortable; 14) 50-ft Fast pace; 15)10 m Fast pace; 16)Stair ascent and descent; 17)10 m walk; 18)Timed up and Go; 19)Mobility; 20)FOG score; 21)Time up GO; 22)Treadmill walking (TMW); 23)2.45 up and go (Tables 2 and 3).

For neuromotor outcome the identified tests were: 1)UPDRS III motor; 2)Motor learning sequence; 3)Ankle range of motion (ROM); 4)Gait speed; 5)Step length; 6)Stride length; 7)Hip ROM; 8)Knee ROM; 9)Power; 10)Cadence; 11)Gait departure; 12)Gait return; 13)Knee flexor; (14)Peak muscle activation and force; 15)Relative peak muscle activation; 16)Knee extensor muscle activation, 1RM and peak power; 17)Muscle strength; 18) Muscle volume; 19)Average torque; 20)Fatigue; 21)Motor unit activation; 22)Leg press specific strength; 23)Single Leg Balance test; 24)Skeletal muscle index; 25)Thigh muscle mass; 26)2 min knee flexion; 27)Body and upper body flexibility (Tables 2 and 3).

High-Intensity Aerobic Training on Functional Capacity and Neuromotor Outcomes of Parkinson's Disease Patients

Eleven studies verified the effect of HIAT on non-neuromotor and neuromotor functional capacity were evaluated and neuromotor outcomes of Parkinson's Disease. HIAT promoted improvements in functional capacity on parameters of 2-minute step (repetitions), mobility, velocity (deg/s) and Six-minute walk (m)(5,7-9);. On the other hand, there were decreases on total time (sec), stand-sit duration and 10 m fast pace(7,10). Regarding the other parameters, no differences were observed between the groups (Table 2).

In the neuromotor parameters, HIAT caused increases in motor learning sequence, ankle ROM (deg), gait speed (m/s), step length (m), stride length (m), hip ROM, knee ROM, CSP, knee flexor and peak muscle activation and relative peak muscle activation (5,11,12). Furthermore, UPDRS III motor and Knee extensor muscle activation tests found reduced results after training protocol(5,8). In relation to the other tests, no differences were observed (Table 2).

High-Intensity Resistance Training on Functional Capacity and Neuromotor Outcomes and of Parkinson's Disease Patients

Four studies verified the effect of HIRT on functional capacity and neuromotor outcomes of Parkinson's Disease. The training protocol promoted a decrease of the stair ascent and descent (sec), TMW, 2.45up and go and Sit-to-stand tests(13, 14). However, it was able to increase 10 m walk (m/s) and timed up and go (s) in the PD patients(15). Regarding the other investigated parameters, no differences were observed (Table 3).

In the neuromuscular outcomes, HIRT leaded to an increase in muscle volume (cm^3), peak muscle force and knee extension peak power (N), knee extension 1RM (kg), knee extension peak power (W), leg press specific strength (Kg) and, single leg balance test (sec)(13,15). On the other hand, Fatigue Severity Scale, UPDRS

Section III (Motor), Motor Unit Activation, 2 min Knee flexion, Arm-Curls were reduced after intervention (14,16). (Table 3).

Quality Assessment of Controlled Intervention Studies

All studies were considered adequate according to the NIH tool assessment (Table 4). It was observed that most studies were not conducted with population samples, hence, randomly allocated. No study presented significant sample losses, presented the same sample characteristics at the beginning of the study, absence of other interventions, high adherence to the protocol and valid evaluation measures.

This study effectively contributes to the growth and development of the scientific literature knowledge on the benefits of the exercise to PD patients. The main results were that both training modalities (HIA and HIRT) can improve functional capacity variables in PD subjects. For the first time, a systematic review describes the impacts promoted by two high intensity training modalities (aerobic and resistance) on functional capacity components including cardiorespiratory fitness, gait, body balance, and neuromuscular aspects of patients with PD.

Robust evidence demonstrates the importance of maintaining and developing cardiorespiratory fitness in healthy individuals and those with different chronic diseases, including PD(17,18). Petkus *et al.*(18), evaluated 33 PD patients and demonstrated that patients with higher cardiorespiratory fitness performed better in cognitive functions including episodic memory, executive function, and visuospatial performance. It is well known that high-intensity training can increase cardiorespiratory fitness(19), however, some of the HIAT studies included in this review did not find such improvement, even characterizing their protocol as high-intensity interval training. As the increase in HIE-related cardiorespiratory fitness is mainly related to the amount of work performed at or near maximal VO_2 usage, we believe that the inability of the PD patients to engage the intensity required and/or maladjustment of the exercise protocol (i.e. I, intensity and duration of the stimulus; II, intensity and duration of the rest; III, number and duration of the series), see detailed in(19), could be responsible for the absence of this cardiorespiratory improvement. This idea is corroborated by a systematic review with meta-analysis conducted by Oliveira et. al.(20), which evaluating general aerobic exercise protocols did not observe significant changes in the cardiorespiratory fitness in PD patients.

Regarding the neuromuscular outcomes, both HIAT and HIRT demonstrated to be beneficial to PD patients, especially the resistance model, wherein increasing in the muscle mass and in its activation, as well as a better score in the UPDRS motor section were the most frequent improvements quoted. The benefits of resistance training in neuromuscular components are widely described and it can benefit different populations, including elderly and individuals with Parkinson(21,22). Yang & Wang(23), in a systematic review with meta-analysis, observed that PD patients engaged in a progressive resistance training improved their walking ability and muscle strength regardless of the training emphasis (e.g. trunk, upper or lower limbs).

Literature describes that resistance training (RT) related muscle strength gain relies on both neural and morphologic changes, wherein the neural adaptations are predominant in an initial period of training(24,25). Into neurobiology exercise field, it is described the importance of the executive requirements of RT to brain health, triggering benefits that can persist for some time, even when the exercise regimen is stopped(26,27). Besides, it is shown that cognitive, gait and some motor skills share common brain networks, thus, the neural adaptations promoted by exercise, especially RT, seem to be essential to patients with neurodegenerative diseases(28).

Table 2 – Impact of high-intensity aerobic training on aerobic capacity and neuromotor outcomes of Parkinson's disease patients

Author	**Functional Capacity**	
	Non-Neuromotor outcomes	**Neuromotor outcomes**
Cancela *et al.* (20)	↑ 2 Minute Step (repetitions); = Tinetti Balance; Six-Minute Walk (m); 8-Foot Up-and-Go (sec)	↓UPDRS III motor
Duchesne *et al.* (23)	-	↑ Motor Learning Sequence
Fiorelli *et al.*(2)	= Workload (W)	-
Fisher *et al.* (24)	= Cadence (step/min); Velocity (m/s); ↑ Sit-to-Stand; CSP (m/s)	= UPDRS motor score; ↑ Ankle ROM (deg); Gait speed; Step length (m); Stride length (m); Hip ROM (deg); Knee ROM (deg); CSP (m/s)
Harvey *et al.*(3)	= 6 Minute Walk (m)	-
Jennifer *et al.*	↑ 6 Minute Walk (m)	-
Mandy Miller *et al.*(7)	↑ Mobility; Velocity (deg/s); ↓ Total time (sec); Stand-Sit duration	= Power (W); Cadence (RPM); Gait departure (sec); Gait Return (sec);
Rose *et al.*(5)	-	↑ Knee flexor and peak muscle activation; relative peak muscle activation. ↓ Knee extensor muscle activation
Rose *et al.* (29)	↑ Six-Minute Walk (m);	↓UPDRS III motor
Schenkman *et al.*(6)	= Total step Count	-
Shulman *et al.* (30)	= 6 Minute Walk (m); 10 m Comfortable; 50-ft Fast pace ↓ 10 m Fast pace;	= UPDRS III motor; Muscle strength (leg press and extension).

Deg: Degrees; m: meters; **m/s**: meters/seconds; rpm: rotations per minute; **UPDRS**: Unified Parkinson's Disease Rating Scale; **W**:watts.

Table 3 – Impact of high-intensity resistance training on Functional Capacity of Parkinson's disease patients.

Author	**Functional Capacity**	
	Non-Neuromotor Outcomes	**Neuromuscular Outcomes**
Dibble *et al.* (21)	↑ Six-minute walk (m); ↓ Stair ascent and descent (sec)	↑ Muscle volume (cm^3); = UPDRS motor score; Average torque (NM)
Dibble *et al.* (22)	↑ 10 m walk (m/s); Timed up and Go (s); Mobility (%)	↑ Peak muscle force (N); = UPDRS motor subsection
Kelly *et al.* (26)	= Mobility (%); FOG score; 6 Minute Walk test (m);	↓ Fatigue Severity Scale; UPDRS Section III (Motor); Motor Unit Activation; ↑ Knee Extension 1RM (kg); Knee Extension Peak Power (W); Leg Press Specific Strength (Kg); Single Leg Balance test (sec); = Skeletal Muscle Index ($kg.m^2$); Thigh Muscle Mass (Kg)
Morberg *et al.* (28)	↓ Time up Go (sec); TMW; 2.45up and go; Sit-to-stand;	↓ UPDRS Motor score; 2 min Knee flexion; Arm-Curls; = Lower Body flexibility; Upper Body flexibility

Deg: Degrees; m: meters; **m/s**: meters/seconds; rpm: rotations per minute; **UPDRS**: Unified Parkinson's Disease Rating Scale; **W**:watts.

Table 4 – Quality Assessment of Controlled Intervention Studies

Author	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Q14	Quality Rating
Cancela *et al.* (20)	Y	Y	NA	NA	NA	Y	Y	Y	Y	Y	Y	N	Y	Y	Good
Dibble *et al.* (21)	N	Y	NA	NA	NA	Y	Y	Y	Y	Y	Y	Y	Y	Y	Good
Dibble *et al.* (22)	N	Y	NA	NA	NA	Y	Y	Y	Y	Y	Y	Y	Y	Y	Good
Duchesne *et al.* (23)	N	N	NA	NA	NA	Y	Y	Y	Y	Y	Y	N	Y	Y	Good
Fiorelli *et al.* (2)	N	Y	NA	NA	NA	Y	Y	Y	Y	Y	Y	N	Y	Y	Good
Fisher *et al.* (24)	Y	Y	NA	NA	NA	Y	Y	Y	Y	Y	Y	N	Y	Y	Good
Harvey *et al.*(3)	Y	Y	NA	NA	NA	Y	Y	Y	Y	Y	Y	Y	Y	Y	Good
Reed *et al.* (25)	Y	Y	NA	NA	NA	Y	Y	Y	Y	Y	Y	Y	Y	Y	Good
Kelly *et al.* (26)	N	N	NA	NA	NA	Y	Y	Y	Y	Y	Y	N	Y	Y	Good
Rosenfeldt *et al.* (27)	N	N	NA	NA	NA	Y	Y	Y	Y	Y	Y	N	Y	Y	Good
Morberg *et al.* (28)	N	N	NA	NA	NA	Y	Y	Y	Y	Y	Y	Y	Y	Y	Good
O'Callaghan *et al.*(4)	N	Y	NA	NA	NA	Y	Y	Y	Y	Y	Y	N	Y	Y	Good
Rose *et al.*(5)	N	N	NA	NA	NA	Y	Y	Y	Y	Y	Y	N	Y	Y	Good
Rose *et al.* (29)	N	N	NA	NA	NA	Y	Y	Y	Y	Y	Y	N	Y	Y	Good
Schenkman *et al.*(6)	Y	Y	NA	NA	NA	Y	Y	Y	Y	Y	Y	Y	Y	Y	Good
Shulman *et al.* (30)	Y	Y	NA	NA	NA	Y	Y	Y	Y	Y	Y	N	Y	Y	Good

Q1: Was the study described as randomized, a randomized trial, a randomized clinical trial, or an RCT?; Q2: Was the method of randomization adequate (i.e., use of randomly generated assignment)?; Q3: Was the treatment allocation concealed (so that assignments could not be predicted)?; Q4: Were study participants and providers blinded to treatment group assignment?; Q5: Were the people assessing the outcomes blinded to the participants' group assignments?; Q6: Were the groups similar at baseline on important characteristics that could affect outcomes (e.g., demographics, risk factors, co-morbid conditions)?; Q7: Was the overall drop-out rate from the study at endpoint 20% or lower of the number allocated to treatment?; Q8: Was the differential drop-out rate (between treatment groups) at endpoint 15 percentage points or lower?; Q9: Was there high adherence to the intervention protocols for each treatment group?; Q10: Were other interventions avoided or similar in the groups (e.g., similar background treatments)?; Q11: Were outcomes assessed using valid and reliable measures, implemented consistently across all study participants?; Q12: Did the authors report that the sample size was sufficiently large to be able to detect a difference in the main outcome between groups with at least 80% power?; Q13: Were outcomes reported or subgroups analyzed prespecified (i.e., identified before analyses were conducted)?; Q14: Were all randomized participants analyzed in the group to which they were originally assigned, i.e., did they use an intention-to-treat analysis?; Y, yes; N, no; NA, not applicable.

Among the exercise-induced molecular outcomes, neurotrophic factors such as those derivatives from brain and glia, brain-derived neurotrophic factor (BNDF) and Glial cell line-derived neurotrophic factor (GNDF), respectively, have been standing out due to their neuroplasticity effects. In this context, González *et al.* reviewing blood changes followed by PE, indicate that patients with neurodegenerative diseases, especially Parkinson, must engage in regular PE as a coadjutant strategy in the disease management, wherein higher levels of BDNF protect the brain function(29,30). Although the correlation between PE and increase in BDNF has been described in the literature, it is unknown how this neurotrophic factor affects the development of neuromuscular components, thus, a rationale cause-effect among the variables need to be further evaluated.

HIAT programs were designed around 70-75% of heart rate reserve with volume progression toward the maximal individual sustainability, while the intensity in the HIRT ranged from 65-85% of 1RM and comprised 5-6 exercises(23,24,5,30). Both protocols increased mobility capacity regardless improvements in the traditional metabolic/physiologic parameters related to HIE, especially cardiorespiratory fitness (evaluated in the studies by six-minute walk)(26,28). It is feasible to assume that the intensity requested by the protocols up-regulate pathways involved in muscle activation, both in cerebral and neuromuscular circuits, increasing coordination and strength.

Strong points and limitations of the study

The relevance of the study was highlighted because results contributes to enable health professionals and researchers to better understand general characteristics of aerobic and resistance protocols and how they can promote improvements in the analyzed variables. Finally, with all the elements in the present investigation, one can envisage opportunities for planning, elaborating, and managing protocols of physical training in high intensity, with safety and effectiveness of this non-pharmacological tool, in the promotion of longevity with quality of life of these patients with PD.

The main limitation in the study is the lack of randomized clinical studies that comparatively analyze these two methods/modalities of high-intensity training in patients with PD. In addition, HIAT studies flaw in determine and conduce standard High intensity protocols (i.e., prescribing interval stimulus intensity, rest and logical outcomes related). We understand the difficult in conducting a high intensity exercise in patients with PD, however, exercise protocols must be better described, at least the basic variables of any training program (intensity, volume, frequency, duration, and progression way), allowing the readers to apply the training properly. Finally, the availability of quantitative data for performing a meta-analysis (mean; standard deviation and number of subjects) would add greater reliability to the present study

Conclusion

HIAT and HIRT improved non-neuromotor and neuromotor components (muscle strength, power, balance) related to functional capacity in patients with PD aiming to promote their health and quality of life. This systematic review summarized the literature findings related to the impacts of High-Intensity Aerobic and High-Intensity Resistance Training protocols on functional capacity of patients with PD.

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Conflict of interest

The authors declare that they have no conflict of interest.

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