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**Rewiring movement in Parkinson's disease: exercise,
neuromodulation, and motor control -
bridging neuroplasticity, gait biomechanics, and fatigue
management for advanced rehabilitation**

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**Rewiring movement in Parkinson's disease: exercise,
neuromodulation, and motor control -
bridging neuroplasticity, gait biomechanics, and fatigue
management for advanced rehabilitation**

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If you dream so big, it is because that version of you already exists in the future.

To my grandfather Andrea.

This thesis is dedicated to his memory, to the strength and dignity with which he faced Parkinson's disease, and to the quiet inspiration he has been throughout my journey.

I also dedicate this work to my family, to my sister Miriam, and to all those who have supported my human and professional growth over these years.

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ABSTRACT

This doctoral thesis investigates the effects of physical exercise and combined motor–cognitive interventions on motor, neuromuscular, and neuroplastic outcomes in individuals with Parkinson’s disease (PD), adopting a multi-level and mechanism-informed perspective. The work integrates evidence from systematic reviews, an umbrella review, and an experimental study to examine how exercise characteristics and task demands influence functional performance and underlying neural mechanisms in PD.

First, a systematic review and meta-analysis examined changes in brain-derived neurotrophic factor (BDNF) following different exercise protocols in PD, showing that higher exercise intensity is positively associated with increases in BDNF levels, supporting a potential role of exercise-induced neuroplasticity.

Second, a randomized controlled study explored baseline neuromuscular and corticospinal function of the upper limb in early-stage PD, revealing preserved muscle structure and corticospinal excitability, with functional asymmetries suggesting central, rather than structural, mechanisms underlying motor impairment.

Third, a systematic review on dual-task walking highlighted consistent biomechanical gait alterations in PD, including reduced stride length, gait speed, and increased variability, accompanied by compensatory prefrontal cortex activation, indicating a shift from automatic to cognitively controlled locomotion.

Finally, an umbrella review of systematic reviews synthesized the broader effects of physical exercise in PD, demonstrating that fitness-oriented exercise produces global motor and physical benefits, while motor–cognitive training more effectively targets balance and dual-task gait deficits; combined interventions may further potentiate neuroplastic adaptations.

Overall, the findings support a shift toward targeted, mechanism-based exercise prescription in PD, emphasizing the role of exercise intensity, task complexity, and combined approaches to optimize motor function, cognitive–motor integration, and neuroplastic potential.

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Glossary

1RM (One-Repetition Maximum): The maximum amount of force a muscle can generate during a single maximal effort in a given exercise, used to prescribe resistance training intensity.

6MWT (Six-Minute Walk Test): A submaximal exercise test used to assess aerobic capacity and endurance by measuring the distance walked over six minutes.

ADL (Activities of Daily Living): Basic self-care tasks such as bathing, dressing, and eating, often used as an outcome measure for functional independence.

AMSTAR-2 (A MeaSurement Tool to Assess systematic Reviews - 2): A critical appraisal tool used to evaluate the methodological quality of systematic reviews.

AT (Aerobic Training): Exercise that improves the efficiency of the cardiovascular system in absorbing, transporting, and utilizing oxygen.

AXIS (Appraisal tool for Cross-Sectional Studies): A tool designed to assess the quality and risk of bias in cross-sectional studies.

BDNF (Brain-Derived Neurotrophic Factor): A protein that supports neuron survival, growth, and differentiation, and is a key mediator of neuroplasticity and neuroprotection.

BFRE (Blood Flow Restriction Exercise): A training method involving the use of a cuff to partially restrict arterial inflow and fully restrict venous outflow in a limb during low-intensity exercise, aimed at stimulating hypertrophy and strength gains.

BT (Balance Training): Exercises specifically designed to improve postural stability and reduce the risk of falls.

CCA (Corrected Covered Area): A metric used in umbrella reviews to quantify the degree of overlap of primary studies across multiple meta-analyses.

Cohen's d: A statistic measuring the standardized difference between two means, commonly used to calculate effect size.

CRUNCH (Compensation-Related Utilization of Neural Circuits Hypothesis): A model suggesting that older adults or patients recruit additional brain regions, particularly prefrontal areas, to compensate for cognitive or motor deficits, especially under high task demands.

CSA (Cross-Sectional Area): In muscle physiology, the area of a cross-section of a muscle, used as a measure of muscle size.

DBS (Deep Brain Stimulation): A surgical treatment involving the implantation of a medical device that sends electrical impulses to specific parts of the brain to alleviate symptoms of movement disorders like Parkinson's disease.

DT (Dual-Task): A paradigm that involves performing a cognitive or motor secondary task concurrently with a primary task (e.g., walking), used to assess attentional demands and automaticity.

DTAiR (Dual-Task Assessment in R): A standardized battery for assessing dual-task performance, providing a framework for calculating a global dual-task cost.

DTC (Dual-Task Cost): The percentage or quantitative decline in performance on one or both tasks when performed simultaneously compared to when they are performed alone.

EHI (Edinburgh Handedness Inventory): A questionnaire used to assess the dominance of a person's right or left hand in everyday activities.

EMG (Electromyography): A technique for recording and evaluating the electrical activity produced by skeletal muscles.

ENB-2 (Esame Neuropsicologico Breve 2): A brief neuropsychological assessment battery used in Italian clinical practice to evaluate cognitive functions.

FAB (Frontal Assessment Battery): A short neuropsychological tool designed to assess executive functions at the bedside.

FFQ (Food Frequency Questionnaire): A dietary assessment tool used to estimate the frequency and, in some cases, the portion size of food and beverage consumption over a specific period.

fNIRS (Functional Near-Infrared Spectroscopy): A neuroimaging technique that measures cortical blood oxygenation, providing an indirect measure of brain activity.

FoG (Freezing of Gait): A debilitating symptom of PD characterized by a brief, episodic absence or marked reduction of forward progression of the feet despite the intention to walk.

FSS (Fatigue Severity Scale): A self-report questionnaire used to assess the severity of fatigue and its impact on daily functioning.

GRADE (Grading of Recommendations, Assessment, Development, and Evaluations): A transparent framework for developing and presenting summaries of evidence and provides a systematic approach for making clinical practice recommendations.

H&Y (Hoehn and Yahr Scale): A commonly used system for describing the progression of motor symptoms in Parkinson's Disease.

Hedges' g: A measure of effect size used in meta-analysis that includes a correction for small sample bias.

HIBC (High-Intensity Multimodal Exercise Boot Camp): A structured, intensive exercise program combining various types of training at high intensity.

HIIT (High-Intensity Interval Training): An exercise strategy alternating short periods of intense anaerobic exercise with less intense recovery periods.

HIRT (High-Intensity Resistance Training): A resistance training approach characterized by high effort and intensity, typically using heavy loads.

HRmax (Maximum Heart Rate): The highest heart rate an individual can achieve during maximal physical exertion.

HRR (Heart Rate Reserve): The difference between a person's maximum heart rate and resting heart rate, used to prescribe exercise intensity.

ICH (International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use): An organization that sets guidelines for good clinical practice (GCP).

IMU (Inertial Measurement Unit): A device composed of multiple sensors, including an accelerometer, gyroscope, and magnetometer, that measures acceleration, angular velocity, and magnetic field strength.

iTBS (Intermittent Theta Burst Stimulation): A form of repetitive transcranial magnetic stimulation (TMS) that uses bursts of high-frequency stimulation to enhance cortical excitability and neuroplasticity.

LRI (Locomotor Rehabilitation Index): A metric that relates self-selected walking speed to the individual's optimal speed for minimizing metabolic cost, used to assess locomotor economy.

MCI (Mild Cognitive Impairment): A neurocognitive disorder which involves cognitive impairments beyond those expected based on an individual's age and education but which are not significant enough to interfere with instrumental activities of daily living.

MDS-UPDRS (Movement Disorder Society – Unified Parkinson's Disease Rating Scale): A comprehensive tool for assessing the various symptoms and signs of Parkinson's disease, including motor and non-motor experiences of daily living.

MEP (Motor Evoked Potential): The electrical potential recorded from muscles following stimulation of the corresponding motor cortex, used to measure corticospinal excitability.

MEP AUC (Motor Evoked Potential Area Under the Curve): A measure of the total area under the MEP waveform, reflecting the magnitude of corticospinal activation.

MET (Metabolic Equivalent of Task): A physiological measure expressing the energy cost of physical activities, defined as the ratio of metabolic rate during the activity to a resting metabolic rate.

MoCA (Montreal Cognitive Assessment): A cognitive screening test used to detect mild cognitive impairment, assessing domains such as attention, memory, and executive function.

MST (Maximal Strength Training): A training method aimed at increasing maximal force production by focusing on high-load, low-repetition exercises to improve primarily motor unit recruitment.

MVC (Maximal Voluntary Contraction): The maximal force-generating capacity of a muscle or group of muscles.

NASA-TLX (NASA Task Load Index): A multidimensional assessment tool that provides a subjective workload score based on six subscales: Mental Demand, Physical Demand, Temporal Demand, Performance, Effort, and Frustration.

NIBS (Non-Invasive Brain Stimulation): A group of neuromodulation techniques, such as TMS and tDCS, that alter brain activity without the need for surgery.

NW (Nordic Walking): A form of aerobic walking using specially designed poles to engage the upper body, improving gait parameters, posture, and cardiovascular fitness.

PD (Parkinson's Disease): A progressive neurodegenerative disorder characterized by the loss of dopaminergic neurons in the substantia nigra, leading to motor symptoms such as bradykinesia, rigidity, tremor, and postural instability.

PDQ-8/PDQ-39 (Parkinson's Disease Questionnaire): Patient-reported outcome measures that assess health-related quality of life in individuals with Parkinson's Disease.

PEDro Scale (Physiotherapy Evidence Database Scale): A tool used to rate the methodological quality of randomized controlled trials in physiotherapy.

PCI (Phase Coordination Index): A measure of the consistency and accuracy of left-right stepping phase generation during walking.

PICOS: A framework used to define the key elements of a systematic review question: Population, Intervention, Comparison, Outcome, Study design.

PIGD (Postural Instability and Gait Difficulty): A motor subtype of Parkinson's disease dominated by axial symptoms such as impaired balance and gait disturbance, as opposed to tremor.

PNS (Peripheral Nerve Stimulation): Electrical stimulation applied to a peripheral nerve, often used in research to elicit a direct muscle response (M-wave).

PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses): An evidence-based minimum set of items for reporting in systematic reviews and meta-analyses.

PRO (Patient-Reported Outcome): A report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else.

PROSPERO (International Prospective Register of Systematic Reviews): An international database for prospectively registering systematic reviews.

qDPOT (Dynamic Peak Torque): A measure of the peak torque produced during a dynamic (movement-based) muscle contraction.

qIPOT (Isometric Peak Torque): A measure of the peak torque produced during an isometric (static) muscle contraction.

QoL (Quality of Life): A broad multidimensional concept that usually includes subjective evaluations of both positive and negative aspects of life, often measured by instruments like the PDQ-8.

RAGT (Robot-Assisted Gait Training): A rehabilitation method that uses robotic devices to support, guide, and enhance walking practice.

RCT (Randomized Controlled Trial): A study design that randomly assigns participants into an experimental group or a control group to measure the effectiveness of an intervention.

RFD (Rate of Force Development): A measure of how quickly force can be generated by a muscle or group of muscles.

RMT (Resting Motor Threshold): In TMS, the minimum stimulus intensity required to elicit a motor evoked potential of a predefined size in a relaxed muscle.

ROBINS-I (Risk Of Bias In Non-randomized Studies of Interventions): A tool for assessing the risk of bias in the results of non-randomized studies that compare the health effects of two or more interventions.

RPE (Rating of Perceived Exertion): A scale used to measure the intensity of exercise based on the physical sensations a person experiences during physical activity.

RT (Resistance Training): A form of exercise designed to improve muscular strength and endurance by exercising a muscle or muscle group against external resistance.

SMD (Standardized Mean Difference): A statistical measure used in meta-analysis to standardize the results of different studies to a uniform scale before they are combined.

SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials): An evidence-based guideline for minimum content of a clinical trial protocol.

SSWS (Self-Selected Walking Speed): The comfortable, freely chosen walking speed of an individual, a key indicator of mobility and functional status.

ST (Single-Task): Performing one task in isolation, without any concurrent secondary task.

STROBE (Strengthening the Reporting of Observational Studies in Epidemiology): A guideline for reporting observational studies in epidemiology.

tDCS (Transcranial Direct Current Stimulation): A non-invasive brain stimulation technique that uses a constant, low current delivered to the brain area of interest via electrodes on the scalp to modulate neuronal excitability.

TD (Tremor-Dominant): A motor subtype of Parkinson's disease where tremor is the predominant symptom, as opposed to postural instability and gait difficulty (PIGD).

TIDieR-REHAB (Template for Intervention Description and Replication - Rehabilitation): An extension of the TIDieR checklist for better reporting of rehabilitation interventions.

TMS (Transcranial Magnetic Stimulation): A non-invasive technique that uses magnetic fields to stimulate nerve cells in the brain to assess or modulate corticospinal excitability.

TMT (Trail Making Test): A neuropsychological test of visual attention and task switching.

TMT-A (Trail Making Test Part A): A neuropsychological test that assesses visual search, scanning, speed of processing, and mental flexibility (Part A focuses on basic sequencing).

TMT-B (Trail Making Test Part B): A more complex version of the TMT that adds a task-switching component, assessing executive functions.

TOT (Task-Oriented Training): A therapeutic approach focused on practicing functional tasks that are meaningful to the individual.

TUG (Timed Up and Go Test): A simple test used to assess a person's mobility, requiring them to rise from a chair, walk a short distance, turn around, walk back, and sit down.

UC (Usual Care): The standard treatment or management that a patient would normally receive, often used as a control condition in clinical trials.

UPDRS (Unified Parkinson's Disease Rating Scale): The predecessor to the MDS-UPDRS, a rating scale used to follow the longitudinal course of Parkinson's disease.

VR (Virtual Reality): A simulated experience that can be similar to or completely different from the real world, used in rehabilitation to create engaging and controlled training environments.

WBV (Whole-Body Vibration): A passive physical modality where the individual stands or sits on a vibrating platform, with limited evidence for motor benefits in PD.

Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disorder, representing a rapidly growing global health challenge with over 6 million cases worldwide (Dorsey E. R. 2018). While traditionally characterized by the loss of dopaminergic neurons in the substantia nigra and the classic motor triad of bradykinesia, rigidity, and tremor, PD is now recognized as a complex multisystem synucleinopathy (Morris, Spillantini et al. 2024). The pathogenesis is driven by the prion-like spread of pathological alpha-synuclein aggregates throughout the nervous system, a process that begins years before clinical motor onset and involves multiple neurotransmitter systems, neuroinflammation, and genetic factors (Bloem, Okun et al. 2021, Morris, Spillantini et al. 2024). This refined understanding underscores that PD is more than a dopamine deficiency disorder, encompassing a wide spectrum of debilitating motor and non-motor symptoms.

However, PD is now recognized as a complex multi-system disorder, where non-motor symptoms such as cognitive decline, depression, apathy, and fatigue profoundly impact patients' quality of life and present a primary therapeutic challenge (Schapira, Chaudhuri et al. 2017). Pharmacological management, with levodopa as the cornerstone, provides effective symptomatic control, particularly in the early stages of the disease (Poewe, Seppi et al. 2017). Nonetheless, its efficacy wanes over time, leading to debilitating motor fluctuations and dyskinesias, and no currently available drug has been proven to slow the underlying neurodegenerative progression (Lang and Espay 2018).

This therapeutic impasse has accelerated the search for complementary non-pharmacological strategies that can not only alleviate symptoms but also promote neuroprotective and brain plasticity mechanisms (Petzinger, Fisher et al. 2013). Within this context, structured physical exercise has emerged as a powerful and versatile intervention. Robust evidence demonstrates that various forms of exercise can improve motor function, balance, gait, and quality of life in PD (Ernst, Folkerts et al. 2023). It is hypothesized that these benefits are mediated, at least in part, by the upregulation of neurotrophic factors, which support neuronal survival, dopaminergic function, and synaptic plasticity (Hirsch, van Wegen et al. 2018). Brain-derived neurotrophic factor (BDNF) is a key regulator of these processes (Zuccato and Cattaneo 2009). While preclinical models clearly demonstrate exercise-induced increases in BDNF, the translation of these findings to the PD patient population remains less consistent and is marked by methodological heterogeneity. Thus, a primary knowledge gap lies in understanding how different exercise parameters (type, intensity, volume) specifically

influence BDNF levels in people with PD, information essential for optimizing exercise prescriptions based on mechanisms of action (Mak, Wong-Yu et al. 2017).

Concurrently, non-invasive brain stimulation techniques, such as Transcranial Magnetic Stimulation (TMS) and, in particular, the efficient Intermittent Theta Burst Stimulation (iTBS) protocol, have demonstrated the ability to modulate cortical excitability and promote lasting neuroplasticity (Huang, Edwards et al. 2005). While often investigated as standalone treatments, their potential synergistic effects when combined with peripheral training (e.g., strength training) are largely unexplored. This approach is particularly relevant for addressing often-neglected motor deficits, such as upper limb dysfunction and neuromuscular fatigue, which significantly impair independence in daily activities (Proud, Miller et al. 2013). A second gap thus exists in determining whether a combined central (iTBS) and peripheral (e.g., Maximal Strength Training) approach can yield superior functional outcomes compared to either intervention alone.

Furthermore, the efficacy of rehabilitative interventions must be validated in functionally relevant contexts. Real-world mobility requires the seamless integration of motor and cognitive functions, a challenge starkly revealed under dual-task conditions. In PD, the loss of gait automaticity necessitates a greater reliance on attentional resources, rendering walking particularly susceptible to cognitive interference (Yogev-Seligmann, Hausdorff et al. 2008). While it is well-documented that dual-tasking worsens walking performance, a third gap pertains to a detailed understanding of the specific biomechanical alterations that underpin this deterioration, knowledge crucial for developing targeted interventions to improve safe ambulation in complex environments (Kelly, Eusterbrock et al. 2012).

Finally, the growing volume of primary studies and systematic reviews on exercise in PD can be overwhelming for clinicians and researchers. A fourth, overarching gap is the need for a clear, high-level synthesis of the available evidence. An umbrella review can provide an overview of the strength and consistency of the evidence, identify the most effective modalities for specific symptoms, and highlight persistent knowledge gaps (Fusar-Poli and Radua 2018).

The Thesis Research Programme

This doctoral project was designed to address these interconnected gaps through four complementary studies. The research programme progresses from the molecular level to the design of a novel combined intervention, examines a critical ecologically relevant functional challenge, and culminates in a broad evaluation of the existing evidence.

1. Study 1 (Systematic Review) examines the clinical evidence on the effects of exercise on BDNF levels in PD, systematically investigating the impact of exercise parameters to provide a mechanistic foundation for exercise prescription.
2. Study 2 (RCT) is designed to test synergistic effects of combining iTBS and Maximal Strength Training (MST) on upper limb function and fatigue, thereby bridging central neuromodulation and peripheral training.

3. Study 3 (Systematic Review) analyses the biomechanical gait alterations under dual-task conditions in PD, aiming to delineate the specific motor control deficits that occur when cognitive resources are divided.
4. Study 4 (Umbrella Review) synthesises the highest level of evidence on the effects of physical exercise across all domains of PD, validating the therapeutic approach explored throughout the thesis and mapping the landscape of current knowledge.

Collectively, this research programme aims to advance the understanding of PD management by moving from fundamental mechanisms to innovative clinical applications and functional relevance, with the goal of contributing to the development of more personalised, evidence-based, and effective rehabilitation strategies for people living with PD. By bridging neuroplasticity, biomechanics, and clinical application, this work aims to rewire movement and improve lives.

2. Changes of Brain-Derived Neurotrophic Factor (BDNF) levels after different exercise protocols: a systematic review of clinical studies in Parkinson's disease

Introduction

About 6 million individuals are affected by Parkinson's Disease (PD) worldwide and more than 200,000 people died from this condition in 2016 (Dorsey E. R. 2018). PD, which is associated with loss of dopaminergic neurons in the substantia nigra (Fearnley and Lees 1991), is typically characterized by both motor symptoms, such as bradykinesia, rigidity, rest tremor and postural instability and non-motor features, including cognitive impairment and depression (Lee and Gilbert 2016). First-line treatment of PD is based on levodopa and other dopamine agonists and it is directed at symptoms, but no therapy can slow down the progression of PD (Bloem, Okun et al. 2021).

Physical exercise (i.e., a structured exercise program (Caspersen, Powell et al. 1985)) is a non-pharmacological intervention which is a major component of physiotherapy for management of PD (Bouca-Machado, Rosario et al. 2020) and is often adopted as part of an integrated therapeutic approach (Bloem, Okun et al. 2021). In an observational cohort study, people with PD who exercised regularly, that is more than 150 min/week, showed better physical function and less cognitive decline after 1 year compared to sedentary people with PD and those who exercised less frequently (Caspersen, Powell et al. 1985). Exercise can improve bone metabolism (Amato, Baldassano et al. 2022), balance and walking ability, motor symptoms (bradykinesia, gait and turning) and non-motor symptoms (cognitive deficits, sleep disorders, mood disturbances, and sensory abnormalities) (Xu, Fu et al. 2019). In addition, people with PD may need smaller drug doses, because the effect of levodopa is often improved by exercise (Muhlack, Welnic et al. 2007).

Although many types of physical exercise can help improve movement and quality of life for people with PD, there is no evidence that certain exercise types work better than others (Ernst, Folkerts et al. 2023). NICE recommends physiotherapy and occupational therapy for people with PD who experience difficulties in motor function and daily living activities, without specifying the type of exercise (Rogers, Davies et al. 2017). Similarly, European physiotherapy

guidelines recommend that people with PD reduce their daily sitting time and exercise at least 150 min/week, according to their own preferences and physical capabilities (Keus SHJ 2014).

It was suggested that aerobic training (AT) improves motor function, although long-term effects are not clear (Schootemeijer, van der Kolk et al. 2020). Other studies reported that Nordic walking, dance, cycling, Tai Chi and Qigong and walking improve physical fitness and mobility (Song, Grabowska et al. 2017, Tiihonen, Westner et al. 2021, Peyre-Tartaruga, Martinez et al. 2022). It was also reported that resistance training (RT) improves physical function and quality of life in PD (Gollan, Ernst et al. 2022). The American College of Sports Medicine recommends that people with PD engage in Balance Training (BT) in addition to the regular practice of AT and RT (American College of Sports Medicine. 2020). A recent meta-analysis of 109 trials showed that dancing was superior to other types of exercise in improving motor function, whereas Nordic walking and Qigong were the most effective exercises that improved mobility and manual dexterity, respectively (Zhang, Li et al. 2023).

The effect of exercise on these clinical outcomes can be explained by a variety of mechanisms (Xu, Fu et al. 2019), including the synthesis of several neurotrophic factors, as reported in a review of animal studies and in a systematic review in people with PD (da Silva, Domingues et al. 2016, Li, Loevaas et al. 2023). Brain-Derived Neurotrophic Factor (BDNF) protects the brain against destruction of dopaminergic neurons and acts as a growth factor for dopaminergic neurons of the substantia nigra pars compacta (Hyman, Hofer et al. 1991). People with PD have decreased serum levels of BDNF compared to healthy individuals (Rahmani, Saghazadeh et al. 2019); furthermore, severity of PD symptoms is inversely associated with BDNF concentration (Scalzo, Kummer et al. 2010).

It is known that regular exercise impacts resting BDNF levels in healthy participants, with a moderate effect size (Hyman, Hofer et al. 1991, Szuhany, Bugatti et al. 2015). A meta-analysis of exercise programs in older adults showed that strength training significantly increased BDNF concentration, while AT did not exert such an effect (Marinus, Hansen et al. 2019). Another systematic review reported that the increase in BDNF concentrations was larger after AT compared to RT (Dinoff, Herrmann et al. 2016), whereas a recent network meta-analysis found that changes in BDNF were greater after RT than AT, but results were pooled from mixed populations, with only a minority of studies including people with PD (Zhou, Wang et al. 2022).

There is uncertainty not only about the type of exercise that should be recommended to people with PD, but also regarding its frequency and intensity (Martignon, Pedrinolla et al. 2021, Cui, Li et al. 2023, El Hayek, Lobo Jofili Lopes et al. 2023). A synthesis of exercise guidelines suggests that people with mild to moderate PD should engage in three to five sessions of AT

at moderate intensity (40%–60% maximum heart rate) per week and two to three sessions of RT, but the evidence base is less consistent compared to other neurological conditions (Kim, Lai et al. 2019). A high intensity (>75% maximum heart rate for AT and >70% 1-repetition maximum for RT) is needed according to some scholars but not others (Machado, Teixeira et al. 2022, Rotondo, Proietti et al. 2023). Recently, a feasible, safe and accessible home-based high-intensity program was proposed (Harpham, Gunn et al. 2023). It has also been suggested that the health benefits of physical activity are linked to the total amount of exercise (volume), rather than each component (intensity, type, frequency) (Pate, Pratt et al. 1995). A meta-analysis of observational studies showed an inverse association between weekly physical activity volume and risk of developing PD in men (Fang, Han et al. 2018).

Previous research, including recent systematic reviews on the effect of exercise on BDNF levels, limited the analysis to controlled trials only (Hirsch, van Wegen et al. 2018, Li, Loevaas et al. 2023, Rotondo, Proietti et al. 2023). Randomised trials provide evidence of efficacy of interventions in “ideal” settings, whereas non-randomised studies more accurately reflect usual clinical practice (Sørensen, Lash et al. 2006). Furthermore, exercise interventions in PD are so heterogeneous that they were classified into 18 different combinations of duration, intensity and type (Zhou, Wang et al. 2022, Rotondo, Proietti et al. 2023). This heterogeneity, coupled with a very limited number of trials, makes the evaluation of the effectiveness of exercise intervention extremely hard. Recent meta-analyses aimed at assessing whether exercise determined an improvement of BDNF levels (Hirsch, van Wegen et al. 2018, Li, Loevaas et al. 2023, Rotondo, Proietti et al. 2023), but a quantitative estimate of the effect of exercise intensity and volume is still lacking. Since it is not known which characteristics of exercise determine the largest benefits for people with PD, this study aimed at assessing to what extent intensity, volume and type of exercise are associated with changes in BDNF levels in people with PD.

Methods

We used the methods proposed in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page, McKenzie et al. 2021). This systematic review and meta-analysis was registered in the International Prospective Register of Systematic Reviews (PROSPERO) with the protocol number CRD42023418629, which is available online at https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=418629.

Search strategy and selection criteria

We searched clinicaltrials.gov, CINAHL, Embase, PubMed, Scopus, Web of Science for studies listed from 1 January 2003 to 31 December 2022. A further literature review update was performed in May 2023.

The following string of terms was used: (Parkinson*) AND (exercise OR “physical activity” OR training OR sport* OR rehabilit* OR “physical therapy” OR physiotherapy) AND (BDNF OR plastic* OR synap* OR neuro* OR cognit* OR biomarker*) NOT (rat OR animal OR mouse OR mice) NOT review. Supplementary Material S1 details the string for each bibliographic database. Reference lists of eligible studies were manually examined for further identification of relevant articles.

Data extraction

After removing duplicates and reviewing the title and abstract of potential studies, we systematically assessed the full text of identified manuscripts for eligibility. The following data were extracted by two authors (AP and GP) for each study and study arm:

- (1) study characteristics (title, authors and year of publication, type of study, sample size);
- (2) participants’ information (age, sex, diagnosis, disease duration (years), disease stage (Hoehn and Yahr), motor examination (MDS-UPDRS part 3), pharmacological treatment;
- (3) characteristics of the exercise protocol (duration in weeks, number of weekly sessions, duration of each exercise session, description of exercise);
- (4) biological sample examined, method of analysis, mean and standard deviation of BDNF at baseline and at the end of the exercise protocol (at least 12 h after the final exercise session). If more than two measures of BDNF were reported after the training, the measurement closer in time to the end of the training was chosen. Supplementary Material S2 describes the methods of BDNF measurement for each study.

Any discrepancies in data extraction were resolved by reference to the original article and discussion between the researchers. If the two authors reached no consensus, a third author (BF) made the final judgement. In case of doubts, we asked the original investigators for additional data and clarification of methods. If the response was unsatisfactory, we extracted relevant data from a previous review (Li, Loevaas et al. 2023).

To be eligible for inclusion, studies had to meet the following criteria: 1) they recruited human participants with diagnosis of PD; 2) they used an experimental design with or without a control group; 3) they contained physical exercise training; 4) they assessed BDNF before and after the exercise protocol. Study protocols, review articles and observational studies were excluded. We also excluded study arms (but not studies) that contained, in addition to the exercise interventions, other interventions that were not exercise-based, such as diet or other

techniques, such as transcranial magnetic stimulation (Aftanas, Gevorgyan et al. 2018, Oliveira, Iraci et al. 2020).

Study quality assessment

To assess the risk of bias of randomized trials, the Cochrane Risk of Bias tool was used (Higgins, Altman et al. 2011). Risk of bias was assessed within seven domains: 1) random sequence generation, 2) allocation concealment, 3) blinding of participants and personnel, 4) blinding of outcome assessment, 5) incomplete outcome data, 6) selective reporting, 7) other sources of bias. The Risk Of Bias In Non-randomized Studies of Interventions (ROBINS-I) tool was used to assess the risk of bias for non-randomized studies (Sterne, Hernan et al. 2016). This tool includes seven domains: 1) bias due to confounding, 2) bias in selection of participants into the study, 3) bias in classification of interventions, 4) bias due to deviations from intended interventions, 5) bias due to missing data, 6) bias in measurement of outcomes, and 7) bias in selection of the reported results. These assessments were performed independently by two reviewers (AP, BF). If the two authors reached no consensus, a third reviewer (GP) made the final judgement.

Data-analysis

Intensity of exercise was estimated with the use of the Metabolic Equivalent of Task (MET), a measure which describes the energy expenditure of a specific activity relative to a rest state (Committee 2008). Firstly, we chose the MET values of the activity that best matched the exercise described in the study protocol using ACSM conversion tables and Ainsworth compendium (Ainsworth, Haskell et al. 2011, Garber, Blissmer et al. 2011). Secondly, since exercise interventions often comprised multiple exercise activities, we computed a time-weighted average of MET values (Gomersall, Olds et al. 2011). Inactive control groups under routine or usual care that did not follow a specific exercise protocol, were assigned MET = 1.

The total volume of exercise (expressed in MET-hours) was calculated by multiplying the average weekly training volume (in MET-hours/week) for the duration in weeks of the exercise protocol. For each exercise activity, the assigned MET value was multiplied by the duration in minutes of the training session and by the number of weekly sessions. When an exercise protocol included more than one activity, MET-hours/week of each activity were summed up. Volume of physical activity (in MET-hours) was calculated in a previous observational cohort study in a similar manner (Yang, Trolle Lagerros et al. 2015). We also calculated the proportion of volume spent practicing different types of exercise (aerobic, resistance, balance and other) (American College of Sports Medicine. 2020); the type with the largest volume was used to define the “dominant” type of each exercise protocol.

We computed two distinct standardized measures of effects. In the first analysis (controlled studies only), we computed Hedges' g to estimate the standardized mean difference (SMD) between experimental and control group in pre-post intervention BDNF changes (Matthias Egger (Editor) 2022). When mean and standard deviation of BDNF were not available in the original studies we derived Hedges' g from a previous review (Li, Loevaas et al. 2023). In the second analysis, which included both controlled and non-controlled studies, we computed a measure of pre-post intervention change in BDNF values for each study arm, calculating Cohen's d (Matthias Egger (Editor) 2022).

We conducted a random-effects meta-analysis to obtain a summary estimate of the effect of exercise interventions. The I^2 statistic was used to assess inconsistency between studies. In addition, we conducted several meta-regression models to assess whether the heterogeneity among controlled studies could be explained by differences in intensity, volume and type of exercise. Similarly, in the analysis that included both controlled and non-controlled studies, we built several linear regression models to assess whether the heterogeneity in the effect measure could be explained by differences in intensity, volume and type of exercise among study arms. These analyses were not included in the original protocol, which was limited to the calculation of correlation coefficients between SMD and the three dimensions of exercise. We later realised that the use of a regression framework instead of correlation, would reveal a clearer picture of the study findings.

A sensitivity analysis was performed by excluding all exercise activities with MET ≤ 2.5 under the assumption that exercise can only increase BDNF levels through physical conditioning, thus requiring higher intensity (Nofuji, Suwa et al. 2012, Kelly, Wood et al. 2017).

All analyses were done with the statistical software STATA release 18 (StataCorp LP, Texas, USA), while Robvis was used to visualize risk-of-bias assessments (McGuinness and Higgins 2020).

Results

Search results

A total of 3,179 records were identified after removing duplicates. Fifty-three studies were considered potentially relevant by screening titles and abstracts and 16 studies (8 two-arm trials (Frazzitta, Maestri et al. 2014, Sajatovic, Ridgel et al. 2017, Landers, Navalta et al. 2019, O'Callaghan, Harvey et al. 2020, Segura, Eraso et al. 2020, Szymura, Kubica et al. 2020, Soke, Kocer et al. 2021, Freidle, Johansson et al. 2022) and 8 single-arm trials (Zoladz, Majerczak et al. 2014, Angelucci, Piermaria et al. 2016, da Silva Germanos, Vieira et al. 2019, Ponde, Neto et al. 2019, Oliveira, Iraci et al. 2020, Stuckenschneider, Abeln et al. 2021, Harro, Shoemaker et al. 2022, Schaeffer, Roeben et al. 2022)), which included a total of 370 people with PD, were finally

deemed eligible for the systematic review. The PRISMA flow diagram illustrating the number of studies excluded at each stage of the systematic review is shown in Figure 1. The studies excluded and the reasons for exclusion are reported in Supplementary Material S3.

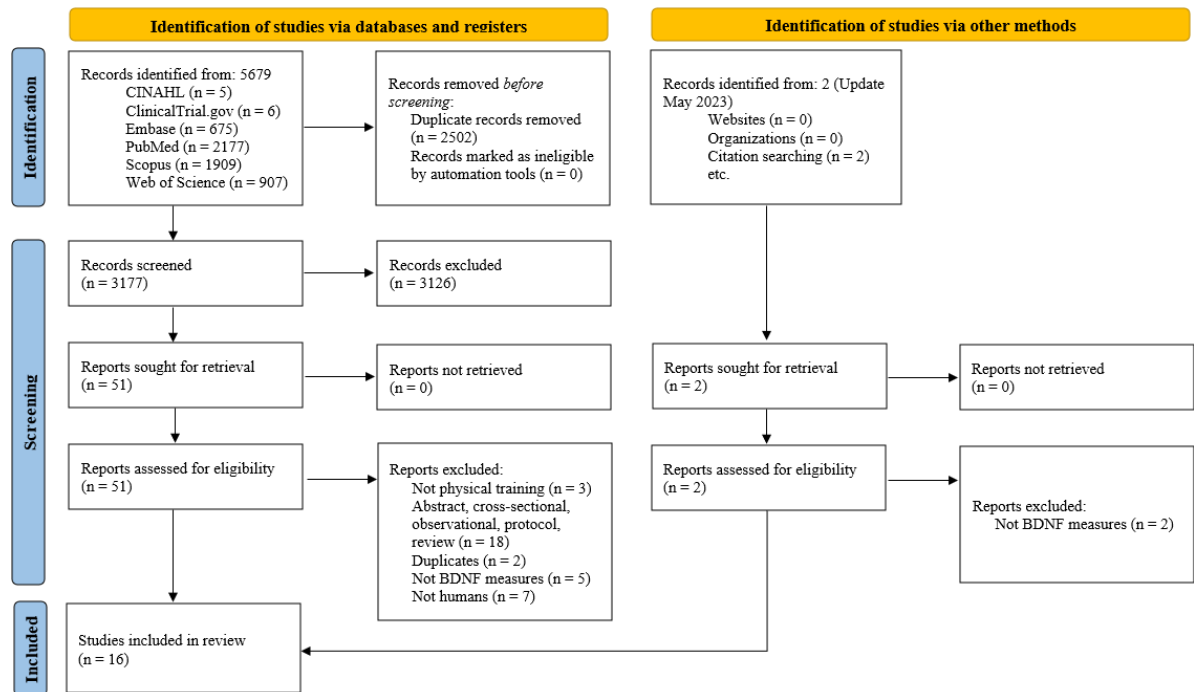


Figure 1. PRISMA 2020 flow diagram for new systematic reviews which included searches of databases, registers and other sources.

Study characteristics

Table 1 contains a summary description of patient characteristics and interventions for each study arm of the selected studies. A large variability emerged in terms of clinical characteristics and exercise interventions. Sample size ranged from 8 to 95 participants with PD and was often smaller than 20 while mean disease duration varied between 8 months and 14 years. About half of the studies did not report data on MDS-UPDRS and only two studies described the amount of daily levodopa (Landers, Navalta et al. 2019, Freidle, Johansson et al. 2022). Most of the interventions were aerobic, followed by resistance and balance and then other components.

Table 1. Patients' characteristics and description of the exercise intervention by study arm

Author and year	Age**	Hoen & Yahr***	Years with disease**	N. of subjects	Study arm*	Description of exercise protocol	Duration (weeks)
Angelucci et al. 2016 (Angelucci, Piermaria et al. 2016)	62.8 ± 6.7	2-3	11.8 ± 7.4	9	Multimodal	Relaxation and breathing, flexibility, postural; treadmill with a heart reserve ≤60% and maximum speed of treadmill scrolling of 3.5-4 km/h; stationary bike with maximum speed of 25-30 km/h; Wii Fit Balance Board; mobility (exercises to promote control of strength and movement velocity); coordination (exercises to promote control of strength and movement velocity)	4
Da Silva Germanos et al. 2019 (da Silva Germanos, Vieira et al. 2019)	65.1 ± 6.7	1-3	-	9	Multimodal	Aquatic exercises: stretching and mobility; strengthening, gait, balance, proprioception; dual task (exercises in combination with games with playful connotations to stimulate group integration)	4
De Oliveira et al. 2020 (Oliveira, Iraci et al. 2020)	65.5 ± 2.2	1-4	-	9	Multimodal	Mobility and coordination (strength, agility, double task and body control); deep water running (endurance) with distance and speed determined in periodization; balance; stretching and relaxation	4
Frazzitta et al. 2014 (Frazzitta, Maestri et al. 2014)	67.0 ± 5.0	1-1.5	0.7 ± 0.4	14	Multimodal	Cardiovascular exercises (warm up), stretching, mobility, postural; balance and gait using a stabilometric platform with a visual cue, treadmill training with both a visual and an auditory cue (heart rate reserve ≤60% and a maximum speed of treadmill scrolling of 3.5 km/h); occupational therapy	4
Freidle et al. 2022 (Freidle, Johansson et al. 2022)	65 ± 4 71.0 ± 5.9	1-1.5 2-3	0.7 ± 0.2 5.5 ± 7	10 48	None Multimodal	HiBalance (sensory integration, motor agility, anticipatory postural adjustments and stability limits); home exercises (functional aerobic, strength exercises)	10

	71.1 ± 6.3	2-4	3 ± 4	47	Speech and communication	HiCommunication (voice sound level, articulatory precision, word retrieval, memory); home exercises (voice, speech function)	10
Harro et al. 2022 (Harro, Shoemaker et al. 2022)	67.2 ± 9.2	1.5-3	4.5 ± 3.2	12	Endurance	Nordic walking: warm up, low intensity aerobic exercise at 4-6/10 RPE with intermittent high intensity short intervals of aerobic exercise at 7-8/10 RPE during training progressions, cool down	6
Landers et al. 2019 (Landers, Navalta et al. 2019)	63.5 ± 10.9	1-3	4.9 ± 5.1	13	Multimodal (high intensity)	High-intensity multimodal exercise boot camp (HIBC): moderate-high intensity aerobic exercise at 70%-80% of HRmax (treadmill, overground walking on the indoor track, stair climber, bike, recumbent bike, rowing machine), strengthening the major muscle groups of the trunk and upper/lower extremities at 50-80 1RM, postural, dynamic gait and sensory orientation, stretching; home exercises at 13-20 RPE	8
	64.6 ± 6.0	1-4	4.7 ± 3.9	11	Multimodal (low intensity)	Usual care exercise program (UC): aerobic exercise at 50%-65% of HRmax (treadmill, overground walking on the indoor track, stair climber, bike, recumbent bike, rowing machine), strengthening the major muscle groups of the trunk and upper/lower extremities (no more than 50% of their 1RM), step touch task, stretching; home exercises at 13-20 RPE	8
O'Callaghan et al. 2019 (O'Callaghan, Harvey et al. 2020)	70.4 ± 7.2	1-3	-	13	Aerobic + Resistance	Moderate-intensity continuous training at 60-80 HRmax: aerobic exercises included warm-up, treadmill walking/running, sit-to-stand, marching/step ups, hand cycling, recumbent cycling and boxing; resistance exercises included upright rowing, lateral arm raises, triceps kick-backs, chest stretch at 90° and bicep curls (circuit with 12 workstations); stretching	12

	64.6 ± 8.6	1-3	-	14	None		
	68.8 ± 7.9	1-3	-	9	High-Intensity Interval Training	High intensity interval training at ≥85% HRmax: warm-up which progressed in intensity and contained whole-body movements (e.g., power clean and press, step and press, squat, pull-down to squat, high pull, bent over row); cool down	12
	69.0 ± 6.6	1-3	-	8	None		
Pondé et al. 2019 (Ponde, Neto et al. 2019)	60.6 ± 14.5	2-3	9.4 ± 5.9	8	Aerobic	Aerobic training (treadmill) at 50-70% HRmax; motor imagery training including concentration with instrumental music, imaginary practice, return of images (video projection) recorded in physical training (real), referring to the running on a treadmill, relaxation EXCEED (Enhanced ExerCise thErapy) at 60-80% HRmax: warm up, fast-paced, low-resistance cycling, progressive sequence of resistance bands, cool down	8
Sajatovic et al. 2017 (Sajatovic, Ridgel et al. 2017)	69.8 ± 2.3	1-3	7.3 ± 3.4	13	Aerobic + Resistance (peer support)	SGE (Self-guided exercise) at 60-80% HRmax: warm up, fast-paced, low-resistance cycling, progressive sequence of resistance bands, cool down	12
	70.3 ± 6.5	1-3	6.4 ± 6.7	15	Aerobic + Resistance	Exergame training (“Virtual smash”, “Light race” and “Kardio boxing” from the game pack “Your shape: Fitness evolved”) combined aspects of moderate intensity aerobic fitness training with elements of coordination and speed	12
Schaeffer et al. 2022 (Schaeffer, Roeben et al. 2022)	58 ± 10	1-2.5	5.6 ± 5.0	17	Aerobic	Warm up (low resistance pedalling at 30-40 rpm), stationary tandem bicycle at 80% HRmax (while pedalling at 80 rpm or faster), cool down (30-40 rpm), stretching	6
Segura et al. 2020 (Segura, Eraso et al. 2020)	57.8	1-3	2-14	6	Aerobic		16
	56	1-3	2-24	7	None		

Soke et al. 2021 (Soke, Kocer et al. 2021)	57.1 ± 8.2	1-3	8.1 ± 4.8	15	Aerobic + Resistance	Warm up, treadmill at 60-80% HRmax, cool down, task-oriented training (TOT): circuit with 11 workstations (12-15 RPE)	8
	58.1 ± 8.9	1-3	7.6 ± 3.9	14	Aerobic	Warm up, treadmill at 60-80% HRmax, cool down	8
Stuckenschneider et al. 2021 (Stuckenschneider, Abeln et al. 2021)	71.4	1.5-4	-	8	Multimodal	Standing on even or uneven ground with eyes open or closed (balance), sitting on a chair while lifting one's toes or heels and throwing and catching a ball at the same time (dual task); wall pushups, holding medicine balls with outstretched arms, squats, or crunches (resistance) at least 13 RPE; walking or running exercises (aerobic) at least 13 RPE	8
Szymura et al. 2020 (Szymura, Kubica et al. 2020)	66.0 ± 2.6	2-3	-	16	Aerobic	Warm up, Wii Fit Balance Board at 60-70% HRmax, cool down	12
	65.2 ± 7.4	2-3	-	13	None		
Zoladz et al. 2014 (Zoladz, Majerczak et al. 2014)	70 ± 3	1-3	8.5 ± 4.5	12	Aerobic	The moderate-intensity interval training session (IT) consisted of warm up, interval exercise including cycling at 80-90 rpm (fast phase of IT) and cycling less than 60 rpm (slow phase of IT) at 60-75% HRmax, cool down	8

*Definition of exercise intervention according to Zhou B et al. in Aging Neurosci 2022 (Zhou, Wang et al. 2022)

**Mean ± Standard Deviation

***Range

Supplementary Material S4 details all exercise activities included in each study arm according to type (Aerobic, Resistance, Balance, Others), MET, number of sessions per week and minutes per session. Table 2 shows average intensity, total and weekly volume, and proportion of volume according to exercise type by study arm. Exercise protocols had a median intensity of 3.5 MET (inter-quartile range 3.1–3.9); weekly and total volume were highly variable.

TABLE 2. Intensity, weekly and total volume, and proportion of exercise type by study arm.

Author and year	Study arm ^a	Intensity (time- weighted average of MET)	Total volume (MET-hours)	Proportion Aerobic	Proportion Balance	Proportion Resistance	Proportion Others
Angelucci et al. 2016	Multimodal	2.5	123.2	0.32	0.12	0	0.55
Da Silva Germanos et al. 2019	Multimodal	3.7	24.7	0.32	0	0.54	0.14
De Oliveira et al. 2020	Multimodal	3.9	32.8	0.70	0.16	0	0.14
Frazzitta et al. 2014	Multimodal	2.4	103.7	0.39	0.12	0	0.49
Freidle et al. 2022	Multimodal	3.1	73.3	0.16	0.68	0.16	0
	Speech and communication	1.3	28.2	0	0	0	1
Harro et al. 2022	Endurance	4.2	60.4	1	0	0	0
Landers et al. 2019	Multimodal (high intensity)	3.8	215.4	0.38	0.13	0.38	0.1
	Multimodal (low intensity)	2.7	90	0.31	0.19	0.33	0.17
O'Callaghan et al. 2019	Aerobic + Resistance	3.5	123.1	0.72	0	0.23	0.04
	High-Intensity Interval Training	5.3	111	0	0	1	0
Pondé et al. 2019	Aerobic	2.5	36	0.89	0	0	0.11
Sajatovic et al. 2017	Aerobic + Resistance (peer support)	3.5	105	0.60	0	0.40	0
	Aerobic + Resistance	3.5	105	0.60	0	0.40	0
Schaeffer et al. 2022	Aerobic	4	54	1	0	0	0
Segura et al. 2020	Aerobic	4.3	144.4	0.87	0	0	0.13
Soke et al. 2021	Aerobic + Resistance	3.9	98.8	0.47	0	0.53	0
	Aerobic	3.8	46	1	0	0	0

Stuckenschneider et al. 2021	Multimodal	3.6	65.6	0.38	0.23	0.38	0
Szymura et al. 2020	Aerobic	3.2	114	0.13	0.87	0	0
Zoladz et al. 2014	Aerobic	3.2	76	1	0	0	0

^aDefinition of exercise intervention according Zhou B et al. in Aging Neurosci 2022 (Zhou, Wang et al. 2022).

Main analysis

Supplementary Material S5 shows pre-post exercise BDNF levels of experimental and comparison groups with SMD (Hedges' g) in randomized studies. Only two out of eight controlled studies showed significant differences in BDNF changes over time between experimental and comparison groups.

Two separate meta-analyses were performed (Figure 2): the first one included only those studies ($n = 5$) which reported mean and standard deviation of BDNF, allowing us to directly estimate SMD. The second meta-analysis added data on SMD derived from a previous systematic review (American College of Sports Medicine et al., 2020). According to the first meta-analysis, exercise interventions show a significant improvement in BDNF levels compared to the control group, with $SMD = 0.70$ (95% CI: 0.03, 1.38). There was substantial heterogeneity between studies ($I^2 = 76.0\%$). A smaller but more precise estimate of SMD is present in the meta-analysis of all controlled studies.

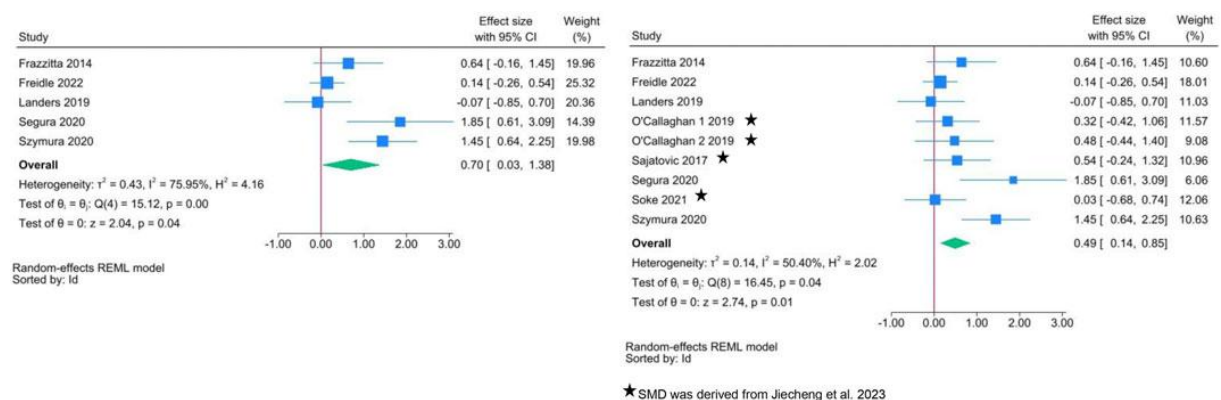


FIGURE 2. Forest plots of exercise interventions in a subset of 5 controlled studies with available data on BDNF (left) and in the complete set of 9 controlled studies (right).

Table 3 shows the results of the meta-regressions: between-group differences in intensity were positively associated with SMD in the analysis limited to the subset of 5 studies, but not in the complete set of controlled studies. There was no difference according to exercise type. This latter finding is also confirmed in Figure 3A: when the comparison group receives “usual care” (i.e., inactive group), the increase in BDNF change is clear regardless of exercise type. A large variability in SMD is present, especially for aerobic and balance exercise.

	5 studies			9 studies		
	Coefficient	(95% CI)	P value	Coefficient	(95% CI)	P value
Δ Time-weighted average of MET*	0.99	(0.10 1.87)	0.028	0.16	(-0.13 0.46)	0.278
Δ Total MET-hours (x100)*	0.82	(-1.17 2.81)	0.419	0.38	(-0.42 1.18)	0.351
Type						
Identical (Aerobic + Resistance)	Reference			Reference		
Aerobic	1.25	(-0.93 3.43)	0.262	0.58	(-0.64 1.79)	0.350
Balance	0.81	(-1.29 2.91)	0.449	0.45	(-0.80 1.70)	0.476
Resistance				0.00	(-1.31 1.31)	0.999

*Difference between experimental and control group

TABLE 3. Meta-regression of between-group differences in intensity, volume and type of exercise on changes in BDNF levels (controlled studies only).

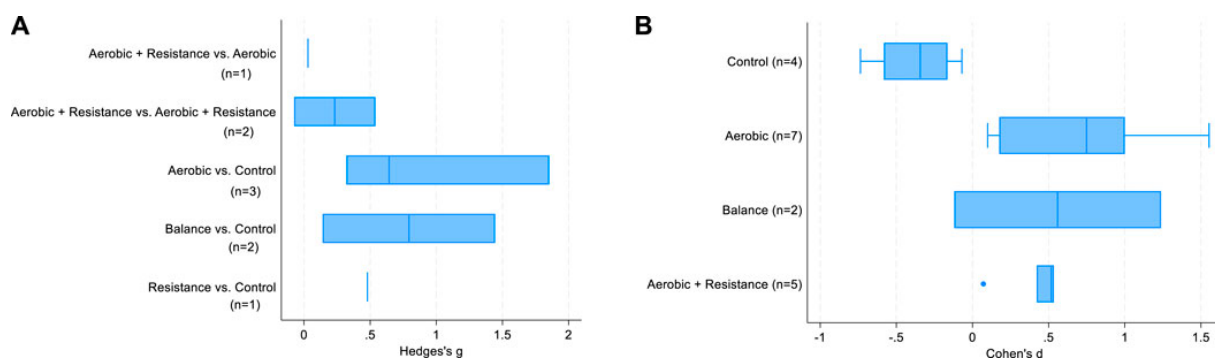


FIGURE 3. Box-plots of SMD in controlled studies (A) and in the analysis by study arms of controlled and non-controlled studies (B).

Supplementary Material S6 shows pre-post exercise BDNF levels with SMD (Cohen's d) separately by study arm in controlled and non-controlled studies. The SMD was significantly different from zero in 4 study arms. Mean and standard deviation of BDNF were not reported in 4 studies, and the corresponding 8 study arms.

Supplementary File 6. Pre-post exercise BDNF levels denoted separately by study arm in controlled and non-controlled studies.

The linear regression models (Table 4) showed that time-weighted average of MET and total volume were positively associated with BDNF change over time. All types of exercise were significantly associated with SMD, with effects of similar magnitude. This finding clearly emerges in Figure 3B as well, which again suggests a substantial effect of exercise on BDNF changes over time regardless of exercise type. A large variability for aerobic and balance exercise is evident.

	Coefficient	(95% CI)	P value
Time-weighted average of MET	0.38	(0.16 0.59)	0.002
Total MET-hours (x100)	0.50	(0.05 0.95)	0.032
Type	None as reference group		
Aerobic	1.10	(0.50 1.70)	0.002
Balance	0.93	(0.10 1.77)	0.031
Aerobic + Resistance	0.79	(0.14 1.43)	0.020

TABLE 4. Linear regression of intensity, volume and type of exercise on change in BDNF (study arms of controlled and non-controlled studies).

The results of the sensitivity analysis largely overlapped with those of the primary analysis, with the only relevant difference being the estimate of the effect of exercise intensity (Supplementary Material S7). Time-weighted average of MET was again significant in the meta-regression of 5 controlled studies (Beta coefficient = 0.41, $p = 0.04$) and nearly significant (Beta coefficient = 0.14, $p = 0.12$) in the complete set of controlled studies.

Risk of bias

The risk of bias assessment for each study is summarized in Supplementary Materials S8, S9. Overall, most controlled studies were at low risk of bias (75%) and the remainder were uncertain. On the other hand, we found a moderate risk of bias for single-arm studies.

Discussion

This systematic review shows that exercise increases BDNF levels in people with PD, irrespective of type. Exercises of greater intensity determined the largest improvement. The positive effect of exercise on BDNF levels found in this study confirms the results of previous reviews (Hirsch, van Wegen et al. 2018, Ruiz-Gonzalez, Hernandez-Martinez et al. 2021, Li, Loevaas et al. 2023, Rotondo, Proietti et al. 2023). To the best of our knowledge, this is the first

systematic review in people with PD that attempts at evaluating the effect on BDNF levels of different characteristics of exercise, such as intensity, volume and type. A similar analysis was carried out in previous systematic reviews of the literature in youth and athletes (Lesinski, Prieske et al. 2016, Wu, Xu et al. 2021), but not in people with PD.

As far as intensity of exercise is concerned, our results suggest a positive dose-response association with BDNF levels, resembling the findings of previous reviews in people with PD (Ellis and Rochester 2018, Alberts and Rosenfeldt 2020, Machado, Teixeira et al. 2022), healthy participants and animal models (Petzinger, Fisher et al. 2010, Huang, Larsen et al. 2014). High-intensity exercise may promote the synthesis or availability of BDNF in the brain through different mechanisms, such as increased permeability of the blood brain barrier due to hyperthermia (Walsh and Tschakovsky 2018), brain hypoxia and muscle damage (Jiménez-Maldonado, Rentería et al. 2018), and circulating molecules such as lactate (Sobral-Monteiro-Junior, Maillot et al. 2019).

In the analysis by study arm, total exercise volume was associated with increased BDNF levels over time. A previous study in people with different neurodegenerative disorders showed that neither weekly volume nor duration of exercise were associated with BDNF (Ruiz-Gonzalez, Hernandez-Martinez et al. 2021). Since total exercise volume comprehends weekly volume and duration of the intervention, its positive effect on BDNF may be explained by the impact of exercise programs of longer duration. However, total volume was associated with increase in BDNF only in the analysis by study arm, and not in the analysis of controlled studies: it is possible that this positive effect is an artifact due to the high risk of bias of non-controlled studies. De la Rosa et al. reported that trained men have lower circulating levels of BDNF but increased binding sites as a result of an adaptation to regular physical activity (De la Rosa, Solana et al. 2019).

The type of exercise that should be recommended to people with PD is controversial (Li, Loevaas et al. 2023). In this study we found that all types of exercise were useful, but no exercise type was superior to the others, contrary to previous reviews which either favored AT or RT (Dinoff, Herrmann et al. 2016, Zhou, Wang et al. 2022). On the other hand, exercises of greater intensity showed the largest benefits in this study. We suggest that people with mild to moderate disease severity, when appropriately supervised, engage in high-intensity aerobic training (HIIT) or high-intensity resistance training (HIRT) exercises, as recommended by other authors (Zhou, Wang et al. 2022).

Different mechanisms may explain the effect on BDNF levels of aerobic and resistance exercise, which include increases in Ca^{++} levels and reactive oxygen species in neuronal cells (Radak, Suzuki et al. 2016, Fernandes, Arida et al. 2017, Pinho, Aguiar et al. 2019). It was also shown

that the release of BDNF from muscle contraction induces the phosphorylation cascades of different signaling pathways, such as cAMP-response element-binding protein (CREB) and mammalian target of rapamycin (mTOR), resulting in additional secretion of BDNF in the brain (Pinho, Aguiar et al. 2019). As far as balance exercise is concerned, the mechanism of action leading to increased BDNF is poorly understood (Kubica, Szymura et al. 2019).

The present study may be affected by several limitations, such as the scarcity of published studies, most of which had small sample sizes, as well as the large variability in participant features and exercise protocols. A recent review on the effect of exercise in PD examined 156 experimental studies (Ernst, Folkerts et al. 2023), but only a minority reported data on BDNF, as shown in this and previous systematic reviews (Hirsch, van Wegen et al. 2018, Li, Loevaas et al. 2023, Rotondo, Proietti et al. 2023). It is likely that the limited sample size, which was often smaller than 20 participants, combined with between-study participant differences, affected the precision of our estimates. The large heterogeneity in the effect measures, especially for aerobic and balance exercises, may derive from the presence of a few influential studies. Despite the selected studies widely differed in intensity, type and volume, we were able to demonstrate that part of the heterogeneity could be explained by differences in intensity between experimental and control group.

Intensity, volume, and typology are not the only dimensions of exercise. Other scholars suggested that “complex” exercise interventions may be particularly effective in people with PD (Petzinger, Fisher et al. 2010, Janssen Daalen, Schootemeijer et al. 2022). These interventions may combine cognitive and motor rehabilitation (Ferrazzoli, Ortelli et al. 2018). Unfortunately, the description of exercise protocols was often poor, so we chose to focus on the dimensions (intensity, volume and type) that were more clearly reported.

Another limitation of this study is the use of 2011 compendium and ACSM tables, which contain reference values of exercise intensity for healthy, and not diseased populations. For instance, it was shown that, for the same relative intensity, the metabolic rate of obese elderly people with type 2 diabetes was lower than that of healthy controls (Zanuso, Bergamin et al. 2016). Thus, tabulated values of MET may have not correctly reflected the physiological demands of exercise in people with PD. In addition, selected studies did not consider those activities which are normally carried out by every person with PD, including those belonging to “true” control groups: as a result, differences in exercise volume and intensity between the “active” experimental group and the “inactive” control group may have been artificially inflated. Further, most studies did not report the presence of genetic variants, which may either promote BDNF synthesis after AT or interfere with neuroplasticity (Mang, Campbell et al. 2013, Lemos, Alves et al. 2016).

Conclusion

This systematic review offers consistent evidence that exercise is beneficial for people with PD, irrespective of exercise typology. The evidence derives from both controlled and non-controlled studies and is especially strong for exercises of greater intensity. This latter finding may be of great value to practitioners for the design and implementation of physical exercise interventions in people with PD. We suggest that people with mild to moderate disease severity, when appropriately supervised, engage in high-intensity exercise.

Future studies should improve the description of exercise interventions, carefully detailing their intensity using standardised measures such as MET or % Heart Rate Reserve (American College of Sports Medicine. 2020, Rotondo, Proietti et al. 2023). This will enable researchers to assess more accurately the intensity of the exercise protocol and evaluate its effect on BDNF and other participant outcomes.

3. Evaluating the combined effects of Intermittent Theta Burst Stimulation and Maximal Strength Training on upper limb function and neuromuscular fatigue in Parkinson's Disease patients: a randomized controlled study

Introduction

Parkinson's disease (PD) currently affects approximately 6 million of people (Dorsey E. R. 2018), with an age-standardized prevalence rate increase of 21.7% from 1990 to 2016. Parkinson's disease is characterized by the loss of dopaminergic neurons in the substantia nigra (Fearnley and Lees 1991) and is typically marked by both motor symptoms such as bradykinesia, rigidity, resting tremor, and postural instability, as well as non-motor features, including cognitive decline and depression (Lee and Gilbert 2016). From a phenomenological perspective people with PD often report fatigue as a sense of diminished energy or an increased exertion required for their daily activities, this fatigue is distinguishable from feelings of sleepiness, lack of motivation and depression (Kluger, Brown et al. 2014). Fatigue can influence spatiotemporal parameters such as gait, leading to reduced step length and increased instability (Schlachetzki, Barth et al. 2017). This fatigue, commonly reported by PD patients, is not only a subjective sensation but also has measurable effects on motor performance. A specific type of fatigue relevant to PD is neuromuscular fatigue, which refers to the decline in muscle force generation during sustained effort (Bigland-Ritchie and Woods 1984). Neuromuscular fatigue in PD has been linked to alterations in brain circuits affecting voluntary activation and motor unit recruitment (Stevens-Lapsley, Balter et al. 2012), potentially contributing to the gait impairments described by Schlachetzki et al. (2017) (Schlachetzki, Barth et al. 2017). Another important factor is the difference in the magnitude of motor impairment symptoms between the left or right body side. The differences between the

right and left-sided cohorts (i.e., groups of patients categorized based on the predominant side of motor impairment) are particularly evident when testing muscle isokinetic strength at 90°/s (Frazzitta, Ferrazzoli et al. 2015). Studies on physical rehabilitation in PD often focus on lower limb impairments, such as gait and balance issues (Dibble, Addison et al. 2009, Schilling, Pfeiffer et al. 2010, Vieira de Moraes Filho, Chaves et al. 2020). Meanwhile, most research on upper limbs assesses factors like coordination, strength, power, bradykinesia, and functionality (Proud, Miller et al. 2013).

Among treatments for PD, methods of non-invasive brain stimulation (NIBS), utilizing techniques like Transcranial Magnetic Stimulation (TMS) or transcranial Direct Current Stimulation (tDCS), have demonstrated the ability to induce plastic reorganization processes in the brain (Haraldsson, Ferrarelli et al. 2004). High-frequency rTMS (≥ 5 Hz) induces excitability in the cortex, while low-frequency rTMS (≤ 1 Hz) has an inhibitory effect (Brunoni, Chaimani et al. 2017). Theta-burst stimulation (TBS) is another form of rTMS protocol with both high-frequency and low-intensity stimulation capable of inducing neuroplastic changes (Rossi, Antal et al. 2021) and increases cortical excitability (Chu, Cheng et al. 2021). In comparison to traditional rTMS protocols, TBS demonstrates consistent and enduring impacts on motor-evoked potentials (MEPs) with a shorter duration of stimulation (Huang, Edwards et al. 2005). Corticospinal excitability and post-activation potentiation are crucial mechanisms underlying the development of muscle force. Post-exercise facilitation and post-exercise depression, signifying an increase and decrease, respectively, in the amplitude of evoked potentials, are observed in both fresh and fatigued muscles, including the biceps brachii (Gandevia, Petersen et al. 1999). The recent literature highlighted potential positive effects for the combination of TBS with exercise training or rehabilitation in patients with stroke, schizophrenia, and other diseases. This combination has shown efficacy in improving upper limb motor function with dual task (Kim and Yim 2018), and there is currently an ongoing study on clinical symptoms of dysphagia, aphasia, and cognitive function following a stroke (Park and Yoon 2015, Arheix-Parras, Barrios et al. 2021).

Other potential nonpharmacological approaches for ameliorating the neuromuscular components of force and the development of neuromuscular fatigue is Maximal Strength Training (MST). With this exercise training method, Helgerud et al. (Helgerud, Thomsen et al. 2020) showed a clear increase in the maximal force and motor unit recruitment in patients with PD. Indeed, most of the reported literature is focused on the lower limbs (Lin, Chen et al. 2022), but very little is known about the effects on the upper limbs. Moreover, the combined effect of MST and TBS has never been evaluated. Furthermore, the potential effects of physical therapy interventions on the motor function of the upper limbs and the overall quality of life in PD patients remain unclear (Correa, da Silva Rocha Paz et al. 2020). Motor impairments in the upper limbs of individuals with PD are typically addressed through programs focusing on fine-motor hand exercises, practice-based interventions, visual and auditory cueing (Bryant, Rintala et al. 2010), resistance training (Kadkhodaie, Sharifnezhad et al. 2020), and rhythmic

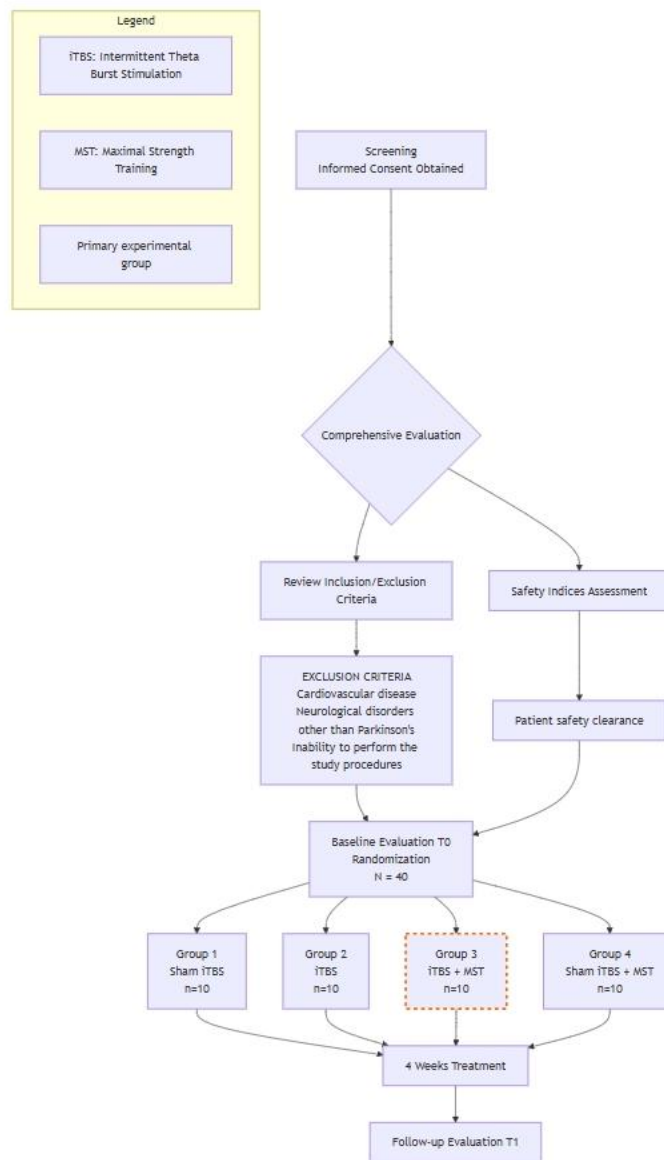
auditory stimulation (Fan, Li et al. 2022). In light of this, it is necessary to clarify which interventions may lead to a reduction in limb differences in patients with PD, especially when attempting to combine two interventions, TBS and MST.

Aims: The purpose of this study was to determine the effects of intermittent Theta Burst Stimulation (iTBS) and Maximal Strength Training (MST) on maximal force and neuromuscular fatigue in the more-affected upper limb of individuals with Parkinson's disease. The combined effects of iTBS and MST were also evaluated.

Methods

For this randomized trial, we recruited 40 patients with PD. Patients were randomly assigned to: 1) sham iTBS, 2) iTBS, 3) sham iTBS + MST 4) iTBS + MST. The study lasted for 4 weeks, with three sessions per week. An additional group of age- and sex-matched healthy participants also underwent baseline assessments to provide normative reference values for neuromuscular and cognitive measures. This group was not part of the factorial design but served as a physiological comparator.

An *a priori* power analysis was conducted using G*Power software (version 3.1.9.7). The calculation was based on the primary outcome of change in maximal voluntary contraction (MVC) force. The effect size was estimated from a previous study that implemented an identical maximal strength training (MST) protocol in people with Parkinson's disease, which reported a large effect on MVC (Cohen's $d \approx 1.03$) (Helgerud, Thomsen et al. 2020). Using a conservative converted effect size of $f = 0.4$, an alpha (α) of 0.05, and a power ($1-\beta$) of 0.90 for a repeated-measures analysis of variance (ANOVA) with between-within interaction, the analysis indicated a required total sample size of $N = 36$. To account for a potential 10-15% dropout rate, we aim to recruit a total of 40 participants with Parkinson's disease.



Participants were recruited from the Azienda Ospedaliera Universitaria Integrata Verona – “Parkinson’s Center and Movement Disorders”, as well as from the Associazione Unione Parkinsoniani Verona. They were informed about the study through direct referrals from their treating neurologists, printed materials (e.g., brochures, posters), and informational meetings held at participating clinics and association meetings. Eligible participants were screened based on predefined inclusion and exclusion criteria.

All participants provided written informed consent after receiving detailed information about the study's aims and procedures. The study protocol was approved by the local Ethics Committee and conducted in accordance with the ethical standards of the Declaration of Helsinki.

This protocol and the informed consent forms were reviewed and approved by the applicable ethical committees of the Azienda Ospedaliera Universitaria Integrata of Verona with respect

to scientific content and compliance with applicable research and human participant regulations. This protocol was ethically conducted following the latest revision of the Declaration of Helsinki as well as the Declaration of Oviedo. The study was designed and conducted in adherence to good clinical practice principles and procedures, in compliance with Italian legislation, as described in the following documents and accepted by the investigators with their signatures: 1) ICH Harmonized Tripartite Guidelines for Good Clinical Practice (1996); 2) Directive 91/507/EEC, The Rules Governing Medicinal Products in the European Community; 3) D. L.vo n.211 of 24 June 2003; 4) D. L.vo n.200 of 6 November 2007; and, 5) D.M. 21 December 2007.

The study comprised four examination phases following a previous study (Martignon, Laginestra et al. 2022). The participants underwent clinical and physical screening using rating scales and questionnaires, including the Unified Parkinson's Disease Rating Scale (UPDRS) (Goetz, Tilley et al. 2008), the Hoehn and Yahr Scale (Hoehn and Yahr 1967), the Montreal Cognitive Assessment (MoCA) (Nasreddine, Phillips et al. 2005), the Fatigue Severity Scale (FSS) (Krupp, LaRocca et al. 1989), the Parkinson's Disease Questionnaire-8 (PDQ-8) (Jenkinson, Fitzpatrick et al. 1997), the Food Frequency Questionnaire (FFQ) (Willett, Sampson et al. 1985), and the Edinburgh Handedness Inventory (EHI) (Oldfield 1971). They were then familiarized with the experimental procedures in the laboratory and provided with a wristwatch (Polar Vantage V, Polar Electro Oy, Kempele, Finland) for daily energy expenditure (DEE) assessment.

Inclusion Criteria. Patients with a confirmed diagnosis of PD, according to the 2015 MDS-PD criteria (Postuma, Berg et al. 2015), were included. Eligible patients must have had a disease stage $\leq$ III on the Hoehn & Yahr scale (Hoehn and Yahr 1967), be aged 40–70 years and have no dementia (MoCA score $\geq$ 21, based on PD-specific validation (Dalrymple-Alford, MacAskill et al. 2010). Additionally, fatigue was assessed using the Fatigue Severity Scale (FSS) (Krupp, LaRocca et al. 1989), with a required score of $\geq$ 4. All participants provided written informed consent.

Exclusion Criteria. Exclusion criteria included: severe depression, as assessed by a score of >18 on the Beck Depression Inventory-II (BDI-II) (Beck, Steer et al. 1996) or clinical diagnosis; significant apathy, as assessed by a score of ≥ 40 on the Apathy Evaluation Scale (AES) (Marin, Biedrzycki et al. 1991) or clinical evaluation; psychosis, based on clinical history or evaluation; advanced chronic illnesses (e.g., advanced cancer, cachexia); severe orthopedic conditions impairing exercise performance; and cardiopulmonary diseases contraindicating physical activity. Participants with pacemakers, a history of seizures, or non-medical metallic implants were also excluded in accordance with international safety guidelines for TMS (Rossi, Antal et al. 2021).

Pre-intervention assessments include cognitive and motor tests. The experimental setup involved electromyography (EMG), a system with surface EMG electrodes placed on the

muscle of interest (including the biceps), proper skin preparation for optimal electrode contact, a Force Measurement Device (using a force transducer or dynamometer), and Electrical Stimulation Equipment to deliver targeted electrical stimulation to motor nerves or muscles. The primary goal was to achieve specific physiological outcomes through targeted stimulation. For the brachial plexus, motor wave (Mwave) was used to induce controlled muscle contractions in the biceps brachii.

Figure 1

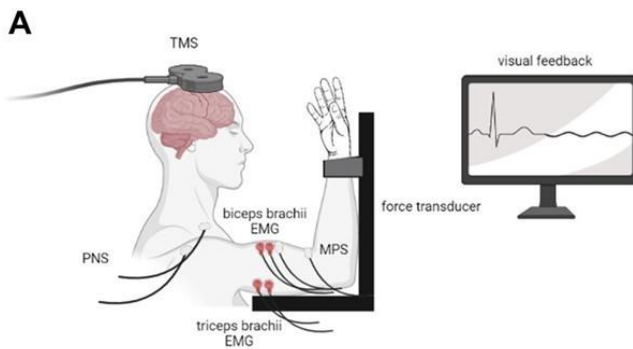


Figure 1: set up of experimental protocol in laboratory

Neuromuscular fatigue was assessed using a combination of electromyography (EMG), maximal voluntary contraction (MVC) tests, and fatiguing protocols. Specifically:

- **Maximal Voluntary Contraction (MVC):** Participants will perform six MVCs with interpolated twitches to assess muscle strength and voluntary activation.
- **Electromyography (EMG):** Surface EMG electrodes will be placed on the biceps brachii to record muscle activity and detect changes in motor unit recruitment.
- **Fatiguing Task:** A sustained 2-minute MVC will be performed to induce fatigue, after which neuromuscular parameters (force generation, EMG amplitude, and motor unit firing rates) will be re-evaluated.
- **Corticospinal Excitability:** Transcranial Magnetic Stimulation (TMS) will be used to measure motor-evoked potentials (MEPs) before and after the fatiguing task, allowing assessment of central fatigue mechanisms.

Maximal force assessments involve six Maximum Voluntary Contractions (MVC) with interpolated twitches (stimulation at the motor point) to assess muscle strength and voluntary activation. Corticospinal excitability will be measured via the utilization of TMS during MVC and 20% EMG calculated on MVC, including six Motor Evoked Potentials (MEP) by stimulating the motor cortex and one Peripheral Nerve Stimulation (PNS) to assess both voluntary activation and peripheral nerve response. The evaluation protocol will be: 3 MVCs

with interpolated twitch (stimulation during MVC and stimulation at rest of the motor point); at least 1 and a half minutes of rest between each; 3 MVCs with TMS and stimulation of the brachial plexus; 1 contraction at 20% EMG with 4 TMS pulses and one stimulation of the brachial plexus; Fatiguing task: 2 minutes of maximal voluntary contraction, then the neuromuscular evaluation will be repeated. All assessments will be performed primarily on the limb with the greatest motor impairment, while the contralateral limb will be assessed as a reference to allow comparison between the more and less affected sides, both before and after the intervention.

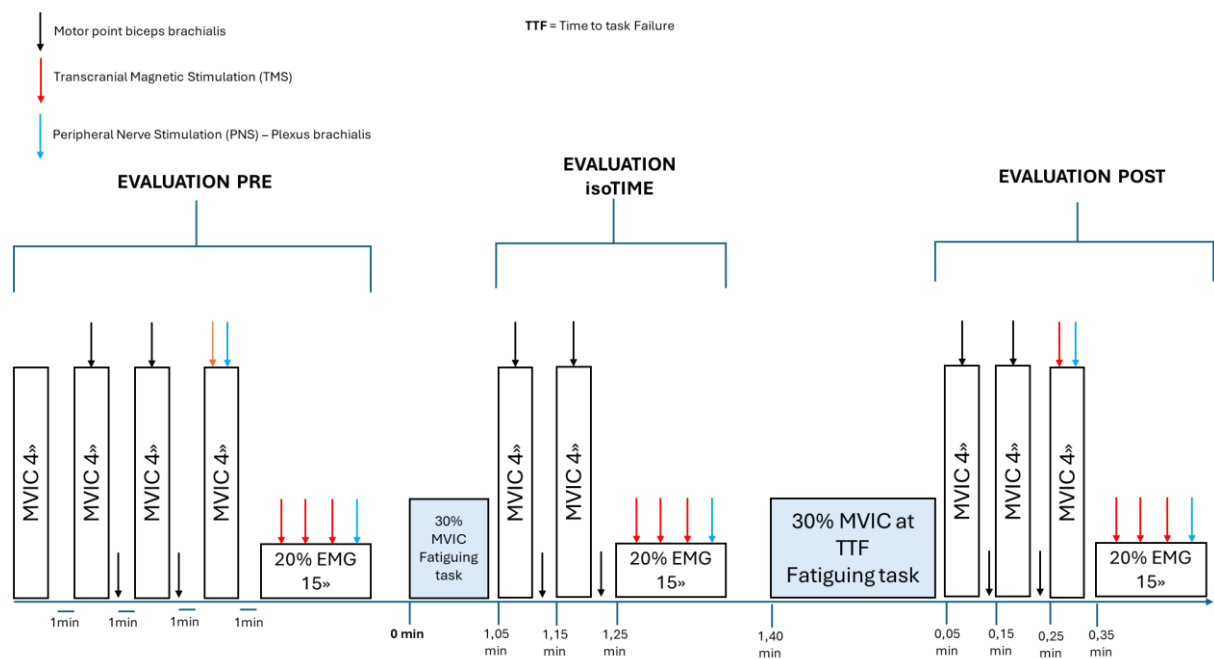


Figure 2. Experimental protocol for assessing muscle fatigue and electromyographic (EMG) activation. The figure illustrates an example of the protocol used in the preliminary phase of the study, with different percentages compared to those applied in the final protocol, which is described in detail in the Methods section.

Surface electromyography. The EMG of the biceps brachii will be recorded with two solid adhesive hydrogel electrodes (H59P; Tyco Healthcare Group, Mansfield, MA) positioned longitudinally over the muscle belly, aligned with the arrangement of the underlying muscle fibers, and with an interelectrode distance of 20 mm (center-to-center). Before applying the electrodes, the skin will be shaved and cleaned with a cotton swab soaked in alcohol to minimize electrical impedance.

Neuromuscular assessment and nerve stimulation. Maximal voluntary and electrically induced muscle contractions of the biceps brachii muscle will be measured using a custom-

made setup. Participants will be seated in an upright position with back support, and seat belts will be applied to secure them to the chair and prevent movement of other body parts. The elbow will be flexed at 90°, and the ankle of the dominant limb will be attached to the force transducer. The output from the force transducer will be amplified and recorded with a PowerLab-16/35 data acquisition system.

Cognitive function was assessed using a battery of standardized tests including: the Montreal Cognitive Assessment (MoCA) to screen for dementia (with a score <26 indicating cognitive impairment) (Nasreddine, Phillips et al. 2005); the Frontal Assessment Battery (FAB) to evaluate executive functions (Dubois, Slachevsky et al. 2000); the Trail Making Test (TMT) Parts A and B to assess attention, processing speed, and task-switching (Reitan 1958); the Stroop Test to measure response inhibition and executive control (Stroop 1935); the Interference Memory test from the ENB-2 battery (Mondini, Mapelli et al. 2011); and the Digit Span test to evaluate working memory (Wechsler 2008). This comprehensive battery evaluates multiple cognitive domains, including attention, executive functions, memory, and overall cognitive performance.

Each patient from their respective randomized group will come to the laboratory to perform activities with sham iTBS or real iTBS. Afterward, they will go to the gym to carry out the MST in the case of Group 4 or Group 3, which will only perform MST training with a preceding sham iTBS.

1. Sham iTBS. On sham stimulation, a panel that is placed between the coil and the scalp is commonly referred to as a "shield" or "panel shield" as a barrier to modify or control the magnetic field distribution during TMS procedures which does not induce any significant physiological transcranial effect on the brain, will be used.

2. iTBS. iTBS (Magstim Rapid2, Whitland, UK) will use standard, internationally approved parameters: 80% resting motor threshold (RMT) stimulation intensity; triplet 50 Hz bursts, repeated at 5 Hz for 2 s on and 8 s off, 10 times; 600 pulses per session; for a total duration of 3 min 20 s. To measure the RMT, the figure-of-eight coil is positioned with its center aimed at the base of the scalp in the area of cerebral cortex movement. The patient is instructed to relax completely, and the intensity of transcranial magnetic stimulation output is gradually adjusted. Five consecutive single stimulations are performed, and to be considered valid, at least five of them must induce movement-evoked potentials with an amplitude greater than 50 μ V at the minimum stimulation intensity (Sakamaki, Furusawa et al. 2022).

3. sham iTBS + MST. Sham stimulation will be applied by the same iTBS protocol using the sham coil. Immediately after sham stimulation they will start with the MST with the more affected upper limb, with the training sessions that will include lat machine exercises. Regarding the tests, the lat machine will be performed using a vertical lat machine apparatus. In accordance with the previous training procedure, the exercise will begin with an eccentric

phase, starting from an angle of approximately 180° in the elbow joint and progressing to a flexion of the elbow at 90°. The concentric phase then will follow a brief pause (about 0.5 seconds) and will be executed with maximal force mobilization, returning to an arm angle of about 180°, with arm raises at the end of the concentric lifting phase to engage the training of the brachial biceps.

The 1-RM assessment will be conducted following the National Strength and Conditioning Association (NSCA) guidelines (Strength and Association 2021). The initial 1RM will be estimated during a familiarization session by having the participant perform repetitions with a submaximal load, and then using the Brzycki equation to predict the 1RM (Brzycki 1993). The formal 1-RM assessment will then include a standardized warm-up, consisting of two sets of eight repetitions at 50% of the estimated 1RM. During both lifts, the participants will observe a marked stop (approximately 0.5 seconds) between the eccentric (muscle lengthening) and concentric (muscle shortening) phases of contraction. The load for each lift will be progressively increased until the participant can no longer perform the movement, constituting failure. A rest period of 3–4 minutes will be provided between attempts. The highest load successfully lifted within three to six attempts will be recorded as the 1RM for each exercise. The training will consist of four sets of four repetitions at 90% of 1RM, with an emphasis on slow velocity in the eccentric phase and maximal intentional contraction velocity in the concentric phase, using the unilateral limb with the greater deficit. It is important to note that a short pause (about 0.5 seconds) will be applied between the eccentric and concentric contraction phases. The sets will be separated by a 3-minute rest. If participants are able to complete more than four repetitions in a set, the load will be increased by 5.0 kg on the lat machine (Strength and Association 2021).

Patients will be encouraged to maintain their typical daily activities during the intervention period (Helgerud, Thomsen et al. 2020).

4. iTBS + MST. iTBS (Magstim Rapid2, Whitland, UK) will use standard, internationally approved parameters: 80% resting motor threshold (RMT) stimulation intensity; triplet 50 Hz bursts, repeated at 5 Hz for 2 s on and 8 s off, 10 times; 600 pulses per session; for a total duration of 3 min 20 s. To measure the RMT, the figure-of-eight coil is positioned with its center aimed at the base of the scalp in the area of cerebral cortex movement. The patient is instructed to relax completely, and the intensity of transcranial magnetic stimulation output is gradually adjusted. Five/Ten consecutive single stimulations are performed, and to be considered valid, at least five of them must induce movement-evoked potentials with an amplitude greater than 50 μ V at the minimum stimulation intensity (Sakamaki, Furusawa et al. 2022). Immediately after stimulation, they will start with the MST with the more affected upper limb, with the training sessions that will include lat machine exercises. Regarding the tests, the lat machine will be performed using a vertical lat machine apparatus. In accordance with the previous training procedure, the exercise will begin with an eccentric phase, starting

from an angle of approximately 180° in the elbow joint and progressing to a flexion of the elbow at 90°. The concentric phase then will follow a brief pause (about 0.5 seconds) and will be executed with maximal force mobilization, returning to an arm angle of about 180°, with arm raises at the end of the concentric lifting phase to engage the training of the brachial biceps. MST will be performed using the lat machine for the upper limbs, employing the 4x4 procedure from the Helgerud 2020 protocol (Helgerud, Thomsen et al. 2020).

5. Control group (healthy). This group will only undergo the baseline neuromuscular assessments without receiving any iTBS or MST intervention. The purpose of including this group is to provide a healthy reference population, matched for age, sex, height, and weight with the PD group, thereby controlling for potential confounding factors and facilitating a more accurate interpretation of the magnitude of disease-related impairments and intervention effects.

Planned Statistical Analysis

The primary analysis for the intervention study will follow a 2x2 factorial design to assess the independent and combined effects of the two factors: iTBS (real vs. sham) and MST (present vs. absent) in the patient groups. For the primary and secondary outcomes (e.g., MVC force, voluntary activation, corticospinal excitability measures, cognitive test scores), a two-way repeated-measures ANOVA will be performed with *Time* (pre- vs. post-intervention) as the within-subjects factor and *Intervention Group* (the four PD groups) as the between-subjects factor. Bonferroni correction will be used for *post hoc* analyses of significant interactions. The healthy control group, serving as a physiological comparator, will not be included in this factorial model. Baseline comparisons between all PD patients and the healthy control group will be conducted using independent samples t-tests. Statistical significance will be set at $p < 0.05$. Data will be presented as mean $\pm$ standard deviation (SD).

Expected results. With the four reference groups, we would expect the following scenarios:

1. Sham iTBS Group: With a panel that is placed between the coil and the scalp, no effect on the brain is expected, as it simulates sound and touch without inducing any physiological transcranial impact. We expect no changes in maximum strength, rate of force development (RFD), voluntary activation, motor evoked potential, silent period, corticospinal signal excitability, or neuromuscular fatigue of the limb with a greater deficit compared to the other, at both central and peripheral levels for both upper limbs. From a cognitive perspective, no changes in attention and executive functions are anticipated for this group.

2. iTBS-only Group: Stimulation of the primary motor cortex (M1) is anticipated, leading to neuroplastic changes centrally along the corticospinal tract. We expect small but significant changes in maximum strength, RFD, an increase in voluntary activation and excitability of corticospinal signals, and small but significant changes in neuromuscular fatigue of the limb

with a greater deficit compared to the other, primarily mediated by central adaptations. These changes will also be present in the contralateral arm, but the magnitude of the change will be smaller.

3. Sham iTBS combined with MST Group: The unilateral MST is expected to improve maximal strength and RFD, motor unit recruitment, but with greater central effects seen in the iTBS-only group. Neuromuscular fatigue would be ameliorated via an increase in muscular recruitment and at the peripheral level by the better muscle contractility. These positive effects will also extend to the contralateral arm, although the central effects are expected to be smaller than those observed in the iTBS-only group. Ultimately, MST can lead to improvements in executive function and attention.

4. iTBS combined with MST Group: This group is likely to experience a more significant impact on neuroplasticity due to the combined effects on the M1 area and subsequent central effects with MST training on the more affected limb. This is expected to improve maximal strength and RFD, voluntary activation, motor evoked potential, and silent period, as well as corticospinal signal excitability, and reduce neuromuscular fatigue at both central and peripheral levels. Also, for this case, we expect a positive on the contralateral limb. By combining the two interventions, a favorable cognitive outcome is expected, which is likely to significantly impact attention and executive functions.

5. Control group (healthy). None change.

Preliminary Results

Participants

Ten male patients with Parkinson's disease (PD; all right-handed, disease stage 1–2) and seven healthy male controls were initially recruited. For the analyses reported here, data from six PD patients and six controls were included. Participants were matched for age and hand dominance.

Maximal Voluntary Contraction (MVC)

Mean MVC force for the left and right hand is shown in Figure 1. No significant differences were observed between PD and controls (Left: $P = 0.17$; Right: $P = 0.24$). Within-group analyses revealed a significant left–right difference in PD ($P = 0.009$), while controls showed only a trend ($P = 0.054$). Overall, MVC performance was comparable between groups, with slightly higher right-hand force in PD participants.

Torque and Torque Normalized to CSA

Mean torque values (Figure 2) and torque normalized to muscle CSA (Figure 3) did not differ significantly between groups (Torque Left: $P = 0.09$; Right: $P = 0.11$; Normalized Torque Left: $P = 0.32$; Right: $P = 0.60$). Both groups exhibited significant left–right asymmetry in torque (PD:

$P = 0.009$; Controls: $P = 0.043$), while only the PD participants maintained asymmetry after normalization ($P = 0.03$).

Muscle Cross-Sectional Area (CSA)

Absolute and relative CSA values for left and right sides are shown in Figures 4 and 5. No significant between-group or within-group differences were detected (Absolute CSA Left: $P = 0.99$, Right: $P > 0.99$; Relative CSA Left: $P = 0.97$, Right: $P > 0.99$), indicating comparable muscle structure across groups.

Dynamic Peak Torque (qDPOT and qIPOT)

Normalized qDPOT (Figure 6) and absolute qIPOT (Figure 7) values showed no significant differences between groups or sides (all $P > 0.99$), indicating preserved dynamic torque capacity in early-stage PD.

Maximal Voluntary Activation (MVA)

Figure 7 shows MVA (%) for left and right sides. Similar values across groups and sides suggest that voluntary muscle activation is largely preserved in PD.

Corticospinal Excitability

MEP amplitude (P2P; Figure 8) and area under the curve (AUC; Figure 9) did not differ significantly between PD and controls for either hemisphere (Amplitude Left: $P = 0.89$, Right: $P = 0.29$; AUC Left: $P = 0.96$, Right: $P = 0.16$). Within-group comparisons revealed no hemispheric asymmetry in PD, while controls showed a non-significant trend for AUC ($P = 0.06$).

Statistical Analysis for Preliminary Data

For the baseline comparisons between PD patients and healthy controls, data were analyzed using two-way repeated-measures analysis of variance (ANOVA). The model included the between-subjects factor Group (PD, Control) and the within-subjects factor Side (Left, Right). When a significant interaction or main effect was found, Bonferroni post hoc tests were applied for multiple comparisons. Statistical significance was set at $p < 0.05$. Data in the text and figures are presented as mean $\pm$ standard deviation (SD).

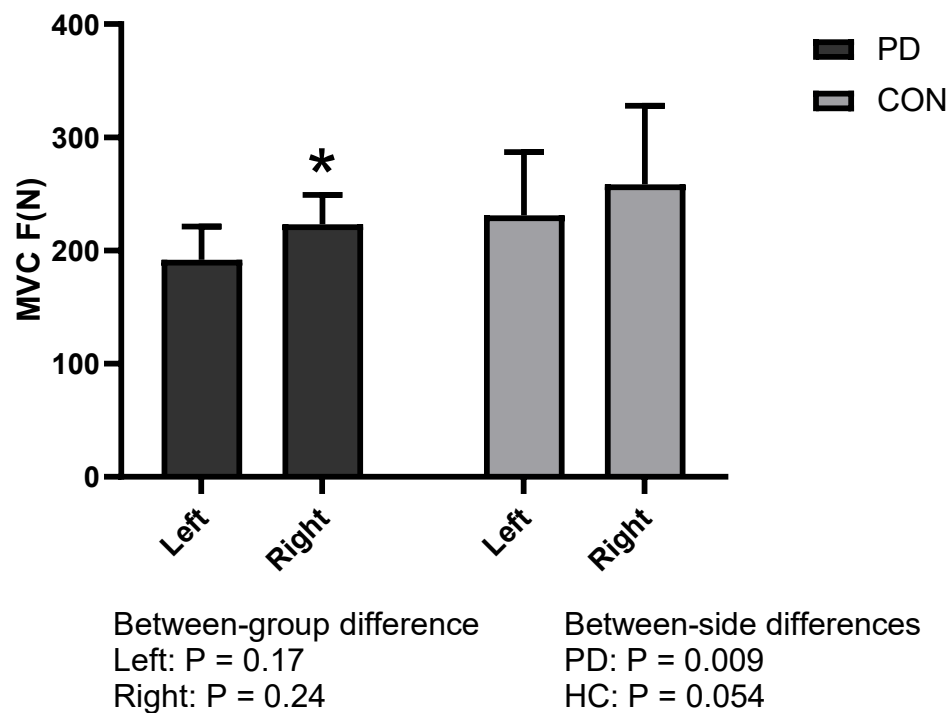


Figure 1 Maximal Voluntary Contraction (MVC) force. Bar graph showing the mean MVC force (N) for the left and right hand in PD patients and healthy controls. PD participants exhibit significant lateralization (higher right-hand force), whereas no significant differences were observed between groups.

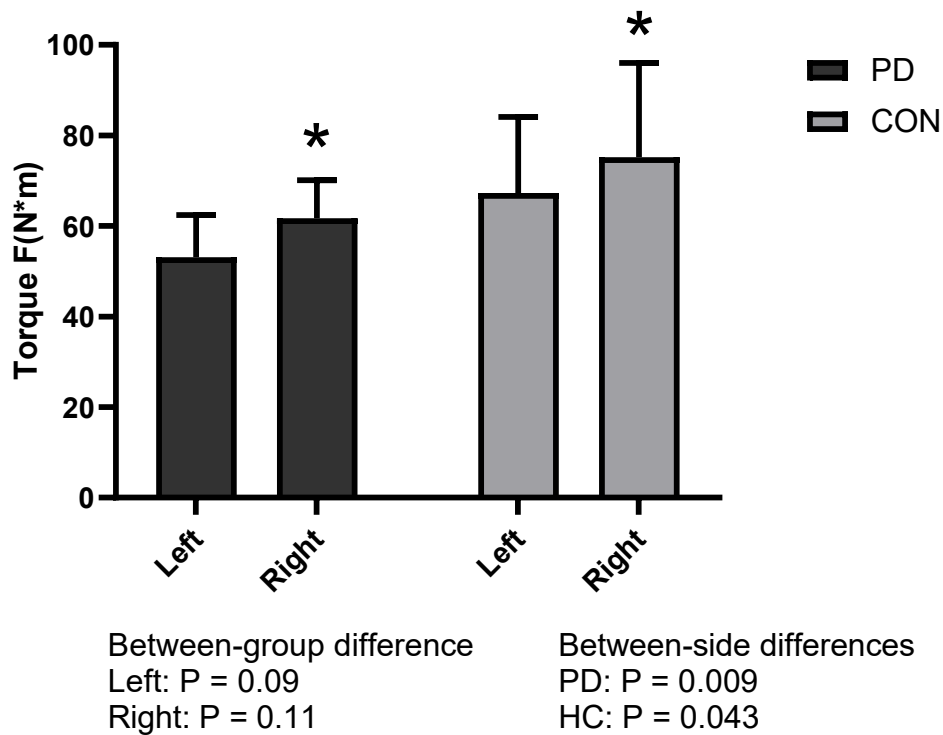


Figure 2 Torque values (N·m). Bar graph illustrating the mean torque for left and right sides in PD and control groups. Both groups display slightly higher torque on the right side; PD participants show significant lateralization, whereas controls show a smaller trend.

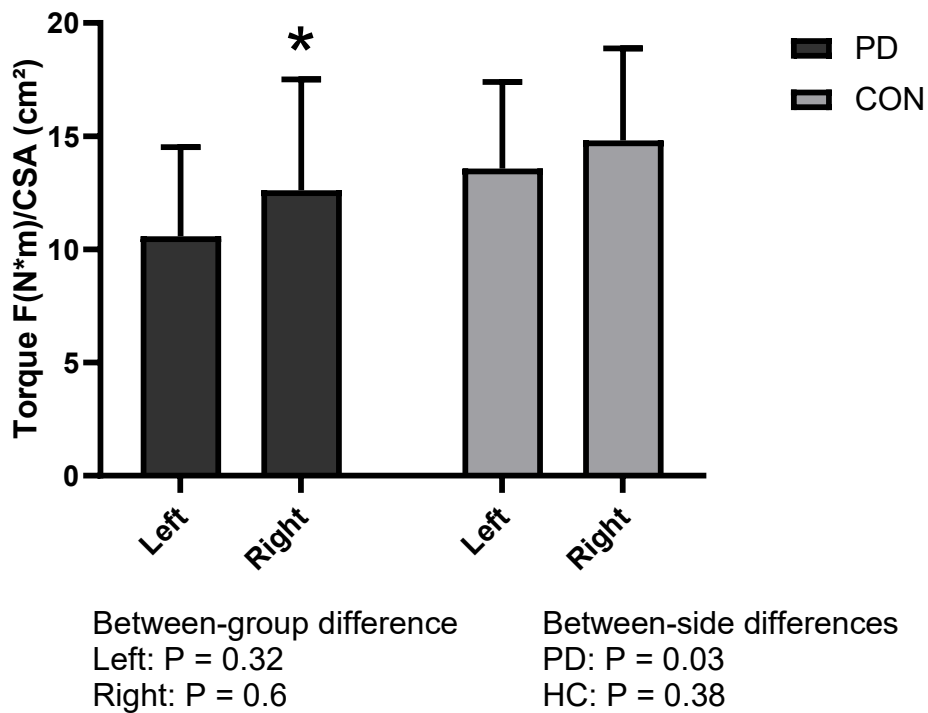


Figure 3 Torque normalized to muscle cross-sectional area ($\text{N}\cdot\text{m}/\text{cm}^2$). Mean normalized torque for left and right sides in PD and control groups. PD participants demonstrate significant left–right differences; no significant between-group differences are observed.

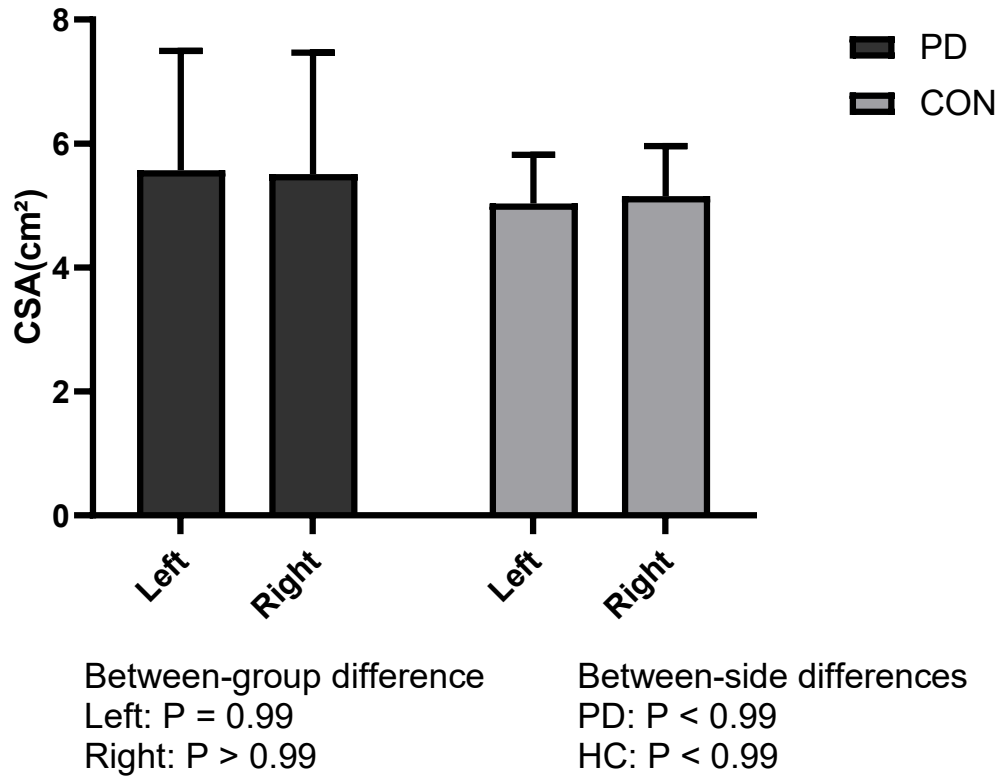


Figure 4 Absolute muscle cross-sectional area (CSA, cm^2). Bar graph showing CSA for left and right sides in PD and controls. No significant differences are observed between groups or between sides within groups.

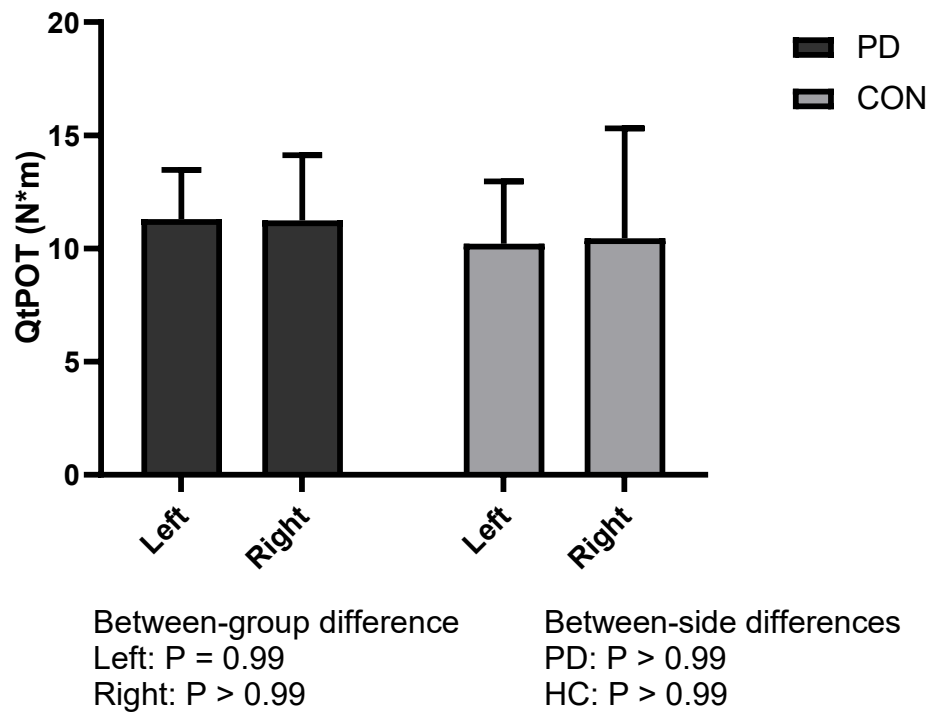


Figure 5 Normalized qDPOT ($\text{N}\cdot\text{m}^2/\text{cm}^2$) in PD and CON participants for the left and right sides. No significant group or side differences were found (*all* $P > 0.99$).

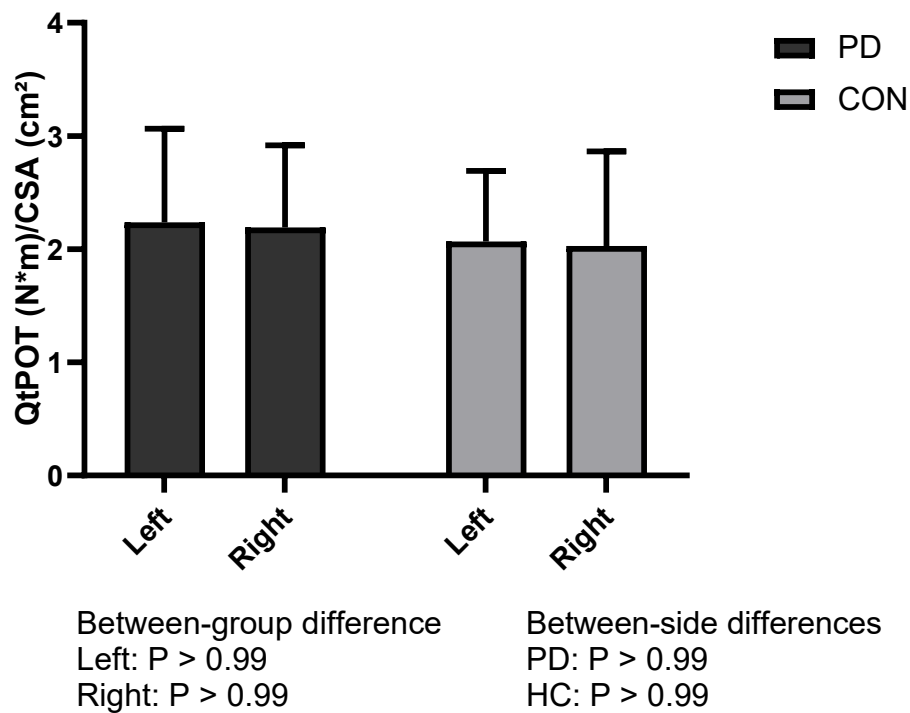


Figure 6 Absolute qIPOT (N·m) in PD and CON participants for the left and right sides. No significant group or side differences were detected (*all* $P > 0.99$).

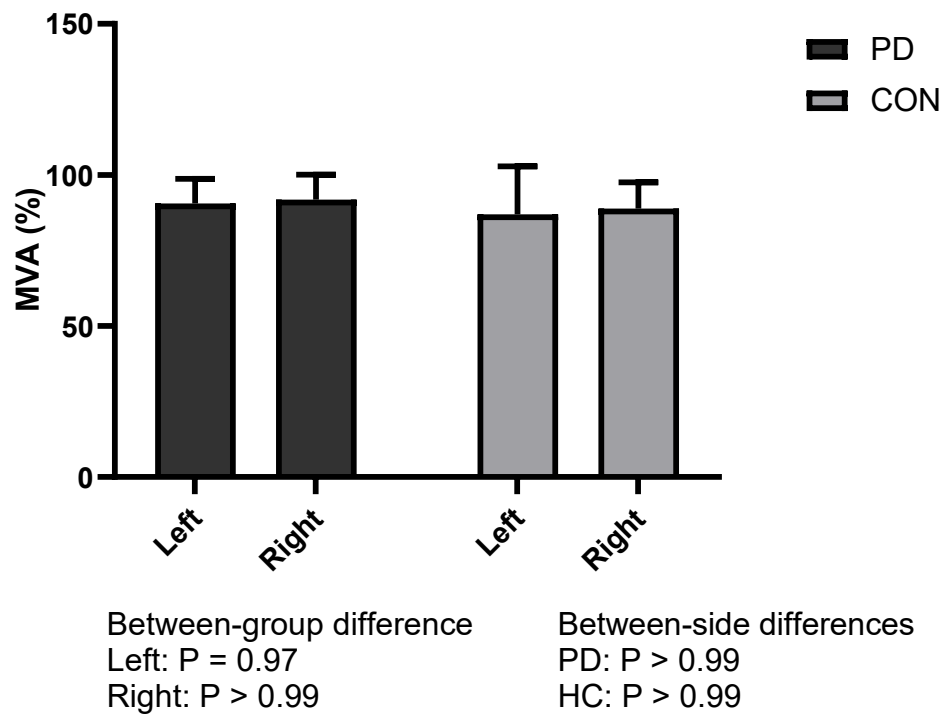


Figure 7 Maximal Voluntary Activation (MVA, %). Percentage of maximal voluntary activation for left and right sides in PD and control participants. Similar values across groups and sides indicate that the ability to fully activate the muscles voluntarily is comparable.

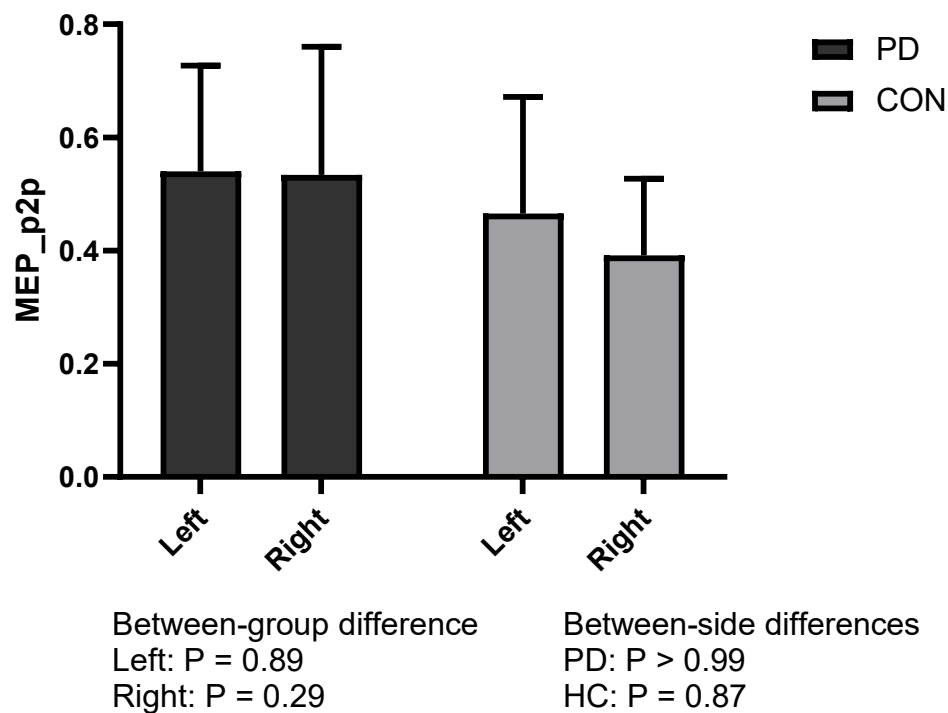


Figure 8 MEP amplitude ratios. Bar graph representing MEP amplitude ratios for left and right hemispheres in PD and control groups. No significant differences were detected between groups or hemispheres.

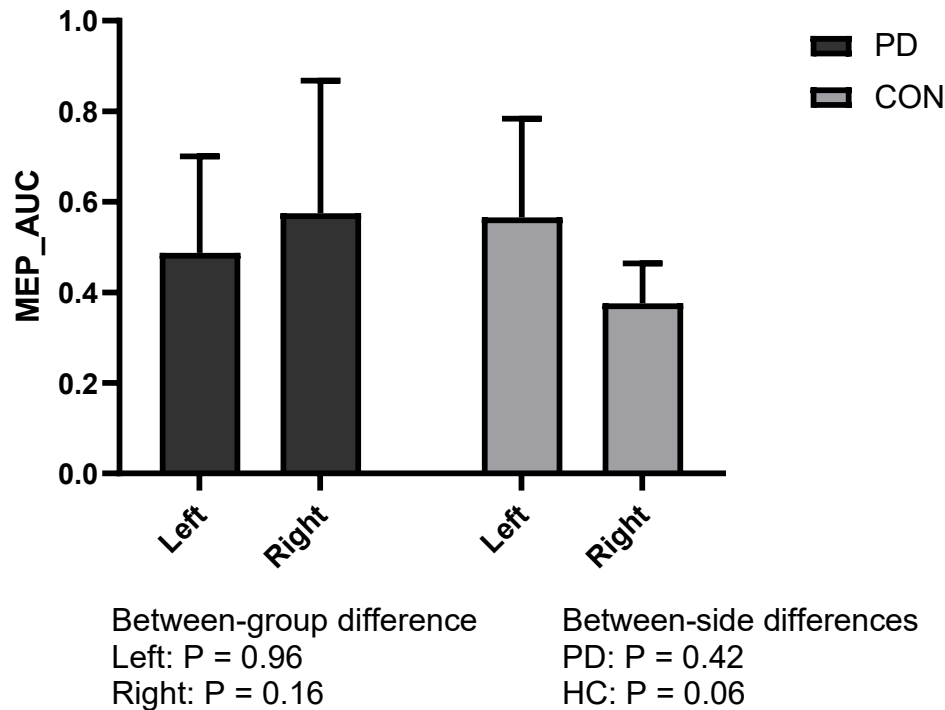


Figure 9 MEP area under the curve (AUC). Mean MEP_AUC values for left and right hemispheres in PD and controls. No significant differences are observed, indicating preserved corticospinal excitability in early-stage PD.

Discussion

This study protocol describes a randomized controlled trial designed to evaluate the effects of intermittent theta burst stimulation (iTBS) and maximal strength training (MST), alone and in combination, on upper limb maximal force production and neuromuscular fatigue in patients with Parkinson's disease (PD). To our knowledge, this is the first trial to explore the synergistic effects of iTBS and MST specifically targeting the most affected upper limb in PD patients.

Most rehabilitation studies in PD have focused on lower limb impairments, particularly gait and balance (Dibble, Addison et al. 2009, Schilling, Pfeiffer et al. 2010, Vieira de Moraes Filho, Chaves et al. 2020), whereas upper limb dysfunctions remain less investigated, despite their critical impact on autonomy and quality of life (Proud, Miller et al. 2013). Moreover, non-invasive brain stimulation techniques such as TMS have been increasingly studied for their potential to induce neuroplastic changes (Huang, Edwards et al. 2005, Chu, Cheng et al. 2021, Rossi, Antal et al. 2021), but data on their interaction with strength training interventions in PD are limited. This trial addresses this gap by combining a neuromodulatory approach with evidence-based resistance training.

Baseline neuromuscular function

Across all measures, including maximal voluntary contraction (MVC, Figure 1), torque (Figures 2–3), muscle cross-sectional area (CSA, Figures 4–5), dynamic peak torque (qDPOT and qIPOT, Figures 6–7), maximal voluntary activation (MVA, Figure 7), and corticospinal excitability (MEP amplitude and AUC, Figures 8–9), early-stage PD patients exhibited largely preserved neuromuscular function relative to controls. No significant between-group differences were observed, indicating that early-stage PD does not entail substantial deficits in muscle strength, structure, or corticospinal drive.

Functional lateralization

Within-group analyses revealed lateralized asymmetries in PD patients, with higher MVC and torque on the more dominant and affected limb (Figures 1–3). These functional differences were not accompanied by structural disparities (Figures 4–5), suggesting that asymmetries are likely mediated by central neural mechanisms rather than peripheral muscle properties. This pattern aligns with the typical asymmetric progression of PD and supports the rationale for targeting unilateral training interventions on the most affected limb.

Corticospinal excitability

Measures of corticospinal excitability, including MEP amplitude and AUC, did not differ between PD and controls or between hemispheres (Figures 8–9). The preserved corticospinal function at baseline indicates that any post-intervention changes observed following iTBS, MST, or their combination can be interpreted as genuine neuroplastic adaptations rather than recovery from pre-existing deficits.

Implications for intervention

The preservation of baseline neuromuscular capacity suggests that iTBS and MST interventions have the potential to enhance neuromuscular plasticity rather than merely restore deficits. The lateralized asymmetries observed further justify the focus on unilateral training of the most affected limb.

The rationale for combining iTBS with MST is grounded in the concept of 'gating' or 'priming' neuroplasticity. iTBS is postulated to transiently increase cortical excitability and lower the threshold for long-term potentiation (LTP)-like plasticity within the corticospinal pathway targeting the trained muscle (Huang, Edwards et al. 2005, Suppa, Quartarone et al. 2017). When performed immediately prior to MST, a potent stimulus for both neural drive and muscle adaptation, this primed state may facilitate superior encoding of the motor task, leading to greater and more sustained gains in strength and fatigue resistance compared to either intervention alone (Cirillo, Todd et al. 2011, Carson and Kennedy 2013).

While maximal force production is our primary mechanistic outcome, a key secondary aim is to assess whether gains in strength translate to improved resistance to neuromuscular fatigue, a common and debilitating symptom in PD that contributes to reduced physical activity and quality of life (Friedman, Brown et al. 2007, Lou 2009). Fatigue will be quantified using a sustained submaximal contraction protocol, measuring the decline in force output and

changes in electromyographic (EMG) spectral properties (central vs. peripheral components) over time (Gandevia, 2001; Enoka & Duchateau, 2008)(Gandevia 2001).

The safety and tolerability profiles of both iTBS (Rossi, Antal et al. 2021) and MST (Bickel, Cross et al. 2011) are well-established in neurological and older populations. This trial will systematically monitor and report adverse events, adherence rates, and participant satisfaction to inform future clinical implementation.

Limitations

Finally, this study has some limitations. Its single-center nature may introduce a potential selection bias, and the preliminary sample is small and homogeneous. Furthermore, adherence to the MST protocol may vary depending on individual daily fatigue levels, which are typical of PD; however, supervised sessions are implemented to mitigate this issue. Nonetheless, if successful, this trial will provide foundational evidence supporting the integration of iTBS and MST into rehabilitation programs for PD, with direct clinical implications for improving upper limb function.

Looking beyond the horizon of this specific protocol, its translational potential to home-based or community settings represents a compelling future direction, increasingly facilitated by technological advances (Evancho, Tyler et al. 2023). A hybrid 'supervision-initiated, self-management-sustained' model appears to be the logical evolution (Godinho, Domingos et al. 2016, Evancho, Tyler et al. 2023). In this framework, the intensive clinical phase described here, characterized by neuronavigated iTBS and high-intensity MST with isotonic machines, would serve as a powerful "priming" intervention to maximize neuromuscular and neuroplastic adaptations (e.g., those mediated by BDNF) (Bolognini, Pascual-Leone et al. 2009, Celnik 2015). Subsequently, for the long-term maintenance phase at home, the neuromodulation component could be transitioned into portable, remotely supervised devices for transcranial direct current stimulation (tDCS) or alternating current stimulation (tACS) (Kasschau, Sherman et al. 2015, Charvet, Dobbs et al. 2018), providing a practical tool to help sustain corticospinal excitability.

Concerning the strength training component, it is crucial to emphasize that a simple switch to standard elastic bands would likely be insufficient to preserve the high-level neural adaptations induced by the original MST. However, the scientific literature robustly demonstrates that once improvements are achieved, the volume and intensity required to *maintain* strength and neural adaptations are significantly lower than those required to *induce* them (Taaffe, Duret et al. 1999, Bickel, Cross et al. 2011). Therefore, the home-based phase does not necessarily need to replicate the peak intensity of the clinical phase but must be sufficiently challenging to prevent detraining. Future studies should test home-based protocols utilizing compact yet quantifiable equipment (e.g., digitally adjustable resistance systems, adjustable dumbbells, or high-resistance elastic bands with monitored rate of perceived exertion) (Lopes, Machado et al. 2019), all within a structured framework of remote supervision and periodic in-clinic booster sessions.

This decentralized approach would not only significantly enhance the accessibility and sustainability of high-quality rehabilitation, thereby reducing the burden on patients and healthcare systems, but also promote long-term adherence by integrating therapy into daily life and actively empowering patients. Subsequent studies can validate this hybrid pipeline by

examining its long-term effects in larger, multicenter cohorts and measuring its crucial impact on activities of daily living and quality of life.

Future directions

Future research should incorporate neuroimaging techniques, such as fMRI or EEG, during maximal contractions to map cortical activation patterns and assess post-intervention changes in central connectivity (Polania, Nitsche et al. 2018, Ciccarelli, Colombo et al. 2022). Larger cohorts and longer-term follow-ups will be necessary to evaluate the sustainability and generalizability of the observed effects (Corcos, Robichaud et al. 2013). Extending beyond the scope of the present protocol, a logical next step to unravel the underlying biology would be to incorporate biomarker and genetic analyses. For example, one could collect blood samples at baseline and post-intervention to analyze serum levels of BDNF and relevant myokines (e.g., irisin) using ELISA (Wrann, White et al. 2013, Polacchini, Metelli et al. 2015). Additionally, DNA could be extracted for genotyping of the BDNF val66met polymorphism (rs6265) (Egan, Kojima et al. 2003). Such analyses would help explore the humoral and genetic mediators of intervention response (Venezia, Quinlan et al. 2017). These mechanistic insights would be crucial for personalizing interventions and for informing the next step in the translational pipeline: the development of a sustainable, hybrid care model.

Conclusions

Preliminary data indicate that in early-stage PD, strength, muscle structure, and corticospinal excitability are largely preserved relative to healthy controls. Functional lateralization supports the use of targeted unilateral training interventions. The combined iTBS and MST design has the potential to induce true neuroplastic adaptations rather than merely restoring baseline function. These baseline findings provide a solid foundation for interpreting post-intervention changes and highlight the clinical relevance of the trial. Future studies should examine the relationship between cortical connectivity changes and functional improvements, as well as long-term effects in larger and more diverse cohorts.

4. Biomechanical gait alterations under dual-tasking in Parkinson's disease: A systematic review

Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disorder now recognized as a complex multisystem synucleinopathy (Morris, Spillantini et al. 2024). While traditionally characterized by the degeneration of dopaminergic neurons in the substantia nigra pars compacta, leading to classic motor deficits such as bradykinesia, rigidity, resting tremor, and postural instability (Poewe, Seppi et al. 2017), the underlying pathophysiology extends beyond dopamine deficiency to involve widespread neural networks critical for both motor and cognitive function (Bloem, Okun et al. 2021). This systems-level disruption provides the neurobiological substrate for the complex interplay between motor and cognitive deficits that characterizes PD. These motor impairments are often accompanied by cognitive deficits, particularly in executive function, attention, and working memory, which further limit functional independence and quality of life (Goldman and Litvan 2011, Kehagia, Barker et al. 2013). Among the most disabling manifestations, gait and balance disturbances significantly increase fall risk, reduce mobility, and compromise autonomy (Hausdorff 2009, Lord, Baker et al. 2011).

Dual-task (DT) paradigms, in which a cognitive or motor secondary task is performed concurrently with walking, highlight the interaction between motor and cognitive deficits in PD, a phenomenon observed across neurodegenerative diseases, including Alzheimer's and Parkinson's (Kelly, Eusterbrock et al. 2012, Yogev-Seligmann, Giladi et al. 2013, Longhurst, Rider et al. 2023). In healthy adults, gait is largely automatic; however, in PD, basal ganglia dysfunction impairs automaticity, necessitating increased attentional control via prefrontal circuits (Wu, Hallett et al. 2015). DT performance in PD is associated with slower gait, reduced stride length, increased variability, and higher fall risk, and the decline from single-task (ST) to DT walking is commonly quantified as the dual-task cost (DTC). Cognitive secondary tasks, such as serial subtraction or verbal fluency, generally elicit a higher DTC than motor tasks due to greater attentional demands (Wild, de Lima et al. 2013). Disease progression further reduces

attentional capacity and motor automaticity, amplifying reliance on compensatory mechanisms (Fritz, Cheek et al. 2015, Wu, Hallett et al. 2015).

Neuroimaging and electrophysiological studies link DT deficits in PD to compensatory prefrontal activation and basal ganglia dysfunction, in line with the Compensation-Related Utilization of Neural Circuits Hypothesis (CRUNCH) (Kim and Fraser 2022). Dopamine depletion disrupts automatic gait control, increasing reliance on prefrontal cognitive resources for motor regulation (Orcioli-Silva, Vitorio et al. 2020). Functional neuroimaging and electrophysiological studies also report altered theta and beta oscillations in the prefrontal cortex, subthalamic nucleus, and pedunculopontine nucleus during DT walking, reflecting a shift from automatic to controlled locomotor strategies (Nwogo, Kammermeier et al. 2022). Further, a previous study has observed DTC seems to be related to cognitive state and neuromuscular function (Ivaniski-Mello, Müller et al. 2023). These findings emphasize the importance of cognitive-motor integration interventions for improving gait and mobility (Sarasso, Parente et al. 2024).

While DT clearly impairs gait performance, the specific biomechanical changes underlying these deficits remain less explored. Most meta-analyses have focused on spatiotemporal parameters such as velocity, cadence, and stride time variability (Raffegau, Krehbiel et al. 2019, Sarasso, Parente et al. 2024), whereas kinematic measures, including joint angles and range of motion, and kinetic parameters, such as joint moments and power generation, have received less attention. Recent studies provide important insights into these aspects, showing altered lower-limb joint kinematics during DT walking, changes in dynamic joint stiffness and joint power generation (Galna, Lord et al. 2012), longitudinal variations in DTC across disease stages (Kocer, Gulsen et al. 2023), and modulation of gait outcomes by attention prioritization and cueing strategies (Bianchini, Warmerdam et al. 2022, Van Crielinge, Sahu et al. 2024). Understanding these biomechanical alterations is crucial for explaining the stooped posture, shuffling gait, and instability typical of PD, and for guiding targeted rehabilitation strategies.

A major limitation in the literature is methodological heterogeneity, including differences in DT protocols, walking conditions (treadmill versus overground), and biomechanical analysis techniques, which restrict comparability across studies (Fritz, Cheek et al. 2015, Parati, Ambrosini et al. 2022). This heterogeneity extends to the measurement of dual-task interference itself, underscoring the need for novel, standardized assessment tools with demonstrated reliability and validity in neurodegenerative populations (Longhurst, Rider et al. 2022). Critically, variability in task prioritization instructions (e.g., "focus on walking" vs. "focus on the cognitive task") and the use of cueing techniques are also significant problems, as they directly influence attentional resource allocation and DT outcomes (Kelly, Eusterbrock et al. 2012, Strouwen, Molenaar et al. 2017). While instrumented treadmills and walkways provide reliable spatiotemporal data, these fundamental differences in experimental design pose a substantial challenge for standardization and the synthesis of findings.

By synthesizing biomechanical evidence from observational and interventional studies, this systematic review aims to characterize gait alterations under DT conditions in PD, identify methodological gaps in assessment, and provide recommendations for standardized protocols, such as those recently proposed by Longhurst et al. (2022), as well as targeted rehabilitation strategies (Longhurst, Rider et al. 2022). A better understanding of DT gait alterations will support the development of more precise rehabilitation approaches aimed at improving mobility and reducing fall risk in individuals with PD.

Methods

Search strategy and selection criteria

For this review, a systematic literature search was conducted across multiple databases, including Cochrane Library, EBSCO, PubMed, Scopus, and Web of Science. The search strategy involved using a combination of key terms related to PD, Parkinsonism, dual-tasking, and gait biomechanics. Specifically, the search string included terms such as “Parkinson’s disease” OR “Parkinsonism,” along with “dual-task” OR “dual-tasking,” and various gait-related terms like “gait,” “walking,” and “locomotion,” as well as biomechanical measures like “joint kinematics,” “hip angles,” “knee angles,” and “stride length.” This broad search was designed to maximize study inclusion, ensuring that all relevant studies were captured, regardless of language or publication date.

However, to refine the search results, we applied specific language and time filters. Only studies published in English, Portuguese, or Spanish were considered, and we focused on studies published from January 1, 2000, to March 11, 2025. These parameters were chosen to ensure that the studies included in this review were both contemporary and linguistically accessible to the research team, ensuring accurate data extraction and critical appraisal. While the inclusion of Italian-language research would have been relevant given the authors' affiliation, the decision to exclude it was pragmatic, aligning with the most common languages in the international scientific literature in this field and maintaining a feasible scope for the systematic review process. This review follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page, McKenzie et al. 2021) and has been registered in PROSPERO (registration CRD420251004404). No amendments were made to the review protocol as registered in PROSPERO. The completed PRISMA 2020 checklist is provided as Supplementary File 1.

The studies eligible for inclusion met specific criteria outlined by the PECOS DTR Model (Methley, Campbell et al. 2014), which were carefully defined to ensure consistency and relevance across the studies selected.

Population (P): Eligible studies included individuals diagnosed with Parkinson's disease (PD) who were evaluated during the "on" medication phase, irrespective of age, sex, or disease stage. Studies were excluded if they: (1) focused on specific populations such as essential

tremor, postural alterations (e.g., camptocormia or Pisa syndrome), or de novo PD; or (2) focused on, or included a dedicated analysis of, Freezing of Gait (FoG). This exclusion criterion applies both to studies where FoG was the primary research focus (e.g., explicit "FoG vs. non-FoG" comparisons) and to those where patients with FoG were analyzed as a distinct subgroup. No data extraction or selective analysis of non-FoG subgroups from such studies was performed. Consequently, the synthesis is based exclusively on studies investigating general PD cohorts without a specific focus on FoG.

Exposure (E): All participants were required to undergo dual-task conditions during a walking evaluation, which could either be free walking or treadmill walking, with kinematic analysis. There was no separate intervention group, meaning that all participants performed the same tasks but under different conditions. Studies were excluded if participants exhibited significant differences in walking speed between the lower limbs. This criterion was applied to minimize biomechanical heterogeneity and ensure that dual-task effects on gait could be interpreted consistently across participants. Large inter-limb speed differences could confound kinematic measures and obscure the specific impact of dual-task conditions on walking performance.

Comparison (C): Healthy, age-matched individuals were used as the comparison group. Studies that included individuals with comorbidities that significantly affect gait, such as neurological disorders (e.g., stroke, multiple sclerosis, dementia), musculoskeletal disorders (e.g., severe osteoarthritis), cardiovascular diseases (e.g., heart failure), vestibular disorders (e.g., chronic dizziness), and metabolic diseases (e.g., diabetes with complications) were excluded. Additionally, studies lacking a control group were also excluded.

Outcome (O): The primary outcomes of interest were spatiotemporal gait measures and biomechanical parameters. These included, but were not limited to, self-selected walking speed (SSWS), stride length, cadence, step width, and various joint kinematics such as hip, knee, and ankle angles. Postural control measures, such as the center of pressure trajectory, were also taken into consideration. Studies were excluded if they did not report the variables of interest or contained duplicate data.

Duration (D): Only studies that involved acute evaluations, such as a single session or measurement under dual-task conditions, were included. Longitudinal studies were considered only if the data came from the baseline (pre-intervention) measurement.

Study Design (S): Eligible study designs included both observational and experimental studies that had a healthy control group. For longitudinal studies that measured biomechanical parameters more than once, only the first measurement (baseline) was considered. Studies involving animal models, books, conference abstracts, editorials, meta-analyses, narrative reviews, protocols, and systematic reviews were excluded.

In terms of language and time filters, only studies published in English, Portuguese, or Spanish were considered, and the time frame was limited to research published between January 1, 2000, and March 11, 2025.

A structured search strategy was employed using Boolean operators (AND, OR, NOT) and keywords related to PD, dual-tasking, gait, and relevant biomechanical measures. Specific search strings were tailored for each database to ensure optimal retrieval of relevant studies. For example, in PubMed, the search string was constructed as follows:

(Parkinson Disease[MeSH Terms] OR Parkinson Disease*) AND (Dual-Task* OR Double-task*) AND (Gait[MeSH Terms] OR Neurologic Gait Disorder [MeSH Terms] OR Gait Analysis[MeSH Terms] OR Walking[MeSH Terms] OR Walking Speed[MeSH Terms] OR Biomechanical Phenomena[MeSH Terms] OR Locomotion[MeSH Terms] OR Biomechanic* OR Gait OR Walking OR Step OR Kinematic OR Spatiotemporal Parameter OR Walking Speed OR Stride Length OR Stride Frequency OR Cadence OR Step Width OR Double Support Duration OR Single Support Duration OR Swing Time OR Range of Motion OR Joint Angles) AND (Control Group OR Healthy Control* OR Age-Matched Control*) NOT (Meta-Analysis[Title/Abstract] OR Systematic Review [Title/Abstract])

This search string was adjusted for each database to ensure a comprehensive and relevant selection of studies.

Study Selection and Data Extraction. Two independent reviewers screened studies based on their titles and abstracts, followed by a full-text review. Any disagreements were resolved through discussion or consultation with a third reviewer. Data from eligible studies were extracted using a standardized form that included information on population characteristics (age, sex, disease stage, and medication status), task or experimental conditions (dual-task conditions and walking conditions), comparison group characteristics, and outcome measures. Additional data related to study design, methodology, and potential confounders (e.g., cognitive status, comorbidities) were also collected.

Study quality assessment

The methodological quality and risk of bias of the included studies were assessed independently by two reviewers. Given that the focus of this review was on baseline dual-task performance (prior to any intervention), all studies were considered as observational cross-sectional studies for the purpose of quality assessment. Consequently, a single, unified tool, the AXIS tool (Appraisal tool for Cross-Sectional Studies), was employed to evaluate all studies (Downes, Brennan et al. 2016). Although the AXIS tool does not provide formal cut-off points, a pragmatic categorization of study quality was applied to facilitate comparison across studies. Specifically, studies scoring ≥ 16 were classified as high quality, those scoring 11–15 as moderate quality, and those scoring ≤ 10 as low quality. These thresholds were defined a priori and align with approaches commonly adopted in previous systematic and umbrella reviews.

The reporting quality of observational studies was assessed with reference to the STROBE guidelines (Vandenbroucke, von Elm et al. 2007) to ensure transparent and complete reporting.

To specifically evaluate the methodological rigor of the dual-task (DT) protocols, a key focus of this review, a customized checklist was applied. This checklist was adapted from established methodological frameworks for DT paradigms, primarily drawing on the work of Plummer-D'Amato et al. (2011) and Plummer & Eskes (2015) (Plummer-D'Amato, Altmann et al. 2011, Plummer and Eskes 2015), which have been cited in previous reviews for assessing key elements such as task standardization, real-world applicability of the tasks, and cognitive load assessment. The framework proposed by Yogev-Seligmann (2008) also informed the evaluation of attentional prioritization aspects (Yogev-Seligmann, Hausdorff et al. 2008). Furthermore, the checklist incorporated the principle of measuring subjective cognitive load (e.g., using tools like the NASA-TLX) (Hart and Staveland 1988). This tailored tool enabled a consistent and transparent evaluation of the DT-specific methodology across all included studies.

Discrepancies in quality assessment were resolved through discussion or consultation with a third reviewer.

Data analysis

A narrative synthesis was conducted to describe biomechanical gait alterations under DT conditions in individuals with PD compared to single-task (ST) walking and healthy controls. Differences were analyzed based on disease severity, as measured by the H&Y and MDS-UPDRS III scales, type of secondary task (cognitive, motor, or mixed), and walking conditions, distinguishing between treadmill and overground walking. Additional factors included baseline cognitive function, as indicated by MoCA scores, and symptom lateralization, considering the affected side (dominant vs. non-dominant). All included data were collected during the ON phase of dopaminergic medication, and only baseline measures were considered, with no analysis of post-training or intervention effects.

If sufficient homogeneity was present across studies, a random-effects meta-analysis was conducted to estimate the overall effect. Standardized Mean Differences (SMD) and 95% Confidence Intervals (CI) were calculated for biomechanical parameters. Heterogeneity was assessed using the I^2 statistic, with thresholds of $I^2 < 25\%$ indicating low heterogeneity, 25–50% moderate heterogeneity, and $>50\%$ high heterogeneity.

Meta-regression analyses explored associations between biomechanical alterations and clinical severity markers (MDS-UPDRS III, H&Y), demographic variables (age, disease duration), assessment tools (GAITRite vs. IMU vs. motion capture), DT type (cognitive vs. motor vs. mixed), dopaminergic state (ON only), cognitive function (MoCA score), presence of FoG, and lateralization effects.

A sensitivity analysis was performed to ensure the robustness of findings by excluding studies with a high risk of bias or small sample sizes, conducting separate analyses with and without the inclusion of RCT baseline data, assessing measurement tool variability by comparing GAITRite, IMU, and motion capture, investigating the impact of dopaminergic states by analyzing ON vs. OFF conditions, and examining the influence of cognitive impairment severity based on MoCA cutoff values.

Missing data (e.g., unreported standard deviations) were not imputed. The synthesis was based solely on the data available in the included studies.

Publication bias

A formal assessment of publication bias for the present narrative synthesis was not feasible due to the significant heterogeneity of the included studies and the lack of a pooled effect size. An assessment of publication bias using statistical methods (e.g., funnel plots and the test by Egger et al., 1997)(Egger, Davey Smith et al. 1997) will be conducted as part of a planned future meta-analysis, once enough homogeneous studies are available for quantitative synthesis.

Considerations or intervention strategies

A subgroup comparison of different dual-task conditions was performed to explore whether cognitive or motor secondary tasks had differing impacts on gait performance according to disease severity. Long-term effects or neuroplastic adaptations could not be evaluated, as the included studies only reported baseline assessments.

Preliminary results

Figure 1 illustrates the study selection process for a systematic review on PD and dual-task activities, following the PRISMA 2020 guidelines (Page, McKenzie et al. 2021). A total of 1,960 records were identified from five databases: PubMed (220 records), Scopus (821 records), EBSCO (305 records), Cochrane Library (220 records), and Web of Science (394 records). Before screening, 621 duplicate records were removed, along with 20 records due to import failures or formatting issues. From the initial 1,315 records screened, 1,236 were excluded. The remaining 79 full-text reports were assessed for eligibility. Of these, 35 were excluded due to irrelevant outcomes, population, or study design (e.g., for focusing on FOG). One additional record (Nishida et al., 2020) was excluded as it was a review article published in a language other than English, Portuguese, or Spanish, thereby failing both the publication type and language criteria. Finally, 44 studies met the inclusion criteria and were included in the systematic review. The diagram provides a clear overview of the selection process, highlighting the key screening stages and exclusion criteria applied to ensure the relevance and quality of the studies analyzed. The characteristics of the included study samples, including demographic and clinical data, are synthesized in Table 1. The experimental

protocols, detailing dual-task paradigms, outcome measures, and methodological setups, are summarized in Table 2.

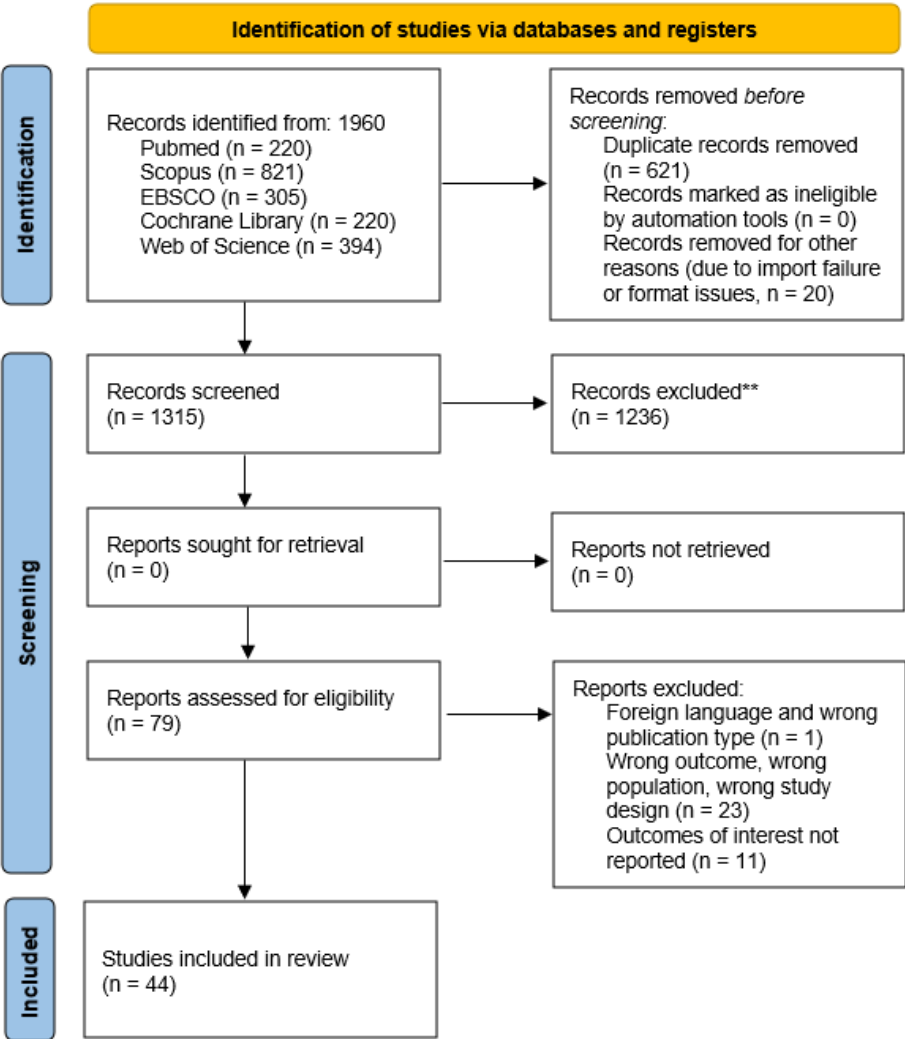


Figure 1. PRISMA 2020 flow diagram for new systematic reviews, which included searches of databases, registers, and other sources. A detailed table of excluded studies with specific reasons is provided in Supplementary Table S1.

Data Synthesis

A formal meta-analysis was not conducted at this stage due to the significant methodological, clinical, and statistical heterogeneity among the included studies. The results are, therefore, presented as a narrative synthesis. A quantitative synthesis (meta-analysis) of the data is

planned as a subsequent phase of this project once additional data standardization and collection are complete.

Characteristics of the Included Studies

This systematic review incorporated a total of 44 studies, published over a span of more than two decades (2002–2025), reflecting the growing and sustained interest in the biomechanics of DT walking in PD. The collective evidence presents a methodologically rich and diverse landscape, characterized by a range of designs, participant profiles, and technological approaches.

Study Designs and Populations

The foundational evidence comes from a majority of observational, cross-sectional studies (e.g., Alcock et al., 2016; Álvarez et al., 2020; Rochester et al., 2014)(Rochester, Galna et al. 2014, Alcock, Galna et al. 2016, Alvarez, Latorre et al. 2020), which provide critical snapshots of DT interference across the PD spectrum. This corpus is robustly complemented by experimental and repeated-measures designs that investigate the effects of specific manipulations. For instance, Baker et al. (2008) and Brown et al. (2009)(Baker, Rochester et al. 2008, Brown, de Bruin et al. 2009) employed within-subject designs to dissect the impact of different cueing types on gait variability, while Harrison et al. (2018) implemented a randomized crossover trial to compare distinct age groups and PD patients (Harrison, Horin et al. 2018).

The scope of the included studies is evidenced by their sample sizes, which range from focused, in-depth investigations with smaller cohorts (e.g., n=9 PD, Fernandes et al., 2016; n=10 PD, Brown et al., 2009)(Brown, de Bruin et al. 2009, Fernandes, Sousa et al. 2016) to large-scale studies that enable powerful analyses and subgroup stratification (e.g., n=121 PD, Rochester et al., 2014; n=97 PD, Seuthe et al., 2024; n=111 total, Krupička et al. 2024)(Rochester, Galna et al. 2014, Krupička, Malá et al. 2024, Seuthe, Hermanns et al. 2024).

A detailed analysis of participant characteristics reveals a consistent clinical profile

The mean age of PD participants typically fell between 60 and 75 years, accurately reflecting the demographic most affected by the disease. Sex distribution was generally balanced, although a slight male predominance was noted in several cohorts (Stuart, Lord et al. 2018, Graham, Armitage et al. 2023). Disease severity predominantly assessed using the Hoehn and Yahr (H&Y) scale (Hoehn and Yahr 1967), clustered in the mild to moderate stages (I-III), indicating a focus on ambulatory patients where gait rehabilitation is most relevant. Disease duration varied widely, from newly diagnosed cohorts (Rochester, Galna et al. 2014) to those with long-standing disease exceeding 10 years (Rochester, Hetherington et al. 2005). The systematic assessment of global cognition via the Mini-Mental State Examination (MMSE) or Montreal Cognitive Assessment (MoCA) confirmed that most studies involved patients without dementia, thus isolating the motor-cognitive interference of DT from major cognitive decline (Folstein, Folstein et al. 1975, Nasreddine, Phillips et al. 2005). Importantly, a

significant number of studies deliberately stratified their analysis by clinically relevant subgroups, specifically focusing on patients with Mild Cognitive Impairment (MCI+)(Amboni, Barone et al. 2012), FoG (Baker, Rochester et al. 2008), or specific motor phenotypes such as Postural Instability/Gait Difficulty (PIGD) and Tremor-Dominant (TD)(Micó-Amigo, Kingma et al. 2019, Álvarez, Latorre et al. 2020).

Technological sophistication and multi-modal assessment

A hallmark of the contemporary literature included in this review is the deployment of sophisticated, often multi-modal, assessment technologies. The quantification of gait has moved far beyond simple stopwatch timing, leveraging:

- **High-Fidelity Motion Capture Systems:** A substantial number of studies utilized comprehensive 3D motion analysis systems, such as Vicon (Alcock, Galna et al. 2016, Corradini, Silveira-Ciola et al. 2022) and Qualisys (Amboni, Barone et al. 2012), to obtain precise kinematic data on joint angles and segment movements.
- **Instrumented Walkways:** Systems like GAITRite (Baker, Rochester et al. 2008, Rochester, Galna et al. 2014, Harrison, Horin et al. 2018) and Proto-Kinetics Zeno Walkway (Ehgoetz Martens, Silveira et al. 2018) were frequently employed for their efficiency and reliability in capturing a wide array of spatiotemporal parameters (velocity, cadence, stride length, step time, and their variability).
- **Wearable Sensor Technology:** The use of inertial measurement units (IMUs) is a prominent and growing trend, facilitating ecologically valid assessments outside the laboratory. Studies utilized systems from APDM Mobility Lab (Graham, Armitage et al. 2023, Xu, Geng et al. 2023), SENSY (Dragasevic-Miskovic, Bobic et al. 2021), and other wearable platforms (Hua, Nguyen et al. 2022) to capture gait in more naturalistic settings.
- **Force Platforms and Instrumented Treadmills:** Several studies incorporated force plates (Fernandes, Sousa et al. 2016, Nardello, Bombieri et al. 2020) or instrumented treadmills (Mak, Yu et al. 2013, Fernandez-Lago, Bello et al. 2015) to analyze kinetic parameters like ground reaction forces and center of pressure dynamics.

A critical and innovative trend was the integration of gait analysis with neurophysiological recordings. A significant subset of studies combined kinematic or spatiotemporal measurements with functional Near-Infrared Spectroscopy (fNIRS) to concurrently monitor prefrontal cortex (PFC) activation during walking. This multi-modal approach, exemplified by Al-Yahya et al. (2019)(Al-Yahya, Mahmoud et al. 2018), Orcioli-Silva et al. (2020)(Orcioli-Silva, Vitorio et al. 2020), and Sousani et al. (2025)(Sousani, Fernandez Rojas et al. 2025), provides direct insights into the neural correlates of DT interference, marking a paradigm shift from simply describing gait changes to understanding their underlying central mechanisms.

Dual-Task Paradigms and Walking Conditions

Dual-task paradigms were a universal component, though the specific protocols exhibited considerable heterogeneity, reflecting different research questions. The cognitive secondary tasks employed ranged from simple attention-demanding activities like serial subtraction (Yogev, Plotnik et al. 2007, Corradini, Silveira-Ciola et al. 2022) to more complex executive function tests such as the Stroop test and verbal fluency tasks (Wild, de Lima et al. 2013, Ginis, Pirani et al. 2017).

The walking conditions themselves were also varied, enhancing the ecological validity of the findings. While many studies used standard straight-path walkways (typically between 5m and 10m), others designed more complex scenarios. These included: Circular walking paths (Micó-Amigo, Kingma et al. 2019), Oval circuits (Rochester, Galna et al. 2014, Ranchet, Hoang et al. 2020), Specific turning tasks (Nardello, Bertoli et al. 2020), Obstacle negotiation (Pieruccini-Faria, Ehgoetz Martens et al. 2014, Corradini, Silveira-Ciola et al. 2022), The Timed Up and Go (TUG) test (Kocer, Gulsen et al. 2023, Sousani, Fernandez Rojas et al. 2025).

This methodological diversity, detailed comprehensively in Table 1, provides a rich and multifaceted evidence base. It enables a nuanced synthesis of how DT walking impacts PD gait across various clinical profiles, measurement techniques, and real-world walking challenges, which is presented in the following sections.

The methodological quality and risk of bias of the included studies were rigorously appraised using standardized tools, and the results are summarized in Table 3. The assessment offers a comprehensive evaluation of the strengths and limitations inherent in the body of evidence.

Synthesis of Results

Overall, the dual-task effect on gait results in a loss of automaticity. The collective evidence consistently indicates that dual-task (DT) conditions exacerbate gait impairments in PD, systematically degrading performance across key parameters (Rochester, Galna et al. 2014, Ehgoetz Martens, Silveira et al. 2018). The most consistent finding is a significant reduction in gait speed and stride length, coupled with a marked increase in gait variability.

Macro-Level Changes: In a large cohort study, Rochester et al. (2014) (n=121 PD)(Rochester, Galna et al. 2014) quantified this as a reduction in walking speed by approximately 0.15 m/s and a shortening of stride length by over 10 cm under DT conditions compared to single-task (ST) walking. This was not merely a slowing but a fundamental alteration of the gait pattern.

Micro-Level Instability: The loss of rhythmicity is a critical marker. Yogev et al. (2005) (Yogev, Giladi et al. 2005) found that the coefficient of variation for swing time, a measure of step-to-step consistency, increased by over 40% in PD patients during a cognitive DT, while healthy controls (HC) remained stable. This indicates a breakdown in the automatic, rhythmic control of gait.

Dual-Task Cost (DTC): The vulnerability of the PD motor system is encapsulated by the DTC. Studies like Ehgoetz Martens et al. (2018) and Dragasevic-Miskovica et al. (2021) reported DTCs for gait speed and stride time variability that were 2 to 3 times higher in PD groups compared to HC (Ehgoetz Martens, Silveira et al. 2018, Dragasevic-Miskovic, Bobic et al. 2021). This disproportionate cost highlights the specific inability of the PD brain to efficiently allocate attention between concurrent tasks.

Impact of Cognitive Task Domain and Complexity: A Hierarchy of Interference

The magnitude of gait deterioration is not uniform; it follows a hierarchy directly related to the cognitive demand of the secondary task.

High-Executive Demand Tasks: Tasks that heavily engage the central executive network, particularly the prefrontal cortex (PFC), induce the most profound disruptions. Serial subtraction (e.g., subtracting 7s) not only requires working memory but also continuous updating and inhibition, leading to significant reductions in velocity and stride length (Yogev, Plotnik et al. 2007). Similarly, the Stroop test, which demands conflict resolution and response inhibition, was shown by Orcioli-Silva et al. (2020) to be particularly detrimental, correlating with a measurable increase in PFC activation (Orcioli-Silva, Vitorio et al. 2020).

Verbal Fluency vs. Arithmetic: A nuanced finding is that while verbal fluency tasks (e.g., category word generation) are disruptive, they often have a slightly lesser impact than arithmetic. LaPointe et al. (2010) suggested this may be because word generation, while demanding, relies on somewhat more automated lexical networks compared to the purely computational and sequential load of arithmetic (LaPointe, Stierwalt et al. 2010).

Motor-Cognitive Tasks: Even seemingly simple motor tasks reveal underlying deficits. Baker et al. (2008) demonstrated that the act of carrying a tray task requiring upper-limb coordination and stability significantly increased the coefficient of variation for step time in PD patients, indicating that any additional motor planning load can destabilize gait control (Baker, Rochester et al. 2008).

Influence of disease severity and motor subtype: identifying vulnerable phenotypes, DT performance acts as a functional biomarker, sensitive to disease progression and subtype.

Disease Severity: A clear dose-response relationship appeared to exist between disease severity and DT interference. Rochester et al. (2014) and Seuthe et al. (2024) found that patients in Hoehn & Yahr (H&Y) stage III exhibited DTCs for stride length and double-support time that were significantly larger than those in stage II (Rochester, Galna et al. 2014, Seuthe, Hermanns et al. 2024). This suggests that as the neurodegenerative process advances, the "cognitive reserve" for managing gait diminishes.

Motor Phenotype (PIGD vs. TD): The most striking differentiation is between motor subtypes. Multiple studies consistently report that the Postural Instability/Gait Difficulty (PIGD) subtype is disproportionately impaired under DT (Mico-Amigo, Kingma et al. 2019, Graham, Armitage et al. 2023). This subgroup exhibits greater reductions in speed and increased variability compared to the Tremor-Dominant (TD) subtype. This is clinically crucial, as it indicates that the pathophysiological processes underlying PI GD (involving non-dopaminergic systems and axial structures) render gait control exceptionally vulnerable to cognitive distraction.

FoG: The Extreme of Dual-Task Vulnerability. Graham et al. (2023) and Stuart et al. (2017) showed that patients with FoG not only walk slower with shorter steps but are also more likely to experience actual freezing episodes during DT, especially during the cognitively challenging moment of initiating a turn (Stuart, Galna et al. 2017, Graham, Armitage et al. 2023).

Neurophysiological and cognitive correlates: the neural cost of walking advanced instrumentation reveals the "brain cost" of walking in PD under DT.

Compensatory Prefrontal Hyperactivation: fNIRS studies provide direct evidence of neural compensation. Orcioli-Silva et al. (2020), Ranchet et al. (2020), and Sousani et al. (2025) all documented a significant increase in PFC oxy-haemoglobin concentration during DT walking in PD (Orcioli-Silva, Vítório et al. 2020, Ranchet, Hoang et al. 2020, Sousani, Fernandez Rojas et al. 2025). This hyperactivation, reflected in increased prefrontal oxy-haemoglobin concentration during DT walking, is interpreted as a compensatory recruitment of higher-order cognitive circuits to support and control a motor process that is no longer automatic in PD (Orcioli-Silva, Vítório et al. 2020, Ranchet, Hoang et al. 2020, Sousani, Fernandez Rojas et al. 2025). In some cases, the magnitude of PFC activation is inversely correlated with gait performance, suggesting an inefficient neural strategy. Crucially, this inefficient neural strategy is not only cognitively taxing but is also hypothesized to have a direct metabolic cost, contributing to the higher energy expenditure of walking in PD (Clark 2015, Mirelman, Bonato et al. 2019). This neurophysiological evidence provides a mechanistic basis for the degradation of locomotor economy observed under DT conditions, a concept we explore in the Discussion.

Visual Sacrifice: The reallocation of attentional resources comes at a cost to environmental awareness. Eye-tracking research by Galna et al. (2012) and Stuart et al. (2018) revealed that under DT, PD patients make fewer saccades and have longer fixation durations, effectively employing a "staring" strategy (Galna, Lord et al. 2012, Stuart, Lord et al. 2018). This reduction in visual exploration compromises their ability to anticipate obstacles and navigate safely, directly linking cognitive load to increased fall risk.

Effects of interventions and modulating factors. The DT deficit, while profound, is modifiable. Evidence shows that various interventions can mitigate its impact.

External Cueing: Rhythmic auditory cues (Lohnes and Earhart 2011) and visual cues (Mak, Yu et al. 2013) act as external pacers, bypassing impaired internal timing mechanisms. They have been shown to reduce gait variability and increase stride length under DT, effectively "re-automating" the step rhythm by providing an external temporal scaffold.

Dopaminergic Medication: Among the included studies that assessed medication state, levodopa was found to provide partial relief from DT-related gait deterioration. For instance, Orcioli-Silva et al. (2020) demonstrated that in the ON-medication state, patients maintained a longer stride length during DT walking compared to the OFF state. (Orcioli-Silva, Vítório et al. 2020). This pattern suggests a modulatory, albeit incomplete, benefit of dopaminergic therapy on dual-task walking performance in PD.

Task Prioritization: The findings of Yogev-Seligmann et al. (2012) are critical for clinical assessment and rehabilitation. When patients are instructed to prioritize walking, their gait parameters significantly improve, but their cognitive task performance (e.g., accuracy in serial subtractions) declines (Yogev-Seligmann, Rotem-Galili et al. 2012). This trade-off underscores the competitive nature of resource allocation in PD and highlights that assessment instructions can dramatically influence the observed results.

Quality Assessment of the Included Studies

The methodological quality of the included studies was evaluated using tools appropriate to their design. For the majority of observational and cross-sectional studies, the AXIS tool was applied (Downes, Brennan et al. 2016). Total AXIS scores ranged from 13 to 17 out of 20, indicating moderate to high methodological quality overall (see Supplementary Table S1 for detailed item-level ratings). Studies such as Ehgoetz Martens et al., 2018; Graham et al., 2023; Orcioli-Silva et al., 2020 achieved the highest scores, reflecting clear objectives, robust methodology, and comprehensive statistical analyses (Ehgoetz Martens, Silveira et al. 2018, Orcioli-Silva, Vítório et al. 2020, Graham, Armitage et al. 2023), whereas studies with smaller samples or missing information on non-responders generally scored lower (e.g., Baker et al., 2008, 13/20)(Baker, Rochester et al. 2008).

The reporting quality was assessed using the STROBE guidelines (Vandenbroucke, von Elm et al. 2007), with most studies meeting reporting criteria, indicating transparent and complete reporting of study methods and results.

To specifically assess the rigor of the DT protocols, a customized DT Checklist was applied. Most studies scored 3/5 or 4/5, highlighting strengths such as counterbalanced task orders, ecologically valid secondary tasks (e.g., talking, carrying an object, serial subtractions), and detailed analysis of both gait and cognitive performance. Studies such as Yogev-Seligmann et al., 2012 were particularly notable for providing explicit instructions on task prioritization (Yogev-Seligmann, Rotem-Galili et al. 2012).

Despite these strengths, common limitations were observed across studies:

- Lack of cognitive load measurement, with no study using validated tools such as the NASA Task Load Index (NASA-TLX).
- Small sample sizes, particularly in studies involving complex instrumentation (e.g., motion capture, fNIRS).
- Lack of assessor blinding, introducing potential performance and detection bias.
- Absence of familiarization phases with the dual-task paradigms before data collection.

Using the GRADE framework, the overall certainty of the evidence was rated. The majority of studies were assigned a “Moderate” level, reflecting acceptable methodological quality but some risk of bias. A few studies with high AXIS scores and rigorous DT protocols (e.g., Orcioli-Silva et al., 2020; Rochester et al., 2014)(Rochester, Galna et al. 2014, Orcioli-Silva, Vitorio et al. 2020) were rated “High”, indicating greater confidence in the findings.

Supplementary Table S1 provides a complete item-level AXIS assessment for all included studies, enabling transparent evaluation of study quality across the 20 criteria.

Discussion

This systematic review provides a comprehensive synthesis of biomechanical and cognitive-motor alterations during dual-task (DT) walking in PD. Our findings not only confirm the well-documented spatiotemporal deficits (Hausdorff 2009, Raffegau, Krehbiel et al. 2019) but highlight a characteristic pattern of DT interference, reflected in the observed reductions in stride length, gait speed, and sagittal plane joint kinematics, which collectively indicate compromised propulsion. This signature is strongly correlated with neurophysiological evidence of a system under cognitive strain, offering a more mechanistic understanding of why gait fails in real-world, complex environments and solidifying the model of a shift from automatic to controlled movement (Wu, Hallett et al. 2015, Kim and Fraser 2022).

Interpretation of key findings: from behavior to mechanism

Consistent with the results, reductions in ankle, knee, and hip range of motion under DT suggest a stiffening strategy of the locomotor system (Galna, Lord et al. 2012). This is not merely a generalized slowing but a targeted alteration of motor control, likely adopted to reduce the degrees of freedom that need to be monitored and controlled under divided attention. This interpretation is powerfully supported by the fNIRS data, which consistently show compensatory prefrontal cortex (PFC) hyperactivation (Orcioli-Silva, Vitorio et al. 2020, Ranchet, Hoang et al. 2020). We posit that this PFC activity reflects the conscious, effortful control being exerted to maintain stability at the expense of efficient, fluid movement, a direct neural correlate of the “postural second” strategy and a key tenet of the CRUNCH hypothesis (Kim and Fraser 2022).

The partial amelioration of DT deficits by levodopa, as observed in our synthesis, suggests that dopaminergic circuits facilitate motor-cognitive integration but are not solely responsible

for DT interference. The limited efficacy of dopaminergic medication on axial symptoms like gait and balance underscores the significant contribution of non-dopaminergic pathways. A growing body of evidence indicates that gait control is largely mediated by cholinergic systems, with dysfunction in the pedunculopontine nucleus (PPN) and basal forebrain contributing directly to postural instability and gait difficulty (PIGD) (Rochester, Yarnall et al. 2012, Bohnen, Frey et al. 2013). Furthermore, since acetylcholine is crucial for attentional processes (Gratwicke and Foltynie 2018), its deficiency in PD likely creates a shared vulnerability, where the neural resources needed for both gait control and cognitive task performance are simultaneously compromised. This cholinergic deficit provides a compelling mechanism for the pronounced dual-task costs observed, particularly in the PIGD subtype (Bohnen, Kanel et al. 2018), and explains why dopaminergic replacement alone is insufficient to restore automaticity during complex, attention-demanding walking.

Our synthesis reveals that this is a protective stiffening strategy, along with the associated significant cognitive effort, has profound implications for locomotor control and energy economy. This is because the shorter steps are biomechanically linked to the observed stiffening strategy and reduced joint range of motion, particularly at the ankle, which compromises the generation of propulsive power (Galna, Lord et al. 2012, Stuart, Lord et al. 2018). Crucially, this disruption of the normal push-off mechanism not only hinders forward progression but also degrades the pendulum-like mechanics of gait. The concurrent reduction in visual exploration, as captured by eye-tracking studies (Galna, Lord et al. 2012, Stuart, Lord et al. 2018), completes this picture: attentional resources are withdrawn from environmental monitoring and funneled into the cognitively demanding task of basic locomotor control, potentially increases the risk of falls (Lord, Baker et al. 2011).

Our synthesis reveals that the reduced gait speed under DT conditions is primarily driven by a significant reduction in stride length, a consistent and fundamental finding across literature. Beyond being a simple marker of bradykinesia, this alteration has profound implications for locomotor control and energy economy. The shorter steps are biomechanically linked to the observed stiffening strategy and reduced joint range of motion, particularly at the ankle, which compromises the generation of propulsive power (Galna, Lord et al. 2012). Crucially, this disruption of the normal push-off mechanism not only hinders forward progression but also degrades the pendulum-like mechanics of gait. The efficient transfer of potential and kinetic energy, which characterizes economical walking, is thereby impaired.

This biomechanical inefficiency can be quantified using the Locomotor Rehabilitation Index (LRI), a metric that relates self-selected walking speed to the individual's optimal speed for minimizing metabolic cost (Peyré-Tartaruga and Monteiro 2016). In healthy adults, the LRI averages around 95% (Barboza, Weizemann et al. 2021), indicating a close match between preferred and optimal speeds. However, in PD, the LRI is significantly lower, and it further deteriorates under DT conditions (Ivaniski-Mello, Müller et al. 2023). A lower LRI indicates a greater deviation from energetically optimal gait and is associated with a higher metabolic cost of transport (Peyre-Tartaruga, Martinez et al. 2022). The relationship between

spatiotemporal parameters and LRI is complex, with the stride length-frequency ratio explaining only 16% of the variance in LRI in healthy adults (Barboza, Weizemann et al. 2021). This suggests that LRI captures a broader integration of locomotor function beyond simple spatiotemporal adjustments.

The impaired pendulum-like mechanism in PD, which is a key determinant of the high energy cost, can be directly measured. Leal-Nascimento et al. (2021) demonstrated that individuals with PD show a significant reduction in pendulum-like energy recovery during free walking compared to healthy controls, especially at speeds close to their self-selected pace (Leal-Nascimento, da Silva et al. 2022). Crucially, they found that Nordic Walking (NW) acutely increased this energy recovery in PD, suggesting a potential mechanism for its therapeutic benefit. This improvement in the pendulum mechanism aligns with the chronic improvements in LRI observed after NW training programs (Monteiro, Franzoni et al. 2017, Franzoni, Monteiro et al. 2018). NW not only improves the energy-saving mechanism but also enhances functional balance and postural control after a training period, as evidenced by improvements in the Berg Balance Scale in both NW and Free Walking groups, with a trend favoring NW (Franzoni, Monteiro et al. 2018).

Consequently, individuals with PD likely experience a disproportionate increase in the metabolic cost of transport during DT walking (Peyré-Tartaruga et al., 2022), which directly depletes their limited energy reserves (Peyre-Tartaruga, Martinez et al. 2022). This perspective, framed by the "PPTPARKINSON" approach, reframes DT interference not just as a problem of motor-cognitive capacity, but as a primary driver of the high energetic cost of locomotion in PD. This energy drain provides a direct, biomechanically grounded explanation for the rapid onset of fatigue and the severe curtailment of community ambulation observed in these patients.

Furthermore, the synthesis of walking conditions (treadmill vs. overground) offers insight into the role of external cueing. The reduced biomechanical alterations observed during treadmill walking under DT can be attributed to the constant velocity enforced by the belt. This external rhythm may act as a continuous spatial-temporal cue, partially bypassing the impaired internal cueing mechanisms and reducing the cognitive load required for pace regulation (Peyre-Tartaruga, Martinez et al. 2022). This provides a mechanistic explanation for why gait on a treadmill often appears less impaired, as the environment itself provides a structure that supports movement automation.

Methodological critique and future directions

A critical contribution of this review is its rigorous appraisal of methodological quality, which identified specific and recurring limitations (as detailed in the Quality Assessment). The most significant of these gaps, the near-universal absence of subjective cognitive load measurement, is a critical flaw. Relying solely on performance metrics is limited in scope and fails to capture the full extent of cognitive-motor interference; two patients with identical gait deterioration

under DT may be experiencing vastly different levels of mental effort, with profound implications for their fatigue, function, and rehabilitation potential. Future studies must integrate tools like the NASA-TLX to dissect the subjective experience of dual-tasking, moving beyond a purely performance-based framework.

Furthermore, our quality assessment highlights that the heterogeneity in DT protocols, ranging from the choice of secondary task to walking distance and prioritization instructions, remains a significant barrier to synthesis and clinical translation (Fritz, Cheek et al. 2015, Parati, Ambrosini et al. 2022). We echo the call for the development and adoption of a standardized "DT core outcome set" for PD research. This should include a recommended battery of secondary tasks spanning different cognitive domains (Kelly, Eusterbrock et al. 2012), standardized instructions for prioritization (Yogev-Seligmann, Rotem-Galili et al. 2012), and a minimum set of biomechanical and cognitive load measures. Promising steps in this direction include tools like the Dual-Task Assessment in R (DTAiR) battery, which provides a standardized framework for calculating a global dual-task cost and systematically assessing the effects of attentional prioritization, offering a more comprehensive metric of interference (Longhurst, Rider et al. 2022).

Clinical and phenotypic implications: towards precision rehabilitation

Our synthesis highlights that DT performance is not a unitary construct, but is powerfully moderated by clinical subtypes, and, crucially, is modifiable by the external factors identified in our results. The profound vulnerability of the PIGD phenotype to DT interference suggests that its pathophysiological substrate, involving greater non-dopaminergic deficits and brainstem dysfunction, is exceptionally ill-equipped to handle additional cognitive load (Mico-Amigo, Kingma et al. 2019, Graham, Armitage et al. 2023). This makes DT assessment a potent tool for phenotyping and prognostication. The mitigating effects of external cueing directly inform non-pharmacological intervention strategies. The strong interplay between DT gait and cognitive status, particularly executive function (Goldman and Litvan 2011, Kehagia, Barker et al. 2013), along with the critical trade-off observed during task prioritization, further reinforces the need for an integrated motor-cognitive approach to rehabilitation that teaches patients how to dynamically allocate attention based on environmental demands (Sarasso, Parente et al. 2024).

Furthermore, the synthesis of walking conditions (treadmill vs. overground) offers insight into the role of external cueing. The reduced biomechanical alterations observed during treadmill walking under DT, as noted in the results, can be attributed to the constant velocity enforced by the belt. This external rhythm may act as a continuous spatial-temporal cue, partially bypassing the impaired internal cueing mechanisms and reducing the cognitive load required for pace regulation (Peyre-Tartaruga, Martinez et al. 2022). This provides a mechanistic explanation for why gait on a treadmill often appears less impaired, as the environment itself provides a structure that supports movement automation.

Limitations

Significant methodological heterogeneity across studies, including divergent dual-task protocols, walking conditions, and assessment technologies, precluded a quantitative meta-analysis and limited the direct comparability of findings. The evidence base remains predominantly focused on spatiotemporal parameters, with insufficient investigation of detailed joint kinematics, kinetics, and muscle activation patterns, which hinders a mechanistic understanding of motor control alterations. Furthermore, nearly all included studies failed to quantify subjective cognitive load, relying solely on performance metrics while neglecting perceived mental effort. Ecological validity is constrained by the predominance of laboratory settings, and generalizability is limited by the focus on patients with mild-to-moderate stages of disease in the "ON" medication state. Finally, quality assessment revealed recurring risks of bias, including frequent lack of assessor blinding and small sample sizes in technologically complex studies.

Conclusion

In conclusion, this systematic review establishes that DT walking in PD is characterized by a specific and measurable profile, marking a fundamental shift from automatic to controlled movement (Wu, Hallett et al. 2015). The most consistent and impactful finding is the significant reduction in stride length.

The mechanisms underlying this alteration are twofold. From a motor control perspective, it reflects a protective stiffening strategy and reduced sagittal plane kinematics, likely adopted to simplify control under divided attention. This is neurally supported by compensatory prefrontal cortex (PFC) hyperactivation (Orcioli-Silva, Vítório et al. 2020), a direct correlate of the CRUNCH model (Kim and Fraser 2022). Crucially, from a locomotion standpoint, this altered gait pattern has severe energetic consequences. The shortened stride and compromised ankle push-off degrade the pendulum-like mechanism of gait, leading to a lower Locomotor Rehabilitation Index (LRI) and a significantly higher metabolic cost of transport (Peyré-Tartaruga and Monteiro 2016, Barboza, Weizemann et al. 2021). This reframes DT interference not just as a cognitive-motor problem, but as a primary driver of the high energetic cost of walking in PD.

The evidence also shows this deficit is modifiable. The reduced biomechanical alterations on a treadmill are explained by the belt's constant velocity, which acts as an external spatiotemporal cue, bypassing impaired internal timing and reducing the cognitive load for pace regulation.

Therefore, the DT paradigm is a powerful functional biomarker. The profound vulnerability of the PIGD subtype underscores its utility for phenotyping. Addressing the key methodological gap, the absence of subjective cognitive load measurement, is the essential next step. By standardizing protocols and integrating tools like the NASA-TLX, we can

translate this understanding into effective, personalized rehabilitation that improves not only gait safety but also locomotor economy in people living with PD.

5. Effects of Physical Exercise in Parkinson's Disease: An Umbrella Review of Systematic Reviews

Introduction

Parkinson's Disease (PD) is a progressive neurodegenerative disorder primarily affecting motor functions such as bradykinesia, rigidity, and tremor. Non-motor symptoms, including cognitive decline and mood disorders, also severely impact quality of life (Schrag, Jahanshahi et al. 2000, Poewe, Seppi et al. 2017). With the rising global prevalence of PD (Pringsheim, Jette et al. 2014), the need for effective therapies is urgent. While pharmacological treatments are central for managing specific symptoms, exercise and physical therapy are now recognized as fundamental, disease-modifying therapies (Fox, Katzenschlager et al. 2018). A growing evidence base supports their vital role in improving motor and non-motor outcomes, and potentially modifying disease progression (Petzinger, Fisher et al. 2010, Mak, Wong-Yu et al. 2017).

Physical exercise has been shown to enhance neuroplasticity, reduce neuroinflammation, and stimulate the release of neurotrophic factors, such as Brain-Derived Neurotrophic Factor (BDNF), which contribute to improvements in both motor and cognitive functions in PD (Hirsch and Farley 2009, Frazzitta, Maestri et al. 2014, Paillard, Rolland et al. 2015). Structured exercise programs, such as aerobic training, strength exercises, and motor learning techniques, have demonstrated significant benefits in enhancing balance, mobility, and overall quality of life (Tomlinson, Herd et al. 2014, Schenkman, Moore et al. 2018).

Furthermore, physical exercise has proven effective in addressing non-motor symptoms, including depression, anxiety, cognitive decline, and sleep disturbances (Cugusi, Solla et al. 2015, Wu, Zhang et al. 2022). A recent umbrella review by Moratelli et al. (2024) analyzed evidence from 20 systematic reviews, consolidating these findings and highlighting the positive effects of various physical activity interventions on non-motor symptoms, particularly in alleviating depression and enhancing cognition. The review also emphasized the need for clearer guidelines on exercise frequency and duration, while underscoring the importance of integrating physical exercise into rehabilitation programs alongside pharmacological treatments (Moratelli, Lima et al. 2024).

Parallel to exercise, innovative rehabilitation methods, such as virtual reality (VR), have shown promise in improving functional outcomes for PD patients. VR creates enriched, task-specific environments that may enhance motor learning and engagement (Mirelman, Rochester et al.

2016). A recent umbrella review by Yu et al. (2024) examined the efficacy of VR training on motor performance, activities of daily living (ADL), and quality of life (QoL). The review found significant improvements in balance, stride length, ADL, and QoL with VR training, though walking speed and motor function during VR sessions showed no statistically significant change. Despite some methodological limitations, the evidence supports VR as a potential intervention to improve key PD outcomes (Yu, Wu et al. 2023).

Furthermore, dance-based interventions have also emerged as a promising therapeutic approach for individuals with PD. Dance integrates aerobic exercise, balance, coordination, rhythm, and social interaction, potentially targeting multiple brain pathways (Shanahan, Morris et al. 2015). An umbrella review by Pinto et al. (2024) analyzed evidence from 55 systematic reviews and found that dance, particularly when combined with pharmacological care, outperforms standard treatments in improving motor symptoms, such as balance and mobility. Dance was notably effective in addressing motor severity and depressive symptoms, although its impact on gait distance and overall quality of life remains unclear. While recent reviews have framed it as an adjunct therapy (Pinto, Simon Myra et al. 2024), its mechanisms align more precisely with those of a targeted exercise modality within PD rehabilitation, highlighting its value for improving specific motor and non-motor outcomes.

Despite the growing body of evidence, including numerous systematic reviews and meta-analyses, it remains unclear which specific exercise types are most beneficial across a range of PD outcomes. A recent umbrella review by Padilha et al. (2023) synthesized findings from 139 systematic reviews, classifying physical exercises into five categories: aerobic, strength, combined, sensorimotor, and other protocols. Results suggest that all exercise categories improve balance and mobility, with combined exercises and strength training showing notable benefits for both motor and non-motor outcomes, including quality of life. However, limitations in the quality and reporting of these interventions highlight the need for more rigorous studies to guide clinical practice (Padilha, Souza et al. 2023).

This reflects a critical, unresolved challenge: significant heterogeneity in how interventions are defined, classified, and delivered limits the ability to draw overarching conclusions about *which type* of therapeutic movement is best for specific PD deficits (Lenka and Jankovic 2023). Is the primary benefit driven by improving general physiological fitness, by retraining specific motor skills, or by synergistically combining movement with neuromodulation?

To address this conceptual and methodological challenge, the present umbrella review employed a novel analytical framework that categorizes interventions based on their primary therapeutic target and underlying mechanism of action. To our knowledge, this classification represents a departure from previous umbrella reviews that have typically categorized interventions by activity type (Tomlinson, Herd et al. 2014, Padilha, Souza et al. 2023):

1. **Physical Exercise:** Defined as structured, planned, and repetitive physical activity aimed primarily at improving or maintaining components of physical fitness (e.g., aerobic capacity, muscular strength, flexibility), in line with standard definitions from leading authorities such as the American College of Sports Medicine (American College of Sports Medicine. 2020) and the World Health Organization (Bull, Al-Ansari et al. 2020).

2. **Motor and Motor-Cognitive Training:** Interventions that use movement as a medium but are primarily aimed at improving specific motor functions, gait parameters, or cognitive-motor integration through principles of motor learning, sensory cueing (Nieuwboer, Kwakkel et al. 2007), and task-specific practice, including dual-task paradigms (Kelly, Eusterbrock et al. 2012).
3. **Combined or Adjunctive Interventions:** Innovative protocols in which physical exercise is synergistically combined with a distinct, non-exercise modality (e.g., non-invasive brain stimulation) to potentiate neuroplastic effects and enhance functional outcomes (Kaski, Dominguez et al. 2014).

This framework will allow for a more nuanced and mechanistically informed comparison of intervention types, moving beyond a simple description of activities to an analysis based on therapeutic intent.

Therefore, following best practices for evidence synthesis (Fusar-Poli and Radua 2018), the aim of this review was to conduct an umbrella review accompanied by a higher-order meta-analytic synthesis. This involved quantitatively integrating results from multiple meta-analyses and systematic reviews to evaluate consistency, effect sizes, and the strength of evidence across interventions (Rucker and Schwarzer 2015, Rodrigues-de-Paula, Lana et al. 2018). By systematically aggregating and evaluating findings across existing systematic reviews and meta-analyses within this structured framework, this review provides a broader, more robust, and clinically relevant understanding of the therapeutic potential of physical activity in PD. The analysis assesses the strength and consistency of the evidence for each category and generates meaningful insights to inform both practice and future research.

Methods

Search Strategy

A systematic literature search was conducted across five electronic databases: Cochrane Library, EBSCO, PubMed, Scopus, and Web of Science. The search strategy combined medical subject headings (MeSH) and free-text terms related to PD and various forms of physical exercise. Keywords included terms such as “Parkinson’s disease,” “exercise,” “physical activity,” “rehabilitation,” “aerobic training,” “resistance training,” “dance,” “Tai Chi,” “virtual reality,” and “multimodal interventions.” Boolean operators (AND, OR, NOT) were used to optimize the comprehensiveness and sensitivity of the search across all databases. The search strategy was tailored to each platform to account for differences in indexing and syntax, and no restrictions were placed on language or publication date to ensure maximum coverage of eligible studies.

This review adhered to the PRISMA 2020 guidelines (Page, McKenzie et al. 2021) and was registered on PROSPERO (registration number: CRD420251025503). The search aimed to identify all relevant systematic reviews and meta-analyses that evaluated the effects of physical exercise interventions on individuals with PD or validated animal models of the condition.

Eligibility Criteria

Studies were considered eligible for inclusion based on a predefined set of criteria informed by the PICOS framework and aligned with the review's objectives. The population of interest included adult individuals (aged 18 or older) formally diagnosed with PD. Additionally, preclinical studies involving validated animal models, such as rodents or non-human primates, were included if they examined pathophysiological mechanisms or therapeutic responses to physical exercise that are directly measurable and comparable to outcomes assessed in human studies, such as motor performance, neuroplasticity markers, or neurotrophic factor expression.

Eligible interventions included structured physical exercise programs, such as aerobic training, resistance exercises, multimodal approaches, virtual reality-based rehabilitation, Tai Chi, yoga, and dance. Both acute interventions (single-session protocols) and long-term exercise programs were included. The studies had to report on outcomes related to motor or non-motor symptoms, or neuroprotective mechanisms associated with PD. Acceptable comparators included no-exercise groups, usual care, or other types of exercise interventions.

Reviews were excluded if they focused on pharmacological treatments, surgical interventions, or passive therapies without any physical activity component. Additional exclusions applied to reviews that included participants without a formal diagnosis of PD, studies involving unstructured or poorly defined exercise programs, and those with mixed populations from which PD-specific data could not be extracted. Abstracts, conference posters, preprints, theses, and other non-peer-reviewed literature were also excluded.

Intervention Categorization Framework

To address heterogeneity in intervention types and facilitate a structured synthesis, included interventions were classified into three mutually exclusive categories based on their primary therapeutic target and operational principles:

1. **Physical Exercise (Fitness-Oriented):** This category includes structured, planned, and repetitive physical activities primarily aimed at improving or maintaining components of physical fitness, as defined by major sports and health organizations. This encompassed strength and resistance training (e.g., progressive resistance with weights, bands, or machines). aerobic/endurance training (e.g., walking, cycling, treadmill). Flexibility, range of motion, and multimodal fitness exercises (e.g., conventional physiotherapy packages, Tai Chi, yoga, or Pilates) were included in this category when the primary focus was on improving general physical capacity, consistent with standard classifications (American College of Sports Medicine. 2020).
2. **Motor and Motor-Cognitive Training (Function-Oriented):** This category included interventions where movement was used as a medium, but the primary aim was the direct improvement of motor function, gait parameters, or cognitive-motor integration through principles of motor learning and task-specificity. This encompassed: balance and postural control training (including both reactive and anticipatory balance

control), cueing strategies (auditory, visual, or somatosensory), dual-task training, task-specific training of Activities of Daily Living (ADLs), and reactive or perturbation-based balance training.

3. **Combined or Adjunctive Interventions:** This category was reserved for innovative protocols where a physical exercise component (from Category 1 or 2) was systematically combined in a single session with a distinct, non-exercise modality to leverage synergistic or potentiating effects. This included but was not limited to: Exercise combined with Non-Invasive Brain Stimulation (e.g., TMS, tDCS). Exercise combined with targeted pharmacological agents beyond standard levodopa therapy.

Classification was performed during data extraction based on the detailed description of the intervention provided in each systematic review. Reviews investigating multi-component interventions that did not fit neatly into one category were classified based on the predominant component as emphasized by the review authors. This framework was consistently applied to all included reviews, enabling comparative analysis.

Study Selection and Data Extraction

All titles and abstracts identified through the database searches were independently screened by two reviewers to determine initial eligibility. Full texts of potentially relevant reviews were then retrieved and assessed for inclusion. Any disagreements in the selection process were resolved through discussion or, if necessary, consultation with a third reviewer to ensure consistency.

Data extraction was performed using a standardized form developed for this review. The form captured key characteristics of each included review, such as author(s), year of publication, review type (systematic review or meta-analysis), number and type of primary studies included, participant demographics (age, sex, disease stage), and details of the intervention (type, intensity, frequency, duration). Outcome measures were also extracted, including motor function (e.g., UPDRS, gait speed), non-motor symptoms (e.g., depression, anxiety, cognitive impairment), quality of life assessments, and neuroprotective biomarkers. Information on statistical analyses, reported effect sizes, heterogeneity metrics, and sensitivity analyses were also collected where available.

Risk of Bias and Quality Assessment

The methodological quality of the included systematic reviews and meta-analyses was assessed using AMSTAR-2, a validated tool for evaluating the quality of reviews of healthcare interventions (Shea, Reeves et al. 2017). In addition, to assess redundancy across reviews and the overlap of included primary studies, the Corrected Covered Area (CCA), as described by Pieper et al. (2014), was calculated (Pieper, Antoine et al. 2014). The CCA provided a quantitative measure of the degree to which studies were included in multiple reviews. Interpretation thresholds followed standard criteria: 0–5% (slight overlap), 6–10% (moderate overlap), 11–15% (high overlap), and over 15% (very high overlap). This metric was

particularly important for minimizing the risk of double-counting evidence in cases where meta-analyses shared a large number of primary studies.

To explore the presence of publication bias, funnel plots were visually inspected and Egger's test was applied (Egger, Davey Smith et al. 1997). When asymmetry suggested potential bias, trim-and-fill adjustments were used to estimate its impact on summary estimates.

Data Synthesis and Analysis

Given the anticipated variability in reviews regarding study populations, interventions, and outcomes, a narrative synthesis was initially undertaken to summarize and compare findings across studies. This included a qualitative analysis of the types of interventions studied, outcome measures reported, and the magnitude and direction of observed effects on both motor and non-motor symptoms of PD.

Where data allowed, a secondary meta-analysis was conducted to pool effect estimates from existing meta-analyses using a random-effects model (Higgins, Altman et al. 2011). This statistical approach accounted for heterogeneity across studies and allowed for more conservative estimates of overall effects. Standardized Mean Differences (SMDs) with 95% Confidence Intervals (CI) were used for continuous outcomes. Heterogeneity was quantified using the I^2 statistic, with thresholds of 25%, 50%, and 75% representing low, moderate, and high heterogeneity, respectively.

Meta-regression analyses were performed when sufficient data were available to explore the potential influence of moderator variables, including age, disease duration, Hoehn & Yahr stage, cognitive status, intervention type, and exercise dosage. Further sensitivity analyses were conducted to assess the robustness of the findings by excluding studies with a high risk of bias or limited sample sizes, and by comparing studies that used different measurement tools (e.g., wearable sensors, GAITRite systems, motion capture).

Finally, subgroup analyses were carried out to investigate whether specific exercise modalities, such as dance, VR, or Tai Chi, produced differential effects across different PD phenotypes or stages of disease severity. Where follow-up data were reported, we also explored whether certain interventions showed evidence of long-term benefits or neuroplastic adaptation.

Preliminary results

Study selection and overview

The initial systematic search identified 6,636 records from the Cochrane Library (n = 56), EBSCO (n = 606), PubMed (n = 1,421), Scopus (n = 3,493), and Web of Science (n = 1,060). Following the removal of 2,581 duplicates, 4,055 records were screened for eligibility based on title and abstract. After excluding 3,606 records that did not meet the inclusion criteria, the full texts of 449 reports were retrieved, and all were deemed eligible for inclusion. This comprehensive selection provides a robust foundation for synthesizing current evidence on the effects of exercise interventions in PD.

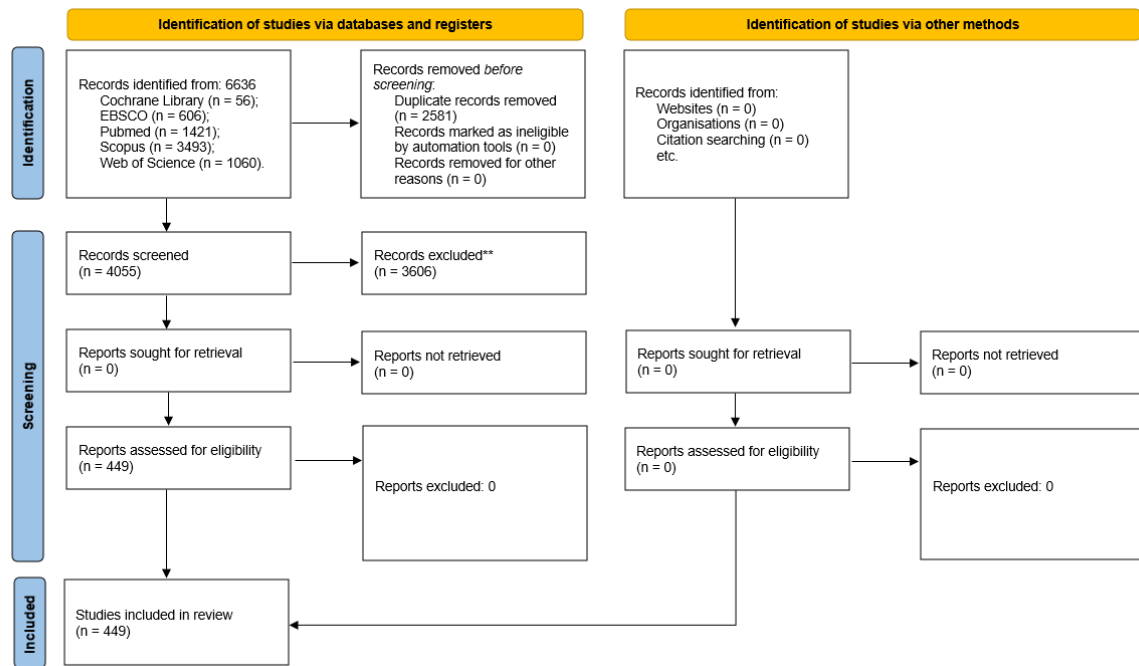


Figure 1. Study selection strategy flowchart according to the PRISMA model

The characteristics of the included SRoMAs, summarized in the accompanying evidence table (see Supplementary Table 1), provide a structured, quantitative overview essential for clinicians and researchers to appraise the scope and generalizability of the findings. The table delineates the first author, year, study design, number of included studies and participants, intervention type, population characteristics, primary outcomes, intervention dose and duration, control group details, and critical comments.

A detailed analysis of this corpus reveals the following key characteristics:

- **Population:** Most of the evidence is derived from studies involving adults with mild-to-moderate PD (Hoehn & Yahr stages I–III) (Hoehn and Yahr 1967). This focus is a significant consideration for clinical extrapolation. While this represents the largest group for non-pharmacological interventions, reporting of specific age ranges and disease duration was sometimes inconsistent or incomplete across primary studies, actively limiting confident extrapolation of the findings to individuals with advanced PD (Hoehn & Yahr IV–V) (Hoehn and Yahr 1967).
- **Interventions:** The interventions were categorized into a clinically oriented framework: 1) Physical Exercise (e.g., aerobic, resistance, multimodal), 2) Motor and Motor-Cognitive Training, which includes both traditional approaches (e.g., balance, dance, dual-task) and modern, technology-assisted modalities (e.g., VR, RAGT), and 3) Combined Interventions (e.g., physical-cognitive training). A small number of reviews

also examined select pharmacological adjuncts for non-motor symptoms like fatigue, providing a comparator for non-pharmacological approaches.

- **Outcomes:** The synthesized evidence spanned a comprehensive range of outcomes: Motor Symptoms: Unified Parkinson's Disease Rating Scale Part III (UPDRS-III/MDS-UPDRS-III) scores, specific measures of balance (e.g., Berg Balance Scale), gait parameters (speed, stride length, cadence), and functional mobility (e.g., Timed Up-and-Go); Non-Motor Symptoms: Cognition (global and domain-specific), mood (depression, anxiety), fatigue, sleep quality, and Health-Related Quality of Life (HRQoL); Mechanistic & Neurobiological Markers: Circulating levels of neurotrophic factors (BDNF, IGF-1) and outcomes from neuroimaging studies (functional and structural MRI).
- **Scale and Scope:** The included SRoMAs varied considerably in scale, ranging from focused reviews of 5–10 trials to large-scale Network Meta-Analyses (NMAs) incorporating up to 154 randomized controlled trials (RCTs) (e.g., Ernst et al., 2024; Radder et al., 2020)(Radder, Lígia Silva de Lima et al. 2020, Ernst, Folkerts et al. 2024). These large NMAs synthesize extensive evidence and provide a high level of statistical power, often serving as influential references within the field.
- **Intervention Characteristics (Dosage):** The evidence table captures the critical parameters of exercise prescription. The typical session frequency was 2–5 times per week, with total program durations ranging from 4 to 24 weeks. The total exercise volume, when quantifiable, spanned a wide range from approximately 200 to over 1,000 MET-min/week, with higher volumes generally associated with greater improvements. The prescribed intensity was inherently modality-specific and varied by study design, from light-intensity mind-body exercises to high-intensity interval training.
- **Safety and Tolerability:** A consistent and reassuring finding across the vast majority of included reviews was that serious adverse events were rare, and reported events were typically minor (e.g., muscle soreness, transient fatigue). This is supported by a large Cochrane review, which concluded that exercise-based interventions are safe for people with Parkinson's disease and do not increase the risk of adverse events (Ernst, Folkerts et al. 2023). The data robustly support that the prescribed exercise interventions, across all modalities, are well-tolerated and possess a favorable risk-benefit profile for the target population.

This detailed characterization of the evidence base establishes a firm foundation for the synthesis that follows, allowing for a nuanced understanding of the strength, scope, and limitations of the current knowledge on exercise in PD.

To transcend a simple enumeration of effects and provide a clinically actionable framework, we have categorized the evidence into three primary therapeutic targets: 1) Physical Exercise (Fitness-Oriented) to build foundational capacity, 2) Motor and Motor-Cognitive Training

(Function-Oriented) to retrain specific neural circuits, and 3) Combined Interventions to potentiate neuroplasticity (American College of Sports Medicine. 2020).

1. Physical Exercise (Fitness-Oriented)

This category focuses on improving core physiological attributes (muscular strength, cardiorespiratory capacity, endurance), providing measurable benefits in motor performance and functional capacity.

- Multimodal and Combined Training (integrating aerobic and resistance exercises) emerges as the most effective strategy for improving global motor severity (as measured by UPDRS-III scores), cardiorespiratory fitness, and muscular strength (Radder, Lígia Silva de Lima et al. 2020, Li, Gao et al. 2022, Ernst, Folkerts et al. 2024). A clear dose-response relationship was evident, with higher volumes (e.g., >850 MET-min/week) conferring greater benefit (Cui, Hu et al. 2024, Gao, Zhang et al. 2024, Yuan, Wang et al. 2024, Wang, Yuan et al. 2025). This approach also yielded significant, clinically meaningful improvements in health-related quality of life (HRQoL) (Chen, Tan et al. 2020, Brito, dos Santos et al. 2022).
- Aerobic Exercise (treadmill, cycling) specifically and consistently enhanced gait speed, stride length, and walking endurance (Mehrholz, Friis et al. 2010, de Almeida, Santana et al. 2022, Barbieri, Barbieri et al. 2025, Xie, Yuan et al. 2025). Its impact on overall motor scores was significant, particularly when adhering to ACSM guidelines (Cui, Hu et al. 2024), and it robustly improved cardiorespiratory fitness (VO₂ max) (Ferreira, Binda et al. 2021, Kim, Kang et al. 2025).
- Resistance Training alone was highly effective for increasing muscle strength and power, directly translating to improved functional capacity and walking capacity, especially when programs were progressive (Lima, Scianni et al. 2013, Chung, Thilarajah et al. 2016, de Lima, da Silva et al. 2022, Gollan, Ernst et al. 2022, Yang, Wang et al. 2023).
- High-Intensity Interval Training (HIIT) was established as feasible and safe, offering a potent stimulus for rapidly improving cardiorespiratory fitness, motor function, and disease severity, with effects comparable or superior to moderate-intensity continuous exercise in some studies (Sena et al., 2023; Harpham et al., 2023; Molina Palomino et al., 2021)(Molina Palomino, López López et al. 2021, Harpham, Gunn et al. 2023, Sena, Costa et al. 2023).

2. Motor and Motor-Cognitive Training (Function-Oriented)

This category focused on improving specific motor functions and their integration with cognition, showing greater efficacy compared to Physical Exercise (Fitness-Oriented).

- Balance and Complex Gait: Dance (Tango, Ballroom, Folk) demonstrated moderate-to-large effects, consistently providing larger improvements in dynamic balance, gait under dual-task conditions, motor severity, functional mobility, and quality of life

compared to usual care and other exercises, with high adherence due to its engaging nature (Dos Santos Delabary, Komerowski et al. 2018, Ismail, Lee et al. 2021, Donida, dos Santos Delabary et al. 2023, Mahmoud, Al-Turkistani et al. 2023, Barnish, Reynolds et al. 2025); Virtual Reality (VR) and Exergaming create immersive environments that significantly improve static and dynamic balance and gait, often outperforming conventional therapy. For these modalities, optimal dosing parameters have been identified, suggesting sessions of 30-60 minutes, 2-3 times per week yield significant benefits (Chuang, Chen et al. 2022, Sarasso, Gardoni et al. 2022, Wu, Xiong et al. 2022, Lheureux, Lejeune et al. 2025); Perturbation-Based Balance Training is emerging as a highly effective strategy for fall prevention, as it safely introduces postural disruptions to directly improve reactive postural control and has been shown to reduce actual fall rates more effectively than traditional balance training (Mansfield, Wong et al. 2015, Coelho, de Oliveira et al. 2022).

- **Gait Automation and Rhythmicity:** External Cueing (particularly auditory rhythmic stimulation) is a highly accessible and effective strategy for immediately improving gait speed, stride length, and cadence, directly addressing issues like freezing of gait (Spaulding, Barber et al. 2013, Burrai, Apuzzo et al. 2024, Huang, Dong et al. 2024, Nascimento, Boening et al. 2024).
- **Mind-Body Exercises:** Tai Chi and Qigong were particularly powerful for enhancing balance, reducing fear of falling and fall rates, and improving functional mobility, likely through sensorimotor integration. Specific forms like the 24-form Yang style showed superior benefits (Song, Grabowska et al. 2017, Liu, Yeh et al. 2019, Aras, Seyyar et al. 2022, Lei, Ma et al. 2022, Lou, Xiang et al. 2025). Yoga showed pronounced effects on motor scores (UPDRS-III) and dual-task performance, offering benefits for both physical function and mental well-being (Kwok, Choi et al. 2016, Ban, Yue et al. 2021, Wu, Xu et al. 2021).
- **Dual-Task Training (DTT)** effectively enhanced gait parameters (speed, stride length) and balance under cognitively challenging conditions, demonstrating improved integration of motor and cognitive circuits (De Freitas Tb Ms, Leite et al. 2020, Du, Ma et al. 2023, Garcia-Lopez, de Los Angeles Castillo-Pintor et al. 2023, Johansson, Folkerts et al. 2023).
- **Advanced Technologies and Niche Modalities:** Robot-Assisted Gait Training (RAGT) showed significant benefits for gait speed, endurance, and balance, showing particular utility in patients with more severe impairments or freezing of gait (Alwardat, Etoom et al. 2018, Picelli, Capecchi et al. 2021, Xue, Yang et al. 2023, Jiang, Zhou et al. 2024, Tao, Luo et al. 2024). Boxing Training is a well-tolerated and engaging intervention that has been shown to improve balance, mobility, lower extremity strength, and quality of life. However, its superiority over other exercises was not consistently proven (Chrysagis, Trompouki et al. 2024, Gonzalez-Devesa, Ayan et al. 2024, Wang, Song et al. 2025). Therapies with Inconclusive Evidence: Whole-body

vibration (WBV), a passive physical modality, was considered but excluded from the primary synthesis as it falls outside this review's scope of active exercise interventions. The evidence for its use in PD is weak, showing minimal and inconsistent motor benefits that preclude its recommendation as a standalone therapy (Sitja Rabert, Rigau Comas et al. 2012, He, Su et al. 2020).

3. Combined Interventions: Potentiating Neuroplasticity

This emerging paradigm systematically combined physical exercise with another modality to synergistically enhance effects.

Physical-Cognitive Training: Combined protocols showed promising benefits for addressing both motor and cognitive symptoms simultaneously, though optimal methods (simultaneous dual-task vs. sequential training) require further investigation (Kim, Lee et al. 2023, Chartier, Godard et al. 2024, Gil, Moratelli et al. 2024, Pigott, Armstrong et al. 2024).

Adjunctive Therapies: Preliminary evidence for exercise coupled with non-invasive brain stimulation (e.g., tDCS, TMS) suggests potential for greater improvement in motor learning and cortical excitability than intervention alone. However, this evidence base is still nascent and heterogeneous.

4. Impacts Beyond Motor Function: Non-Motor Symptoms and Neurobiological Mechanisms

The benefits of exercise extend profoundly beyond motor control, addressing the whole person and is underpinned by measurable neurobiological changes.

- **Mental Health:** Evidence suggests that exercise is a potent intervention for depression and anxiety, with mind-body exercises (Yoga, Tai Chi) and resistance training showing large effect sizes (Tian, Kang et al. 2022, Feller, Fox et al. 2023, Costa, Prati et al. 2024, Meliani, Lima et al. 2025).
- **Cognition:** Combined physical-cognitive training and aerobic exercise improved global cognition, executive function, and processing speed. Dance therapy has shown particular promise for enhancing memory and social cognition (Wang, Li et al. 2021, Kim, Lee et al. 2023, Yin, Liu et al. 2023, Chartier, Godard et al. 2024, Gil, Moratelli et al. 2024).
- **Fatigue, Sleep, and Pain:** Physical activity has been shown to be an effective intervention for reducing fatigue (Folkerts, Nielsen et al. 2023). It also significantly improved sleep quality and reduced chronic pain, with modalities like Tai Chi and aquatic therapy being particularly effective (Qureshi, Jamal et al. 2021, Huissoud, Boussac et al. 2024, Tang, Gong et al. 2024, Ying, Sun et al. 2024, Tan, Pan et al. 2025).
- **Neurobiological Mechanisms:** The clinical benefits are supported by compelling evidence of neuroplasticity. **Neurotrophic and Neurochemical Adaptations:** Exercise increased levels of Brain-Derived Neurotrophic Factor (BDNF) and IGF-1 in PD

patients, which correlated with motor and cognitive improvements (Ruiz-Gonzalez, Hernandez-Martinez et al. 2021, Rotondo, Proietti et al. 2023, Kaagman, van Wegen et al. 2024, Paterno, Polsinelli et al. 2024). Neuroimaging Evidence: Human studies demonstrated functional and structural brain changes, including strengthened cortico-subcortical pathways and activation of compensatory networks (Baglio, Pirastru et al. 2022, Li, Gao et al. 2022, Wang, Li et al. 2022). Preclinical and Disease-Modifying Potential: Animal models showed exercise reduces alpha-synuclein aggregation, dampens neuroinflammation, counteracts glutamatergic dysregulation, and improves mitochondrial function (Nhu, Cheng et al. 2021, Ishaq, Shah et al. 2024, Ishaq, Shah et al. 2025). Crucially, long-term human interventions (≥ 6 months) are associated with a reduced requirement for dopaminergic medication, suggesting a potential disease-modifying effect (Okada, Ohtsuka et al. 2021, Ji, Lu et al. 2022, Li, Loevaas et al. 2023).

5. Clinical Implementation: Personalization, Accessibility, and Adherence

Translating the robust evidence for exercise in PD into clinical practice presents a challenge in selecting and applying it. Successful implementation requires a strategic focus on three key areas: personalization, dosage, and accessible delivery models.

- **Personalized Prescription:** The most effective intervention depends on the primary treatment goal. Network meta-analyses allowed for the ranking of therapies, supporting tailored prescriptions (e.g., dance for balance, mood, and cognition; resistance training for strength; Tai Chi for balance and fall prevention; aerobic exercise for gait endurance; cueing for immediate gait improvement) (Mustafaoglu, Ahmed et al. 2022, Alvarez-Bueno, Deeks et al. 2023, Qian, Fu et al. 2023, Yang, Wang et al. 2023, Zhao, Zhang et al. 2024).
- **Dosage:** The included reviews emphasize that adherence to established exercise guidelines (e.g., ACSM)(American College of Sports Medicine. 2020) is associated with greater improvements (Cui, Li et al. 2023, Cui, Hu et al. 2024). Furthermore, the evidence suggests that while optimal dosing (frequency, intensity, duration) is modality-specific, the consensus across reviews is that consistency and long-term engagement are critical for sustaining benefits (Li, Gao et al. 2022, Simpkins and Yang 2023).
- **Accessible and Sustainable Models:** Home-Based and Telerehabilitation programs are feasible, safe, and effective for maintaining balance, mobility, and QoL, offering a scalable solution for long-term management (Flynn, Allen et al. 2019, Vellata, Belli et al. 2021, Cabeleira, da Campo et al. 2022, Yang, Fu et al. 2023, Federico, Cacciante et al. 2024, Gao, Zhang et al. 2024). Group Exercise was as effective as individual therapy for most outcomes and provided social benefits that enhanced long-term adherence (Palm, Swarowsky et al. 2024, Palm, Swarowsky et al. 2025, States, Dewan et al. 2025).

6. Methodological Quality and Overlap

A formal assessment of methodological quality using AMSTAR-2 and an analysis of study overlap via the Corrected Covered Area (CCA) metric are planned components of this review's quality appraisal (Pieper, Antoine et al. 2014, Shea, Reeves et al. 2017). However, a well-recognized challenge in this field is the significant heterogeneity in review quality and the high degree of redundancy across meta-analyses, particularly for popular interventions like dance and VR. This context underscores the inherent value of the present umbrella review in consolidating overlapping evidence and synthesizing clear clinical guidance.

Discussion

This umbrella review provides a comprehensive synthesis of evidence from 449 systematic reviews and meta-analyses examining the effects of exercise and rehabilitative interventions in PD. Across diverse modalities, physical activity consistently demonstrated meaningful benefits on motor symptoms, balance, gait, functional mobility, and non-motor outcomes, including mood, cognition, and overall quality of life (Ernst et al., 2024; Yuan et al., 2024; Mahmoud et al., 2023; Wang et al., 2025)(Mahmoud, Al-Turkistani et al. 2023, Ernst, Folkerts et al. 2024, Yuan, Wang et al. 2024). Notably, interventions such as dance and rhythmically cued exercises yielded moderate to large improvements in motor performance, whereas resistance training and mind-body practices, like Tai Chi and Yoga, provided smaller but clinically relevant gains (Lima, Scianni et al. 2013, Kwok, Choi et al. 2016, Liu, Yeh et al. 2019).

The findings of this review highlight the specificity of intervention effects. High-speed cycling and treadmill-based programs were particularly effective in reducing bradykinesia and improving gait velocity, while interventions emphasizing postural control, such as Tai Chi, Yoga, and dance, consistently enhanced balance and contributed to fall prevention (de Almeida, Porto et al. 2021, Molina Palomino, López López et al. 2021, Fan, Soh et al. 2025). Technology-assisted rehabilitation, including virtual reality (VR), exergaming, and robotic-assisted therapies, has emerged as a feasible adjunct to conventional physiotherapy, demonstrating improvements in static and dynamic balance and promoting patient engagement, though long-term effects remain heterogeneous (Wu, Zhang et al. 2022, Fernandez-Gonzalez, Rodriguez-Costa et al. 2023, Tao, Luo et al. 2024).

Complementing these technology-driven approaches, a specific and highly effective form of aerobic exercise, Nordic Walking, deserves particular emphasis. This modality, which uses specialized poles to engage the upper body in a rhythmic, coordinated pattern, has consistently been shown to improve gait speed, stride length, upright posture, and cardiovascular fitness in PD. Key studies, such as those by Monteiro et al. (2017), Franzoni et al. (2018), and the systematic review by Peyré-Tartaruga et al. (2022), substantiate these benefits (Monteiro, Franzoni et al. 2017, Franzoni, Monteiro et al. 2018, Peyre-Tartaruga, Martinez et al. 2022). A critical point of consideration, however, is that trials with rigorous, standardized control over training load parameters (e.g., intensity monitored via heart rate, specific speed, or perceived exertion) remain relatively rare. This gap underscores the need for

future studies to not only confirm efficacy but also to define the precise dosage required for optimal, personalized prescriptions.

Despite these consistent positive trends, significant heterogeneity existed across studies regarding intervention intensity, duration, frequency, and outcome measures. A major contributor to this heterogeneity, as rightly highlighted in the review process, is the inadequate reporting of intervention details. The consistent use of reporting checklists like TIDieR (Template for Intervention Description and Replication) or its extension for rehabilitation, TIDieR-REHAB, was notably scarce (Hoffmann, Glasziou et al. 2014, Fuller, Colwell et al. 2020). This lack of detailed description regarding the 'active ingredients, dosage (e.g., exact intensity, sets, reps), and tailoring procedures makes it difficult to replicate studies, pool data effectively, and understand which components are essential for efficacy. For example, while dance and rhythm-based programs improved balance and functional mobility, their impact on cognitive outcomes and depressive symptoms was less consistent (Cheng, Quan et al. 2024, Meliani, Lima et al. 2025), a finding that is hard to interpret without a clear understanding of the specific cognitive demands and dosages of each dance program. Similarly, VR and robotic-assisted interventions offered short-term benefits but presented variable long-term effects, highlighting the need for standardized protocols, including the use of TIDieR, and validated outcome assessments to strengthen clinical recommendations (Chartier, Godard et al. 2024, Gao, Zhang et al. 2024).

Mechanistic insights suggest that the beneficial effects of exercise are mediated by neuroplastic adaptations, including increased levels of brain-derived neurotrophic factor (BDNF), enhanced cortico-subcortical connectivity, and neuroprotective effects demonstrated in preclinical and clinical models (Ferreira, Binda et al. 2021, Ruiz-Gonzalez, Hernandez-Martinez et al. 2021, Baglio, Pirastru et al. 2022). Long-term interventions, particularly those lasting more than six months, were associated with sustained motor and cognitive improvements and reductions in levodopa-equivalent dosages, suggesting the potential for disease-modifying effects (Okada, Ohtsuka et al. 2021, Ji, Lu et al. 2022). These findings underscore the importance of integrating structured exercise programs as a core component of PD management rather than as supplementary therapy.

Furthermore, the review identifies promising avenues for future research. Emerging modalities, such as telerehabilitation, exergaming, and home-based VR interventions, offer scalable and accessible solutions, particularly for patients with mobility limitations or restricted access to specialized centers (Vellata, Belli et al. 2021, Federico, Cacciante et al. 2024, Asgharzadeh Chamleh, Afkanpour et al. 2025). However, evidence remains limited for interventions including boxing, blood flow restriction exercise (BFRE), and certain robotic approaches, warranting further high-quality trials to clarify efficacy, optimal dosing, and safety profiles (Picelli, Capecci et al. 2021, Gonzalez-Devesa, Ayan et al. 2024). Importantly, the diversity of PD phenotypes suggests that personalized, symptom-specific rehabilitation programs may maximize therapeutic outcomes, emphasizing the need for tailored exercise prescriptions.

Finally, this umbrella review highlights methodological gaps in existing literature. Many systematic reviews reported moderate to high overlap of primary studies, variable quality, and inconsistencies in reporting, suggesting the necessity of future reviews adhering strictly to established guidelines, such as PRISMA and AMSTAR-2. Such rigor would facilitate evidence synthesis, reduce redundancy, and allow for clearer clinical recommendations.

Overall, the evidence synthesized in this umbrella review underscores the consistent benefits of exercise-based and rehabilitative interventions in PD, despite heterogeneity in study designs, intervention protocols, and outcome reporting. To address the variability in terminology and conceptual framing across studies, we organized interventions into three overarching categories: (i) physical fitness-oriented approaches (e.g., resistance training, cycling, aerobic exercise), (ii) motor-cognitive or rhythm-based interventions (e.g., dance, cueing, dual-task training), and (iii) hybrid or technology-assisted modalities (e.g., VR, exergaming, robotic therapies). This categorization, while simplifying the wide range of protocols, provided a pragmatic framework for comparing intervention effects and clarifying their potential clinical applications.

Importantly, this synthesis does not replace detailed assessments of methodological quality; instead, it highlights the need for greater standardization of intervention reporting, outcome measures, and trial design. Such efforts will enhance comparability between studies and support more robust recommendations for integrating exercise into routine PD management.

Key message and outlook

This umbrella review demonstrates that exercise is not an adjunctive option, but rather a *core* therapeutic strategy in PD. Across 449 systematic reviews and meta-analyses, physical activity consistently improved motor and non-motor outcomes, with certain modalities, such as dance, Tai Chi, cycling, and technology-assisted therapies, offering targeted benefits on gait, balance, and quality of life. These effects are biologically plausible and are supported by evidence of neuroplastic adaptations and potential disease-modifying mechanisms.

Yet, the field remains fragmented. Studies differed widely in their intervention protocols, dosing, and outcome measures, which undermines comparability and limits their translation into guidelines. Moving forward, the mandatory use of reporting guidelines, such as TIDieR-REHAB, is as crucial as the use of PRISMA for reviews; it is a fundamental step to ensure that interventions are not only effective but also replicable and implementable in real-world clinical practice. By categorizing interventions into physical fitness-based, motor-cognitive, and hybrid/technology-assisted approaches, we provided a pragmatic framework to navigate this heterogeneity and inform clinicians, patients, and policymakers. The challenge ahead is not to demonstrate whether exercise works in PD, as it clearly does, but to determine how to prescribe it effectively, sustainably, and equitably. Establishing standardised protocols, implementing long-term follow-up, and adopting personalised approaches should now be the priority for future research and implementation.

Conclusion

The current synthesis confirms that physical exercise and rehabilitation interventions offer significant benefits for both motor and non-motor symptoms in PD. Multimodal approaches, including aerobic and resistance training, dance, mind-body practices, and technology-assisted modalities, contribute to improvements in balance, gait, functional mobility, mood, cognition, and overall quality of life. Neuroplasticity and potential disease-modifying effects provide a biological rationale for these interventions, supporting their inclusion as central components of comprehensive PD management.

While the evidence is largely favorable, heterogeneity in protocols, outcome measures, and study quality highlights the need for standardized intervention guidelines and rigorous, high-quality research. Personalized, symptom-specific exercise prescriptions, combined with scalable home-based and technology-assisted programs, represent promising strategies to optimize patient outcomes. Future investigations should also focus on emerging interventions with limited evidence to expand the therapeutic repertoire for PD, ultimately aiming to enhance both clinical and quality-of-life outcomes for this growing patient population.

6. Cross-Article Synthesis and Interpretation of Findings

This final chapter synthesizes and critically discusses the key findings from the four studies comprising this thesis. First, a narrative synthesis integrates their main results to construct a coherent, multi-level perspective on exercise and neuroplasticity in Parkinson's disease. This integrated narrative then serves as the foundation for a critical discussion of the collective implications, methodological considerations, and future directions for both research and clinical practice.

Synthesis of Key Findings: An Integrated Perspective on Exercise in PD

The four studies, though differing in scope and methodology, collectively build a multi-layered understanding of exercise as a therapeutic intervention in PD. Their findings can be integrated across three levels: from molecular mechanisms and neurophysiological dysfunction to clinical application and future innovation.

1. The Foundational Mechanism: Neuroplasticity (Study 1)

The meta-analysis provides the fundamental molecular rationale for exercise. It demonstrates that structured physical activity reliably increases Brain-Derived Neurotrophic Factor (BDNF), a key mediator of neuroplasticity. This BDNF increase is associated with cognitive improvements, confirming that exercise induces beneficial changes in the brain itself. Critically, this effect was consistent across exercise modalities, establishing a general biological principle: exercise is a potent stimulus for brain health in PD.

2. Emerging Evidence for a Novel Synergistic Approach (Study 2)

The study on combined iTBS and Maximal Strength Training (MST) has progressed from a protocol to a pilot study providing preliminary empirical data. The baseline assessments reveal a crucial finding: individuals with early-stage PD show preserved muscle strength, structure, and corticospinal excitability compared to healthy controls, but exhibit significant functional lateralization (Figures 1-3). This suggests that interventions should aim not at restoring lost function, but at enhancing neuroplasticity to overcome asymmetric neural drive.

- **Proof of Concept:** The study confirms the feasibility and safety of the combined iTBS+MST paradigm.
- **Rationale for Synergy:** The preserved corticospinal function (Figures 8-9) provides a "clean slate" upon which iTBS (a central neuromodulator) can potentially enhance the neural adaptations to MST (a peripheral strength stimulus). This directly tests the hypothesis that priming the motor cortex can amplify training-induced plasticity.

- Targeted Application: By focusing on the more-affected upper limb, this approach addresses a common but often neglected source of disability, moving beyond the traditional focus on gait and balance.

3. The Functional Challenge: Cognitive-Motor Interference (Study 3)

The systematic review on dual-task gait explains the core functional deficit that exercise must address. It shows that gait in PD loses its automaticity, becoming cognitively demanding. The observed biomechanical stiffening (reduced joint movement) and compensatory prefrontal cortex overactivation during dual-tasking provide a neurophysiological model for why people with PD struggle with complex, real-world mobility. This study directly links the cognitive deficits highlighted in Study 1 (where BDNF mediated cognitive gain) to motor performance, revealing the critical interference that occurs in daily life.

4. The Clinical Translation: Efficacy and Specificity (Study 4)

The umbrella review translates the mechanisms and challenges into clinical evidence. It confirms the broad efficacy of exercise for motor and non-motor symptoms and advances the field by demonstrating intervention specificity (e.g., dance for balance, resistance training for strength). This answers the "what works" question. Furthermore, by endorsing the role of neuroplastic mechanisms, it directly connects the clinical benefits back to the BDNF pathway identified in Study 1. The call for "precision prescription" is a direct response to the heterogeneous deficits outlined in Study 3.

Collectively, these works do not merely stand side by side; they engage in a dialectic that constructs a compelling research trajectory. This trajectory can be summarized as a progressive pipeline that moves from fundamental mechanism to personalized application:

- Why it works (Mechanism): Exercise induces neuroplasticity via molecules like BDNF (Study 1).
- What to target (Dysfunction): A key functional impairment is the loss of automatic movement control, requiring excessive cognitive resources and leading to gait deterioration (Study 3).
- How to innovate (Synergy): Preliminary data support exploring combined brain stimulation and high-intensity training to maximally engage plasticity, especially for under-addressed issues like upper limb function and neuromuscular fatigue (Study 2).
- What to prescribe (Evidence): A wide array of exercises is effective, and the choice should be tailored to the patient's specific goal (Study 4).

This integrated perspective positions the new pilot data not as an outlier, but as the logical next step in developing advanced, mechanism-driven rehabilitation strategies for PD. It shifts the narrative from "exercise is beneficial" to "how can we optimize and potentiate exercise-induced neuroplasticity for precise clinical targets?"

Integrated Discussion

From Molecular Mechanisms to Functional Recovery: A Cohesive Narrative

The integration of these four studies reveals a compelling, multi-level narrative that spans from molecular mechanisms to clinical application. Study 1 (Paterno, Polsinelli et al. 2024) provides the foundational molecular piece, demonstrating that structured exercise increases BDNF in PD. BDNF is a well-established critical mediator of synaptic plasticity, neuroprotection, neuronal survival, and synaptogenesis (Miranda, Morici et al. 2019). This finding offers a crucial biological mechanism for the broad functional improvements documented on a large scale by Study 4 (the Umbrella Review), which confirms the efficacy of exercise across motor and non-motor domains. This link between exercise, BDNF, and clinical improvement is supported by a growing consensus that physical activity is a powerful modulator of brain health and function in neurodegeneration (Cotman, Berchtold et al. 2007, Hirsch, Iyer et al. 2016).

Decoding a Core Functional Deficit: The Dual-Task Paradigm

Study 3 (the Systematic Review on DT) provides the critical functional link by elucidating a specific, ecologically relevant deficit: the breakdown of gait under DT conditions with a secondary task (cognitive or motor). The observed biomechanical signature, reduced sagittal plane kinematics and compromised propulsion, is not merely a global slowing but reflects a fundamental loss of automaticity (Wu, Hallett et al. 2015). This forces a shift to a conscious, cognitively driven control strategy, a phenomenon captured by the consistent finding of compensatory prefrontal cortex (PFC) overactivation (Ehgoetz Martens, Silveira et al. 2018, Orcioli-Silva, Vitorio et al. 2020). This aligns with models like “CRUNCH”, which posits that older adults and clinical populations recruit additional prefrontal resources to maintain performance under high cognitive demand (Reuter-Lorenz and Cappell 2008). This vulnerability is particularly pronounced in specific subgroups, such as patients with FOG or the PIGD phenotype, who show greater dual-task costs.

This breakdown has direct biomechanical and metabolic consequences. The impaired ankle push-off, likely due to altered muscle activation patterns (e.g., a shift from phasic to tonic activation of the gastrocnemius), disrupts the generation of propulsive impulse. This, in turn, perturbs the pendulum-like mechanism of gait, degrading its energy-saving efficiency (Leal-Nascimento, da Silva et al. 2022). Consequently, the DT cost in PD represents a shift to a more metabolically costly and unstable gait pattern (Peyre-Tartaruga, Martinez et al. 2022), directly contributing to fatigue and limited community ambulation.

Towards Targeted Interventions: Combining Central and Peripheral Strategies

In this context, Study 2 (the iTBS+MST Protocol) represents the logical next step: a sophisticated intervention designed to directly target the identified pathophysiology via a combined, bidirectional approach.

The protocol employs iTBS to prime the motor cortex. iTBS enhances cortical excitability and promotes neuroplasticity (Huang, Edwards et al. 2005). This "priming" is hypothesized to work, in part, by upregulating the release of neurotrophic factors, such as BDNF, thereby creating a brain state more receptive to subsequent learning (Li Voti, Conte et al. 2014, Suppa, Huang et al. 2016).

This central neuromodulation is synergistically paired with MST. While MST directly improves peripheral neuromuscular function and force generation (Falvo, Schilling et al. 2008), its effects are not confined to the muscle. Vigorous muscular contractions trigger the release of myokines and exerkines (e.g., cathepsin B, FNDC5/irisin), which can cross the blood-brain barrier and further stimulate BDNF production and neuroplasticity in the brain (Pedersen and Febbraio 2012, Wrann, White et al. 2013). Therefore, MST is not merely "training the periphery"; it initiates a powerful humoral signal that feeds back to enhance central adaptation.

This combined strategy of centrally "priming" the cortex and peripherally "training" the muscle, which in turn signals back to the brain, constitutes a promising, closed-loop paradigm in neurorehabilitation (Lefaucheur, Aleman et al. 2020). To directly test these mechanistic hypotheses, future iterations of this protocol should incorporate biomarker analyses. Measuring serum BDNF and myokine levels before and after intervention would clarify the humoral mediators of improvement. Furthermore, genotyping participants for the BDNF val66met polymorphism (rs6265) is crucial, as this common genetic variant significantly impacts activity-dependent BDNF secretion and trafficking, likely influencing individual responsiveness to both iTBS and exercise-based interventions (Egan, Kojima et al. 2003, Notaras and van den Buuse 2019). The application of this sophisticated paradigm to the often-neglected upper limb in PD is a particularly noteworthy aspect of the study design. In contrast, passive modalities such as WBV have shown minimal and inconsistent motor benefits, precluding their recommendation as a standalone therapy and underscoring the importance of active, targeted exercise modalities (Sitja Rabert, Rigau Comas et al. 2012, He, Su et al. 2020).

Between General Efficacy and Personalization: The Future of Rehabilitation

A critical tension, and the field's evolution, is evident between the general evidence and the push for personalization. Study 4 suggests that structured exercise is generally beneficial. For instance, while recent reviews have framed dance as an adjunct therapy (Pinto, Simon Myra et al. 2024), its mechanisms align more precisely with those of a targeted exercise modality for improving balance, mood, and cognition. In contrast, Studies 2 and 3 drive the field toward precision medicine. A promising path forward is to move beyond broad clinical phenotypes and stratify patients based on specific functional subgroups defined by quantifiable deficits (Espay, Schwarzschild et al. 2017). For instance, patients could be categorized by their DT cost profile, degree of propulsive impairment, or distinct biomechanical patterns during complex tasks. Research has already shown that patients with the akinetic-rigid subtype exhibit significantly impaired anticipatory postural adjustments and a more conservative gait pattern

compared to other subtypes (Casal, Peyre-Tartaruga et al. 2021). Such stratification would allow for a more nuanced prescription, matching interventions like the combined iTBS + MST protocol or targeted DT training to individuals whose specific functional impairments predict the greatest benefit.

Bridging the Gap: From Laboratory Evidence to Clinical Implementation

While the chain of evidence, from BDNF modulation (Study 1) through the elucidation of functional deficits under dual-task conditions (Study 3) to innovative combined interventions (Study 2) and the confirmation of large-scale efficacy (Study 4), provides a compelling scientific rationale, a critical translational gap remains. This heterogeneity in assessment, including DT protocols, underscores the need for novel, standardized tools with demonstrated reliability and validity in neurodegenerative populations, such as the Dual-Task Assessment in R (DTAiR) battery (Longhurst, Rider et al. 2022). The ultimate challenge lies in moving these findings from controlled research settings into routine clinical practice. Despite robust efficacy data, the widespread adoption of sophisticated interventions is often hampered by barriers related to resource availability, clinician training, patient adherence, and integration with standard care pathways (Keus SHJ 2014, Ferrazzoli, Ortellì et al. 2018). This implementation gap is well-documented, with studies showing that evidence-based allied health services remain underutilized in routine care despite their proven benefits (Bloem, Eimers et al. 2021). Therefore, the next frontier in PD's rehabilitation is implementation science. Future research must not only ask "what works?" but also "how can this be delivered effectively and sustainably in diverse clinical and community contexts?". For instance, combined central-peripheral approaches, such as the iTBS + MST protocol, require feasibility studies to adapt them for use in real-world rehabilitation centers. Similarly, dual-task assessment and training must be simplified and standardized for busy clinical environments without losing their ecological validity. Closing this gap is paramount to realizing the full potential of the mechanistic and efficacy evidence, ensuring that scientific advances translate into tangible improvements in mobility, cognition, and quality of life for people with PD. In this sense, the umbrella review (Study 4) offers a menu of effective options, but the future lies in creating the practical "recipe" for their delivery, effectively bridging the bench-to-bedside divide.

Clinical Implications and Future Perspectives

- For Clinical Practice: Clinicians can rely on the solid evidence from the Umbrella Review to promote exercise as a therapeutic pillar. However, they should refine prescriptions using specialized knowledge, such as assessing the dual-task deficit to identify patients at higher risk of falls and considering the implications for gait economy. Furthermore, they should consider research that explores combined interventions for specific goals.

- For Future Research: It is crucial to bridge the gap between generic evidence and personalized application. Future studies should follow the methodological rigor exemplified by the Protocol, incorporate biomarkers like BDNF to validate mechanisms of action, and utilize complex functional outcomes, such as dual-tasking and detailed biomechanical and metabolic analyses (e.g., measuring propulsive impulse and energy recovery), to measure efficacy in ecological contexts. It is crucial to bridge the gap between generic evidence and personalized application. Future studies should build upon the preliminary findings and methodological rigor exemplified by the iTBS+MST pilot study (Study 2), incorporate biomarkers like BDNF (Study 1) to validate mechanisms of action, and utilize complex functional outcomes, such as dual-tasking (Study 3), to measure efficacy in ecological contexts.

Limitations of the present analysis

This analysis was limited by the heterogeneity of the included studies (from meta-analysis to a pilot study), which prevented statistical synthesis. Furthermore, while Study 2 now provides preliminary empirical data, these findings are from an initial pilot phase with a small sample size. Consequently, conclusions regarding the efficacy and mechanisms of the combined iTBS+MST intervention remain preliminary until confirmed by the full-powered, definitive randomized controlled trial currently in progress.

7. Summary and conclusion

Summary of the Thesis

This thesis undertakes a comprehensive analysis of non-pharmacological interventions in PD by critically examining four distinct yet interconnected bodies of literature. The objective was to move beyond a simple summary of effectiveness and towards an integrated understanding of the mechanisms, specific applications, and future directions of neuromodulation and physical exercise in PD management.

The journey began at the molecular level with Study 1 (Paterno, Polsinelli et al. 2024), which established a fundamental mechanism of action: structured physical exercise significantly increases BDNF, a key neurotrophin. In the context of PD, elevated BDNF is associated with both enhanced synaptic plasticity, which underlies cognitive and motor learning, and neuroprotection, supporting the survival and function of vulnerable neuronal populations (Petzinger, Holschneider et al. 2015, Miranda, Morici et al. 2019, Palasz, Niewiadomski et al. 2019). This finding provides a compelling biological rationale for the broader functional benefits of exercise, suggesting it may modify disease progression, not just symptomatology (Petzinger, Fisher et al. 2013, Ferrazzoli, Ortelli et al. 2018, Bloem, Eimers et al. 2021).

Building on this, Study 2 (iTBS+MST Protocol) represented a forward-looking methodological proposal. It outlined a protocol for testing a synergistic intervention combining intermittent iTBS, a form of non-invasive brain stimulation targeting cortical excitability (Suppa, Huang et al. 2016), with MST to address upper limb function and fatigue. This study highlighted the shift towards targeted, mechanism-based combination therapies.

The focus then narrowed onto a critical clinical challenge with Study 3 (Dual-Task Review), which detailed the specific biomechanical and cognitive impairments that emerge when individuals with PD walk while performing a secondary task (cognitive or motor). This review identified a core set of alterations that define DT walking in PD: a consistent and profound reduction in stride length and gait velocity, increased gait variability, and a specific impairment in propulsion control linked to reduced sagittal plane kinematics (ankle, knee, hip). These deficits were mechanistically explained by a loss of gait automaticity, necessitating compensatory overactivation of the prefrontal cortex, which led to a less efficient and more energetically costly gait pattern (Wu and Hallett 2005, Maidan, Rosenberg-Katz et al. 2017).

Finally, Study 4 (Umbrella Review) provided the overarching context, synthesizing evidence from hundreds of systematic reviews to offer compelling evidence that physical exercise, in its various forms, is effective in improving a wide range of motor and non-motor symptoms in PD, thereby solidifying its role as a cornerstone of rehabilitation.

Integrated Conclusion

The integration of these four studies leads to several overarching conclusions:

1. **A Multi-Level Evidence Base:** The evidence for non-pharmacological interventions in PD is robust and spans from molecular mechanisms (BDNF increase) to specific functional deficits (dual-task impairment) and overall symptomatic efficacy. This multi-level understanding strengthens the case for integrating these interventions into standard care.
2. **The Primacy of Neuroplasticity:** A central, unifying theme is the role of neuroplasticity. The benefits of exercise are mediated, at least in part, by plasticity-promoting molecules like BDNF. Furthermore, interventions like iTBS are explicitly designed to modulate plasticity, and the reversal of dual-task deficits likely involves plastic reorganization of brain networks. Harnessing neuroplasticity is, therefore, the common goal of these diverse approaches.
3. **From General Principles to Personalization:** The field is evolving from establishing general efficacy ("exercise is good") towards personalizing rehabilitation ("which specific exercise, combined with what, for which patient?"). The tension between the umbrella review's broad conclusions and the highly specific iTBS+MST protocol is not a contradiction but a sign of a maturing field moving towards precision medicine.
4. **Functional Relevance is Key:** The dual-task paradigm reminds us that true improvement is measured in ecologically valid contexts. Future research and clinical practice must prioritize outcomes that reflect real-world challenges, such as walking while talking, to truly enhance patient autonomy and reduce the risk of falls.

Implications and Future Directions

For Clinical Practice:

- **Prescribe Exercise Confidently:** Clinicians should recommend structured exercise as a core, non-negotiable component of PD management, based on the overwhelming evidence.
- **Adhere to and Adapt Dosage:** Prescriptions should follow established dose-response principles, adhering to guidelines for frequency, intensity, and duration (e.g., ≥ 150 minutes of moderate-intensity aerobic exercise weekly, plus 2-3 days of strength and balance training). Crucially, this dosage must be adapted based on the individual's disease stage, fitness level, fatigue, and specific functional goals.
- **Refine Prescriptions:** Assessment should include dual-task testing to identify individuals at high risk of falls who would benefit most from cognitive-motor training.

- Consider the Whole Patient: Rehabilitation programs should not neglect the upper limb and fatigue, areas targeted by emerging protocols and crucial for quality of life.

For Future Research:

- Mechanistic Studies: Future trials should incorporate biomarkers (e.g., BDNF, neuroimaging) to validate mechanisms of action and identify responders.
- Combination Interventions: There is a need for more rigorous RCTs testing the synergy between different modalities (e.g., brain stimulation + physical training, as in the iTBS+MST protocol).
- Personalized Protocols: Research should focus on defining biomarkers and clinical features that can predict which patients will benefit most from which specific intervention.
- Long-Term Outcomes: Studies with longer follow-ups are needed to assess the sustainability of benefits and the potential *disease-modifying* effects of these interventions.

Final Conclusion

In conclusion, this thesis demonstrates that the management of PD is undergoing a significant paradigm shift. The evidence clearly shows that non-pharmacological strategies, ranging from structured physical activity to advanced neuromodulation techniques, are powerful tools that act in concert with, rather than merely alongside, pharmacological treatments (Bloem, de Vries et al. 2015). By understanding the molecular mechanisms, targeting specific functional deficits, and moving towards personalized combination therapies, the future of PD rehabilitation is poised to become more effective, precise, and profoundly impactful on patients' lives. *The journey "from the molecule to the movement" is not only possible but essential for advancing care.*

Bibliography

- (2019). "Abstract book of the 5th World Parkinson Congress, Kyoto, Japan, June 4–7, 2019." Journal of Parkinson's Disease **9**: 1-278.
- Abou, L., A. Alluri, A. Fliflet, Y. T. Du and L. A. Rice (2021). "Effectiveness of Physical Therapy Interventions in Reducing Fear of Falling Among Individuals With Neurologic Diseases: A Systematic Review and Meta-analysis." ARCHIVES OF PHYSICAL MEDICINE AND REHABILITATION **102**(1): 132-154.
- Abuoaf, R., R. AlKaabi, A. Mohamed Saleh, U. Zerough, T. Hartley, S. M. van Niekerk, H. Khalil and L. D. Morris (2023). "The effect of physical exercise on anxiety in people with parkinson's disease: A systematic review of randomized control trials." NeuroRehabilitation **52**(3): 387-402.
- Aburub, A., S. J. Ledger, J. Sim and S. M. Hunter (2020). "Cardiopulmonary Function and Aerobic Exercise in Parkinson's: A Systematic Review of the Literature." Mov Disord Clin Pract **7**(6): 599-606.
- Adamson, B. C., I. Ensari and R. W. Motl (2015). "Effect of exercise on depressive symptoms in adults with neurologic disorders: a systematic review and meta-analysis." Arch Phys Med Rehabil **96**(7): 1329-1338.
- Aftanas, L. I., M. M. Gevorgyan, S. Y. Zhanaeva, S. S. Dzemidovich, K. I. Kulikova, E. L. Al'perina, K. V. Danilenko and G. V. Idova (2018). "Therapeutic Effects of Repetitive Transcranial Magnetic Stimulation (rTMS) on Neuroinflammation and Neuroplasticity in Patients with Parkinson's Disease: a Placebo-Controlled Study." Bull Exp Biol Med **165**(2): 195-199.
- Aguiar, L. P. C., P. A. da Rocha and M. Morris (2016). "Therapeutic Dancing for Parkinson's Disease." International Journal of Gerontology **10**(2): 64-70.
- Ahler, J. R., H. Busk, P. M. Holm, A. Bricca, D. V. Poulsen, S. T. Skou and L. H. Tang (2024). "Benefits and harms of structured outdoor physical activity for people with somatic or mental diseases: A systematic review and meta-analysis." Prev Med **183**: 107966.
- Ain, Z., S. Parveen, C. A. Sehgal, M. D. Manzar and M. M. Noohu (2025). "Effects of remote rehabilitation with modern technologies on impairments in people with Parkinson's disease: A systematic review and meta-analysis." Technology and Disability **37**(1): 45-62.
- Ainsworth, B. E., W. L. Haskell, S. D. Herrmann, N. Meckes, D. R. Bassett, Jr., C. Tudor-Locke, J. L. Greer, J. Vezina, M. C. Whitt-Glover and A. S. Leon (2011). "2011 Compendium of Physical Activities: a second update of codes and MET values." Med Sci Sports Exerc **43**(8): 1575-1581.
- Akrama, G., L. Sitzmann and C. Baumann (2023). "Der Einfluss vom Exergaming mit kommerziell verfügbaren Spielkonsolen auf die Balance und Lebensqualität bei Menschen mit idiopathischem Parkinson-Syndrom–Eine systematische Übersichtsarbeit." physioscience **19**(02): 63-73.
- Al-Yahya, E., W. Mahmoud, D. Meester, P. Esser and H. Dawes (2018). "Neural Substrates of Cognitive Motor Interference During Walking; Peripheral and Central Mechanisms." Front Hum Neurosci **12**: 536.
- Alanazi, M. A. (2024). "The Role of Physical Activity in Adjunctive Nursing Management of Neuro-Degenerative Diseases among Older Adults: A Systematic Review of Interventional Studies." Life (Basel) **14**(5).
- Alberts, J. L. and A. B. Rosenfeldt (2020). "The Universal Prescription for Parkinson's Disease: Exercise." J Parkinsons Dis **10**(s1): S21-s27.
- Alcock, L., B. Galna, S. Lord and L. Rochester (2016). "Characterisation of foot clearance during gait in people with early Parkinson's disease: Deficits associated with a dual task." J Biomech **49**(13): 2763-2769.
- Aldana-Benitez, D., M. J. Caicedo-Pareja, D. P. Sanchez and L. T. Ordonez-Mora (2023). "Dance as a neurorehabilitation strategy: A systematic review." J Bodyw Mov Ther **35**: 348-363.
- Alexandre de Assis, I. S., G. J. Luvizutto, A. C. M. Bruno and L. A. P. Sande de Souza (2020). "The Proprioceptive Neuromuscular Facilitation Concept in Parkinson Disease: A Systematic Review and Meta-Analysis." J Chiropr Med **19**(3): 181-187.

- Alharthi, A. S. (2024). "Interpretable machine learning comprehensive human gait deterioration analysis." *Front Neuroinform* **18**: 1451529.
- Allen, N. E., C. G. Canning, L. R. S. Almeida, B. R. Bloem, S. H. Keus, N. Lofgren, A. Nieuwboer, G. S. Verheyden, T. P. Yamato and C. Sherrington (2022). "Interventions for preventing falls in Parkinson's disease." *Cochrane Database Syst Rev* **6**: Cd011574.
- Allen, N. E., C. Sherrington, S. S. Paul and C. G. Canning (2011). "Balance and falls in Parkinson's disease: a meta-analysis of the effect of exercise and motor training." *Mov Disord* **26**(9): 1605-1615.
- Allen, N. E., C. Sherrington, G. D. Suriyarachchi, S. S. Paul, J. Song and C. G. Canning (2012). "Exercise and motor training in people with Parkinson's disease: a systematic review of participant characteristics, intervention delivery, retention rates, adherence, and adverse events in clinical trials." *Parkinsons Dis* **2012**: 854328.
- Alvarez, I., J. Latorre, M. Aguilar, P. Pastor and R. Llorens (2020). "Validity and sensitivity of instrumented postural and gait assessment using low-cost devices in Parkinson's disease." *J Neuroeng Rehabil* **17**(1): 149.
- Alvarez-Bueno, C., J. J. Deeks, I. Cavero-Redondo, K. Jolly, A. I. Torres-Costoso, M. Price, R. Fernandez-Rodriguez and V. Martinez-Vizcaino (2023). "Effect of Exercise on Motor Symptoms in Patients With Parkinson's Disease: A Network Meta-analysis." *J Geriatr Phys Ther* **46**(2): E87-e105.
- Alves Da Rocha, P., J. McClelland and M. E. Morris (2015). "Complementary physical therapies for movement disorders in Parkinson's disease: a systematic review." *Eur J Phys Rehabil Med* **51**(6): 693-704.
- Alwardat, M., M. Etoom, S. Al Dajah, T. Schirizzi, G. Di Lazzaro, P. Sinibaldi Salimei, N. Biagio Mercuri and A. Pisani (2018). "Effectiveness of robot-assisted gait training on motor impairments in people with Parkinson's disease: a systematic review and meta-analysis." *Int J Rehabil Res* **41**(4): 287-296.
- Aman, J. E., N. Elangovan, I. L. Yeh and J. Konczak (2014). "The effectiveness of proprioceptive training for improving motor function: a systematic review." *Front Hum Neurosci* **8**: 1075.
- Amato, A., S. Baldassano, S. Vasto, G. Schirò, C. Davì, P. Drid, F. A. Dos Santos Mendes, R. Caldarella, M. D'Amelio and P. Proia (2022). "Effects of a Resistance Training Protocol on Physical Performance, Body Composition, Bone Metabolism, and Systemic Homeostasis in Patients Diagnosed with Parkinson's Disease: A Pilot Study." *Int J Environ Res Public Health* **19**(20).
- Amboni, M., P. Barone, L. Iuppariello, I. Lista, R. Tranfaglia, A. Fasano, M. Picillo, C. Vitale, G. Santangelo, V. Agosti, A. Iavarone and G. Sorrentino (2012). "Gait patterns in Parkinsonian patients with or without mild cognitive impairment." *Mov Disord* **27**(12): 1536-1543.
- American College of Sports Medicine., T., W. R., Gordon, N. F., & Pescatello, L. S. (2020). *ACSM's guidelines for exercise testing and prescription*. 10th ed. Philadelphia, Lippincott Williams & Wilkins.
- Amirthalingam, J., G. Paidi, K. Alshowaikh, A. Iroshani Jayarathna, D. Salibindla, K. Karpinska-Leydier and H. E. Ergin (2021). "Virtual Reality Intervention to Help Improve Motor Function in Patients Undergoing Rehabilitation for Cerebral Palsy, Parkinson's Disease, or Stroke: A Systematic Review of Randomized Controlled Trials." *Cureus* **13**(7): e16763.
- Angelucci, F., A. Peppe, G. A. Carlesimo, F. Serafini, S. Zabberoni, F. Barban, J. Shofany, C. Caltagirone and A. Costa (2015). "A pilot study on the effect of cognitive training on BDNF serum levels in individuals with Parkinson's disease." *Front Hum Neurosci* **9**: 130.
- Angelucci, F., J. Piermaria, F. Gelfo, J. Shofany, M. Tramontano, M. Fiore, C. Caltagirone and A. Peppe (2016). "The effects of motor rehabilitation training on clinical symptoms and serum BDNF levels in Parkinson's disease subjects." *Can J Physiol Pharmacol* **94**(4): 455-461.
- Aras, B., G. K. Seyyar, O. Fidan and E. Colak (2022). "The effect of Tai Chi on functional mobility, balance and falls in Parkinson's disease: A systematic review and meta-analysis of systematic reviews." *Explore (NY)* **18**(4): 402-410.
- Arenales Arauz, Y. L., G. Ahuja, Y. P. T. Kamsma, A. Kortholt, E. A. van der Zee and M. J. G. van Heuvelen (2022). "Potential of Whole-Body Vibration in Parkinson's Disease: A Systematic Review and Meta-Analysis of Human and Animal Studies." *Biology (Basel)* **11**(8).
- Arheix-Parras, S., C. Barrios, G. Python, M. Cogne, I. Sibon, M. Engelhardt, P. Dehail, H. Cassoudealle, G. Moucheboeuf and B. Glize (2021). "A systematic review of repetitive transcranial magnetic stimulation in aphasia rehabilitation: Leads for future studies." *Neurosci Biobehav Rev* **127**: 212-241.

- Asgharzadeh Chamleh, M. R., M. Afkanpour, D. Tehrany Dehkordy, N. Norouzkhani and S. Aalaei (2025). "Game-based telerehabilitation in neurological disorders: a systematic review of features, opportunities and challenges." *Disabil Rehabil Assist Technol* **20**(5): 1257-1271.
- Ayán Pérez, C. and J. M. Cancela (2014). "Effectiveness of water-based exercise in people living with Parkinson's disease: a systematic review." *European Review of Aging and Physical Activity* **11**(2): 107-118.
- Azevedo, L. V. D., J. R. Pereira, R. M. S. Santos, N. P. Rocha, A. L. Teixeira, P. P. Christo, V. R. Santos and P. L. Scalzo (2022). "Acute exercise increases BDNF serum levels in patients with Parkinson's disease regardless of depression or fatigue." *EUROPEAN JOURNAL OF SPORT SCIENCE* **22**(8): 1296-1303.
- Baglio, F., A. Pirastru, N. Bergsland, M. Cazzoli and E. Tavazzi (2022). "Neuroplasticity mediated by motor rehabilitation in Parkinson's disease: A systematic review on structural and functional MRI markers." *Reviews in the Neurosciences* **33**(2): 213-226.
- Baglio, F., A. Pirastru, N. Bergsland, M. Cazzoli and E. Tavazzi (2022). "Neuroplasticity mediated by motor rehabilitation in Parkinson's disease: a systematic review on structural and functional MRI markers." *Rev Neurosci* **33**(2): 213-226.
- Baker, K., L. Rochester and A. Nieuwboer (2008). "The effect of cues on gait variability--reducing the attentional cost of walking in people with Parkinson's disease." *Parkinsonism Relat Disord* **14**(4): 314-320.
- Ban, M., X. Yue, P. Dou and P. Zhang (2021). "The Effects of Yoga on Patients with Parkinson's Disease: A Meta-Analysis of Randomized Controlled Trials." *Behav Neurol* **2021**: 5582488.
- Barbieri, F. A., L. Simieli, D. Orcioli-Silva, A. M. Baptista, M. Borkowske Pestana, V. Spiandor Beretta, P. C. R. Dos Santos and L. T. Bucken Gobbi (2018). "Obstacle Avoidance Increases Asymmetry of Crossing Step in Individuals With Parkinson's Disease and Neurologically Healthy Individuals." *J Mot Behav* **50**(1): 17-25.
- Barbieri, R. A., F. A. Barbieri, N. Zelada-Astudillo, V. C. Moreno, C. A. Kalva-Filho and A. R. Zamuner (2025). "Influence of Aerobic Exercise on Functional Capacity and Maximal Oxygen Uptake in Patients With Parkinson Disease: A Systematic Review and Meta- analysis." *Arch Phys Med Rehabil* **106**(1): 134-144.
- Barboza, T. V., C. Weizemann and A. R. Carvalho (2021). "Causal relationship between spatiotemporal parameters of walking and the locomotor rehabilitation index in healthy people." *Gait Posture* **90**: 320-325.
- Barclay, A., S. R. Gray, L. Paul and S. Rooney (2022). "The effects of cycling using lower limb active passive trainers in people with neurological conditions: a systematic review." *International Journal of Therapy And Rehabilitation* **29**(6): 1-21.
- Barnish, M. S. and S. M. Barran (2020). "A systematic review of active group-based dance, singing, music therapy and theatrical interventions for quality of life, functional communication, speech, motor function and cognitive status in people with Parkinson's disease." *BMC Neurol* **20**(1): 371.
- Barnish, M. S., S. E. Reynolds and R. V. Nelson-Horne (2025). "Active group-based performing arts interventions in Parkinson's disease: an updated systematic review and meta-analysis." *BMJ Open* **15**(4): e089920.
- Barry, G., B. Galna and L. Rochester (2014). "The role of exergaming in Parkinson's disease rehabilitation: a systematic review of the evidence." *J Neuroeng Rehabil* **11**: 33.
- Bastioli, G., J. C. Arnold, M. Mancini, A. C. Mar, B. Gamallo-Lana, K. Saadipour, M. V. Chao and M. E. Rice (2022). "Voluntary Exercise Boosts Striatal Dopamine Release: Evidence for the Necessary and Sufficient Role of BDNF." *J Neurosci* **42**(23): 4725-4736.
- Beck, A. T., R. A. Steer and G. Brown (1996). "Beck depression inventory-II." *Psychological assessment*.
- Belchior, L. D., B. S. Tomaz, A. P. V. Abdon, N. A. F. Frota, D. G. B. Mont'Alverne and D. M. Gaspar (2017). "Treadmill in Parkinson's: influence on gait, balance, BDNF and Reduced Glutathione." *Fisioterapia em Movimento* **30**: 93-100.
- Berti, A., M. Pini and F. Ferrarello (2020). "Argentine tango in the care of Parkinson's disease: A systematic review and analysis of the intervention." *Complement Ther Med* **52**: 102474.

Bevilacqua, R., M. Benadduci, F. Barbarossa, G. Amabili, V. Di Donna, C. Martella, G. Pelliccioni, G. R. Riccardi and E. Maranesi (2024). "Effectiveness of Technological Interventions for Older Adults With Parkinson Disease: Systematic Review." *JMIR Serious Games* **12**: e53431.

Bevilacqua, R., E. Maranesi, G. R. Riccardi, V. D. Donna, P. Pelliccioni, R. Luzi, F. Lattanzio and G. Pelliccioni (2019). "Non-Immersive Virtual Reality for Rehabilitation of the Older People: A Systematic Review into Efficacy and Effectiveness." *J Clin Med* **8**(11).

Bianchini, E., E. Warmerdam, R. Romijnders, C. Hansen, F. E. Pontieri and W. Maetzler (2022). "Cognitive dual-task cost depends on the complexity of the cognitive task, but not on age and disease." *Front Neurol* **13**: 964207.

Bickel, C. S., J. M. Cross and M. M. Bamman (2011). "Exercise dosing to retain resistance training adaptations in young and older adults." *Med Sci Sports Exerc* **43**(7): 1177-1187.

Bigland-Ritchie, B. and J. J. Woods (1984). "Changes in muscle contractile properties and neural control during human muscular fatigue." *Muscle Nerve* **7**(9): 691-699.

Bishnoi, A., R. Lee, Y. Hu, J. R. Mahoney and M. E. Hernandez (2022). "Effect of Treadmill Training Interventions on Spatiotemporal Gait Parameters in Older Adults with Neurological Disorders: Systematic Review and Meta-Analysis of Randomized Controlled Trials." *Int J Environ Res Public Health* **19**(5).

Bishnoi, A., M. Shankar, R. Lee, Y. Hu and M. E. Hernandez (2023). "Effects of Therapeutic Intervention on Spatiotemporal Gait Parameters in Adults With Neurologic Disorder: Systematic Review and Meta-analysis." *Arch Phys Med Rehabil* **104**(3): 451-474.

Bispo, D., C. Lins, K. L. Hawkes, S. Tripp and T. K. Khoo (2024). "The Positive Effects of Physical Activity on Quality of Life in Parkinson's Disease: A Systematic Review." *Geriatrics (Basel)* **9**(4).

Bloem, B. R., N. M. de Vries and G. Ebersbach (2015). "Nonpharmacological treatments for patients with Parkinson's disease." *Mov Disord* **30**(11): 1504-1520.

Bloem, B. R., M. Eimers, M. S. van Galen, M. Munneke and S. K. L. Darweesh (2021). "From trials to clinical practice: Temporal trends in the coverage of specialized allied health services for Parkinson's disease." *Eur J Neurol* **28**(3): 775-782.

Bloem, B. R., M. S. Okun and C. Klein (2021). "Parkinson's disease." *Lancet* **397**(10291): 2284-2303.

Bluett, B., E. Bayram and I. Litvan (2019). "The virtual reality of Parkinson's disease freezing of gait: A systematic review." *Parkinsonism Relat Disord* **61**: 26-33.

Bohnen, N. I., K. A. Frey, S. Studenski, V. Kotagal, R. A. Koeppe, P. J. Scott, R. L. Albin and M. L. Muller (2013). "Gait speed in Parkinson disease correlates with cholinergic degeneration." *Neurology* **81**(18): 1611-1616.

Bohnen, N. I., P. Kanel and M. Muller (2018). "Molecular Imaging of the Cholinergic System in Parkinson's Disease." *Int Rev Neurobiol* **141**: 211-250.

Bolognini, N., A. Pascual-Leone and F. Fregni (2009). "Using non-invasive brain stimulation to augment motor training-induced plasticity." *J Neuroeng Rehabil* **6**: 8.

Bombieri, F., F. Schena, B. Pellegrini, P. Barone, M. Tinazzi and R. Erro (2017). "Walking on four limbs: A systematic review of Nordic Walking in Parkinson disease." *Parkinsonism Relat Disord* **38**: 8-12.

Bonnechere, B., B. Jansen, L. Omelina and S. Van Sint Jan (2016). "The use of commercial video games in rehabilitation: a systematic review." *Int J Rehabil Res* **39**(4): 277-290.

Bouca-Machado, R., A. Rosario, D. Caldeira, A. Castro Caldas, D. Guerreiro, M. Venturelli, M. Tinazzi, F. Schena and J. F. J (2020). "Physical Activity, Exercise, and Physiotherapy in Parkinson's Disease: Defining the Concepts." *Mov Disord Clin Pract* **7**(1): 7-15.

Braz de Oliveira, M. P., C. Rigo Lima, S. L. A. da Silva, E. C. Firmino Vaz Figueira, B. David Truax and S. M. Smaili (2024). "Effect of aquatic exercise programs according to the International Classification of Functionality, Disability and Health domains in individuals with Parkinson's disease: a systematic review and meta- analysis with GRADE quality assessment." *Disabil Rehabil* **46**(3): 429-442.

Braz, N. F. T., L. R. Dutra, P. E. S. Medeiros, A. A. Scianni and C. D. C. d. M. Faria (2018). "Effectiveness of Nintendo Wii in functional and health outcomes of individuals with Parkinson's disease: A systematic review." *Fisioterapia e Pesquisa* **25**: 100-106.

Briennesse, L. A. and M. N. Emerson (2013). "Effects of resistance training for people with Parkinson's disease: a systematic review." *J Am Med Dir Assoc* **14**(4): 236-241.

- Brito, K. S., T. R. dos Santos and A. T. Magalhães (2022). "Os efeitos da reabilitação baseada em exercícios sobre a marcha de pacientes com doença de Parkinson: uma revisão sistemática." *Fisioterapia Brasil* **23**(1): 152-172.
- Brown, L. A., N. de Bruin, J. B. Doan, O. Suchowersky and B. Hu (2009). "Novel Challenges to Gait in Parkinson's Disease: The Effect of Concurrent Music in Single- and Dual-Task Contexts." *Archives of Physical Medicine and Rehabilitation* **90**(9): 1578-1583.
- Brunoni, A. R., A. Chaimani, A. H. Moffa, L. B. Razza, W. F. Gattaz, Z. J. Daskalakis and A. F. Carvalho (2017). "Repetitive Transcranial Magnetic Stimulation for the Acute Treatment of Major Depressive Episodes: A Systematic Review With Network Meta- analysis." *JAMA Psychiatry* **74**(2): 143-152.
- Bryant, M. S., D. H. Rintala, E. C. Lai and E. J. Protas (2010). "An investigation of two interventions for micrographia in individuals with Parkinson's disease." *Clin Rehabil* **24**(11): 1021-1026.
- Brzycki, M. (1993). "Strength Testing—Predicting a One-Rep Max from Reps-to-Fatigue." *Journal of Physical Education, Recreation & Dance* **64**(1): 88-90.
- Bull, F. C., S. S. Al-Ansari, S. Biddle, K. Borodulin, M. P. Buman, G. Cardon, C. Carty, J. P. Chaput, S. Chastin, R. Chou, P. C. Dempsey, L. DiPietro, U. Ekelund, J. Firth, C. M. Friedenreich, L. Garcia, M. Gichu, R. Jago, P. T. Katzmarzyk, E. Lambert, M. Leitzmann, K. Milton, F. B. Ortega, C. Ranasinghe, E. Stamatakis, A. Tiedemann, R. P. Troiano, H. P. van der Ploeg, V. Wari and J. F. Willumsen (2020). "World Health Organization 2020 guidelines on physical activity and sedentary behaviour." *Br J Sports Med* **54**(24): 1451-1462.
- Burrai, F., L. Apuzzo and R. Zanotti (2024). "Effectiveness of Rhythmic Auditory Stimulation on Gait in Parkinson Disease: A Systematic Review and Meta-analysis." *Holist Nurs Pract* **38**(2): 109-119.
- Cabeleira, M. E. P., L. A. da Campo, P. S. Corrêa and F. Cechetti (2022). "Home-based exercises with minimal oversight in Parkinson's Disease motor function: A systematic review and meta-analysis." *Scientia Medica* **32**(1): e42035-e42035.
- Calabro, R. S., A. Naro, V. Cimino, A. Buda, G. Paladina, G. Di Lorenzo, A. Manuli, D. Milardi, P. Bramanti and A. Bramanti (2020). "Improving motor performance in Parkinson's disease: a preliminary study on the promising use of the computer assisted virtual reality environment (CAREN)." *Neurol Sci* **41**(4): 933-941.
- Campo-Prieto, P., D. Santos-Garcia, J. M. Cancela-Carral and G. Rodriguez-Fuentes (2021). "Current status of immersive virtual reality as a tool for physical and functional rehabilitation in patients with Parkinson's disease: systematic review." *REVISTA DE NEUROLOGIA* **73**(10): 358-367.
- Campos, C., N. B. Rocha, E. Lattari, F. Paes, A. E. Nardi and S. Machado (2016). "Exercise-induced neuroprotective effects on neurodegenerative diseases: the key role of trophic factors." *Expert Rev Neurother* **16**(6): 723-734.
- Cano Porras, D., P. Siemonsma, R. Inzelberg, G. Zeilig and M. Plotnik (2018). "Advantages of virtual reality in the rehabilitation of balance and gait: Systematic review." *Neurology* **90**(22): 1017-1025.
- Carapellotti, A. M., R. Stevenson and M. Doumas (2020). "The efficacy of dance for improving motor impairments, non-motor symptoms, and quality of life in Parkinson's disease: A systematic review and meta-analysis." *PLoS One* **15**(8): e0236820.
- Cardoso, A., D. C. Sa-Caputo, N. R. Asad, M. J. van Heuvelen, E. A. van der Zee, A. Ribeiro-Carvalho and M. Bernardo-Filho (2022). "Beneficial effects of whole-body vibration exercise for brain disorders in experimental studies with animal models: a systematic review." *Behav Brain Res* **431**: 113933.
- Cardoso, S. V., S. R. Fernandes and M. T. Tomas (2024). "Therapeutic Importance of Exercise in Neuroplasticity in Adults with Neurological Pathology: Systematic Review." *Int J Exerc Sci* **17**(1): 1105-1119.
- Carlson, S. J., Y. F. Chiu, M. R. Landers, N. E. Fritz, V. R. Mishra and J. K. Longhurst (2024). "Dual-Task Performance and Brain Morphologic Characteristics in Parkinson's Disease." *Neurodegener Dis*: 1-11.
- Carmignano, S. M., C. Fundaro, D. Bonaiuti, R. S. Calabro, A. Cassio, D. Mazzoli, E. Bizzarini, I. Campanini, S. Cerulli, C. Chisari, V. Colombo, S. Dalise, V. Gazzotti, D. Mazzoleni, M. Mazzucchelli, C. Melegari, A. Merlo, G. Stampacchia, P. Boldrini, S. Mazzoleni, F. Posteraro, P. Benanti, E. Castelli, F. Draicchio, V. Falabella, S. Galeri, F. Gimigliano, M. Grigioni, S. Mazzon, F. Molteni, G. Morone, M. Petrarca, A. Picelli, M. Senatore, G. Turchetti and E. Andrenelli (2022). "Robot-assisted gait training in

patients with Parkinson's disease: Implications for clinical practice. A systematic review." NeuroRehabilitation **51**(4): 649-663.

Carroll, L. M., M. E. Morris, W. T. O'Connor and A. M. Clifford (2020). "Is Aquatic Therapy Optimally Prescribed for Parkinson's Disease? A Systematic Review and Meta-Analysis." Journal of Parkinson's Disease **10**(1): 59-76.

Carson, R. G. and N. C. Kennedy (2013). "Modulation of human corticospinal excitability by paired associative stimulation." Front Hum Neurosci **7**: 823.

Casal, M. Z., L. A. Peyre-Tartaruga, A. P. J. Zanardi, A. Ivaniski-Mello, L. L. Alves, A. N. Haas and F. G. Martinez (2021). "Postural Adjustments and Biomechanics During Gait Initiation and Obstacle Negotiation: A Comparison Between Akinetic-Rigid and Hyperkinetic Parkinson's Disease." Front Physiol **12**: 723628.

Cascaes da Silva, F., R. Iop Rda, P. Domingos Dos Santos, L. M. Aguiar Bezerra de Melo, P. J. Barbosa Gutierrez Filho and R. da Silva (2016). "Effects of Physical-Exercise-Based Rehabilitation Programs on the Quality of Life of Patients With Parkinson's Disease: A Systematic Review of Randomized Controlled Trials." J Aging Phys Act **24**(3): 484-496.

Caspersen, C. J., K. E. Powell and G. M. Christenson (1985). "Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research." Public Health Rep **100**(2): 126-131.

Celnik, P. (2015). "Understanding and modulating motor learning with cerebellar stimulation." Cerebellum **14**(2): 171-174.

Chang, H., Y. Song and X. Cen (2022). "Effectiveness of Augmented Reality for Lower Limb Rehabilitation: A Systematic Review." Appl Bionics Biomech **2022**: 4047845.

Chartier, C., J. Godard, S. Durand, A. Humeau-Heurtier, E. Menetrier, P. Allain and J. Besnard (2024). "Combinations of physical and cognitive training for subcortical neurodegenerative diseases with physical, cognitive and behavioral symptoms: a systematic review." Neurol Sci **45**(12): 5571-5589.

Charvet, L. E., B. Dobbs, M. T. Shaw, M. Bikson, A. Datta and L. B. Krupp (2018). "Remotely supervised transcranial direct current stimulation for the treatment of fatigue in multiple sclerosis: Results from a randomized, sham-controlled trial." Mult Scler **24**(13): 1760-1769.

Chen, K., Y. Tan, Y. Lu, J. Wu, X. Liu and Y. Zhao (2020). "Effect of Exercise on Quality of Life in Parkinson's Disease: A Systematic Review and Meta-Analysis." Parkinsons Dis **2020**: 3257623.

Chen, S., Y. Zhang, Y. T. Wang, X. Liu, W. Song and X. Du (2020). "The effect of Qigong-based therapy on patients with Parkinson's disease: a systematic review and meta-analysis." Clin Rehabil **34**(12): 1436-1448.

Chen, Y., Q. Gao, C. Q. He and R. Bian (2020). "Effect of Virtual Reality on Balance in Individuals With Parkinson Disease: A Systematic Review and Meta-Analysis of Randomized Controlled Trials." Phys Ther **100**(6): 933-945.

Cheng, W. H., Y. Quan and W. F. Thompson (2024). "The effect of dance on mental health and quality of life of people with Parkinson's disease: A systematic review and three-level meta-analysis." Arch Gerontol Geriatr **120**: 105326.

Chiong, J. D., V. Patel and H. M. Tairan (2019). "Effects of physical exercise on gait and balance in patients with parkinson's disease." Critical Reviews in Physical and Rehabilitation Medicine **31**(3): 217-232.

Choi, H. Y., K. H. Cho, C. Jin, J. Lee, T. H. Kim, W. S. Jung, S. K. Moon, C. N. Ko, S. Y. Cho, C. Y. Jeon, T. Y. Choi, M. S. Lee, S. H. Lee, E. K. Chung and S. Kwon (2020). "Exercise Therapies for Parkinson's Disease: A Systematic Review and Meta- Analysis." Parkinsons Dis **2020**: 2565320.

Chrysagis, N., G. Trompouki, D. Petropaulis, G. A. Koumantakis, G. Krekoulas, G. Theotokatos, E. Skordilis and V. Sakellari (2024). "Effect of Boxing Exercises on the Functional Ability and Quality of Life of Individuals with Parkinson's Disease: A Systematic Review." Eur J Investig Health Psychol Educ **14**(5): 1295-1310.

Chu, H. T., C. M. Cheng, C. S. Liang, W. H. Chang, C. H. Juan, Y. Z. Huang, J. S. Jeng, Y. M. Bai, S. J. Tsai, M. H. Chen and C. T. Li (2021). "Efficacy and tolerability of theta-burst stimulation for major depression: A systematic review and meta-analysis." Prog Neuropsychopharmacol Biol Psychiatry **106**: 110168.

Chuang, C. S., Y. W. Chen, B. Y. Zeng, C. M. Hung, Y. K. Tu, Y. C. Tai, Y. C. Wu, C. W. Hsu, W. T. Lei, S. L. Wu, B. Stubbs, A. F. Carvalho, K. P. Su, T. Y. Chen, P. T. Tseng, M. K. Wu and C. H. Tsai (2022). "Effects of modern technology (exergame and virtual reality) assisted rehabilitation vs conventional rehabilitation in patients with Parkinson's disease: a network meta-analysis of randomised controlled trials." *Physiotherapy* **117**: 35-42.

Chung, C. L., S. Thilarajah and D. Tan (2016). "Effectiveness of resistance training on muscle strength and physical function in people with Parkinson's disease: a systematic review and meta-analysis." *Clin Rehabil* **30**(1): 11-23.

Ciccarelli, N., B. Colombo, F. Pepe, E. Magni, A. Antonietti and M. C. Silveri (2022). "Cognitive reserve: a multidimensional protective factor in Parkinson's disease related cognitive impairment." *Neuropsychol Dev Cogn B Aging Neuropsychol Cogn* **29**(4): 687-702.

Cirillo, J., G. Todd and J. G. Semmler (2011). "Corticomotor excitability and plasticity following complex visuomotor training in young and old adults." *Eur J Neurosci* **34**(11): 1847-1856.

Clark, D. J. (2015). "Automaticity of walking: functional significance, mechanisms, measurement and rehabilitation strategies." *Front Hum Neurosci* **9**: 246.

Coelho, D. B., C. E. N. de Oliveira, M. V. C. Guimaraes, C. Ribeiro de Souza, M. L. Dos Santos and A. C. de Lima-Pardini (2022). "A systematic review on the effectiveness of perturbation-based balance training in postural control and gait in Parkinson's disease." *Physiotherapy* **116**: 58-71.

Committee, P. A. G. A. (2008). Physical Activity Guidelines Advisory Committee Report. Washington, DC: U.S. Department of Health and Human Services.

Comparan, M. (2018). *Dual-task Training vs. Aerobic Training to Improve Gait in Subjects with Parkinson's Disease: A Meta-Analysis*, California State University, Fresno.

Corcos, D. M., J. A. Robichaud, F. J. David, S. E. Leurgans, D. E. Vaillancourt, C. Poon, M. R. Rafferty, W. M. Kohrt and C. L. Comella (2013). "A two-year randomized controlled trial of progressive resistance exercise for Parkinson's disease." *Mov Disord* **28**(9): 1230-1240.

Corradini, J. R., A. P. Silveira-Ciola, V. A. I. Pereira, M. H. Kuroda, M. H. Faria, L. Simieli, J. Tavares and F. A. Barbieri (2022). "Dual tasking reduces gait asymmetry of trajectory deviation during obstacle circumvention in people with Parkinson's disease." *Hum Mov Sci* **83**: 102938.

Corrales Gómez, J. D., T. Torres Naranjo, E. O. Orozco Villa and S. H. Barbosa Granados (2023). "Effects of Exercise and Physical Activity on Quality of Life in Patients with Parkinson's Disease: A Systematic Review." *MHSalud* **20**(2): 115-131.

Correa, T. V., T. da Silva Rocha Paz, S. Allodi, V. L. S. de Britto and C. L. Correa (2020). "Progressive muscle-strength protocol for the functionality of upper limbs and quality of life in individuals with Parkinson's disease: Pilot study." *Complement Ther Med* **52**: 102432.

Cortes-Perez, I., N. Zagalaz-Anula, D. Montoro-Cardenas, R. Lomas-Vega, E. Obrero-Gaitan and M. C. Osuna-Perez (2021). "Leap Motion Controller Video Game-Based Therapy for Upper Extremity Motor Recovery in Patients with Central Nervous System Diseases. A Systematic Review with Meta-Analysis." *Sensors (Basel)* **21**(6).

Cosentino, C., M. Baccini, M. Putzolu, D. Ristori, L. Avanzino and E. Pelosin (2020). "Effectiveness of Physiotherapy on Freezing of Gait in Parkinson's Disease: A Systematic Review and Meta-Analysis." *Mov Disord* **35**(4): 523-536.

Costa, V., A. de Oliveira Barreto Suassuna, T. Souza Silva Brito, T. Frigo da Rocha and A. C. Gianlorenço (2025). "Physical exercise for the management of cognitive symptoms in Parkinson's disease: systematic review and meta-analysis." *Physical & Occupational Therapy In Geriatrics* **43**(1): 68-93.

Costa, V., J. M. Prati, A. de Oliveira Barreto Suassuna, T. Souza Silva Brito, T. Frigo da Rocha and A. C. Gianlorenço (2024). "Physical Exercise for Treating the Anxiety and Depression Symptoms of Parkinson's Disease: Systematic Review and Meta-Analysis." *J Geriatr Psychiatry Neurol* **37**(6): 415-435.

Costa, V., A. O. B. Suassuna, T. S. S. Brito, T. F. da Rocha and A. C. Gianlorenço (2023). "Physical exercise for treating non-motor symptoms assessed by general Parkinson's disease scales: systematic review and meta-analysis of clinical trials." *BMJ Neurol Open* **5**(2): e000469.

Cotman, C. W., N. C. Berchtold and L. A. Christie (2007). "Exercise builds brain health: key roles of growth factor cascades and inflammation." *Trends Neurosci* **30**(9): 464-472.

Cristini, J., M. Weiss, B. De Las Heras, A. Medina-Rincon, A. Dagher, R. B. Postuma, R. Huber, J. Doyon, P. Rosa-Neto, J. Carrier, A. W. Amara and M. Roig (2021). "The effects of exercise on sleep quality in persons with Parkinson's disease: A systematic review with meta-analysis." Sleep Med Rev **55**: 101384.

Crizzle, A. M. and I. J. Newhouse (2006). "Is physical exercise beneficial for persons with Parkinson's disease?" Clin J Sport Med **16**(5): 422-425.

Cruickshank, T. M., A. R. Reyes and M. R. Ziman (2015). "A systematic review and meta-analysis of strength training in individuals with multiple sclerosis or parkinson disease." Medicine (United States) **94**(4).

Cugusi, L., A. Manca, M. Bergamin, A. Di Blasio, M. Monticone, F. Deriu and G. Mercurio (2019). "Aquatic exercise improves motor impairments in people with Parkinson's disease, with similar or greater benefits than land-based exercise: a systematic review." J Physiother **65**(2): 65-74.

Cugusi, L., A. Manca, D. Dragone, F. Deriu, P. Solla, C. Secci, M. Monticone and G. Mercurio (2017). "Nordic Walking for the Management of People With Parkinson Disease: A Systematic Review." Pm r **9**(11): 1157-1166.

Cugusi, L., L. Prosperini and G. Mura (2021). "Exergaming for Quality of Life in Persons Living with Chronic Diseases: A Systematic Review and Meta-analysis." Pm r **13**(7): 756-780.

Cugusi, L., P. Solla, R. Serpe, T. Carzedda, L. Piras, M. Oggianu, S. Gabba, A. Di Blasio, M. Bergamin, A. Cannas, F. Marrosu and G. Mercurio (2015). "Effects of a Nordic Walking program on motor and non-motor symptoms, functional performance and body composition in patients with Parkinson's disease." NeuroRehabilitation **37**(2): 245-254.

Cui, W., Z. Hu, J. Li, S. Wang and R. Xu (2024). "The impact of aerobic exercise dose based on ACSM recommendations on patients with Parkinson's disease: a systematic review and meta-analysis of randomized controlled trials." Front Aging Neurosci **16**: 1419643.

Cui, W., D. Li, L. Yue and J. Xie (2023). "The effects of exercise dose on patients with Parkinson's disease: a systematic review and meta-analysis of randomized controlled trials." J Neurol **270**(11): 5327-5343.

Cusso, M. E., K. J. Donald and T. K. Khoo (2016). "The Impact of Physical Activity on Non-Motor Symptoms in Parkinson's Disease: A Systematic Review." Front Med (Lausanne) **3**: 35.

Cwiekala-Lewis, K. J., M. Gallek and R. E. Taylor-Piliae (2017). "The effects of Tai Chi on physical function and well-being among persons with Parkinson's Disease: A systematic review." J Bodyw Mov Ther **21**(2): 414-421.

da Costa Daniele, T. M., P. F. C. de Bruin, R. S. de Matos, G. S. de Bruin, C. J. Maia Chaves and V. M. S. de Bruin (2020). "Exercise effects on brain and behavior in healthy mice, Alzheimer's disease and Parkinson's disease model-A systematic review and meta- analysis." Behav Brain Res **383**: 112488.

Da Silva, F. C., R. D. R. Iop, L. C. De Oliveira, A. M. Boll, J. G. S. De Alvarenga, P. J. B. G. Filho, L. M. A. B. De Melo, A. J. Xavier and R. Da Silva (2018). "Effects of physical exercise programs on cognitive function in Parkinson's disease patients: A systematic review of randomized controlled trials of the last 10 years." PLoS ONE **13**(2).

da Silva Germanos, S., B. Vieira, I. Reichert Vital da Silva, J. J. da Cunha, S. Nique, V. Striebel, D. Pochmann and V. Rostirola Elsner (2019). "The impact of an aquatic exercise program on BDNF levels in Parkinson's disease patients: short-and long-term outcomes." Funct Neurol **34**(2): 65-70.

da Silva, P. G., D. D. Domingues, L. A. de Carvalho, S. Allodi and C. L. Correa (2016). "Neurotrophic factors in Parkinson's disease are regulated by exercise: Evidence-based practice." J Neurol Sci **363**: 5-15.

Dai, S., H. Yuan, J. Wang, Y. Yang and S. Wen (2023). "Effects of aquatic exercise on the improvement of lower-extremity motor function and quality of life in patients with Parkinson's disease: A meta-analysis." Front Physiol **14**: 1066718.

Dalrymple-Alford, J. C., M. R. MacAskill, C. T. Nakas, L. Livingston, C. Graham, G. P. Crucian, T. R. Melzer, J. Kirwan, R. Keenan, S. Wells, R. J. Porter, R. Watts and T. J. Anderson (2010). "The MoCA: well-suited screen for cognitive impairment in Parkinson disease." Neurology **75**(19): 1717-1725.

Dauwan, M., M. J. H. Begemann, M. I. E. Slot, E. H. M. Lee, P. Scheltens and I. E. C. Sommer (2021). "Physical exercise improves quality of life, depressive symptoms, and cognition across chronic brain disorders: a transdiagnostic systematic review and meta-analysis of randomized controlled trials." J Neurol **268**(4): 1222-1246.

de Almeida, F. O., V. Santana, D. M. Corcos, C. Ugrinowitsch and C. Silva-Batista (2022). Effects of Endurance Training on Motor Signs of Parkinson's Disease: A Systematic Review and Meta-Analysis. Sports Med. New Zealand, (c) 2022. The Author(s), under exclusive licence to Springer Nature Switzerland AG. **52**: 1789-1815.

de Almeida, H. S., F. Porto, M. Porretti, G. Lopes, D. Fiorot, P. D. S. Bunn and E. B. da Silva (2021). "Effect of Dance on Postural Control in People with Parkinson's Disease: A Meta-Analysis Review." J Aging Phys Act **29**(1): 130-141.

de Almeida, S. B., E. S. Tavares Sobreira, C. P. de Lucena Alves, D. P. Lima, J. de Carvalho Bonfadini, M. A. Sobreira-Neto, T. H. Freitas, S. L. do Nascimento and P. Braga-Neto (2025). "Effect of power training on physical functional performance of patients with Parkinson's disease: A systematic review and meta-analysis of randomized controlled trials." PLoS One **20**(2): e0314058.

de Dreu, M. J., A. S. D. van der Wilk, E. Poppe, G. Kwakkel and E. E. H. van Wegen (2012). "Rehabilitation, exercise therapy and music in patients with Parkinson's disease: A meta-analysis of the effects of music-based movement therapy on walking ability, balance and quality of life." Parkinsonism and Related Disorders **18**(SUPPL. 1): S114-S119.

De Freitas Tb Ms, P. T., P. B. Leite, P. T. Doná F PhD, P. T. Pompeu Je PhD, P. T. Swarowsky A PhD and P. T. Torriani-Pasin C PhD (2020). "The effects of dual task gait and balance training in Parkinson's disease: a systematic review." Physiother Theory Pract **36**(10): 1088-1096.

de Goede, C. J., S. H. Keus, G. Kwakkel and R. C. Wagenaar (2001). "The effects of physical therapy in Parkinson's disease: a research synthesis." Arch Phys Med Rehabil **82**(4): 509-515.

De Keersmaecker, E., N. Lefeber, M. Geys, E. Jespers, E. Kerckhofs and E. Swinnen (2019). "Virtual reality during gait training: does it improve gait function in persons with central nervous system movement disorders? A systematic review and meta-analysis." NeuroRehabilitation **44**(1): 43-66.

De la Rosa, A., E. Solana, R. Corpas, D. Bartrés-Faz, M. Pallàs, J. Vina, C. Sanfeliu and M. C. Gomez-Cabrera (2019). "Long-term exercise training improves memory in middle-aged men and modulates peripheral levels of BDNF and Cathepsin B." Sci Rep **9**(1): 3337.

de Lima, K. P., C. N. da Silva, N. F. de Seixas, M. de Santana Maneschy, B. N. Lima, G. V. Junior, A. P. Novo and K. da Silva Almeida (2022). "Effect of resistance training on balance and postural control in people with Parkinson's: A systematic review." Revista Científica de la Sociedad de Enfermería Neurológica (English ed.) **56**: 18-28.

De Natale, G., E. Qorri, J. Todri and O. Lena (2025). "Impact of Virtual Reality Alone and in Combination with Conventional Therapy on Balance in Parkinson's Disease: A Systematic Review with a Meta-Analysis of Randomized Controlled Trials." Medicina (Kaunas) **61**(3).

de Oliveira, L. C., L. C. Mendes, R. A. de Lopes, J. A. S. Carneiro, A. Cardoso, E. A. L. Júnior and A. de Oliveira Andrade (2021). "A systematic review of serious games used for rehabilitation of individuals with Parkinson's disease." Research on Biomedical Engineering **37**(4): 849-865.

de Oliveira, M. P. B., D. F. M. Lobato, S. M. Smaili, C. Carvalho and J. B. C. Borges (2021). "Effect of aerobic exercise on functional capacity and quality of life in individuals with Parkinson's disease: A systematic review of randomized controlled trials." Arch Gerontol Geriatr **95**: 104422.

De Santis, K. K. and I. Kaplan (2020). "The motor and the non-motor outcomes of Nordic Walking in Parkinson's disease: A systematic review." J Bodyw Mov Ther **24**(2): 4-10.

De Vitis, A., A. Battaglini, P. Sinatti, E. A. S. Romero, L. Bissolotti, D. Cotella and J. H. Villafañe (2023). "Effects of telemedicine for postural instability in independent patients with Parkinson's disease: a literature review." Topics in Geriatric Rehabilitation **39**(4): 294-306.

Deane, K. H., D. Jones, C. Ellis-Hill, C. E. Clarke, E. D. Playford and Y. Ben-Shlomo (2001). "A comparison of physiotherapy techniques for patients with Parkinson's disease." Cochrane Database Syst Rev(1): Cd002815.

Deane, K. H., D. Jones, E. D. Playford, Y. Ben-Shlomo and C. E. Clarke (2001). "Physiotherapy for patients with Parkinson's Disease: a comparison of techniques." Cochrane Database Syst Rev(3): Cd002817.

del Pozo-Cruz, B., J. C. Adsuar, J. A. Parraca, J. del Pozo-Cruz, P. R. Olivares and N. Gusi (2012). "Using whole-body vibration training in patients affected with common neurological diseases: a systematic literature review." J Altern Complement Med **18**(1): 29-41.

- Delgado-Alvarado, M., M. Marano, A. Santurtun, A. Urtiaga-Gallano, D. Tordesillas-Gutierrez and J. Infante (2020). "Nonpharmacological, nonsurgical treatments for freezing of gait in Parkinson's disease: A systematic review." *Mov Disord* **35**(2): 204-214.
- Dibble, L. E., O. Addison and E. Papa (2009). "The effects of exercise on balance in persons with parkinson's disease: A systematic review across the disability spectrum." *Journal of Neurologic Physical Therapy* **33**(1): 14-26.
- Dincher, A. (2023). "Effects of a Single Session of Whole Body Vibration Compared to Multiple Sessions—An Updated Review and Meta-Analysis." *Vibration* **6**(4): 932-944.
- Dincher, A., M. Schwarz and G. Wydra (2019). "Analysis of the Effects of Whole-Body Vibration in Parkinson Disease - Systematic Review and Meta-Analysis." *Pm r* **11**(6): 640-653.
- Dinoff, A., N. Herrmann, W. Swardfager, C. S. Liu, C. Sherman, S. Chan and K. L. Lanctot (2016). "The Effect of Exercise Training on Resting Concentrations of Peripheral Brain-Derived Neurotrophic Factor (BDNF): A Meta-Analysis." *PLoS One* **11**(9): e0163037.
- do Amaral, C. M. S., S. B. de Almeida, R. P. de Almeida, S. L. do Nascimento, R. M. Ribeiro and P. Braga-Neto (2024). "Effectiveness of vestibular rehabilitation on postural balance in Parkinson's disease: a systematic review and meta-analysis of randomized controlled trials." *BMC Neurol* **24**(1): 161.
- Dockx, K., E. M. Bekkers, V. Van den Bergh, P. Ginis, L. Rochester, J. M. Hausdorff, A. Mirelman and A. Nieuwboer (2016). "Virtual reality for rehabilitation in Parkinson's disease." *Cochrane Database Syst Rev* **12**: Cd010760.
- Donida, R., M. dos Santos Delabary, R. Costa and A. Haas (2023). "Effects of dance on balance in Parkinson's disease: A Systematic Review with Meta-Analysis." *Revista Andaluza de Medicina del Deporte* **16**.
- Dorsey E. R., E. A., Nichols E., et al. (2018). "Global, regional, and national burden of Parkinson's disease, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016." *Lancet Neurol* **17**(11): 939-953.
- Dos Santos Delabary, M., I. G. Komerowski, E. P. Monteiro, R. R. Costa and A. N. Haas (2018). "Effects of dance practice on functional mobility, motor symptoms and quality of life in people with Parkinson's disease: a systematic review with meta-analysis." *Aging Clin Exp Res* **30**(7): 727-735.
- Doucet, B. M., I. Franc and E. G. Hunter (2021). "Interventions Within the Scope of Occupational Therapy to Improve Activities of Daily Living, Rest, and Sleep in People With Parkinson's Disease: A Systematic Review." *Am J Occup Ther* **75**(3).
- Downes, M. J., M. L. Brennan, H. C. Williams and R. S. Dean (2016). "Development of a critical appraisal tool to assess the quality of cross- sectional studies (AXIS)." *BMJ Open* **6**(12): e011458.
- Dragasevic-Miskovic, N. T., V. Bobic, M. Kostic, I. Stankovic, S. Radovanovic, K. Dimitrijevic, M. Svetel, I. Petrovic and M. Duric-Jovicic (2021). "Impact of depression on gait variability in Parkinson's disease." *Clin Neurol Neurosurg* **200**: 106324.
- Drks (2011). "Morphometric correlates and predictors of impaired gait and balance in Parkinson's Disease-a pilot study." <https://trialsearch.who.int/Trial2.aspx?TrialID=DRKS00003290>.
- Du, Q., Y. Wei, Y. Ma, C. Liu, S. Du, Q. Zhang, X. Gong, J. Yang, Q. Li and K. Li (2025). "Efficacy of Virtual Reality-Based Interventions on Cognitive Function in Patients With Neuropsychiatric Disorders: Systematic Review and Meta- Analysis of Randomized Controlled Trials." *JMIR Serious Games* **13**: e67501.
- Du, Y. H., J. Ma, J. Y. Hu, L. Zhu, L. Y. Wang, R. Y. Yang, L. C. Liang, M. Jiang, M. Cai and J. Pu (2023). "Effects of dual-task training on gait and motor ability in patients with Parkinson's disease: A systematic review and meta-analysis." *Clin Rehabil* **37**(7): 942-953.
- Dubois, B., A. Slachevsky, I. Litvan and B. Pillon (2000). "The FAB: a Frontal Assessment Battery at bedside." *Neurology* **55**(11): 1621-1626.
- Dunabeitia, I., D. Gonzalez-Devesa, N. Blanco-Martinez and C. Ayan-Perez (2025). "The effects of stretching in Parkinson's disease: A systematic review of randomized controlled trials." *Parkinsonism Relat Disord* **134**: 107796.
- DÁVILA-MORÁN, R. C., J. S. MONTENEGRO, J. M. CHÁVEZ-DÍAZ and E. F. PERALTA LOAYZA "USES OF VIRTUAL REALITY IN PHYSICAL REHABILITATION: A SYSTEMATIC REVIEW."

Egan, M. F., M. Kojima, J. H. Callicott, T. E. Goldberg, B. S. Kolachana, A. Bertolino, E. Zaitsev, B. Gold, D. Goldman, M. Dean, B. Lu and D. R. Weinberger (2003). "The BDNF val66met polymorphism affects activity-dependent secretion of BDNF and human memory and hippocampal function." *Cell* **112**(2): 257-269.

Egger, M., G. Davey Smith, M. Schneider and C. Minder (1997). "Bias in meta-analysis detected by a simple, graphical test." *BMJ* **315**(7109): 629-634.

Ehgoetz Martens, K. A., C. R. A. Silveira, B. N. Intzandt and Q. J. Almeida (2018). "Overload From Anxiety: A Non-Motor Cause for Gait Impairments in Parkinson's Disease." *J Neuropsychiatry Clin Neurosci* **30**(1): 77-80.

El Hayek, M., J. L. M. Lobo Jofili Lopes, J. H. LeLaurin, M. E. Gregory, A. M. Abi Nehme, P. McCall-Junkin, K. L. K. Au, M. S. Okun and R. G. Salloum (2023). "Type, Timing, Frequency, and Durability of Outcome of Physical Therapy for Parkinson Disease: A Systematic Review and Meta-Analysis." *JAMA Netw Open* **6**(7): e2324860.

Elbers, R. G., J. Verhoef, E. E. van Wegen, H. W. Berendse and G. Kwakkel (2015). "Interventions for fatigue in Parkinson's disease." *Cochrane Database Syst Rev*(10): Cd010925.

Elena, P., S. Demetris, M. Christina and P. Marios (2021). "Differences Between Exergaming Rehabilitation and Conventional Physiotherapy on Quality of Life in Parkinson's Disease: A Systematic Review and Meta-Analysis." *Front Neurol* **12**: 683385.

Ellis, T. and L. Rochester (2018). "Mobilizing Parkinson's Disease: The Future of Exercise." *J Parkinsons Dis* **8**(s1): S95-s100.

Emmanouilidis, S., M. E. Hackney, S. C. Slade, H. Heng, D. Jazayeri and M. E. Morris (2021). "Dance Is an Accessible Physical Activity for People with Parkinson's Disease." *Parkinsons Dis* **2021**: 7516504.

Ernst, M., A. K. Folkerts, R. Gollan, E. Lieker, J. Caro-Valenzuela, A. Adams, N. Cryns, I. Monsef, A. Dresen, M. Roheger, C. Eggers, N. Skoetz and E. Kalbe (2023). "Physical exercise for people with Parkinson's disease: a systematic review and network meta-analysis." *Cochrane Database Syst Rev* **1**: CD013856.

Ernst, M., A. K. Folkerts, R. Gollan, E. Lieker, J. Caro-Valenzuela, A. Adams, N. Cryns, I. Monsef, A. Dresen, M. Roheger, C. Eggers, N. Skoetz and E. Kalbe (2024). "Physical exercise for people with Parkinson's disease: a systematic review and network meta-analysis." *Cochrane Database Syst Rev* **4**: Cd013856.

Erra, C., I. Mileti, M. Germanotta, M. Petracca, I. Imbimbo, A. De Biase, S. Rossi, D. Ricciardi, A. Pacilli, E. Di Sipio, E. Palermo, A. R. Bentivoglio and L. Padua (2019). "Immediate effects of rhythmic auditory stimulation on gait kinematics in Parkinson's disease ON/OFF medication." *Clin Neurophysiol* **130**(10): 1789-1797.

Espay, A. J., M. A. Schwarzschild, C. M. Tanner, H. H. Fernandez, D. K. Simon, J. B. Leverenz, A. Merola, A. Chen-Plotkin, P. Brundin, M. A. Kauffman, R. Erro, K. Kieburtz, D. Woo, E. A. Macklin, D. G. Standaert and A. E. Lang (2017). "Biomarker-driven phenotyping in Parkinson's disease: A translational missing link in disease-modifying clinical trials." *Mov Disord* **32**(3): 319-324.

Evancho, A., W. J. Tyler and K. McGregor (2023). "A review of combined neuromodulation and physical therapy interventions for enhanced neurorehabilitation." *Front Hum Neurosci* **17**: 1151218.

Fail, L. B., D. A. Marinho, E. A. Marques, M. J. Costa, C. C. Santos, M. C. Marques, M. Izquierdo and H. P. Neiva (2022). "Benefits of aquatic exercise in adults with and without chronic disease-A systematic review with meta-analysis." *Scand J Med Sci Sports* **32**(3): 465-486.

Falvo, M. J., B. K. Schilling and G. M. Earhart (2008). "Parkinson's disease and resistive exercise: rationale, review, and recommendations." *Mov Disord* **23**(1): 1-11.

Fan, W., J. Li, W. Wei, S. H. Xiao, Z. J. Liao, S. M. Wang and K. N. K. Fong (2022). "Effects of rhythmic auditory stimulation on upper-limb movements in patients with Parkinson's disease." *Parkinsonism Relat Disord* **101**: 27-30.

Fan, X., K. G. Soh, C. Y. Mun and K. L. Soh (2025). "Effects of different types of Tai Chi intervention on motor function in older adults: a systematic review." *Aging Clin Exp Res* **37**(1): 32.

Fang, X., D. Han, Q. Cheng, P. Zhang, C. Zhao, J. Min and F. Wang (2018). "Association of Levels of Physical Activity With Risk of Parkinson Disease: A Systematic Review and Meta-analysis." *JAMA network open* **1**(5): e182421.

Farashi, S., L. Kiani and S. Bashirian (2021). "Effect of Exercise on Parkinson's Disease Tremor: A Meta-analysis Study." Tremor Other Hyperkinet Mov (N Y) **11**: 15.

Farshbaf, M. J., K. Ghaedi, T. L. Megraw, J. Curtiss, M. S. Faradonbeh, P. Vaziri and M. H. Nasr-Esfahani (2016). "Does PGC1 alpha/FNDC5/BDNF Elicit the Beneficial Effects of Exercise on Neurodegenerative Disorders?" NEUROMOLECULAR MEDICINE **18**(1): 1-15.

Fearnley, J. M. and A. J. Lees (1991). "Ageing and Parkinson's disease: substantia nigra regional selectivity." Brain **114** (Pt 5): 2283-2301.

Federico, S., L. Cacciante, B. Cieslik, A. Turolla, M. Agostini, P. Kiper and A. Picelli (2024). "Telerehabilitation for Neurological Motor Impairment: A Systematic Review and Meta-Analysis on Quality of Life, Satisfaction, and Acceptance in Stroke, Multiple Sclerosis, and Parkinson's Disease." J Clin Med **13**(1).

Feller, D., I. Fox, P. Gozzer, F. Trentin and D. Papola (2023). "Exercise for Depressive Symptoms in Parkinson Disease: A Systematic Review and Meta-analysis of Randomized Controlled Trials." Arch Phys Med Rehabil **104**(2): 331-339.

Feng, F., H. Xu, Y. Sun, X. Zhang, N. Li, X. Sun, X. Tian and R. Zhao (2023). "Exercise for prevention of falls and fall-related injuries in neurodegenerative diseases and aging-related risk conditions: a meta-analysis." Front Endocrinol (Lausanne) **14**: 1187325.

Fernandes, A., A. S. Sousa, N. Rocha and J. M. Tavares (2016). "Parkinson's Disease and Cognitive-Motor Dual-Task: Is Motor Prioritization Possible in the Early Stages of the Disease?" J Mot Behav **48**(4): 377-383.

Fernandes, J., R. M. Arida and F. Gomez-Pinilla (2017). "Physical exercise as an epigenetic modulator of brain plasticity and cognition." Neurosci Biobehav Rev **80**: 443-456.

Fernandes, Â., T. Coelho, A. Vitória, A. Ferreira, R. Santos, N. Rocha, L. Fernandes and J. M. R. S. Tavares (2015). "Standing balance in individuals with Parkinson's disease during single and dual-task conditions." Gait & Posture **42**(3): 323-328.

Fernandes, Â., A. S. Sousa, N. Rocha and J. M. Tavares (2016). "Parkinson's Disease and Cognitive-Motor Dual-Task: Is Motor Prioritization Possible in the Early Stages of the Disease?" J Mot Behav **48**(4): 377-383.

Fernandez-Gonzalez, D., I. Rodriguez-Costa, I. Sanz-Esteban and C. Estrada-Barranco (2023). "Therapeutic intervention with virtual reality in patients with Parkinson's disease for upper limb motor training: A systematic review." Rehabilitacion (Madr) **57**(2): 100751.

Fernandez-Lago, H., O. Bello, V. Lopez-Alonso, J. A. Sanchez, L. Morenilla and M. A. Fernandez-del-Olmo (2015). "Gait Pattern and Cognitive Performance During Treadmill Walking in Parkinson Disease." AMERICAN JOURNAL OF PHYSICAL MEDICINE & REHABILITATION **94**(11): 931-940.

Ferraz, D., K. Trippo, A. Dominguez and A. Santos Filho JO. Nintendo Wii training on postural balance and mobility rehabilitation of adults with Parkinson's disease: a systematic review. Fisioter Mov. 2017; **30**: 383-393.

Ferrazzoli, D., P. Orтели, G. Madeo, N. Giladi, G. M. Petzinger and G. Frazzitta (2018). "Basal ganglia and beyond: The interplay between motor and cognitive aspects in Parkinson's disease rehabilitation." Neurosci Biobehav Rev **90**: 294-308.

Ferreira, A. F. F., K. H. Binda and C. C. Real (2021). "The effects of treadmill exercise in animal models of Parkinson's disease: A systematic review." Neurosci Biobehav Rev **131**: 1056-1075.

Ferreira, R. N., A. S. de Miranda, N. P. Rocha, E. S. A. C. Simoes, A. L. Teixeira and E. R. da Silva Camargos (2018). "Neurotrophic Factors in Parkinson's Disease: What Have we Learned from Pre-Clinical and Clinical Studies?" Curr Med Chem **25**(31): 3682-3702.

Flach, A., L. Jaegers, M. Krieger, E. Bixler, P. Kelly, E. P. Weiss and S. O. Ahmad (2017). "Endurance exercise improves function in individuals with Parkinson's disease: A meta-analysis." Neurosci Lett **659**: 115-119.

Flynn, A., N. E. Allen, S. Dennis, C. G. Canning and E. Preston (2019). "Home-based prescribed exercise improves balance-related activities in people with Parkinson's disease and has benefits similar to centre-based exercise: a systematic review." J Physiother **65**(4): 189-199.

Folkerts, A. K., M. Ernst, R. Gollan, N. Cryns, I. Monsef, N. Skoetz and E. Kalbe (2024). "Can Physical Exercise Be Considered as a Promising Enhancer of Global Cognition in People with Parkinson's Disease? Results of a Systematic Review and Meta-Analysis." J Parkinsons Dis **14**(s1): S115-s133.

Folkerts, A. K., J. Nielsen, R. Gollan, A. Lansu, D. Solfronk, I. Monsef, M. Ernst, N. Skoetz, K. E. Zeuner and E. Kalbe (2023). "Physical Exercise as a Potential Treatment for Fatigue in Parkinson's Disease? A Systematic Review and Meta-Analysis of Pharmacological and Non-Pharmacological Interventions." J Parkinsons Dis **13**(5): 659-679.

Folstein, M. F., S. E. Folstein and P. R. McHugh (1975). "'Mini-mental state'. A practical method for grading the cognitive state of patients for the clinician." J Psychiatr Res **12**(3): 189-198.

Fong Yan, A., L. L. Nicholson, R. E. Ward, C. E. Hiller, K. Dovey, H. M. Parker, L. F. Low, G. Moyle and C. Chan (2024). "The Effectiveness of Dance Interventions on Psychological and Cognitive Health Outcomes Compared with Other Forms of Physical Activity: A Systematic Review with Meta-analysis." Sports Med **54**(5): 1179-1205.

Fontanesi, C., S. Kvint, G. Frazzitta, R. Bera, D. Ferrazzoli, A. Di Rocco, H. Rebholz, E. Friedman, G. Pezzoli, A. Quartarone, H. Y. Wang and M. F. Ghilardi (2016). "Intensive Rehabilitation Enhances Lymphocyte BDNF-TrkB Signaling in Patients With Parkinson's Disease." Neurorehabil Neural Repair **30**(5): 411-418.

Foster Vander Elst, O., N. H. D. Foster, P. Vuust, P. E. Keller and M. L. Kringelbach (2023). "The Neuroscience of Dance: A Conceptual Framework and Systematic Review." Neurosci Biobehav Rev **150**: 105197.

Fox, S. H., R. Katzenschlager, S. Y. Lim, B. Barton, R. M. A. de Bie, K. Seppi, M. Coelho and C. Sampaio (2018). "International Parkinson and movement disorder society evidence-based medicine review: Update on treatments for the motor symptoms of Parkinson's disease." Mov Disord **33**(8): 1248-1266.

Franzen, E., H. Johansson, M. Freidle, U. Ekman, E. Schalling, A. Lebedev, M. Lovden, S. Holmin, P. Svenningsson and M. Hagstromer (2018). Linking neuroplastic effects to behavioral changes after balance training in Parkinson's disease: a study protocol of a randomized controlled trial. MOVEMENT DISORDERS, WILEY 111 RIVER ST, HOBOKEN 07030-5774, NJ USA.

Franzoni, L. T., E. P. Monteiro, H. B. Oliveira, R. G. da Rosa, R. R. Costa, C. Rieder, F. G. Martinez and L. A. Peyré-Tartaruga (2018). "A 9-Week Nordic and Free Walking Improve Postural Balance in Parkinson's Disease." Sports Med Int Open **2**(2): E28-e34.

Frazzitta, G., D. Ferrazzoli, R. Maestri, R. Rovescala, G. Guaglio, R. Bera, D. Volpe and G. Pezzoli (2015). "Differences in muscle strength in parkinsonian patients affected on the right and left side." PLoS One **10**(3): e0121251.

Frazzitta, G., R. Maestri, M. F. Ghilardi, G. Riboldazzi, M. Perini, G. Bertotti, N. Boveri, S. Buttini, F. L. Lombino, D. Uccellini, M. Turla, G. Pezzoli and C. Comi (2014). "Intensive rehabilitation increases BDNF serum levels in parkinsonian patients: a randomized study." Neurorehabil Neural Repair **28**(2): 163-168.

Freidle, M., H. Johansson, U. Ekman, A. V. Lebedev, E. Schalling, W. H. Thompson, P. Svenningsson, M. Lövdén, A. Abney, F. Albrecht, H. Steurer, B. Leavy, S. Holmin, M. Hagströmer and E. Franzén (2022). "Behavioural and neuroplastic effects of a double-blind randomised controlled balance exercise trial in people with Parkinson's disease." NPJ Parkinsons Dis **8**(1): 12.

Freitag, F., S. M. D. Brucki, A. F. Barbosa, J. Chen, C. O. Souza, D. F. Valente, H. F. Chien, C. Bedeschi and M. C. Voos (2019). "Is virtual reality beneficial for dual-task gait training in patients with Parkinson's disease? A systematic review." Dement Neuropsychol **13**(3): 259-267.

Friedman, J. H., R. G. Brown, C. Comella, C. E. Garber, L. B. Krupp, J. S. Lou, L. Marsh, L. Nail, L. Shulman and C. B. Taylor (2007). "Fatigue in Parkinson's disease: a review." Mov Disord **22**(3): 297-308.

Fritz, N. E., F. M. Cheek and D. S. Nichols-Larsen (2015). "Motor-Cognitive Dual-Task Training in Persons With Neurologic Disorders: A Systematic Review." J Neurol Phys Ther **39**(3): 142-153.

Fuller, D., E. Colwell, J. Low, K. Orychock, M. A. Tobin, B. Simango, R. Buote, D. Van Heerden, H. Luan, K. Cullen, L. Slade and N. G. A. Taylor (2020). "Reliability and Validity of Commercially Available Wearable Devices for Measuring Steps, Energy Expenditure, and Heart Rate: Systematic Review." JMIR Mhealth Uhealth **8**(9): e18694.

Fusar-Poli, P. and J. Radua (2018). "Ten simple rules for conducting umbrella reviews." Evid Based Ment Health **21**(3): 95-100.

- Galletly, R. and S. G. Brauer (2005). "Does the type of concurrent task affect preferred and cued gait in people with Parkinson's disease?" Aust J Physiother **51**(3): 175-180.
- Gallou-Guyot, M., D. Nuic, S. Mandigout, M. Compagnat, M. L. Welter, J. C. Daviet and A. Perrochon (2022). "Effectiveness of home-based rehabilitation using active video games on quality of life, cognitive and motor functions in people with Parkinson's disease: a systematic review." DISABILITY AND REHABILITATION **44**(26): 8222-8233.
- Galna, B., S. Lord, D. Daud, N. Archibald, D. Burn and L. Rochester (2012). "Visual sampling during walking in people with Parkinson's disease and the influence of environment and dual-task." Brain Res **1473**: 35-43.
- Gamborg, M., L. G. Hvid, U. Dalgas and M. Langeskov-Christensen (2022). "Parkinson's disease and intensive exercise therapy - An updated systematic review and meta-analysis." Acta Neurol Scand **145**(5): 504-528.
- Gandevia, S. C. (2001). "Spinal and supraspinal factors in human muscle fatigue." Physiol Rev **81**(4): 1725-1789.
- Gandevia, S. C., N. Petersen, J. E. Butler and J. L. Taylor (1999). "Impaired response of human motoneurons to corticospinal stimulation after voluntary exercise." J Physiol **521 Pt 3**: 749-759.
- Gandhi, P. and C. M. Steele (2022). "Effectiveness of Interventions for Dysphagia in Parkinson Disease: A Systematic Review." Am J Speech Lang Pathol **31**(1): 463-485.
- Gao, X., H. Zhang, X. Fu, Y. Yang and J. Dou (2024). "The effect of home-based exercise on motor and non-motor symptoms with Parkinson's disease patients: A systematic review and network meta-analysis." J Clin Nurs **33**(7): 2755-2774.
- Garber, C. E., B. Blissmer, M. R. Deschenes, B. A. Franklin, M. J. Lamonte, I. M. Lee, D. C. Nieman and D. P. Swain (2011). "American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise." Med Sci Sports Exerc **43**(7): 1334-1359.
- Garcia-Agundez, A., A. K. Folkerts, R. Konrad, P. Caserman, T. Tregel, M. Goosses, S. Gobel and E. Kalbe (2019). "Recent advances in rehabilitation for Parkinson's Disease with Exergames: A Systematic Review." J Neuroeng Rehabil **16**(1): 17.
- Garcia-Lopez, H., M. de Los Angeles Castillo-Pintor, A. M. Castro-Sanchez, I. C. Lara-Palomo, E. Obrero-Gaitan and I. Cortes-Perez (2023). "Efficacy of Dual-Task Training in Patients with Parkinson's Disease: A Systematic Review with Meta-Analysis." Mov Disord Clin Pract **10**(9): 1268-1284.
- Garcia-Lopez, H., E. Obrero-Gaitan, A. M. Castro-Sanchez, I. C. Lara-Palomo, F. A. Nieto-Escamez and I. Cortes-Perez (2021). "Non-Immersive Virtual Reality to Improve Balance and Reduce Risk of Falls in People Diagnosed with Parkinson's Disease: A Systematic Review." Brain Sci **11**(11).
- Gil, P. R., J. A. Moratelli, D. Y. Fausto, K. H. Alexandre, A. A. Garcia Meliani, A. G. Lima and A. C. A. Guimaraes (2024). "The importance of dance for the cognitive function of people with Parkinson's: A systematic review with meta-analysis." J Bodyw Mov Ther **40**: 2091-2098.
- Gilat, M., P. Ginis, D. Zoetewei, J. De Vleeschhauwer, F. Hulzinga, N. D'Cruz and A. Nieuwboer (2021). "A systematic review on exercise and training-based interventions for freezing of gait in Parkinson's disease." NPJ Parkinsons Dis **7**(1): 81.
- Ginis, P., R. Pirani, S. Basaia, A. Ferrari, L. Chiari, E. Heremans, C. G. Canning and A. Nieuwboer (2017). "Focusing on heel strike improves toe clearance in people with Parkinson's disease: an observational pilot study." Physiotherapy **103**(4): 485-490.
- Giorgi, F., D. Platano, L. Berti, D. Donati and R. Tedeschi (2025). "Dancing Towards Stability: The Therapeutic Potential of Argentine Tango for Balance and Mobility in Parkinson's Disease." Diseases **13**(3).
- Godinho, C., J. Domingos, G. Cunha, A. T. Santos, R. M. Fernandes, D. Abreu, N. Goncalves, H. Matthews, T. Isaacs, J. Duffen, A. Al-Jawad, F. Larsen, A. Serrano, P. Weber, A. Thoms, S. Sollinger, H. Graessner, W. Maetzler and J. J. Ferreira (2016). "A systematic review of the characteristics and validity of monitoring technologies to assess Parkinson's disease." J Neuroeng Rehabil **13**: 24.
- Goetz, C. G., B. C. Tilley, S. R. Shaftman, G. T. Stebbins, S. Fahn, P. Martinez-Martin, W. Poewe, C. Sampaio, M. B. Stern, R. Dodel, B. Dubois, R. Holloway, J. Jankovic, J. Kulisevsky, A. E. Lang, A. Lees, S. Leurgans, P. A. LeWitt, D. Nyenhuis, C. W. Olanow, O. Rascol, A. Schrag, J. A. Teresi, J. J. van Hilten

and N. LaPelle (2008). "Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): scale presentation and clinimetric testing results." Mov Disord **23**(15): 2129-2170.

Goh, L., C. G. Canning, J. Song, L. Clemson and N. E. Allen (2023). "The effect of rehabilitation interventions on freezing of gait in people with Parkinson's disease is unclear: a systematic review and meta- analyses." Disabil Rehabil **45**(19): 3199-3218.

Goldberg, A., C. L. Curtis and J. A. Kleim (2015). "Linking Genes to Neurological Clinical Practice: The Genomic Basis for Neurorehabilitation." JOURNAL OF NEUROLOGIC PHYSICAL THERAPY **39**(1): 52-61.

Goldman, J. G. and I. Litvan (2011). "Mild cognitive impairment in Parkinson's disease." Minerva Med **102**(6): 441-459.

Gollan, R., M. Ernst, E. Lieker, J. Caro-Valenzuela, I. Monsef, A. Dresen, M. Roheger, N. Skoetz, E. Kalbe and A. K. Folkerts (2022). Effects of Resistance Training on Motor- and Non-Motor Symptoms in Patients with Parkinson's Disease: A Systematic Review and Meta-Analysis. J Parkinsons Dis. Netherlands. **12**: 1783-1806.

Gomersall, S. R., T. S. Olds and K. Ridley (2011). "Development and evaluation of an adult use-of-time instrument with an energy expenditure focus." J Sci Med Sport **14**(2): 143-148.

Gomes Neto, M., S. S. Pontes, L. O. Almeida, C. M. da Silva, C. da Conceicao Sena and M. B. Saquetto (2020). "Effects of water-based exercise on functioning and quality of life in people with Parkinson's disease: a systematic review and meta-analysis." Clin Rehabil **34**(12): 1425-1435.

Gomes, W. d. L., L. M. d. S. Miranda, N. M. d. Silva, G. K. S. Davi, R. C. S. Costa, I. C. Regalado, R. d. O. Cacho, E. W. A. Cacho and N. M. F. V. Lima (2018). "Analysis of functional profile and mobility in Parkinson's disease: a cross sectional study." Manual Therapy, Posturology & Rehabilitation Journal **0**(0): 1-6.

Gomez, N. G., K. B. Foreman, M. Hunt and A. S. Merryweather (2022). "Upper-extremity kinematics and interlimb movement correlation in persons with Parkinson Disease on irregular terrain, cross-slope, and under dual- task condition." Heliyon **8**(11): e11223.

Gonzalez-Devesa, D., C. Ayan, M. A. Sanchez-Lastra, C. Gutierrez-Hong, A. Garcia-Fresneda and J. C. Diz (2024). "The Efficacy of Boxing Training on Patients with Parkinson's Disease: Systematic Review and Meta-Analysis." Rev Neurol **79**(11): 36478.

Goodwin, V. A., S. H. Richards, R. S. Taylor, A. H. Taylor and J. L. Campbell (2008). "The effectiveness of exercise interventions for people with Parkinson's disease: a systematic review and meta-analysis." Mov Disord **23**(5): 631-640.

Gordt, K., T. Gerhardy, B. Najafi and M. Schwenk (2018). "Effects of Wearable Sensor-Based Balance and Gait Training on Balance, Gait, and Functional Performance in Healthy and Patient Populations: A Systematic Review and Meta-Analysis of Randomized Controlled Trials." Gerontology **64**(1): 74-89.

Graham, L., J. Armitage, R. Vitorio, J. Das, G. Barry, A. Godfrey, C. McDonald, R. Walker, M. Mancini, R. Morris and S. Stuart (2023). "Visual Exploration While Walking With and Without Visual Cues in Parkinson's Disease: Freezer Versus Non-Freezer." Neurorehabil Neural Repair **37**(10): 734-743.

Gratwicke, J. P. and T. Foltynie (2018). "Early nucleus basalis of Meynert degeneration predicts cognitive decline in Parkinson's disease." Brain **141**(1): 7-10.

Guo, X. B. and L. Tang (2024). "Effects of different exercise types on balance function in healthy older adults and Parkinson's patients: a systematic review." Front Aging Neurosci **16**: 1411584.

H, G. and S. L. (2004). " - Rehabilitation for Parkinson's disease: a systematic review of available." Clin Rehabil **18**(5): 463-482.

Hao, Z., X. Zhang and P. Chen (2022). "Effects of Ten Different Exercise Interventions on Motor Function in Parkinson's Disease Patients-A Network Meta-Analysis of Randomized Controlled Trials." Brain Sci **12**(6).

Haraldsson, H. M., F. Ferrarelli, N. H. Kalin and G. Tononi (2004). "Transcranial Magnetic Stimulation in the investigation and treatment of schizophrenia: a review." Schizophr Res **71**(1): 1-16.

Harper, S. A., B. T. Dowdell, J. H. Kim, B. S. Pollock and A. L. Ridgel (2019). "Non-Motor Symptoms after One Week of High Cadence Cycling in Parkinson's Disease." Int J Environ Res Public Health **16**(12).

Harpham, C., H. Gunn, J. Marsden and L. Connolly (2023). "Co-Creating a Feasible, Acceptable and Safe Home-Based High-Intensity Interval Training Programme for People with Parkinson's: The HIIT-Home4Parkinson's Study." *Int J Environ Res Public Health* **20**(9).

Harpham, C., H. Gunn, J. Marsden and L. Connolly (2023). "The feasibility, safety, physiological and clinical effects of high- intensity interval training for people with Parkinson's: a systematic review and meta-analysis." *Aging Clin Exp Res* **35**(3): 497-523.

Harris, D. M., T. Rantalainen, M. Muthalib, L. Johnson and W. P. Teo (2015). "Exergaming as a Viable Therapeutic Tool to Improve Static and Dynamic Balance among Older Adults and People with Idiopathic Parkinson's Disease: A Systematic Review and Meta-Analysis." *Front Aging Neurosci* **7**: 167.

Harrison, E. C., A. P. Horin and G. M. Earhart (2018). "Internal cueing improves gait more than external cueing in healthy adults and people with Parkinson disease." *Sci Rep* **8**(1): 15525.

Harro, C., G. Alderink, L. Hickox, D. W. Zeitler, M. Avery, C. Daman and D. Laker (2024). "Dynamic Measures of Balance during Obstacle-Crossing in Self-Selected Gait in Individuals with Mild-to-Moderate Parkinson's Disease." *Applied Sciences* **14**(3): 1271.

Harro, C. C., M. J. Shoemaker, C. M. Coatney, V. E. Lentine, L. R. Liefers, J. J. Quigley, S. G. Rollins, J. D. Stewart, J. Hall and S. K. Khoo (2022). "Effects of nordic walking exercise on gait, motor/non-motor symptoms, and serum brain-derived neurotrophic factor in individuals with Parkinson's disease." *Front Rehabil Sci* **3**: 1010097.

Hart, S. G. and L. E. Staveland (1988). Development of NASA-TLX (Task Load Index): Results of empirical and theoretical research. *Advances in psychology*, Elsevier. **52**: 139-183.

Hasan, S. M., S. Alshafie, E. A. Hasabo, M. Saleh, W. Elnaiem, A. Qasem, Y. O. Alzu'bi, A. Khaled, M. S. Zaazouee, K. M. Ragab, A. Z. Nourelden and M. F. Doheim (2022). "Efficacy of dance for Parkinson's disease: a pooled analysis of 372 patients." *J Neurol* **269**(3): 1195-1208.

Hausdorff, J. M. (2009). "Gait dynamics in Parkinson's disease: common and distinct behavior among stride length, gait variability, and fractal-like scaling." *Chaos* **19**(2): 026113.

He, C., C. Su, W. Zhang and Q. Wan (2020). "Effects of whole-body vibration on motor function in patients with Parkinson's disease: a systematic review and meta-analysis." *Brain Impairment*: 1-12.

He, S., W. Fang, J. Wu, H. Lv, J. Zhang, T. Wang, Y. Huang, G. Li and M. Li (2023). "Whether mindfulness-guided therapy can be a new direction for the rehabilitation of patients with Parkinson's disease: a network meta- analysis of non-pharmacological alternative motor-/sensory-based interventions." *Front Psychol* **14**: 1162574.

Helgerud, J., S. N. Thomsen, J. Hoff, A. Strandbråten, G. Leivseth, R. Unhjem and E. Wang (2020). "Maximal strength training in patients with Parkinson's disease: impact on efferent neural drive, force-generating capacity, and functional performance." *J Appl Physiol* (1985) **129**(4): 683-690.

Henemann, T. T., L. Truchem, J. Siega, L. Paladini and V. Israel (2023). "Physical therapy interventions to manage pain in Parkinson's disease: A systematic review." *Human Movement* **24**(3): 31-43.

Hidalgo-Agudo, R. D., D. Lucena-Anton, C. Luque-Moreno, A. M. Heredia-Rizo and J. A. Moral-Munoz (2020). "Additional Physical Interventions to Conventional Physical Therapy in Parkinson's Disease: A Systematic Review and Meta-Analysis of Randomized Clinical Trials." *J Clin Med* **9**(4).

Higgins, J. P., D. G. Altman, P. C. Gotzsche, P. Juni, D. Moher, A. D. Oxman, J. Savovic, K. F. Schulz, L. Weeks and J. A. Sterne (2011). "The Cochrane Collaboration's tool for assessing risk of bias in randomised trials." *Bmj* **343**: d5928.

Hirsch, M. A. and B. G. Farley (2009). "Exercise and neuroplasticity in persons living with Parkinson's disease." *European Journal of Physical and Rehabilitation Medicine* **45**(2): 215-229.

Hirsch, M. A., S. S. Iyer and M. Sanjak (2016). "Exercise-induced neuroplasticity in human Parkinson's disease: What is the evidence telling us?" *PARKINSONISM & RELATED DISORDERS* **22**: S78-S81.

Hirsch, M. A., E. E. H. van Wegen, M. A. Newman and P. C. Heyn (2018). "Exercise-induced increase in brain-derived neurotrophic factor in human Parkinson's disease: a systematic review and meta-analysis." *Transl Neurodegener* **7**: 7.

Hodgson, P., A. Jordan, C. Sinani, D. Charura and S. T. Orange (2024). "The relationship between physical function and psychological symptoms in Parkinson's disease: A systematic review and meta-regression analysis." *CNS Neurosci Ther* **30**(2): e14562.

Hoehn, M. M. and M. D. Yahr (1967). "Parkinsonism: onset, progression and mortality." Neurology **17**(5): 427-442.

Hoffmann, T. C., P. P. Glasziou, I. Boutron, R. Milne, R. Perera, D. Moher, D. G. Altman, V. Barbour, H. Macdonald, M. Johnston, S. E. Lamb, M. Dixon-Woods, P. McCulloch, J. C. Wyatt, A. W. Chan and S. Michie (2014). "Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide." Bmj **348**: g1687.

Hooper, P. L., H. D. Durham, Z. Török, T. Crul and L. Vigh (2016). "The central role of heat shock factor 1 in synaptic fidelity and memory consolidation." Cell Stress Chaperones **21**(5): 745-753.

Hortobagyi, T., T. Vetrovsky, G. M. Balbim, N. C. B. Sorte Silva, A. Manca, F. Deriu, M. Kolmos, C. Kruuse, T. Liu-Ambrose, Z. Radak, M. Vaczi, H. Johansson, P. C. R. Dos Santos, E. Franzen and U. Granacher (2022). "The impact of aerobic and resistance training intensity on markers of neuroplasticity in health and disease." Ageing Res Rev **80**: 101698.

Hu, D., Z. H. Liang, X. Ren, M. G. Liu, T. Wang and S. G. Sun (2005). "Genetic polymorphisms of brain-derived neurotrophic factor and sporadic Parkinson disease." Chinese Journal of Clinical Rehabilitation **9**(17): 196-197.

Hua, R., N. Nguyen, A. Jawad, K. Kazmierski, B. White and Y. Wang (2022). "Insole-based falling risk evaluation for patients with Parkinson's disease through walking while holding a cup of water." IEEE Sensors Letters **6**(6): 1-4.

Huang, J., D. Wang and J. Wang (2021). "Clinical Evidence of Tai Chi Exercise Prescriptions: A Systematic Review." Evid Based Complement Alternat Med **2021**: 5558805.

Huang, T., K. T. Larsen, M. Ried-Larsen, N. C. Møller and L. B. Andersen (2014). "The effects of physical activity and exercise on brain-derived neurotrophic factor in healthy humans: A review." Scand J Med Sci Sports **24**(1): 1-10.

Huang, X., K. Dong, C. Gan, Z. Xu, D. Lei, X. Dong, H. Liu and X. Chen (2024). "Effect of Rhythmically Cued Exercise Interventions on Functions in Patients With Parkinson Disease: A Meta-Analysis." Phys Ther **104**(3).

Huang, Y. Z., M. J. Edwards, E. Rounis, K. P. Bhatia and J. C. Rothwell (2005). "Theta burst stimulation of the human motor cortex." Neuron **45**(2): 201-206.

Huissoud, M., M. Boussac, K. Joineau, E. Harroch, C. Brefel-Courbon and E. Descamps (2024). "The effectiveness and safety of non-pharmacological intervention for pain management in Parkinson's disease: A systematic review." Rev Neurol (Paris) **180**(8): 715-735.

Hulzinga, F., V. de Rond, B. Vandendoorent, M. Gilat, P. Ginis, N. D'Cruz, C. Schlenstedt and A. Nieuwboer (2021). "Repeated Gait Perturbation Training in Parkinson's Disease and Healthy Older Adults: A Systematic Review and Meta-Analysis." Front Hum Neurosci **15**: 732648.

Hussain, F., S. Farooqui, A. A. Khan, M. U. Khan, M. A. Khan and A. Hasan (2024). "Effects of nonimmersive virtual reality using Wii-Fit exercises on balance and cognition in Parkinson disease: A meta-analysis." Medicine (Baltimore) **103**(30): e38940.

Hussain, F., S. Farooqui, I. A. Khan, B. Hassan and Z. K. Afridi (2023). "Effects of Exercise-based Management on Motor Symptoms in Parkinson's Disease - A Meta-analysis." J Coll Physicians Surg Pak **33**(8): 919-926.

Hvingelby, V. S., A. N. Glud, J. C. H. Sorensen, Y. Tai, A. S. M. Andersen, E. Johnsen, E. Moro and N. Pavese (2022). "Interventions to improve gait in Parkinson's disease: a systematic review of randomized controlled trials and network meta-analysis." J Neurol **269**(8): 4068-4079.

Hyman, C., M. Hofer, Y. A. Barde, M. Juhasz, G. D. Yancopoulos, S. P. Squinto and R. M. Lindsay (1991). "BDNF is a neurotrophic factor for dopaminergic neurons of the substantia nigra." Nature **350**(6315): 230-232.

Ishaq, S., I. A. Shah, S. D. Lee and B. T. Wu (2024). "Effects of exercise training on nigrostriatal neuroprotection in Parkinson's disease: a systematic review." Front Neurosci **18**: 1464168.

Ishaq, S., I. A. Shah, S. D. Lee and B. T. Wu (2025). "Effects of exercise training on the nigrostriatal glutamatergic pathway and receptor interactions in Parkinson's disease: a systematic review." Front Aging Neurosci **17**: 1512278.

Ismail, S. R., S. W. H. Lee, D. Merom, P. S. N. Megat Kamaruddin, M. S. Chong, T. Ong and N. M. Lai (2021). "Evidence of disease severity, cognitive and physical outcomes of dance interventions for persons with Parkinson's Disease: a systematic review and meta-analysis." *BMC Geriatrics* **21**(1).

Ivaniski-Mello, A., V. T. Müller, L. de Liz Alves, M. Z. Casal, A. N. Haas, L. Correale, A. C. Kanitz, V. F. Martins, A. K. Gonçalves, F. G. Martinez and L. A. Peyré-Tartaruga (2023). "Determinants of Dual-task Gait Speed in Older Adults with and without Parkinson's Disease." *Int J Sports Med* **44**(10): 744-750.

Janssen Daalen, J. M., S. Schootemeijer, E. Richard, S. K. L. Darweesh and B. R. Bloem (2022). "Lifestyle Interventions for the Prevention of Parkinson Disease: A Recipe for Action." *Neurology* **99**(7 Suppl 1): 42-51.

Jenkinson, C., R. Fitzpatrick, V. Peto, R. Greenhall and N. Hyman (1997). "The PDQ-8: Development and validation of a short-form parkinson's disease questionnaire." *Psychology & Health* **12**(6): 805-814.

Ji, X., D. Lu, Q. Yang, L. Xiao, J. Wang and G. Wang (2022). "Physical Therapy for at Least 6 Months Improves Motor Symptoms in Parkinson's Patients: A Meta-Analysis." *Comput Math Methods Med* **2022**: 3393191.

Jiang, X., J. Zhou, Q. Chen, Q. Xu, S. Wang, L. Yuan, D. Zhang, H. Bi and H. Li (2024). "Effect of robot-assisted gait training on motor dysfunction in Parkinson's patients: A systematic review and meta-analysis." *J Back Musculoskeletal Rehabil* **37**(2): 253-268.

Jiang, Y., S. Zhang, Y. Chen, H. Wang, X. He, C. Bin, R. Fu, H. Zhu, M. Pan, Q. Zhang and Y. Lu (2024). "Physical activity and risk of Parkinson's disease: an updated systematic review and meta-analysis." *J Neurol* **271**(12): 7434-7459.

Jiménez-Maldonado, A., I. Rentería, P. C. García-Suárez, J. Moncada-Jiménez and L. F. Freire-Royes (2018). "The Impact of High-Intensity Interval Training on Brain Derived Neurotrophic Factor in Brain: A Mini-Review." *Front Neurosci* **12**: 839.

Jin, X., L. Wang, S. Liu, L. Zhu, P. D. Loprinzi and X. Fan (2019). "The Impact of Mind-body Exercises on Motor Function, Depressive Symptoms, and Quality of Life in Parkinson's Disease: A Systematic Review and Meta- analysis." *Int J Environ Res Public Health* **17**(1).

Johansson, H., A. K. Folkerts, I. Hammarström, E. Kalbe and B. Leavy (2023). "Effects of motor-cognitive training on dual-task performance in people with Parkinson's disease: a systematic review and meta-analysis." *J Neurol* **270**(6): 2890-2907.

Johansson, H., M. Hagstromer, W. J. A. Grooten and E. Franzen (2020). "Exercise-Induced Neuroplasticity in Parkinson's Disease: A Metasynthesis of the Literature." *Neural Plast* **2020**: 8961493.

Jonsson, A. B., S. Krogh, H. S. Laursen, P. Aagaard, H. Kasch and J. F. Nielsen (2024). "Safety and efficacy of blood flow restriction exercise in individuals with neurological disorders: A systematic review." *Scand J Med Sci Sports* **34**(1): e14561.

Kaagman, D. G. M., E. E. H. van Wegen, N. Cignetti, E. Rothermel, T. Vanbellinghen and M. A. Hirsch (2024). "Effects and Mechanisms of Exercise on Brain-Derived Neurotrophic Factor (BDNF) Levels and Clinical Outcomes in People with Parkinson's Disease: A Systematic Review and Meta-Analysis." *Brain Sci* **14**(3).

Kadkhodaie, M., A. Sharifnezhad, S. Ebadi, S. Marzban, S. A. Habibi, A. Ghaffari and B. Forogh (2020). "Effect of eccentric-based rehabilitation on hand tremor intensity in Parkinson disease." *Neurol Sci* **41**(3): 637-643.

Kalron, A. and G. Zeilig (2015). "Efficacy of exercise intervention programs on cognition in people suffering from multiple sclerosis, stroke and Parkinson's disease: A systematic review and meta-analysis of current evidence." *NeuroRehabilitation* **37**(2): 273-289.

Kalyani, H. H. N., K. Sullivan, G. Moyle, S. Brauer, E. R. Jeffrey, L. Roeder, S. Berndt and G. Kerr (2019). "Effects of Dance on Gait, Cognition, and Dual-Tasking in Parkinson's Disease: A Systematic Review and Meta-Analysis." *J Parkinsons Dis* **9**(2): 335-349.

Kamieniarz, A., A. Milert, D. Grzybowska-Ganszczyk, J. Opara and G. Juras (2021). "Tai Chi and Qi Gong therapies as a complementary treatment in Parkinson's disease - a systematic review." *Complement Ther Med* **56**: 102589.

Karim, A., M. S. Iqbal, T. Muhammad and R. Qaisar (2022). "Evaluation of Sarcopenia Using Biomarkers of the Neuromuscular Junction in Parkinson's Disease." *J Mol Neurosci* **72**(4): 820-829.

Karpodini, C. C., P. C. Dinas, E. Angelopoulou, M. A. Wyon, A. N. Haas, M. Bougiesi, S. G. Papageorgiou and Y. Koutedakis (2022). "Rhythmic cueing, dance, resistance training, and Parkinson's disease: A systematic review and meta-analysis." Front Neurol **13**: 875178.

Kashif, M., A. Ahmad, M. A. M. Bandpei, M. Farooq, H. Iram and E. F. R (2022). "Systematic review of the application of virtual reality to improve balance, gait and motor function in patients with Parkinson's disease." Medicine (Baltimore) **101**(31): e29212.

Kaski, D., R. O. Dominguez, J. H. Allum, A. F. Islam and A. M. Bronstein (2014). "Combining physical training with transcranial direct current stimulation to improve gait in Parkinson's disease: a pilot randomized controlled study." Clin Rehabil **28**(11): 1115-1124.

Kasschau, M., K. Sherman, L. Haider, A. Frontario, M. Shaw, A. Datta, M. Bikson and L. Charvet (2015). "A Protocol for the Use of Remotely-Supervised Transcranial Direct Current Stimulation (tDCS) in Multiple Sclerosis (MS)." J Vis Exp(106): e53542.

Kearney, E., S. Shellikeri, R. Martino and Y. Yunusova (2019). "Augmented visual feedback-aided interventions for motor rehabilitation in Parkinson's disease: a systematic review." Disabil Rehabil **41**(9): 995-1011.

Kehagia, A. A., R. A. Barker and T. W. Robbins (2013). "Cognitive impairment in Parkinson's disease: the dual syndrome hypothesis." Neurodegener Dis **11**(2): 79-92.

Kelly, N. A., K. H. Wood, J. B. Allendorfer, M. P. Ford, C. S. Bickel, J. Marstrander, A. W. Amara, T. Anthony, M. M. Bamman and F. M. Skidmore (2017). "High-Intensity Exercise Acutely Increases Substantia Nigra and Prefrontal Brain Activity in Parkinson's Disease." Med Sci Monit **23**: 6064-6071.

Kelly, V. E., A. J. Eusterbrock and A. Shumway-Cook (2012). "A review of dual-task walking deficits in people with Parkinson's disease: motor and cognitive contributions, mechanisms, and clinical implications." Parkinsons Dis **2012**: 918719.

Keus, S. H. J., B. R. Bloem, E. J. M. Hendriks, A. B. Bredero-Cohen, M. Munneke and G. Practice Recommendations Dev (2007). "Evidence-based analysis of physical therapy in Parkinson's disease with recommendations for practice and research." MOVEMENT DISORDERS **22**(4): 451-460.

Keus SHJ, M. M., Graziano M, et al. (2014). European Physiotherapy Guideline for Parkinson's disease.

Khalil, H., M. A. Alomari, O. Khabour, A. Al-Hieshan and J. A. Bajwa (2017). "The Association Between Physical Activity With Cognitive Function and Brain-Derived Neurotrophic Factor in People With Parkinson's Disease: A Pilot Study." J Aging Phys Act **25**(4): 646-652.

Kiepe, M.-S., B. Stöckigt and T. Keil (2012). "Effects of dance therapy and ballroom dances on physical and mental illnesses: A systematic review." The Arts in Psychotherapy **39**(5): 404-411.

Kim, H. and S. Fraser (2022). "Neural correlates of dual-task walking in people with central neurological disorders: a systematic review." J Neurol **269**(5): 2378-2402.

Kim, H., E. Kim, S. J. Yun, M. G. Kang, H. I. Shin, B. M. Oh and H. G. Seo (2022). "Robot-assisted gait training with auditory and visual cues in Parkinson's disease: A randomized controlled trial." Ann Phys Rehabil Med **65**(3): 101620.

Kim, J. and J. Yim (2018). "Effects of High-Frequency Repetitive Transcranial Magnetic Stimulation Combined with Task-Oriented Mirror Therapy Training on Hand Rehabilitation of Acute Stroke Patients." Med Sci Monit **24**: 743-750.

Kim, R., N. Kang, J. H. Lee, H. Lee, T. L. Lee, D. K. Ko, K. Byun, K. Park, J. Y. Lee and B. Jeon (2025). "Moderators of aerobic exercise effects on motor symptoms in patients with Parkinson's disease: A systematic review and meta-analysis." Parkinsonism Relat Disord **134**: 107779.

Kim, R., T. L. Lee, H. Lee, D. K. Ko, B. Jeon and N. Kang (2023). "Effects of Exercise on Depressive Symptoms in Patients With Parkinson Disease: A Meta-analysis." Neurology **100**(4): e377-e387.

Kim, R., T. L. Lee, H. Lee, D. K. Ko, J. H. Lee, H. Shin, D. Lim, J. S. Jun, K. Byun, K. Park, B. Jeon and N. Kang (2023). "Effects of physical exercise interventions on cognitive function in Parkinson's disease: An updated systematic review and meta-analysis of randomized controlled trials." Parkinsonism Relat Disord **117**: 105908.

Kim, Y., B. Lai, T. Mehta, M. Thirumalai, S. Padalabalanarayanan, J. H. Rimmer and R. W. Motl (2019). "Exercise Training Guidelines for Multiple Sclerosis, Stroke, and Parkinson Disease: Rapid Review and Synthesis." Am J Phys Med Rehabil **98**(7): 613-621.

- Klamroth, S., S. Steib, S. Devan and K. Pfeifer (2016). "Effects of Exercise Therapy on Postural Instability in Parkinson Disease: A Meta-analysis." *J Neurol Phys Ther* **40**(1): 3-14.
- Kluger, B. M., R. P. Brown, S. Aerts and M. Schenkman (2014). "Determinants of objectively measured physical functional performance in early to mid-stage Parkinson disease." *Pm r* **6**(11): 992-998.
- Kocer, B., C. Gulsen, F. Soke, E. Ozcan Gulsen, N. Ersoy, O. Tunca Yilmaz and S. S. Comoglu (2023). "Comparison of dual-task costs during different types of walking in people with Parkinson's disease: a controlled study." *Acta Neurol Belg* **123**(6): 2221-2227.
- Kossi, O., J. Raats, J. Wellens, M. Duckaert, S. De Baets, D. Van de Velde and P. Feys (2024). "Efficacy of rehabilitation interventions evaluated in common neurological conditions in improving participation outcomes: A systematic review." *Clin Rehabil* **38**(1): 47-59.
- Krupička, R., C. Malá, S. Neřuková, T. Hubená, F. Havlík, O. Bezdicek, P. Dušek and E. Růžička (2024). "Impaired dual-task gait in Parkinson's disease is associated with brain morphology changes." *J Neural Transm (Vienna)* **131**(12): 1389-1395.
- Krupp, L. B., N. G. LaRocca, J. Muir-Nash and A. D. Steinberg (1989). "The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus." *Arch Neurol* **46**(10): 1121-1123.
- Kubica, J., J. Szymura, A. Domagalik, S. Golda, M. Wiecek, M. Fafrowicz, T. Marek and J. Pera (2019). "Systematic Balance Exercises Influence Cortical Activation and Serum BDNF Levels in Older Adults." *J Clin Med* **8**(11).
- Kwakkel, G., C. J. T. de Goede and E. E. H. van Wegen (2007). "Impact of physical therapy for Parkinson's disease: A critical review of the literature." *PARKINSONISM & RELATED DISORDERS* **13**: S478-S487.
- Kwok, J. Y., K. C. Choi and H. Y. Chan (2016). "Effects of mind-body exercises on the physiological and psychosocial well-being of individuals with Parkinson's disease: A systematic review and meta-analysis." *Complement Ther Med* **29**: 121-131.
- Kwon, S. H., J. K. Park and Y. H. Koh (2023). "A systematic review and meta-analysis on the effect of virtual reality- based rehabilitation for people with Parkinson's disease." *J Neuroeng Rehabil* **20**(1): 94.
- L, W., L. F and T. L (2022). "- Chronic effects of different exercise types on brain activity in healthy." *Front Physiol* **13**(1031803): 1031803.
- Lahude, A. B., P. Souza Correa, P. C. ME and F. Cechetti (2023). "The impact of virtual reality on manual dexterity of Parkinson's disease subjects: a systematic review." *Disabil Rehabil Assist Technol* **18**(7): 1237-1244.
- Lai, J., Y. Cai, L. Yang, M. Xia, X. Cheng and Y. Chen (2022). "Effects of Baduanjin exercise on motor function, balance and gait in Parkinson's disease: a systematic review and meta-analysis." *BMJ Open* **12**(11): e067280.
- Lamotte, G., M. R. Rafferty, J. Prodoehl, W. M. Kohrt, C. L. Comella, T. Simuni and D. M. Corcos (2015). "Effects of endurance exercise training on the motor and non-motor features of Parkinson's disease: a review." *J Parkinsons Dis* **5**(1): 21-41.
- Landers, M. R., J. W. Navalta, A. S. Murtishaw, J. W. Kinney and S. Pirio Richardson (2019). "A High-Intensity Exercise Boot Camp for Persons With Parkinson Disease: A Phase II, Pragmatic, Randomized Clinical Trial of Feasibility, Safety, Signal of Efficacy, and Disease Mechanisms." *J Neurol Phys Ther* **43**(1): 12-25.
- Lang, A. E. and A. J. Espay (2018). "Disease Modification in Parkinson's Disease: Current Approaches, Challenges, and Future Considerations." *Mov Disord* **33**(5): 660-677.
- LaPointe, L. L., J. A. Stierwalt and C. G. Maitland (2010). "Talking while walking: Cognitive loading and injurious falls in Parkinson's disease." *Int J Speech Lang Pathol* **12**(5): 455-459.
- Lau, R. W., T. Teo, F. Yu, R. C. Chung and M. Y. Pang (2011). "Effects of whole-body vibration on sensorimotor performance in people with Parkinson disease: a systematic review." *Phys Ther* **91**(2): 198-209.
- Lazzarini, S. G., B. Mosconi, C. Cordani, C. Arienti and F. Cecchi (2024). "Effectiveness of robot-assisted training in adults with Parkinson's disease: a systematic review and meta-analysis." *J Neurol* **272**(1): 22.

Le Sant, G., T. Lecharte, V. Goreau, A. Nordez, R. Gross and T. Cattagni (2023). "Motor performance, motor impairments, and quality of life after eccentric resistance training in neurological populations: A systematic review and meta-analyses." NeuroRehabilitation **53**(1): 33-50.

Leal-Nascimento, A. H., E. S. da Silva, A. P. J. Zanardi, A. Ivaniski-Mello, E. Passos-Monteiro, F. G. Martinez, A. Rodrigo de Carvalho, R. R. Baptista and L. A. Peyre-Tartaruga (2022). "Biomechanical responses of Nordic walking in people with Parkinson's disease." Scand J Med Sci Sports **32**(2): 290-297.

Lee, A. and R. M. Gilbert (2016). "Epidemiology of Parkinson Disease." Neurol Clin **34**(4): 955-965.

Lee, H.-C., J.-H. Lee and M.-S. Ha (2024). "Role of core-based exercises in improving proprioception among individuals with neurological disorders: a systematic literature review and meta-analysis." Exercise Science **33**(2): 149-159.

Lee, J., M. Choi and Y. Yoo (2017). "A Meta-Analysis of Nonpharmacological Interventions for People With Parkinson's Disease." Clin Nurs Res **26**(5): 608-631.

Lee, J., Y. Kim and Y. L. Kim (2018). "Non-pharmacological therapies for sleep disturbances in people with Parkinson's disease: A systematic review." J Adv Nurs.

Lee, M., C. Youm, B. Noh, H. Park and S. M. Cheon (2020). "Gait Characteristics under Imposed Challenge Speed Conditions in Patients with Parkinson's Disease During Overground Walking." Sensors (Basel) **20**(7).

Lefaucheur, J. P., A. Aleman, C. Baeken, D. H. Benninger, J. Brunelin, V. Di Lazzaro, S. R. Filipovic, C. Grefkes, A. Hasan, F. C. Hummel, S. K. Jaaskelainen, B. Langguth, L. Leocani, A. Londero, R. Nardone, J. P. Nguyen, T. Nyffeler, A. J. Oliveira-Maia, A. Oliviero, F. Padberg, U. Palm, W. Paulus, E. Poulet, A. Quartarone, F. Rachid, I. Rektorova, S. Rossi, H. Sahlsten, M. Schecklmann, D. Szekely and U. Ziemann (2020). "Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS): An update (2014-2018)." Clin Neurophysiol **131**(2): 474-528.

Lei, C., K. Sunzi, F. Dai, X. Liu, Y. Wang, B. Zhang, L. He and M. Ju (2019). "Effects of virtual reality rehabilitation training on gait and balance in patients with Parkinson's disease: A systematic review." PLoS One **14**(11): e0224819.

Lei, H., Z. Ma, K. Tian, K. Liu, J. Wang, X. Zhu, B. Mi, Y. Chen, Q. Yang and H. Jiang (2022). "The effects of different types of Tai Chi exercises on motor function in patients with Parkinson's disease: A network meta-analysis." Front Aging Neurosci **14**: 936027.

Lemos, J. R., Jr., C. R. Alves, S. B. de Souza, J. D. Marsiglia, M. S. Silva, A. C. Pereira, A. L. Teixeira, E. L. Vieira, J. E. Krieger, C. E. Negrão, G. B. Alves, E. M. de Oliveira, W. Bolani, R. G. Dias and I. C. Trombetta (2016). "Peripheral vascular reactivity and serum BDNF responses to aerobic training are impaired by the BDNF Val66Met polymorphism." Physiol Genomics **48**(2): 116-123.

Lenka, A. and J. Jankovic (2023). "How should future clinical trials be designed in the search for disease-modifying therapies for Parkinson's disease?" Expert Rev Neurother **23**(2): 107-122.

Lenoir Dit Caron, R., J. Coquart and M. Gilliaux (2021). "Effect of yoga on health-related quality of life in central nervous system disorders: A systematic review." Clin Rehabil **35**(11): 1530-1543.

Lesinski, M., O. Prieske and U. Granacher (2016). "Effects and dose-response relationships of resistance training on physical performance in youth athletes: a systematic review and meta-analysis." Br J Sports Med **50**(13): 781-795.

Lheureux, A., T. Lejeune, A. Simons, A. Gillis and G. Everard (2025). "Virtual reality effects on balance and mobility in people with Parkinson's disease: A systematic review with meta-analysis." Ann Phys Rehabil Med **68**(6): 101967.

Li, H., C. Cao and Y. Li (2024). "Self-directed physical activity interventions for motor symptoms and quality of life in early and mid-stage Parkinson's disease: A systematic review and meta-analysis." Arch Gerontol Geriatr **116**: 105159.

Li, J., J. Guo, W. Sun, J. Mei, Y. Wang, L. Zhang, J. Zhang, J. Gao, K. Su, Z. Lv, X. Feng and R. Li (2022). "Effects of Exercise on Parkinson's Disease: A Meta-Analysis of Brain Imaging Studies." Front Hum Neurosci **16**: 796712.

Li, J. A., M. B. Loevaas, C. Guan, L. Goh, N. E. Allen, M. K. Y. Mak, J. Lv and S. S. Paul (2023). "Does Exercise Attenuate Disease Progression in People With Parkinson's Disease? A Systematic Review With Meta-Analyses." Neurorehabil Neural Repair **37**(5): 328-352.

- Li, Q. and M. Chen (2021). "Effects of multiple exercise interventions on balance function in patients with Parkinson's disease: a network meta-analysis." Chinese Evidence-Based Nursing 7: 452–460; 474.
- Li, R., Y. Zhang, Y. Jiang, M. Wang, W. H. D. Ang and Y. Lau (2021). "Rehabilitation training based on virtual reality for patients with Parkinson's disease in improving balance, quality of life, activities of daily living, and depressive symptoms: A systematic review and meta- regression analysis." Clin Rehabil 35(8): 1089-1102.
- Li Voti, P., A. Conte, L. Rocchi, M. Bologna, N. Khan, G. Leodori and A. Berardelli (2014). "Cerebellar continuous theta-burst stimulation affects motor learning of voluntary arm movements in humans." Eur J Neurosci 39(1): 124-131.
- Li, X., Z. Chen, Y. Yue, X. Zhou, S. Gu, J. Tao, H. Guo, M. Zhu and Q. Du (2022). "Effect of Wearable Sensor-Based Exercise on Musculoskeletal Disorders in Individuals With Neurodegenerative Diseases: A Systematic Review and Meta-Analysis." Front Aging Neurosci 14: 934844.
- Li, X., Z. Gao, H. Yu, Y. Gu and G. Yang (2022). "Effect of Long-term Exercise Therapy on Motor Symptoms in Parkinson Disease Patients: A Systematic Review and Meta-analysis of Randomized Controlled Trials." Am J Phys Med Rehabil 101(10): 905-912.
- Li, X., J. He, J. Yun and H. Qin (2020). "Lower Limb Resistance Training in Individuals With Parkinson's Disease: An Updated Systematic Review and Meta-Analysis of Randomized Controlled Trials." Front Neurol 11: 591605.
- Li, Y., J. Huang, J. Wang and Y. Cheng (2025). "Effects of different exercises on improving gait performance in patients with Parkinson's disease: a systematic review and network meta-analysis." Front Aging Neurosci 17: 1496112.
- Li, Y., H. Song, L. Shen and Y. Wang (2021). "The efficacy and safety of moderate aerobic exercise for patients with Parkinson's disease: a systematic review and meta-analysis of randomized controlled trials." Ann Palliat Med 10(3): 2638-2649.
- Li, Y., Z. Wang, J. Li, H. Yang and Z. Fang (2024). "The effects of dance interventions on reducing the risk of falls in older adults: a network meta-analysis." Front Public Health 12: 1496692.
- Li, Z., T. Wang, H. Liu, Y. Jiang, Z. Wang and J. Zhuang (2020). "Dual-task training on gait, motor symptoms, and balance in patients with Parkinson's disease: a systematic review and meta-analysis." Clin Rehabil 34(11): 1355-1367.
- Libório, A. M. L., G. de Oliveira Santana, M. C. Macêdo, M. G. Neto, A. F. Baptista and K. N. Sá (2019). "Home-based exercise programs for disabilities of walking activity caused by neurological disorders: Systematic Review with Meta-Analysis." Revista Pesquisa em Fisioterapia 9(4): 539-555.
- Lima, L. O., A. Scianni and F. Rodrigues-de-Paula (2013). "Progressive resistance exercise improves strength and physical performance in people with mild to moderate Parkinson's disease: a systematic review." J Physiother 59(1): 7-13.
- Lin, H. W., K. W. Tam and Y. C. Kuan (2023). "Mindfulness or meditation therapy for Parkinson's disease: A systematic review and meta-analysis of randomized controlled trials." Eur J Neurol 30(8): 2250-2260.
- Lin, X., Y. Zhang, X. Zhang, X. Chen, J. Liu, L. Yang and M. Y. C. Pang (2024). "Comparing the effects of dual-task training and single-task training on walking, balance and cognitive functions in individuals with Parkinson's disease: A systematic review." Chin Med J (Engl) 137(13): 1535-1543.
- Lin, Y. P., R. S. Chen, V. C. Chen, C. H. Liu, H. L. Chan and Y. J. Chang (2022). "Effects of Lower Limb Cycling Training on Different Components of Force and Fatigue in Individuals With Parkinson's Disease." Front Bioeng Biotechnol 10: 829772.
- Lin, Y. P., Lin, II, W. D. Chiou, H. C. Chang, R. S. Chen, C. S. Lu and Y. J. Chang (2023). "The Executive-Function-Related Cognitive-Motor Dual Task Walking Performance and Task Prioritizing Effect on People with Parkinson's Disease." Healthcare (Basel) 11(4).
- Lina, C., C. Guoen, W. Huidan, W. Yingqing, C. Ying, C. Xiaochun and Y. Qinyong (2020). "The Effect of Virtual Reality on the Ability to Perform Activities of Daily Living, Balance During Gait, and Motor Function in Parkinson Disease Patients: A Systematic Review and Meta-Analysis." Am J Phys Med Rehabil 99(10): 917-924.

- Liu, H. H., N. C. Yeh, Y. F. Wu, Y. R. Yang, R. Y. Wang and F. Y. Cheng (2019). "Effects of Tai Chi Exercise on Reducing Falls and Improving Balance Performance in Parkinson's Disease: A Meta-Analysis." *Parkinsons Dis* **2019**: 9626934.
- Liu, W. Y., T. H. Tung, C. Zhang and L. Shi (2022). "Systematic review for the prevention and management of falls and fear of falling in patients with Parkinson's disease." *Brain Behav* **12**(8): e2690.
- Liu, Z., M. Huang, Y. Liao, X. Xie, P. Zhu, Y. Liu and C. Tan (2023). "Long-term efficacy of hydrotherapy on balance function in patients with Parkinson's disease: a systematic review and meta-analysis." *Front Aging Neurosci* **15**: 1320240.
- Lohnes, C. A. and G. M. Earhart (2011). "The impact of attentional, auditory, and combined cues on walking during single and cognitive dual tasks in Parkinson disease." *Gait Posture* **33**(3): 478-483.
- Longhurst, J. K., J. V. Rider, J. L. Cummings, S. E. John, B. Poston, E. C. Held Bradford and M. R. Landers (2022). "A Novel Way of Measuring Dual-Task Interference: The Reliability and Construct Validity of the Dual-Task Effect Battery in Neurodegenerative Disease." *Neurorehabil Neural Repair* **36**(6): 346-359.
- Longhurst, J. K., J. V. Rider, J. L. Cummings, S. E. John, B. Poston and M. R. Landers (2023). "Cognitive-motor dual-task interference in Alzheimer's disease, Parkinson's disease, and prodromal neurodegeneration: A scoping review." *Gait Posture* **105**: 58-74.
- Lopes, J. S. S., A. F. Machado, J. K. Micheletti, A. C. de Almeida, A. P. Cavina and C. M. Pastre (2019). "Effects of training with elastic resistance versus conventional resistance on muscular strength: A systematic review and meta-analysis." *SAGE Open Med* **7**: 2050312119831116.
- Lopez-Liria, R., S. Vega-Tirado, M. A. Valverde-Martinez, A. Calvache-Mateo, A. M. Martinez-Martinez and P. Rocamora-Perez (2023). "Efficacy of Specific Trunk Exercises in the Balance Dysfunction of Patients with Parkinson's Disease: A Systematic Review and Meta-Analysis." *Sensors (Basel)* **23**(4).
- Lord, S., K. Baker, A. Nieuwboer, D. Burn and L. Rochester (2011). "Gait variability in Parkinson's disease: an indicator of non-dopaminergic contributors to gait dysfunction?" *J Neurol* **258**(4): 566-572.
- Lorenzo-Garcia, P., I. Cavero-Redondo, S. Nunez de Arenas-Arroyo, M. J. Guzman-Pavon, S. Priego-Jimenez and C. Alvarez-Bueno (2024). "Effects of physical exercise interventions on balance, postural stability and general mobility in Parkinson's disease: a network meta-analysis." *J Rehabil Med* **56**: jrm10329.
- Lorenzo-Garcia, P., I. Cavero-Redondo, A. I. Torres-Costoso, M. J. Guzman-Pavon, S. Nunez de Arenas-Arroyo and C. Alvarez-Bueno (2021). "Body Weight Support Gait Training for Patients With Parkinson Disease: A Systematic Review and Meta-analyses." *Arch Phys Med Rehabil* **102**(10): 2012-2021.
- Lorenzo-Garcia, P., S. Nunez de Arenas-Arroyo, I. Cavero-Redondo, M. J. Guzman-Pavon, S. Priego-Jimenez and C. Alvarez-Bueno (2023). "Physical Exercise Interventions on Quality of Life in Parkinson Disease: A Network Meta-analysis." *J Neurol Phys Ther* **47**(2): 64-74.
- Lou, J. S. (2009). "Physical and Mental Fatigue in Parkinson's Disease Epidemiology, Pathophysiology and Treatment." *DRUGS & AGING* **26**(3): 195-208.
- Lou, L., C. Xiang, Y. Hu and J. Yang (2025). "Tai Chi improves balance, mobility and gait function of the lower limbs in patients with Parkinson's disease: a systematic review and meta- analysis." *Eur J Med Res* **30**(1): 107.
- Lozano, J. S. and S. M. Pizarro (2024). "Eficacia de la terapia acuática sobre los síntomas motores en pacientes con Parkinson: Revisión sistemática." *Revista andaluza de medicina del deporte* **17**(1): 117-122.
- Lozano, J. S. and S. M. Pizarro (2024). "Hidroterapia para mejorar el equilibrio y la movilidad en pacientes con parkinson leve-moderado: revisión sistemática." *Medicina naturista* **18**(2): 41-48.
- Luna, G., L. F. Pardo-Cocuy, A. Garzon, A. Benitez-Ospina and H. M. Parada-Gereda (2025). "Effectiveness of Lee Silverman Voice Treatment for Improving Motor Function in Patients With Parkinson's Disease: A Systematic Review and Meta-analysis of Randomized Clinical Trials." *Am J Phys Med Rehabil* **104**(12): 1105-1112.
- Lötzke, D., T. Ostermann and A. Büssing (2015). "Argentine tango in Parkinson disease - a systematic review and meta-analysis." *BMC Neurology* **15**(1).
- Machado, S., D. Teixeira, D. Monteiro, C. Imperatori, E. Murillo-Rodriguez, F. P. da Silva Rocha, T. Yamamoto, S. Amatriain-Fernandez, H. Budde, M. G. Carta, L. Caixeta and A. S. de Sa Filho (2022).

"Clinical applications of exercise in Parkinson's disease: what we need to know?" Expert Rev Neurother **22**(9): 771-780.

Mackay, C. P., S. S. Kuys and S. G. Brauer (2017). "The Effect of Aerobic Exercise on Brain-Derived Neurotrophic Factor in People with Neurological Disorders: A Systematic Review and Meta-Analysis." Neural Plast **2017**: 4716197.

Magdi, A., A. M. Sayed Ahmed, E. Elsayed, R. Ahmad, S. Ramakrishnan and M. G. Gabor (2021). "Effects of cueing techniques on gait, gait-related mobility, and functional activities in patients with Parkinson's disease: a systematic review and meta-analysis." Physical Therapy Reviews **26**(3): 188-201.

Mahmoud, H. M., Z. I. Al-Turkistani, M. S. Alayat, E. M. Abd El-Kafy and A. A. R. El Fiky (2023). "Effect of dancing on freezing of gait in patients with Parkinson's disease: A systematic review and meta-analysis." NeuroRehabilitation **53**(3): 269-284.

Mai, A. S., Y. S. Lee, J. H. Yong, D. Teo, Y. M. Wan and E. K. Tan (2024). "Treatment of apathy in Parkinson's disease: A bayesian network meta- analysis of randomised controlled trials." Heliyon **10**(4): e26107.

Maidan, I., F. Nieuwhof, H. Bernad-Elazari, M. F. Reelick, B. R. Bloem, N. Giladi, J. E. Deutsch, J. M. Hausdorff, J. A. Claassen and A. Mirelman (2016). "The Role of the Frontal Lobe in Complex Walking Among Patients With Parkinson's Disease and Healthy Older Adults: An fNIRS Study." Neurorehabil Neural Repair **30**(10): 963-971.

Maidan, I., K. Rosenberg-Katz, Y. Jacob, N. Giladi, J. M. Hausdorff and A. Mirelman (2017). "Disparate effects of training on brain activation in Parkinson disease." Neurology **89**(17): 1804-1810.

Mak, M. K. (2013). "Reduced step length, not step length variability is central to gait hypokinesia in people with Parkinson's disease." Clin Neurol Neurosurg **115**(5): 587-590.

Mak, M. K., I. S. Wong-Yu, X. Shen and C. L. Chung (2017). "Long-term effects of exercise and physical therapy in people with Parkinson disease." Nat Rev Neurol **13**(11): 689-703.

Mak, M. K., L. Yu and C. W. Hui-Chan (2013). "The immediate effect of a novel audio-visual cueing strategy (simulated traffic lights) on dual-task walking in people with Parkinson's disease." Eur J Phys Rehabil Med **49**(2): 153-159.

Malmir, K. and M. Ashrafganjooie (2023). "Effects of HiBalance training program on physical function of individuals with idiopathic Parkinson disease: a systematic review and meta-analysis." Eur Geriatr Med **14**(6): 1273-1288.

Malwanage, K. T., T. D. Dissanayaka, N. E. Allen and S. S. Paul (2024). "Effect of Proprioceptive Training Compared With Other Interventions for Upper Limb Deficits in People With Parkinson Disease: A Systematic Review and Meta-analysis of Randomized Controlled Trials." Arch Phys Med Rehabil **105**(7): 1364-1374.

Mandelbaum, R. and A. C. Lo (2014). "Examining dance as an intervention in Parkinson's disease: a systematic review." American Journal of Dance Therapy **36**(2): 160-175.

Mang, C. S., K. L. Campbell, C. J. Ross and L. A. Boyd (2013). "Promoting neuroplasticity for motor rehabilitation after stroke: considering the effects of aerobic exercise and genetic variation on brain-derived neurotrophic factor." Phys Ther **93**(12): 1707-1716.

Mansfield, A., J. S. Wong, J. Bryce, S. Knorr and K. K. Patterson (2015). "Does Perturbation-Based Balance Training Prevent Falls? Systematic Review and Meta-Analysis of Preliminary Randomized Controlled Trials." PHYSICAL THERAPY **95**(5): 700-709.

Marazzi, S., P. Kiper, K. Palmer, M. Agostini and A. Turolla (2021). "Effects of vibratory stimulation on balance and gait in Parkinson's disease: a systematic review and meta-analysis." Eur J Phys Rehabil Med **57**(2): 254-264.

Marin, R. S., R. C. Biedrzycki and S. Firinciogullari (1991). "Reliability and validity of the Apathy Evaluation Scale." Psychiatry Res **38**(2): 143-162.

Marinus, N., D. Hansen, P. Feys, R. Meesen, A. Timmermans and J. Spildooren (2019). "The Impact of Different Types of Exercise Training on Peripheral Blood Brain-Derived Neurotrophic Factor Concentrations in Older Adults: A Meta- Analysis." Sports Med **49**(10): 1529-1546.

Marotta, N., D. Calafiore, C. Curci, L. Lippi, V. Ammendolia, F. Ferraro, M. Invernizzi and A. de Sire (2022). "Integrating virtual reality and exergaming in cognitive rehabilitation of patients with Parkinson disease: a systematic review of randomized controlled trials." Eur J Phys Rehabil Med **58**(6): 818-826.

Marquez, D. X., S. Aguinaga, P. M. Vasquez, D. E. Conroy, K. I. Erickson, C. Hillman, C. M. Stillman, R. M. Ballard, B. B. Sheppard, S. J. Petruzzello, A. C. King and K. E. Powell (2020). "A systematic review of physical activity and quality of life and well-being." Transl Behav Med **10**(5): 1098-1109.

Martignon, C., F. G. Laginestra, G. Giuriato, A. Pedrinolla, C. Barbi, D. I. V. IA, M. Tinazzi, F. Schena and M. Venturelli (2022). "Evidence that Neuromuscular Fatigue Is not a Dogma in Patients with Parkinson's Disease." Med Sci Sports Exerc **54**(2): 247-257.

Martignon, C., A. Pedrinolla, F. Ruzzante, G. Giuriato, F. G. Laginestra, R. Bouca-Machado, J. J. Ferreira, M. Tinazzi, F. Schena and M. Venturelli (2021). "Guidelines on exercise testing and prescription for patients at different stages of Parkinson's disease." Aging Clin Exp Res **33**(2): 221-246.

Martin-Nunez, J., A. Calvache-Mateo, L. Lopez-Lopez, A. Heredia-Ciuro, I. Cabrera-Martos, J. Rodriguez-Torres and M. C. Valenza (2023). "Effects of Exercise-Based Interventions on Physical Activity Levels in Persons With Parkinson's Disease: A Systematic Review With Meta-analysis." J Geriatr Phys Ther **46**(4): 207-213.

Marusiak, J., E. Zeligowska, J. Mencil, K. Kisiel-Sajewicz, J. Majerczak, J. A. Zoladz, A. Jaskolski and A. Jaskolska (2015). "INTERVAL TRAINING-INDUCED ALLEVIATION OF RIGIDITY AND HYPERTONIA IN PATIENTS WITH PARKINSON'S DISEASE IS ACCOMPANIED BY INCREASED BASAL SERUM BRAIN-DERIVED NEUROTROPHIC FACTOR A repeated-measures, case series pilot study." JOURNAL OF REHABILITATION MEDICINE **47**(4): 372-375.

Matthias Egger (Editor), J. P. T. H. E., George Davey Smith (Editor). June 2022 BMJ Books (2022). Systematic Reviews in Health Research: Meta-Analysis in Context, 3rd Edition.

Mattson, M. P., W. Duan, R. Wan and Z. Guo (2004). "Prophylactic Activation of Neuroprotective Stress Response Pathways by Dietary and Behavioral Manipulations." NeuroRx **1**(1): 111-116.

Mazzarin, C. M., S. R. Valderramas, M. de Paula Ferreira, E. Tiepolo, L. Guérios, D. Parisotto and V. L. Israel (2017). "Effects of dance and of Tai Chi on functional mobility, balance, and agility in Parkinson disease: a systematic review and meta-analysis." Topics in Geriatric Rehabilitation **33**(4): 262-272.

McDermott, A., C. Haberlin and J. Moran (2021). "The use of ehealth to promote physical activity in people living with Parkinson's disease: A systematic review." Physiotherapy Practice and Research **42**(1): 79-92.

McDonnell, M. N., B. Rischbieth, T. T. Schammer, C. Seaforth, A. J. Shaw and A. C. Phillips (2018). "Lee Silverman Voice Treatment (LSVT)-BIG to improve motor function in people with Parkinson's disease: a systematic review and meta-analysis." Clin Rehabil **32**(5): 607-618.

McGuinness, L. A. and J. P. T. Higgins (2020). "Risk-of-bias VISualization (robvis): An R package and Shiny web app for visualizing risk-of-bias assessments." Research Synthesis Methods **n/a**(n/a).

McMahon, L., C. Blake and O. Lennon (2021). "Nonpharmacological interventions for respiratory health in Parkinson's disease: A systematic review and meta-analysis." Eur J Neurol **28**(3): 1022-1040.

McNeely, M. E., R. P. Duncan and G. M. Earhart (2015). "A comparison of dance interventions in people with Parkinson disease and older adults." Maturitas **81**(1): 10-16.

Mehrholz, J., R. Friis, J. Kugler, S. Twork, A. Storch and M. Pohl (2010). "Treadmill training for patients with Parkinson's disease." Cochrane Database Syst Rev(1): Cd007830.

Mehrholz, J., J. Kugler, A. Storch, M. Pohl, K. Hirsch and B. Elsner (2016). "Treadmill training for patients with Parkinson Disease. An abridged version of a Cochrane Review." Eur J Phys Rehabil Med **52**(5): 704-713.

Meliani, A. A. G., A. G. Lima, J. A. Moratelli, J. da Silveira, P. Saraiva, P. R. Gil and A. C. A. Guimaraes (2025). "Can Dance and Yoga Help With the Non-Motor Symptoms of People With Parkinson's? A Systematic Review With Meta-Analysis." J Appl Gerontol: 7334648251328441.

Methajarunon, P., C. Eitvivipart, C. J. Diver and A. Foongchomcheay (2016). "Systematic review of published studies on aquatic exercise for balance in patients with multiple sclerosis, Parkinson's disease, and hemiplegia." Hong Kong Physiother J **35**: 12-20.

Methley, A. M., S. Campbell, C. Chew-Graham, R. McNally and S. Cheraghi-Sohi (2014). "PICO, PICOS and SPIDER: a comparison study of specificity and sensitivity in three search tools for qualitative systematic reviews." BMC health services research **14**(1): 1-10.

- Mico-Amigo, M. E., I. Kingma, S. Heinzel, S. Nussbaum, T. Heger, R. C. van Lummel, D. Berg, W. Maetzler and J. H. van Dieën (2019). "Dual vs. Single Tasking During Circular Walking: What Better Reflects Progression in Parkinson's Disease?" *Front Neurol* **10**: 372.
- Micó-Amigo, M. E., I. Kingma, S. Heinzel, S. Nussbaum, T. Heger, R. C. van Lummel, D. Berg, W. Maetzler and J. H. van Dieën (2019). "Dual vs. Single Tasking During Circular Walking: What Better Reflects Progression in Parkinson's Disease?" *Front Neurol* **10**: 372.
- Migdadi, H., H.-Y. Wang, S. Agarwal, K. Sharma, A. Cucca, A. Quartarone, M. Ghilardi, A. Di Rocco and M. Biagioni (2018). Modulating BDNF Activity in Parkinson's Disease: the Impact of Aerobic Exercise and Transcranial Magnetic Stimulation (P5. 076), AAN Enterprises.
- Miller, K. J., D. Suárez-Iglesias, M. Seijo-Martínez and C. Ayán (2019). "Physiotherapy for freezing of gait in Parkinson's disease: A systematic review and meta-analysis." *Revista de Neurologia* **70**(4): 161-169.
- Miranda, M., J. F. Morici, M. B. Zanoni and P. Bekinschtein (2019). "Brain-Derived Neurotrophic Factor: A Key Molecule for Memory in the Healthy and the Pathological Brain." *Front Cell Neurosci* **13**: 363.
- Mirelman, A., P. Bonato, R. Camicioli, T. D. Ellis, N. Giladi, J. L. Hamilton, C. J. Hass, J. M. Hausdorff, E. Pelosin and Q. J. Almeida (2019). "Gait impairments in Parkinson's disease." *Lancet Neurol* **18**(7): 697-708.
- Mirelman, A., L. Rochester, I. Maidan, S. Del Din, L. Alcock, F. Nieuwhof, M. O. Rikkert, B. R. Bloem, E. Pelosin, L. Avanzino, G. Abbruzzese, K. Dockx, E. Bekkers, N. Giladi, A. Nieuwboer and J. M. Hausdorff (2016). "Addition of a non-immersive virtual reality component to treadmill training to reduce fall risk in older adults (V-TIME): a randomised controlled trial." *Lancet* **388**(10050): 1170-1182.
- Molina, M. C. and I. C. Muñoz (2019). "Efectos de los estímulos rítmicos externos auditivos o visuales sobre la marcha en pacientes con enfermedad de Parkinson: revisión sistemática." *Fisioterapia* **41**(3): 143-156.
- Molina Palomino, F. M., L. López López, J. Rodríguez Torres, M. Granados Santiago, A. Ortiz Rubio, I. Cabrera Martos and M. C. Valenza (2021). "Efectividad del trabajo de resistencia y de cicloergómetro a alta velocidad sobre la bradicinesia en la enfermedad de Parkinson: revisión sistemática." *Fisioterapia* **43**(4): 230-238.
- Mondini, S., D. Mapelli, G. Arcara and P. S. Bisiacchi (2011). *Esame Neuropsicologico Breve 2, ENB-2*.
- Monteiro, E. P., L. T. Franzoni, D. M. Cubillos, A. de Oliveira Fagundes, A. R. Carvalho, H. B. Oliveira, P. D. Pantoja, F. B. Schuch, C. R. Rieder, F. G. Martinez and L. A. Peyre-Tartaruga (2017). "Effects of Nordic walking training on functional parameters in Parkinson's disease: a randomized controlled clinical trial." *Scand J Med Sci Sports* **27**(3): 351-358.
- Monteiro-Junior, R. S., T. Cevada, B. R. Oliveira, E. Lattari, E. M. Portugal, A. Carvalho and A. C. Deslandes (2015). "We need to move more: Neurobiological hypotheses of physical exercise as a treatment for Parkinson's disease." *Med Hypotheses* **85**(5): 537-541.
- Mooventhan, A. and L. Nivethitha (2017). "Evidence based effects of yoga in neurological disorders." *J Clin Neurosci* **43**: 61-67.
- Morales-Gomez, S., I. Elizagaray-Garcia, O. Yepes-Rojas, L. de la Puente-Ranea and A. Gil-Martinez (2018). "Effectiveness of virtual immersion programmes in patients with Parkinson's disease. A systematic review." *REVISTA DE NEUROLOGIA* **66**(3): 69-80.
- Moratelli, J. A., A. G. Lima, K. H. Alexandre, D. Y. Fausto, A. N. Haas and A. C. de Azevedo Guimarães (2024). "Evidence of physical activity interventions on non-motor symptoms of people with Parkinson's disease: An umbrella review." *Sport Sciences for Health* **20**(2): 321-336.
- Moritz, T. A., D. A. Snowdon and C. L. Peiris (2020). "Combining aquatic physiotherapy with usual care physiotherapy for people with neurological conditions: A systematic review." *Physiother Res Int* **25**(1): e1813.
- Morris, H. R., M. G. Spillantini, C. M. Sue and C. H. Williams-Gray (2024). "The pathogenesis of Parkinson's disease." *Lancet* **403**(10423): 293-304.
- Morris, M. E., T. D. Ellis, D. Jazayeri, H. Heng, A. Thomson, A. P. Balasundaram and S. C. Slade (2019). "Boxing for Parkinson's Disease: Has Implementation Accelerated Beyond Current Evidence?" *Front Neurol* **10**: 1222.

Moumdjian, L., T. Sarkamo, C. Leone, M. Leman and P. Feys (2017). "Effectiveness of music-based interventions on motricity or cognitive functioning in neurological populations: a systematic review." Eur J Phys Rehabil Med **53**(3): 466-482.

Mrowczynski, W. (2019). "Health Benefits of Endurance Training: Implications of the Brain-Derived Neurotrophic Factor-A Systematic Review." Neural Plast **2019**: 5413067.

Muhlack, S., J. Welnic, D. Woitalla and T. Muller (2007). "Exercise improves efficacy of levodopa in patients with Parkinson's disease." Mov Disord **22**(3): 427-430.

Mura, G., M. G. Carta, F. Sancassiani, S. Machado and L. Prosperini (2018). "Active exergames to improve cognitive functioning in neurological disabilities: a systematic review and meta-analysis." Eur J Phys Rehabil Med **54**(3): 450-462.

Murray, D. K., M. A. Sacheli, J. J. Eng and A. J. Stoessl (2014). "The effects of exercise on cognition in Parkinson's disease: a systematic review." Transl Neurodegener **3**(1): 5.

Mustafaoglu, R., I. Ahmed and M. Y. C. Pang (2022). "Which type of mind-body exercise is most effective in improving functional performance and quality of life in patients with Parkinson's disease? A systematic review with network meta-analysis." Acta Neurol Belg **122**(6): 1433-1446.

Narayanasetti, N., K. Bansal and A. Thomas (2025). "Physiotherapy for managing tremors in patients with Parkinson's disease—a systematic review." Neuroscience Research Notes **8**(1): 359.351-359.311.

Nardello, F., E. Bertoli, F. Bombieri, M. Bertucco and A. Monte (2020). "The Effect of a Secondary Task on Kinematics during Turning in Parkinson's Disease with Mild to Moderate Impairment." Symmetry **12**(8): 1284.

Nardello, F., F. Bombieri and A. Monte (2020). "Leverage mechanical alterations during walking at self-selected speed in patients with Parkinson's disease." Gait Posture **79**: 175-182.

Nascimento, L. R., A. Boening, R. J. Rocha, W. A. do Carmo and L. Ada (2024). "Walking training with auditory cueing improves walking speed more than walking training alone in ambulatory people with Parkinson's disease: a systematic review." J Physiother **70**(3): 208-215.

Nasreddine, Z. S., N. A. Phillips, V. Bedirian, S. Charbonneau, V. Whitehead, I. Collin, J. L. Cummings and H. Chertkow (2005). "The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment." J Am Geriatr Soc **53**(4): 695-699.

Navarro-Lozano, F., P. Kiper, C. Carmona-Perez, S. Rutkowski, E. Pinero-Pinto and C. Luque-Moreno (2022). "Effects of Non-Immersive Virtual Reality and Video Games on Walking Speed in Parkinson Disease: A Systematic Review and Meta-Analysis." J Clin Med **11**(22).

Navas-Otero, A., A. Pineda-Nogueras, A. Ortiz-Rubio, A. Calvache Mateo, I. Torres-Sanchez, M. Carmen Valenza and M. Granados-Santiago (2024). "Effects of Tai-Chi on Quality of Life in People With Neurodegenerative Diseases. A systematic Review of Randomised Clinical Trials." Am J Health Promot **38**(6): 873-882.

Nhu, N. T., Y. J. Cheng and S. D. Lee (2021). "Effects of Treadmill Exercise on Neural Mitochondrial Functions in Parkinson's Disease: A Systematic Review of Animal Studies." Biomedicines **9**(8).

Ni, M., J. B. Hazzard, J. F. Signorile and C. Luca (2018). "Exercise Guidelines for Gait Function in Parkinson's Disease: A Systematic Review and Meta-analysis." Neurorehabil Neural Repair **32**(10): 872-886.

Ni, X., S. Liu, F. Lu, X. Shi and X. Guo (2014). "Efficacy and safety of Tai Chi for Parkinson's disease: a systematic review and meta-analysis of randomized controlled trials." PLoS One **9**(6): e99377.

Nieuwboer, A., G. Kwakkel, L. Rochester, D. Jones, E. van Wegen, A. M. Willems, F. Chavret, V. Hetherington, K. Baker and I. Lim (2007). "Cueing training in the home improves gait-related mobility in Parkinson's disease: the RESCUE trial." J Neurol Neurosurg Psychiatry **78**(2): 134-140.

Nishida, A., D. Kanbe, N. Sawamoto and R. Takahashi (2020). "Relationship between gait and cognition in Parkinson's disease." Clinical neurology **60**: S342.

Nofuji, Y., M. Suwa, H. Sasaki, A. Ichimiya, R. Nishichi and S. Kumagai (2012). "Different circulating brain-derived neurotrophic factor responses to acute exercise between physically active and sedentary subjects." J Sports Sci Med **11**(1): 83-88.

Norwitz, N. G., D. J. Dearlove, M. Lu, K. Clarke, H. Dawes and M. T. Hu (2020). "A Ketone Ester Drink Enhances Endurance Exercise Performance in Parkinson's Disease." Front Neurosci **14**: 584130.

Notaras, M. and M. van den Buuse (2019). "Brain-Derived Neurotrophic Factor (BDNF): Novel Insights into Regulation and Genetic Variation." *Neuroscientist* **25**(5): 434-454.

Nwogo, R. O., S. Kammermeier and A. Singh (2022). "Abnormal neural oscillations during gait and dual-task in Parkinson's disease." *Front Syst Neurosci* **16**: 995375.

O'Callaghan, A., M. Harvey, D. Houghton, W. K. Gray, K. L. Weston, L. L. Oates, B. Romano and R. W. Walker (2020). "Comparing the influence of exercise intensity on brain-derived neurotrophic factor serum levels in people with Parkinson's disease: a pilot study." *Aging Clin Exp Res* **32**(9): 1731-1738.

O'Connor, R. J. and M. U. Kini (2011). "Non-pharmacological and non-surgical interventions for tremor: a systematic review." *Parkinsonism Relat Disord* **17**(7): 509-515.

O'Shea, S., M. E. Morris and R. Iansek (2002). "Dual task interference during gait in people with Parkinson disease: effects of motor versus cognitive secondary tasks." *Phys Ther* **82**(9): 888-897.

Oh, S. and S. Lee (2021). "Effect of aquatic exercise on physical function and QOL in individuals with neurological disorder: A systematic review and meta-analysis." *J Bodyw Mov Ther* **27**: 67-76.

Ohara, M., K. Hirata, M. Hallett, T. Matsubayashi, Q. Chen, S. Kina, K. Shimano, A. Hirakawa, T. Yokota and T. Hattori (2023). "Long-term levodopa ameliorates sequence effect in simple, but not complex walking in early Parkinson's disease patients." *Parkinsonism Relat Disord* **108**: 105322.

Okada, Y., H. Ohtsuka, N. Kamata, S. Yamamoto, M. Sawada, J. Nakamura, M. Okamoto, M. Narita, Y. Nikaido, H. Urakami, T. Kawasaki, S. Morioka, K. Shomoto and N. Hattori (2021). "Effectiveness of Long-Term Physiotherapy in Parkinson's Disease: A Systematic Review and Meta-Analysis." *J Parkinsons Dis* **11**(4): 1619-1630.

Okemuo, A. J., D. Gallagher and Y. M. Dairo (2023). "Effects of rebound exercises on balance and mobility of people with neurological disorders: A systematic review." *PLoS One* **18**(10): e0292312.

Oldfield, R. C. (1971). "The assessment and analysis of handedness: the Edinburgh inventory." *Neuropsychologia* **9**(1): 97-113.

Oliveira, G. S., L. Iraci, G. S. Pinheiro, M. Z. Casal, A. N. Haas, D. Pochmann, F. G. Martinez, V. Elsner and C. Dani (2020). "Effect of exercise and grape juice on epigenetic modulation and functional outcomes in PD: A randomized clinical trial." *Physiol Behav* **227**: 113135.

Omar Ahmad, S., J. Longhurst, D. Stiles, L. Downard and S. Martin (2023). "A meta-analysis of exercise intervention and the effect on Parkinson's Disease symptoms." *Neurosci Lett* **801**: 137162.

Ono, K., J. Nishimoto, T. Imura, T. Mitsutake, Y. Inoue, S. Tanaka and R. Tanaka (2023). "The effects of walking training with poles on walking ability: A systematic review and meta-analysis of randomized controlled trials." *Pm r* **15**(8): 1026-1037.

Orcioli-Silva, D., R. Vitorio, P. Nobrega-Sousa, N. R. da Conceicao, V. S. Beretta, E. Lirani-Silva and L. T. B. Gobbi (2020). "Levodopa Facilitates Prefrontal Cortex Activation During Dual Task Walking in Parkinson Disease." *Neurorehabil Neural Repair* **34**(7): 589-599.

Orcioli-Silva, D., R. Vitorio, P. Nobrega-Sousa, N. R. da Conceição, V. S. Beretta, E. Lirani-Silva and L. T. B. Gobbi (2020). "Levodopa Facilitates Prefrontal Cortex Activation During Dual Task Walking in Parkinson Disease." *Neurorehabil Neural Repair* **34**(7): 589-599.

Ozcan Gulsen, E. and O. Tunca Yilmaz (2023). "Dual task effect on upper and lower extremity skills in different stages of Parkinson's disease." *Acta Neurol Belg* **123**(3): 865-872.

Padilha, C., R. Souza, F. S. Grossl, A. P. M. Gauer, C. A. de Sa and S. A. Rodrigues-Junior (2023). "Physical exercise and its effects on people with Parkinson's disease: Umbrella review." *PLoS One* **18**(11): e0293826.

Page, M. J., J. E. McKenzie, P. M. Bossuyt, I. Boutron, T. C. Hoffmann, C. D. Mulrow, L. Shamseer, J. M. Tetzlaff, E. A. Akl, S. E. Brennan, R. Chou, J. Glanville, J. M. Grimshaw, A. Hrobjartsson, M. M. Lalu, T. Li, E. W. Loder, E. Mayo-Wilson, S. McDonald, L. A. McGuinness, L. A. Stewart, J. Thomas, A. C. Tricco, V. A. Welch, P. Whiting and D. Moher (2021). "The PRISMA 2020 statement: an updated guideline for reporting systematic reviews." *Bmj* **372**: n71.

Pagnussat, A. S., A. F. R. Kleiner, C. R. M. Rieder, A. Frantz, J. Ehlers, C. Pinto, G. Dorneles, C. A. Netto, A. Peres and M. Galli (2018). "Plantar stimulation in parkinsonians: From biomarkers to mobility - randomized-controlled trial." *Restor Neurol Neurosci* **36**(2): 195-205.

Paillard, T., Y. Rolland and P. de Souto Barreto (2015). "Protective Effects of Physical Exercise in Alzheimer's Disease and Parkinson's Disease: A Narrative Review." *J Clin Neurol* **11**(3): 212-219.

- Palasz, E., W. Niewiadomski, A. Gasiorowska, A. Mietelska-Porowska and G. Niewiadomska (2019). "Neuroplasticity and neuroprotective effect of treadmill training in the chronic mouse model of Parkinson's disease." Neural Plasticity **2019**.
- Palm, D., A. Swarowsky, M. Gullickson, H. Shilling and M. Wolden (2024). "Effects of Group Exercise on Motor Function and Mobility for Parkinson Disease: A Systematic Review and Meta-Analysis." Phys Ther **104**(4).
- Palm, D., A. Swarowsky, M. Kelly, S. Grugel, C. Stiers and M. Wolden (2025). "Effect of group exercise on quality of life for Parkinson disease: systematic review and meta-analysis." Disabil Rehabil **47**(17): 4366-4378.
- Parati, M., E. Ambrosini, D. E. M. B, M. Gallotta, L. A. Dalla Vecchia, G. Ferriero and S. Ferrante (2022). "The reliability of gait parameters captured via instrumented walkways: a systematic review and meta-analysis." Eur J Phys Rehabil Med **58**(3): 363-377.
- Park, C. and B. C. Lee (2024). "A Systematic Review of the Effects of Interactive Telerehabilitation with Remote Monitoring and Guidance on Balance and Gait Performance in Older Adults and Individuals with Neurological Conditions." Bioengineering (Basel) **11**(5).
- Park, I. S. and J. G. Yoon (2015). "The effect of computer-assisted cognitive rehabilitation and repetitive transcranial magnetic stimulation on cognitive function for stroke patients." J Phys Ther Sci **27**(3): 773-776.
- Pate, R. R., M. Pratt, S. N. Blair, W. L. Haskell, C. A. Macera, C. Bouchard, D. Buchner, W. Ettinger, G. W. Heath, A. C. King and et al. (1995). "Physical activity and public health. A recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine." Jama **273**(5): 402-407.
- Patel, R. D. and K. B. Mans (2022). "Effect of supplemental activities on motor and nonmotor outcomes in the Parkinson's population." American Journal of Dance Therapy **44**(2): 210-240.
- Paterno, A., G. Polsinelli and B. Federico (2024). "Changes of brain-derived neurotrophic factor (BDNF) levels after different exercise protocols: a systematic review of clinical studies in Parkinson's disease." Front Physiol **15**: 1352305.
- Patterson, C. G., E. Joslin, A. B. Gil, W. Spigle, T. Nemet, L. Chahine, C. L. Christiansen, E. Melanson, W. M. Kohrt, M. Mancini, D. Josbeno, K. Balfany, G. Griffith, M. K. Dunlap, G. Lamotte, E. Suttman, D. Larson, C. Branson, K. E. McKee, L. Goelz, C. Poon, B. Tilley, U. J. Kang, M. G. Tansey, N. Luthra, C. M. Tanner, J. M. Haus, G. Fantuzzi, N. R. McFarland, P. Gonzalez-Latapi, T. Foroud, R. Motl, M. A. Schwarzschild, T. Simuni, K. Marek, A. Naito, C. Lungu and D. M. Corcos (2022). "Study in Parkinson's disease of exercise phase 3 (SPARX3): study protocol for a randomized controlled trial." Trials **23**(1): 855.
- Patterson, K. K., J. S. Wong, E. C. Prout and D. Brooks (2018). "Dance for the rehabilitation of balance and gait in adults with neurological conditions other than Parkinson's disease: A systematic review." Heliyon **4**(3): e00584.
- Pedersen, B. K. and M. A. Febbraio (2012). "Muscles, exercise and obesity: skeletal muscle as a secretory organ." Nat Rev Endocrinol **8**(8): 457-465.
- Pedro, K. P. P., I. M. de Oliveira, J. M. C. Carral and I. M. Cardalda (2023). "Effects of MOTOMed® movement therapy on the motor function and main symptoms of patients with Parkinson's disease: a systematic review." Retos: nuevas tendencias en educación física, deporte y recreación(47): 249-257.
- Peng, W., R. Zhao, Z. Huang, J. Zhou, Q. Sun, Z. Li, X. Li, J. Yu, N. Wang and Z. Chen (2024). "Efficacy of Oriental Exercises for Non-Motor Symptoms and Quality of Life in Parkinson's Disease: A Systematic Review and Meta-Analysis." Am J Chin Med **52**(8): 2233-2254.
- Perrochon, A., B. Borel, D. Istrate, M. Compagnat and J. C. Daviet (2019). "Exercise-based games interventions at home in individuals with a neurological disease: A systematic review and meta-analysis." Ann Phys Rehabil Med **62**(5): 366-378.
- Perry, S. I. B., P. M. Nelissen, P. Siemonsma and C. Lucas (2019). "The effect of functional-task training on activities of daily living for people with Parkinson's disease, a systematic review with meta-analysis." Complement Ther Med **42**: 312-321.

Petzinger, G. M., B. E. Fisher, S. McEwen, J. A. Beeler, J. P. Walsh and M. W. Jakowec (2013). "Exercise-enhanced neuroplasticity targeting motor and cognitive circuitry in Parkinson's disease." Lancet Neurol **12**(7): 716-726.

Petzinger, G. M., B. E. Fisher, J. E. Van Leeuwen, M. Vukovic, G. Akopian, C. K. Meshul, D. P. Holschneider, A. Nacca, J. P. Walsh and M. W. Jakowec (2010). "Enhancing neuroplasticity in the basal ganglia: the role of exercise in Parkinson's disease." Mov Disord **25 Suppl 1**(0 1): S141-145.

Petzinger, G. M., D. P. Holschneider, B. E. Fisher, S. McEwen, N. Kintz, M. Halliday, W. Toy, J. W. Walsh, J. Beeler and M. W. Jakowec (2015). "The Effects of Exercise on Dopamine Neurotransmission in Parkinson's Disease: Targeting Neuroplasticity to Modulate Basal Ganglia Circuitry." Brain Plast **1**(1): 29-39.

Peyre-Tartaruga, L. A., F. G. Martinez, A. P. J. Zanardi, M. Z. Casal, R. G. Donida, M. S. Delabary, E. Passos-Monteiro, M. Coertjens and A. N. Haas (2022). "Samba, deep water, and poles: a framework for exercise prescription in Parkinson's disease." Sport Sci Health **18**(4): 1119-1127.

Peyré-Tartaruga, L. and E. P. Monteiro (2016). "A new integrative approach to evaluate pathological gait: locomotor rehabilitation index." Clin Transl Degener Dis **1**(2): 86-90.

Picelli, A., M. Camin, M. Tinazzi, A. Vangelista, A. Cosentino, A. Fiaschi and N. Smania (2010). "Three-dimensional motion analysis of the effects of auditory cueing on gait pattern in patients with Parkinson's disease: a preliminary investigation." Neurol Sci **31**(4): 423-430.

Picelli, A., M. Capecci, M. Filippetti, V. Varalta, C. Fonte, D. I. C. R, A. Zadra, I. Chignola, S. Scarpa, A. P. Amico, R. Antenucci, A. Baricich, P. Benanti, L. Bissolotti, P. Boldrini, D. Bonaiuti, E. Castelli, L. Cavalli, D. I. S. G, F. Draicchio, V. Falabella, S. Galeri, F. Gimigliano, M. Grigioni, J. Jonsdottir, C. Lentino, P. Massai, S. Mazzoleni, S. Mazzon, F. Molteni, S. Morelli, G. Morone, D. Panzeri, M. Petrarca, F. Posteraro, M. Senatore, E. Taglione, G. Turchetti, T. Bowman and A. Nardone (2021). "Effects of robot-assisted gait training on postural instability in Parkinson's disease: a systematic review." Eur J Phys Rehabil Med **57**(3): 472-477.

Pieper, D., S. L. Antoine, T. Mathes, E. A. Neugebauer and M. Eikermann (2014). "Systematic review finds overlapping reviews were not mentioned in every other overview." J Clin Epidemiol **67**(4): 368-375.

Pieruccini-Faria, F., K. A. Ehgoetz Martens, C. R. Silveira, J. A. Jones and Q. J. Almeida (2014). "Interactions between cognitive and sensory load while planning and controlling complex gait adaptations in Parkinson's disease." BMC Neurol **14**: 250.

Pigott, J. S., M. Armstrong, N. Tabassum, N. Davies and A. Schrag (2024). "Effectiveness and Feasibility of Nonpharmacological Interventions for People With Parkinson's Disease and Cognitive Impairment on Patient-Centred Outcomes: Systematic Review and Meta-Analysis." Parkinsons Dis **2024**: 3654652.

Pilgram, L. M., G. M. Earhart and K. A. Pickett (2016). "Impact of limiting visual input on gait: Individuals with Parkinson disease, age-matched controls, and healthy young participants." Somatosens Mot Res **33**(1): 29-34.

Pinho, R. A., A. S. Aguiar, Jr. and Z. Radák (2019). "Effects of Resistance Exercise on Cerebral Redox Regulation and Cognition: An Interplay Between Muscle and Brain." Antioxidants (Basel) **8**(11).

Pinto, C., A. P. Salazar, R. R. Marchese, C. Stein and A. S. Pagnussat (2019). "The Effects of Hydrotherapy on Balance, Functional Mobility, Motor Status, and Quality of Life in Patients with Parkinson Disease: A Systematic Review and Meta-analysis." Pm r **11**(3): 278-291.

Pinto, C., R. Simon Myra, A. Severo do Pinho, F. Pereira, G. Orgs and A. S. Pagnussat (2024). "Quality assessment and umbrella review of systematic reviews about dance for people with Parkinson's disease." PLoS One **19**(12): e0311003.

Plotnik, M., N. Giladi and J. M. Hausdorff (2009). "Bilateral coordination of gait and Parkinson's disease: the effects of dual tasking." J Neurol Neurosurg Psychiatry **80**(3): 347-350.

Plummer, P. and G. Eskes (2015). "Measuring treatment effects on dual-task performance: a framework for research and clinical practice." Front Hum Neurosci **9**: 225.

Plummer-D'Amato, P., L. J. Altmann and K. Reilly (2011). "Dual-task effects of spontaneous speech and executive function on gait in aging: exaggerated effects in slow walkers." Gait Posture **33**(2): 233-237.

Poewe, W., K. Seppi, C. M. Tanner, G. M. Halliday, P. Brundin, J. Volkmann, A. E. Schrag and A. E. Lang (2017). "Parkinson disease." Nat Rev Dis Primers **3**: 17013.

- Polacchini, A., G. Metelli, R. Francavilla, G. Baj, M. Florean, L. G. Mascaretti and E. Tongiorgi (2015). "A method for reproducible measurements of serum BDNF: comparison of the performance of six commercial assays." Sci Rep **5**: 17989.
- Polania, R., M. A. Nitsche and C. C. Ruff (2018). "Studying and modifying brain function with non-invasive brain stimulation." Nat Neurosci **21**(2): 174-187.
- Pompeu, S., E. Okamoto and M. E. Piemonte (2011). "Dual-task performance assessment: motor performance of gait, balance, posture and manual skill in dual-tasks." Physiotherapy (united kingdom) **97**: eS1014.
- Ponde, P. D. S., W. K. Neto, D. N. Rodrigues, L. Cristina, M. F. Bastos, I. C. Sanches and E. F. Gama (2019). "CHRONIC RESPONSES OF PHYSICAL AND IMAGERY TRAINING ON PARKINSON'S DISEASE." REVISTA BRASILEIRA DE MEDICINA DO ESPORTE **25**(6): 503-508.
- Postuma, R. B., D. Berg, M. Stern, W. Poewe, C. W. Olanow, W. Oertel, J. Obeso, K. Marek, I. Litvan, A. E. Lang, G. Halliday, C. G. Goetz, T. Gasser, B. Dubois, P. Chan, B. R. Bloem, C. H. Adler and G. Deuschl (2015). "MDS clinical diagnostic criteria for Parkinson's disease." Mov Disord **30**(12): 1591-1601.
- Pringsheim, T., N. Jette, A. Frolkis and T. D. Steeves (2014). "The prevalence of Parkinson's disease: a systematic review and meta- analysis." Mov Disord **29**(13): 1583-1590.
- Pritchard, M. O., J. V. Laster, L. J. Rogers, M. A. Schultz and R. M. Babl (2019). "The effects of aquatic therapy on gait, balance, and quality of life in patients with Parkinson's disease." The Journal of Aquatic Physical Therapy **27**(2): 10-24.
- Prosperini, L., V. Tomassini, L. Castelli, A. Tacchino, G. Brichetto, D. Cattaneo and C. M. Solaro (2021). "Exergames for balance dysfunction in neurological disability: a meta- analysis with meta-regression." J Neurol **268**(9): 3223-3237.
- Proud, E. L., K. J. Miller, C. L. Martin and M. E. Morris (2013). "Upper-limb assessment in people with Parkinson disease: is it a priority for therapists, and which assessment tools are used?" Physiother Can **65**(4): 309-316.
- Proud, E. L., K. J. Miller, M. E. Morris, J. L. McGinley and J. M. Blennerhassett (2024). "Effects of Upper Limb Exercise or Training on Hand Dexterity and Function in People With Parkinson Disease: A Systematic Review and Meta-analysis." Arch Phys Med Rehabil **105**(7): 1375-1387.
- Qian, Y., X. Fu, H. Zhang, Y. Yang and G. Wang (2023). "Comparative efficacy of 24 exercise types on postural instability in adults with Parkinson's disease: a systematic review and network meta- analysis." BMC Geriatr **23**(1): 522.
- Quan, W., S. Liu, M. Cao and J. Zhao (2024). "A comprehensive review of virtual reality technology for cognitive rehabilitation in patients with neurological conditions." Applied Sciences **14**(14): 6285.
- Quirosa-Galán, I., S. García-Bravo, A. C. Fabara-Rodríguez, M. P. Rodríguez-Pérez, E. Huertas-Hoyas, J. Pérez-Corrales, G. Fernández-Gómez, M. Donovan and C. Garcia-Bravo (2024). "Video games in rehabilitation programs for people with Parkinson's disease: A systematic review." Applied Sciences **15**(1): 311.
- Qureshi, A. R., M. K. Jamal, E. Rahman, D. A. Paul, Y. S. Oghli, M. T. Mulaffer, D. Qureshi, M. A. Danish and A. Q. Rana (2021). "Non-pharmacological therapies for pain management in Parkinson's disease: A systematic review." Acta Neurol Scand **144**(2): 115-131.
- Radak, Z., S. Kumagai, A. W. Taylor, H. Naito and S. Goto (2007). "Effects of exercise on brain function: role of free radicals." APPLIED PHYSIOLOGY NUTRITION AND METABOLISM-PHYSIOLOGIE APPLIQUEE NUTRITION ET METABOLISME **32**(5): 942-947.
- Radak, Z., K. Suzuki, M. Higuchi, L. Balogh, I. Boldogh and E. Koltai (2016). "Physical exercise, reactive oxygen species and neuroprotection." Free Radic Biol Med **98**: 187-196.
- Radder, D. L. M., A. Lígia Silva de Lima, J. Domingos, S. H. J. Keus, M. van Nimwegen, B. R. Bloem and N. M. de Vries (2020). "Physiotherapy in Parkinson's Disease: A Meta-Analysis of Present Treatment Modalities." Neurorehabil Neural Repair **34**(10): 871-880.
- Raffegau, T. E., L. M. Krehbiel, N. Kang, F. J. Thijs, L. J. P. Altmann, J. H. Cauraugh and C. J. Hass (2019). "A meta-analysis: Parkinson's disease and dual-task walking." Parkinsonism Relat Disord **62**: 28-35.

Rahmani, F., A. Saghaizadeh, M. Rahmani, A. L. Teixeira, N. Rezaei, V. Aghamollaei and H. E. Ardebili (2019). "Plasma levels of brain-derived neurotrophic factor in patients with Parkinson disease: A systematic review and meta-analysis." Brain Research **1704**: 127-136.

Ramazzina, I., B. Bernazzoli and C. Costantino (2017). "Systematic review on strength training in Parkinson's disease: an unsolved question." Clin Interv Aging **12**: 619-628.

Ramírez-Nieto, M., R. Ortiz-Gutiérrez and R. Cano-de la Cuerda (2018). "Eficacia de los videojuegos comerciales en el tratamiento del equilibrio y la marcha en la enfermedad de Parkinson." Rehabilitación **52**(2): 114-124.

Ranchet, M., I. Hoang, M. Cheminon, R. Derollepot, H. Devos, S. Perrey, J. Luauté, T. Danaila and L. Paire-Ficout (2020). "Changes in Prefrontal Cortical Activity During Walking and Cognitive Functions Among Patients With Parkinson's Disease." Front Neurol **11**: 601686.

Reitan, R. M. (1958). "Validity of the Trail Making Test as an indicator of organic brain damage." Perceptual and motor skills **8**(3): 271-276.

Reuter-Lorenz, P. A. and K. A. Cappell (2008). "Neurocognitive aging and the compensation hypothesis." Current Directions in Psychological Science **17**(3): 177-182.

Reyes, A., M. Ziman and K. Nosaka (2013). "Respiratory muscle training for respiratory deficits in neurodegenerative disorders: A systematic review." Chest **143**(5): 1386-1394.

Robinson, A. G., A. M. Dennett and D. A. Snowdon (2019). "Treadmill training may be an effective form of task-specific training for improving mobility in people with Parkinson's disease and multiple sclerosis: a systematic review and meta-analysis." Physiotherapy **105**(2): 174-186.

Rochester, L., B. Galna, S. Lord and D. Burn (2014). "The nature of dual-task interference during gait in incident Parkinson's disease." Neuroscience **265**: 83-94.

Rochester, L., V. Hetherington, D. Jones, A. Nieuwboer, A. M. Willems, G. Kwakkel and E. Van Wegen (2005). "The effect of external rhythmic cues (auditory and visual) on walking during a functional task in homes of people with Parkinson's disease." ARCHIVES OF PHYSICAL MEDICINE AND REHABILITATION **86**(5): 999-1006.

Rochester, L., A. J. Yarnall, M. R. Baker, R. V. David, S. Lord, B. Galna and D. J. Burn (2012). "Cholinergic dysfunction contributes to gait disturbance in early Parkinson's disease." Brain **135**(Pt 9): 2779-2788.

Rodrigues-de-Paula, F., R. C. Lana, L. K. R. Lopes, F. Cardoso, A. R. R. Lindquist, M. E. P. Piemonte, C. L. Correa, V. L. Israel, F. Mendes and L. O. Lima (2018). "Determinants of the use of physiotherapy services among individuals with Parkinson's disease living in Brazil." Arq Neuropsiquiatr **76**(9): 592-598.

Rodriguez, M. A., L. Albillos-Almaraz, I. Lopez-Aguado, I. Crespo, M. Del Valle and H. Olmedillas (2021). "Vigorous Aerobic Exercise in the Management of Parkinson Disease: A Systematic Review." Pm r **13**(8): 890-900.

Rodriguez, M. A., I. Crespo, M. Del Valle and H. Olmedillas (2020). "Should respiratory muscle training be part of the treatment of Parkinson's disease? A systematic review of randomized controlled trials." Clin Rehabil **34**(4): 429-437.

Rodriguez-Mansilla, J., C. Bedmar-Vargas, E. M. Garrido-Ardila, S. T. Torres-Piles, B. Gonzalez-Sanchez, M. T. Rodriguez-Dominguez, M. V. Ramirez-Duran and M. Jimenez-Palomares (2023). "Effects of Virtual Reality in the Rehabilitation of Parkinson's Disease: A Systematic Review." J Clin Med **12**(15).

Roeder, L., J. T. Costello, S. S. Smith, I. B. Stewart and G. K. Kerr (2015). "Effects of Resistance Training on Measures of Muscular Strength in People with Parkinson's Disease: A Systematic Review and Meta-Analysis." PLoS One **10**(7): e0132135.

Rogers, G., D. Davies, J. Pink and P. Cooper (2017). "Parkinson's disease: summary of updated NICE guidance." Bmj **358**: j1951.

Rossi, S., A. Antal, S. Bestmann, M. Bikson, C. Brewer, J. Brockmoller, L. L. Carpenter, M. Cincotta, R. Chen, J. D. Daskalakis, V. Di Lazzaro, M. D. Fox, M. S. George, D. Gilbert, V. K. Kimiskidis, G. Koch, R. J. Ilmoniemi, J. P. Lefaucheur, L. Leocani, S. H. Lisanby, C. Miniussi, F. Padberg, A. Pascual-Leone, W. Paulus, A. V. Peterchev, A. Quartarone, A. Rotenberg, J. Rothwell, P. M. Rossini, E. Santarnecchi, M. M. Shafi, H. R. Siebner, Y. Ugawa, E. M. Wassermann, A. Zangen, U. Ziemann and M. Hallett (2021). "Safety and recommendations for TMS use in healthy subjects and patient populations, with updates on training, ethical and regulatory issues: Expert Guidelines." Clin Neurophysiol **132**(1): 269-306.

Rothman, S. M., K. J. Griffioen, R. Q. Wan and M. P. Mattson (2012). Brain-derived neurotrophic factor as a regulator of systemic and brain energy metabolism and cardiovascular health. BRAIN AND OBESITY. G. Cizza and K. I. Rother. **1264**: 49-63.

Rotondo, R., S. Proietti, M. Perluigi, E. Padua, F. Stocchi, M. Fini, V. Stocchi, D. Volpe and M. F. De Pandis (2023). "Physical activity and neurotrophic factors as potential drivers of neuroplasticity in Parkinson's Disease: A systematic review and meta- analysis." Ageing Res Rev **92**: 102089.

Rotondo, R., S. Proietti, M. Perluigi, E. Padua, F. Stocchi, M. Fini, V. Stocchi, D. Volpe and M. F. De Pandis (2023). "Physical activity and neurotrophic factors as potential drivers of neuroplasticity in Parkinson's Disease: A systematic review and meta-analysis." Ageing Res Rev: 102089.

Rucker, G. and G. Schwarzer (2015). "Ranking treatments in frequentist network meta-analysis works without resampling methods." BMC Med Res Methodol **15**: 58.

Ruiz-Gonzalez, D., A. Hernandez-Martinez, P. L. Valenzuela, J. S. Morales and A. Soriano-Maldonado (2021). "Effects of physical exercise on plasma brain-derived neurotrophic factor in neurodegenerative disorders: A systematic review and meta-analysis of randomized controlled trials." Neurosci Biobehav Rev **128**: 394-405.

Rutz, D. G. and D. H. Benninger (2020). "Physical Therapy for Freezing of Gait and Gait Impairments in Parkinson Disease: A Systematic Review." Pm r **12**(11): 1140-1156.

Römling, F., K. Brixius, K. Klier and K. Petrowski (2025). "The Role of Boxing in Parkinson's Disease: Evidence, Benefits, and Future Directions."

Sajatovic, M., A. L. Ridgel, E. M. Walter, C. M. Tatsuoka, K. Colón-Zimmermann, R. K. Ramsey, E. Welter, S. A. Gunzler, C. M. Whitney and B. L. Walter (2017). "A randomized trial of individual versus group-format exercise and self-management in individuals with Parkinson's disease and comorbid depression." Patient Prefer Adherence **11**: 965-973.

Sakamaki, T., Y. Furusawa, A. Hayashi, M. Otsuka and J. Fernandez (2022). "Remote Patient Monitoring for Neuropsychiatric Disorders: A Scoping Review of Current Trends and Future Perspectives from Recent Publications and Upcoming Clinical Trials." Telemedicine and e-Health **28**(9): 1235-1250.

Salari, N., A. Hayati, M. Kazeminia, A. Rahmani, M. Mohammadi, R. Fatahian and S. Shohaimi (2022). "The effect of exercise on balance in patients with stroke, Parkinson, and multiple sclerosis: a systematic review and meta-analysis of clinical trials." Neurol Sci **43**(1): 167-185.

Salazar, R. D., X. Ren, T. D. Ellis, N. Toraif, O. J. Barthelemy, S. Neargarder and A. Cronin-Golomb (2017). "Dual tasking in Parkinson's disease: Cognitive consequences while walking." Neuropsychology **31**(6): 613-623.

Salse-Batan, J., M. A. Sanchez-Lastra, D. Suarez-Iglesias, S. Varela and C. Ayan (2022). "Effects of Nordic walking in people with Parkinson's disease: A systematic review and meta-analysis." Health Soc Care Community **30**(5): e1505-e1520.

Saltychev, M., E. Barlund, J. Paltamaa, N. Katajapuu and K. Laimi (2016). "Progressive resistance training in Parkinson's disease: a systematic review and meta-analysis." BMJ Open **6**(1): e008756.

San Martin Valenzuela, C., L. Duenas Moscardo, J. Lopez-Pascual, P. Serra-Ano and J. M. Tomas (2020). "Interference of functional dual-tasks on gait in untrained people with Parkinson's disease and healthy controls: a cross-sectional study." BMC Musculoskelet Disord **21**(1): 396.

Santos, P., G. Scaldaferrri, L. Santos, N. Ribeiro, M. Neto and A. Melo (2019). "Effects of the Nintendo Wii training on balance rehabilitation and quality of life of patients with Parkinson's disease: A systematic review and meta-analysis." NeuroRehabilitation **44**(4): 569-577.

Sarasso, E., A. Gardoni, A. Tettamanti, F. Agosta, M. Filippi and D. Corbetta (2022). "Virtual reality balance training to improve balance and mobility in Parkinson's disease: a systematic review and meta-analysis." J Neurol **269**(4): 1873-1888.

Sarasso, E., M. P. Parente, F. Agosta, M. Filippi and D. Corbetta (2024). "Dual-Task vs. Single-Task Gait Training to Improve Spatiotemporal Gait Parameters in People with Parkinson's Disease: A Systematic Review and Meta-Analysis." Brain Sci **14**(5).

Sarbaz, Y. and H. Pourakbari (2019). "The Effects of Counting the Stride Numbers on the Parkinsonian Gait: Suggesting a Possible Reason for Dual Task Interference." Basic Clin Neurosci **10**(3): 269-279.

Scalzo, P., A. Kummer, T. L. Bretas, F. Cardoso and A. L. Teixeira (2010). "Serum levels of brain-derived neurotrophic factor correlate with motor impairment in Parkinson's disease." J Neurol **257**(4): 540-545.

Schaeffer, E., B. Roeben, O. Granert, A. Hanert, I. Liepelt-Scarfone, E. Leks, S. Otterbein, P. Saraykin, J. H. Busch, M. Synofzik, E. Stransky, T. Bartsch and D. Berg (2022). "Effects of exergaming on hippocampal volume and brain-derived neurotrophic factor levels in Parkinson's disease." Eur J Neurol **29**(2): 441-449.

Schapira, A. H. V., K. R. Chaudhuri and P. Jenner (2017). "Non-motor features of Parkinson disease." Nat Rev Neurosci **18**(7): 435-450.

Schenkman, M., C. G. Moore, W. M. Kohrt, D. A. Hall, A. Delitto, C. L. Comella, D. A. Josbeno, C. L. Christiansen, B. D. Berman, B. M. Kluger, E. L. Melanson, S. Jain, J. A. Robichaud, C. Poon and D. M. Corcos (2018). "Effect of High-Intensity Treadmill Exercise on Motor Symptoms in Patients With De Novo Parkinson Disease A Phase 2 Randomized Clinical Trial." JAMA NEUROLOGY **75**(2): 219-226.

Schilling, B. K., R. F. Pfeiffer, M. S. Ledoux, R. E. Karlage, R. J. Bloomer and M. J. Falvo (2010). "Effects of moderate-volume, high-load lower-body resistance training on strength and function in persons with Parkinson's disease: a pilot study." Parkinsons Dis **2010**: 824734.

Schlachetzki, J. C. M., J. Barth, F. Marxreiter, J. Gossler, Z. Kohl, S. Reinfelder, H. Gassner, K. Aminian, B. M. Eskofier, J. Winkler and J. Klucken (2017). "Wearable sensors objectively measure gait parameters in Parkinson's disease." PLoS One **12**(10): e0183989.

Schootemeijer, S., N. M. van der Kolk, B. R. Bloem and N. M. de Vries (2020). "Current Perspectives on Aerobic Exercise in People with Parkinson's Disease." Neurotherapeutics **17**(4): 1418-1433.

Schrag, A., M. Jahanshahi and N. Quinn (2000). "How does Parkinson's disease affect quality of life? A comparison with quality of life in the general population." Mov Disord **15**(6): 1112-1118.

Segura, C., M. Eraso, J. Bonilla, C. O. Mendivil, G. Santiago, N. Useche, O. Bernal-Pacheco, G. Monsalve, L. Sanchez, E. Hernández, M. J. Peláez-Jaramillo and A. Cárdenas-Mojica (2020). "Effect of a High-Intensity Tandem Bicycle Exercise Program on Clinical Severity, Functional Magnetic Resonance Imaging, and Plasma Biomarkers in Parkinson's Disease." Front Neurol **11**: 656.

Sena, I. G., A. V. D. Costa, I. K. D. Santos, D. P. Araujo, F. Gomes, J. Cavalcanti, M. I. Knackfuss, M. F. Andrade, P. K. M. Melo and I. A. T. Fonseca (2023). "Feasibility and effect of high-intensity training on the progression of motor symptoms in adult individuals with Parkinson's disease: A systematic review and meta-analysis." PLoS One **18**(11): e0293357.

Seuthe, J., N. D'Cruz, P. Ginis, B. Weisser, D. Berg, G. Deuschl, A. Nieuwboer and C. Schlenstedt (2019). "Split-belt treadmill walking in patients with Parkinson's disease: A systematic review." Gait Posture **69**: 187-194.

Seuthe, J., H. Hermanns, F. Hulzinga, N. D'Cruz, G. Deuschl, P. Ginis, A. Nieuwboer and C. Schlenstedt (2024). "Gait asymmetry and symptom laterality in Parkinson's disease: two of a kind?" J Neurol **271**(7): 4373-4382.

Sevcenko, K. and I. Lindgren (2022). "The effects of virtual reality training in stroke and Parkinson's disease rehabilitation: a systematic review and a perspective on usability." Eur Rev Aging Phys Act **19**(1): 4.

Shahhar, A. Z. M., M. Qasheesh and M. A. Shaphe (2022). "Effectiveness of Nintendo Wii on Balance in People with Parkinson's Disease: A Systematic Review." J Lifestyle Med **12**(3): 105-112.

Shahien, M., A. Elaraby, M. Gamal, E. Abdelazim, B. Abdelazeem, H. S. Ghaith and A. Negida (2023). "Physical therapy interventions for the management of hand tremors in patients with Parkinson's disease: a systematic review." Neurol Sci **44**(2): 461-470.

Shanahan, J., M. E. Morris, O. N. Bhriain, J. Saunders and A. M. Clifford (2015). "Dance for people with Parkinson disease: what is the evidence telling us?" Arch Phys Med Rehabil **96**(1): 141-153.

Shanahan, J., M. E. Morris, O. N. Bhriain, D. Volpe, M. Richardson and A. M. Clifford (2015). "Is Irish set dancing feasible for people with Parkinson's disease in Ireland?" Complement Ther Clin Pract **21**(1): 47-51.

Sharififar, S., R. A. Coronado, S. Romero, H. Azari and M. Thigpen (2014). "The effects of whole body vibration on mobility and balance in Parkinson disease: a systematic review." Iran J Med Sci **39**(4): 318-326.

Sharp, K. and J. Hewitt (2014). "Dance as an intervention for people with Parkinson's disease: a systematic review and meta-analysis." Neurosci Biobehav Rev **47**: 445-456.

Shea, B. J., B. C. Reeves, G. Wells, M. Thuku, C. Hamel, J. Moran, D. Moher, P. Tugwell, V. Welch, E. Kristjansson and D. A. Henry (2017). "AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both." Bmj **358**: j4008.

Shen, X., I. S. Wong-Yu and M. K. Mak (2016). "Effects of Exercise on Falls, Balance, and Gait Ability in Parkinson's Disease: A Meta-analysis." Neurorehabil Neural Repair **30**(6): 512-527.

Sherrington, C., Z. A. Michaleff, N. Fairhall, S. S. Paul, A. Tiedemann, J. Whitney, R. G. Cumming, R. D. Herbert, J. C. T. Close and S. R. Lord (2017). "Exercise to prevent falls in older adults: an updated systematic review and meta-analysis." Br J Sports Med **51**(24): 1750-1758.

Shruthi, R. and K. Krishnaprasad (2021). "Review of Recent Rehabilitation Techniques for Fall Prevention in Parkinson's Disease." Journal of Pharmaceutical Research International **33**(58B): 184-192.

Shu, H. F., T. Yang, S. X. Yu, H. D. Huang, L. L. Jiang, J. W. Gu and Y. Q. Kuang (2014). "Aerobic exercise for Parkinson's disease: a systematic review and meta- analysis of randomized controlled trials." PLoS One **9**(7): e100503.

Simpkins, C. and F. Yang (2023). "Do dance style and intervention duration matter in improving balance among people with Parkinson's disease? A systematic review with meta- analysis." Parkinsonism Relat Disord **106**: 105231.

Sitja Rabert, M., D. Rigau Comas, A. Fort Vanmeerhaeghe, C. Santoyo Medina, M. Roque i Figuls, D. Romero-Rodriguez and X. Bonfill Cosp (2012). "Whole-body vibration training for patients with neurodegenerative disease." Cochrane Database Syst Rev(2): Cd009097.

Sivertseva, S. A., K. S. Anfilofeva, A. V. Zotova, M. A. Sherman, M. E. Guseva and A. N. Boyko (2022). "[Dance therapy in the rehabilitation of neurological diseases]." Zh Nevrol Psikhiatr Im S S Korsakova **122**(7. Vyp. 2): 31-35.

Sklivas, A. B., L. E. Robinson, T. L. Uhl, E. E. Dupont-Versteegden and K. P. Mayer (2022). "Efficacy of power training to improve physical function in individuals diagnosed with frailty and chronic disease: A meta-analysis." Physiol Rep **10**(11): e15339.

Skorkowska-Telichowska, K., K. Kropielnicka, K. Bulinska, U. Pilch, M. Wozniowski, A. Szuba and R. Jasinski (2016). "Nordic walking in the second half of life." Aging Clin Exp Res **28**(6): 1035-1046.

Smith, M., R. Barker, G. Williams, J. Carr and R. Gunnarsson (2020). "The effect of exercise on high-level mobility in individuals with neurodegenerative disease: a systematic literature review." Physiotherapy **106**: 174-193.

Soares, M. D., J. K. Dos Viana Santos, F. A. Da Costa and L. P. De Melo (2014). "Wii rehabilitation and neurological physiotherapy: A systematic review." Revista Neurociencias **23**(1): 81-88.

Sobral-Monteiro-Junior, R., P. Maillot, V. Gatica-Rojas, W. R. M. Ávila, A. M. B. de Paula, A. L. S. Guimarães, S. H. S. Santos, C. C. B. Pupe and A. C. Deslandes (2019). "Is the "lactormone" a key-factor for exercise-related neuroplasticity? A hypothesis based on an alternative lactate neurobiological pathway." Med Hypotheses **123**: 63-66.

Soke, F., B. Kocer, I. Fidan, P. Keskinoglu and A. Guclu-Gunduz (2021). "Effects of task-oriented training combined with aerobic training on serum BDNF, GDNF, IGF-1, VEGF, TNF-alpha, and IL-1 beta levels in people with Parkinson's disease: A randomized controlled study." EXPERIMENTAL GERONTOLOGY **150**.

Somaa, F. b. d.-e. d.-s. and A. Asghar (2021). "Paramedical Therapies for Parkinson Disease: A Systematic Review." Journal of Research in Medical and Dental Science **9**(11): 278-283.

Song, H., S. Ge, J. Li, C. Jiao and L. Ran (2025). "Effects of aerobic and resistance training on walking and balance abilities in older adults with Parkinson's disease: A systematic review and meta-analysis." PLoS One **20**(1): e0314539.

Song, R., W. Grabowska, M. Park, K. Osypiuk, G. P. Vergara-Diaz, P. Bonato, J. M. Hausdorff, M. Fox, L. R. Sudarsky, E. Macklin and P. M. Wayne (2017). "The impact of Tai Chi and Qigong mind-body exercises on motor and non- motor function and quality of life in Parkinson's disease: A systematic review and meta-analysis." Parkinsonism Relat Disord **41**: 3-13.

Sousani, M., R. Fernandez Rojas, E. Preston and M. Ghahramani (2025). "Exploring Brain-Body Interactions in Parkinson's Disease: A Study on Dual-Task Performance." IEEE Trans Neural Syst Rehabil Eng **33**: 984-993.

Spaulding, S. J., B. Barber, M. Colby, B. Cormack, T. Mick and M. E. Jenkins (2013). "Cueing and gait improvement among people with Parkinson's disease: a meta-analysis." Arch Phys Med Rehabil **94**(3): 562-570.

Speciali, D. S., E. M. de Oliveira, N. M. dos Santos, F. V. Pereira, A. C. Fracini, T. Y. Fukuda, C. S. Oliveira, J. C. Correa and P. R. Lucareli (2013). "Use of the Gait Deviation Index and spatiotemporal variables for the assessment of dual task interference paradigm." J Bodyw Mov Ther **17**(1): 19-27.

Speciali, D. S., E. M. Oliveira, J. R. Cardoso, J. C. Correa, R. Baker and P. R. Lucareli (2014). "Gait profile score and movement analysis profile in patients with Parkinson's disease during concurrent cognitive load." Braz J Phys Ther **18**(4): 315-322.

Stanmore, E., B. Stubbs, D. Vancampfort, E. D. de Bruin and J. Firth (2017). "The effect of active video games on cognitive functioning in clinical and non-clinical populations: A meta-analysis of randomized controlled trials." Neurosci Biobehav Rev **78**: 34-43.

States, R. A., B. Dewan, P. Lynam, N. Mensah and O. Pottorf (2025). "Group exercise for balance in people with Parkinson's disease: a systematic review with meta-analysis." Physiother Theory Pract **41**(4): 872-889.

Steendam-Oldekamp, E. and T. van Laar (2024). "The Effectiveness of Inpatient Rehabilitation in Parkinson's Disease: A Systematic Review of Recent Studies." J Parkinsons Dis **14**(s1): S93-s112.

Stegemoller, E. L., J. P. Wilson, A. Hazamy, M. C. Shelley, M. S. Okun, L. J. Altmann and C. J. Hass (2014). "Associations between cognitive and gait performance during single- and dual-task walking in people with Parkinson disease." Phys Ther **94**(6): 757-766.

Stein Jr, E. and S. C. Maidanchen (2016). "O USO DA DANÇA COMO ESTRATÉGIA DE TRATAMENTO FISIOTERAPÊUTICO PARA INDIVÍDUOS COM DOENÇA DE PARKINSON: UMA REVISÃO SISTEMÁTICA." Revista Inspirar Movimento & Saude **11**(4).

Sterne, J. A., M. A. Hernan, B. C. Reeves, J. Savovic, N. D. Berkman, M. Viswanathan, D. Henry, D. G. Altman, M. T. Ansari, I. Boutron, J. R. Carpenter, A. W. Chan, R. Churchill, J. J. Deeks, A. Hrobjartsson, J. Kirkham, P. Juni, Y. K. Loke, T. D. Pigott, C. R. Ramsay, D. Regidor, H. R. Rothstein, L. Sandhu, P. L. Santaguida, H. J. Schunemann, B. Shea, I. Shrier, P. Tugwell, L. Turner, J. C. Valentine, H. Waddington, E. Waters, G. A. Wells, P. F. Whiting and J. P. Higgins (2016). "ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions." Bmj **355**: i4919.

Stevens-Lapsley, J. E., J. E. Balter, P. Wolfe, D. G. Eckhoff and W. M. Kohrt (2012). "Early neuromuscular electrical stimulation to improve quadriceps muscle strength after total knee arthroplasty: a randomized controlled trial." Phys Ther **92**(2): 210-226.

Stickdorn, I., D. Marks, C. Thiel and T. Braun (2018). "Effects of Lee Silverman Voice Treatment (LSVT)-BIG Training on Motor Functioning of People with Parkinson's Disease-A Systematic Review." Physioscience **14**(4): 153-160.

Still, A., L. Hale, S. Alam, M. E. Morris and P. Jayakaran (2024). "Relationships between physical activities performed under free-living conditions and non-motor symptoms in people with Parkinson's: A systematic review and meta-analysis." Clin Rehabil **38**(11): 1534-1551.

Strength, N.-N. and C. Association (2021). Essentials of strength training and conditioning, Human kinetics.

Stroop, J. R. (1935). "Studies of interference in serial verbal reactions." Journal of experimental psychology **18**(6): 643.

Strouwen, C., E. Molenaar, L. Müinks, S. H. J. Keus, J. C. M. Zijlmans, W. Vandenberghe, B. R. Bloem and A. Nieuwboer (2017). "Training dual tasks together or apart in Parkinson's disease: Results from the DUALITY trial." Mov Disord **32**(8): 1201-1210.

Stuart, S., B. Galna, L. S. Delicato, S. Lord and L. Rochester (2017). "Direct and indirect effects of attention and visual function on gait impairment in Parkinson's disease: influence of task and turning." Eur J Neurosci **46**(1): 1703-1716.

Stuart, S., S. Lord, B. Galna and L. Rochester (2018). "Saccade frequency response to visual cues during gait in Parkinson's disease: the selective role of attention." Eur J Neurosci **47**(7): 769-778.

Stuckenschneider, T., V. Abeln, T. Foitschik, T. Abel, M. C. Polidori and H. K. Strüder (2021). "Disease-inclusive exercise classes improve physical fitness and reduce depressive symptoms in individuals with and without Parkinson's disease-A feasibility study." Brain Behav **11**(10): e2352.

Stuckenschneider, T., C. D. Askew, A. L. Meneses, R. Baake, J. Weber and S. Schneider (2019). "The Effect of Different Exercise Modes on Domain-Specific Cognitive Function in Patients Suffering from Parkinson's Disease: A Systematic Review of Randomized Controlled Trials." *J Parkinsons Dis* 9(1): 73-95.

Suarez-Iglesias, D., K. J. Miller, M. Seijo-Martinez and C. Ayan (2019). "Benefits of Pilates in Parkinson's Disease: A Systematic Review and Meta- Analysis." *Medicina (Kaunas)* 55(8).

Suarez-Iglesias, D., L. Santos, M. A. Sanchez-Lastra and C. Ayan (2022). "Systematic review and meta-analysis of randomised controlled trials on the effects of yoga in people with Parkinson's disease." *Disabil Rehabil* 44(21): 6210-6229.

Sumec, R., P. Filip, K. Sheardova and M. Bares (2015). "Psychological Benefits of Nonpharmacological Methods Aimed for Improving Balance in Parkinson's Disease: A Systematic Review." *Behav Neurol* 2015: 620674.

Suppa, A., Y. Z. Huang, K. Funke, M. C. Ridding, B. Cheeran, V. Di Lazzaro, U. Ziemann and J. C. Rothwell (2016). "Ten Years of Theta Burst Stimulation in Humans: Established Knowledge, Unknowns and Prospects." *Brain Stimul* 9(3): 323-335.

Suppa, A., A. Quartarone, H. Siebner, R. Chen, V. Di Lazzaro, P. Del Giudice, W. Paulus, J. C. Rothwell, U. Ziemann and J. Classen (2017). "The associative brain at work: Evidence from paired associative stimulation studies in humans." *Clin Neurophysiol* 128(11): 2140-2164.

Szuhany, K. L., M. Bugatti and M. W. Otto (2015). "A meta-analytic review of the effects of exercise on brain-derived neurotrophic factor." *J Psychiatr Res* 60: 56-64.

Szymura, J., J. Kubica, M. Wiecek and J. Pera (2020). "The Immunomodulatory Effects of Systematic Exercise in Older Adults and People with Parkinson's Disease." *J Clin Med* 9(1).

Sørensen, H. T., T. L. Lash and K. J. Rothman (2006). "Beyond randomized controlled trials: a critical comparison of trials with nonrandomized studies." *Hepatology* 44(5): 1075-1082.

Taaffe, D. R., C. Duret, S. Wheeler and R. Marcus (1999). "Once-weekly resistance exercise improves muscle strength and neuromuscular performance in older adults." *J Am Geriatr Soc* 47(10): 1208-1214.

Tambosco, L., L. Percebois-Macadre, A. Rapin, J. Nicomette-Bardel and F. C. Boyer (2014). "Effort training in Parkinson's disease: a systematic review." *Ann Phys Rehabil Med* 57(2): 79-104.

Tan, J. W. and X. P. Wu (2017). "Effect of whole body vibration on low extremity functions and chronic diseases in the elderly." *Chinese Journal of Tissue Engineering Research* 21(8): 1288-1293.

Tan, W., Z. Pan, J. He, T. Wu, F. Wu, Y. Xu, L. Liu, Z. Yang, C. Li, Y. Hu and M. Liao (2025). "Traditional Chinese exercises for the treatment of neuropsychiatric symptoms in Parkinson's disease: A systematic review and meta-analysis." *Complement Ther Med* 89: 103134.

Tang, L., Y. Fang and J. Yin (2019). "The effects of exercise interventions on Parkinson's disease: A Bayesian network meta-analysis." *J Clin Neurosci* 70: 47-54.

Tang, R., S. Gong, J. Li, W. Hu, J. Liu and C. Liao (2024). "Efficacy of non-pharmacological interventions for sleep quality in Parkinson's disease: a systematic review and network meta-analysis." *Front Neurosci* 18: 1337616.

Tao, P. b. d.-e. d.-s., X. b. d.-e. d.-s. Shao, Y. b. d.-e. d.-s. Zhang, D. b. d.-e. d.-s. Huang and J. Han (2024). 帕金森病患者跌倒干预效果的系统评价 Effect of fall intervention in patients with Parkinson's disease: a systematic review. Shanghai, China, Academic Journal of Naval Medical University. 45.

Tao, Y., J. Luo, J. Tian, S. Peng, H. Wang, J. Cao, Z. Wen and X. Zhang (2024). "The role of robot-assisted training on rehabilitation outcomes in Parkinson's disease: a systematic review and meta-analysis." *Disabil Rehabil* 46(18): 4049-4067.

Terrens, A. F., S. E. Soh and P. E. Morgan (2018). "The efficacy and feasibility of aquatic physiotherapy for people with Parkinson's disease: a systematic review." *Disabil Rehabil* 40(24): 2847-2856.

Thorson, C. L., B. E. Hogan and P. S. Brown (2022). "Aquatic Therapy Intervention, Including the 4-Walls Drill, for Persons With Hoehn and Yahr Stage IV Parkinson's Disease: A Retrospective Data Analysis." *The Journal of Aquatic Physical Therapy* 30(1): 2-7.

Tian, J., Y. Kang, P. Liu and H. Yu (2022). "Effect of Physical Activity on Depression in Patients with Parkinson's Disease: A Systematic Review and Meta-Analysis." *Int J Environ Res Public Health* 19(11).

Tiihonen, M., B. U. Westner, M. Butz and S. S. Dalal (2021). "Parkinson's disease patients benefit from bicycling - a systematic review and meta-analysis." *NPI Parkinsons Dis* 7(1): 86.

Tillman, A., M. Muthalib, A. M. Hendy, L. G. Johnson, T. Rantalainen, D. J. Kidgell, P. G. Enticott and W. P. Teo (2015). "Lower limb progressive resistance training improves leg strength but not gait speed or balance in Parkinson's disease: a systematic review and meta-analysis." *Front Aging Neurosci* 7: 40.

Tobar, A., A. P. Jaramillo, S. C. Costa, K. T. Costa and S. S. Garcia (2023). "A Physical Rehabilitation Approach for Parkinson's Disease: A Systematic Literature Review." *Cureus* 15(9): e44739.

Toda, K., M. Iijima and K. Kitagawa (2019). "Periventricular White Matter Lesions Influence Gait Functions in Parkinson's Disease." *Eur Neurol* 81(3-4): 120-127.

Toh, S. F. M. (2013). "A systematic review on the effectiveness of Tai Chi exercise in individuals with Parkinson's disease from 2003 to 2013." *Hong Kong Journal of Occupational Therapy* 23(2): 69-81.

Tomlinson, C. L., C. P. Herd, C. E. Clarke, C. Meek, S. Patel, R. Stowe, K. H. Deane, L. Shah, C. M. Sackley, K. Wheatley and N. Ives (2014). "Physiotherapy for Parkinson's disease: a comparison of techniques." *Cochrane Database Syst Rev*(6): Cd002815.

Tomlinson, C. L., S. Patel, C. Meek, C. P. Herd, C. E. Clarke, R. Stowe, L. Shah, C. Sackley, K. H. Deane, K. Wheatley and N. Ives (2012). "Physiotherapy intervention in Parkinson's disease: systematic review and meta-analysis." *Bmj* 345: e5004.

Tomlinson, C. L., S. Patel, C. Meek, C. P. Herd, C. E. Clarke, R. Stowe, L. Shah, C. M. Sackley, K. H. Deane, K. Wheatley and N. Ives (2013). "Physiotherapy versus placebo or no intervention in Parkinson's disease." *Cochrane Database Syst Rev*(9): Cd002817.

Toneti, B. F., R. F. M. Barbosa, L. Y. Mano, L. O. Sawada, I. G. Oliveira and N. O. Sawada (2020). "Benefits of Qigong as an integrative and complementary practice for health: a systematic review." *Rev Lat Am Enfermagem* 28: e3317.

Tonkin, P. G., T. D. Miller, T. E. Hartmann and M. Skein (2023). "The effects of exercise on non-motor experiences of daily living experienced in Parkinson's Disease: A systematic review and network meta-analysis." *Clin Park Relat Disord* 9: 100203.

Triegaardt, J., T. S. Han, C. Sada, S. Sharma and P. Sharma (2020). "The role of virtual reality on outcomes in rehabilitation of Parkinson's disease: meta-analysis and systematic review in 1031 participants." *Neurol Sci* 41(3): 529-536.

Truijen, S., A. Abdullahi, D. Bijsterbosch, E. van Zoest, M. Conijn, Y. Wang, N. Struyf and W. Saeys (2022). "Effect of home-based virtual reality training and telerehabilitation on balance in individuals with Parkinson disease, multiple sclerosis, and stroke: a systematic review and meta-analysis." *Neurol Sci* 43(5): 2995-3006.

Tseng, I. J., C. Jeng and R. Y. Yuan (2012). "Comparisons of forward and backward gait between poorer and better attention capabilities in early Parkinson's disease." *Gait Posture* 36(3): 367-371.

Tuon, T., S. S. Valvassori, G. C. Dal Pont, C. S. Paganini, B. G. Pozzi, T. F. Luciano, P. S. Souza, J. Quevedo, C. T. Souza and R. A. Pinho (2014). "Physical training prevents depressive symptoms and a decrease in brain-derived neurotrophic factor in Parkinson's disease." *Brain Res Bull* 108: 106-112.

Uhrbrand, A., E. Stenager, M. S. Pedersen and U. Dalgas (2015). "Parkinson's disease and intensive exercise therapy--a systematic review and meta-analysis of randomized controlled trials." *J Neurol Sci* 353(1-2): 9-19.

Uribe, P., N. Fuentes, J. Álvarez-Ruf, I. Cornejo and J. J. Mariman (2022). "Differentiation of the motor cost associated with cognitive tasks in Parkinson's disease: A dual-task study." *Eur J Neurosci* 56(7): 5106-5115.

Van Crielinge, T., U. Sahu and T. Bhatt (2024). "Effect of Explicit Prioritization on Dual Tasks During Standing and Walking in People With Neurologic and Neurocognitive Disorders: A Systematic Review and Meta-analysis." *Arch Phys Med Rehabil* 105(11): 2166-2183.

van de Wetering-van Dongen, V. A., J. G. Kalf, P. J. van der Wees, B. R. Bloem and M. J. Nijkrake (2020). "The Effects of Respiratory Training in Parkinson's Disease: A Systematic Review." *J Parkinsons Dis* 10(4): 1315-1333.

van Wegen, E. E. H., M. A. Hirsch, W. D. J. van de Berg, C. Vriend, M. B. Rietberg, M. A. Newman, T. Vanbellingen and O. A. van den Heuvel (2020). "High-Intensity Interval Cycle Ergometer Training in Parkinson's Disease: Protocol for Identifying Individual Response Patterns Using a Single-Subject Research Design." *Front Neurol* 11: 569880.

Vandenbroucke, J. P., E. von Elm, D. G. Altman, P. C. Gotzsche, C. D. Mulrow, S. J. Pocock, C. Poole, J. J. Schlesselman and M. Egger (2007). "Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration." *Epidemiology* **18**(6): 805-835.

Vasquez-Morales, A., J. Sanz-Valero and C. Wanden-Berghe (2013). "[Eccentric exercise as preventive physical option in people over 65 years: a systematic review of the scientific literature]." *Enferm Clin* **23**(2): 48-55.

Vasu, D. T., M. Hui Lim, W. H. Fong, P. K. Choong and L. W. Chou (2024). "Evidence-Based Physiotherapeutic Interventions Enhancing Hand Dexterity, Activities of Daily Living and Quality of Life of Parkinson's Disease Patients: A Systematic Review." *Can J Neurol Sci*: 1-13.

Veer, K. and S. Pahuja (2022). "Gender based assessment of gait rhythms during dual-task in Parkinson's disease and its early detection." *Biomedical Signal Processing and Control* **72**: 103346.

Vellata, C., S. Belli, F. Balsamo, A. Giordano, R. Colombo and G. Maggioni (2021). "Effectiveness of Telerehabilitation on Motor Impairments, Non-motor Symptoms and Compliance in Patients With Parkinson's Disease: A Systematic Review." *Front Neurol* **12**: 627999.

Venezia, A. C., E. Quinlan and S. M. Roth (2017). "A single bout of exercise increases hippocampal Bdnf: influence of chronic exercise and noradrenaline." *Genes Brain Behav* **16**(8): 800-811.

Vieira de Moraes Filho, A., S. N. Chaves, W. R. Martins, G. P. Tolentino, R. de Cassia Pereira Pinto Homem, G. Landim de Farias, B. L. Fischer, J. A. Oliveira, S. K. A. Pereira, S. E. Vidal, M. R. Mota, R. Moreno Lima and R. Jaco de Oliveira (2020). "Progressive Resistance Training Improves Bradykinesia, Motor Symptoms and Functional Performance in Patients with Parkinson's Disease." *Clin Interv Aging* **15**: 87-95.

Vinolo Gil, M. J., G. Gonzalez-Medina, D. Lucena-Anton, V. Perez-Cabezas, M. D. C. Ruiz-Molinero and R. Martin-Valero (2021). "Augmented Reality in Physical Therapy: Systematic Review and Meta-analysis." *JMIR Serious Games* **9**(4): e30985.

Wallin, A., E. Franzén, J. Studsgaard, M. B. Hansen, S. Johansson and J. K. Brincks (2025). "Balance exercise interventions in Parkinson's disease: A systematic mapping review of components, progression, and intensity." *Parkinsonism Relat Disord*: 107310.

Walsh, J. J. and M. E. Tschakovsky (2018). "Exercise and circulating BDNF: Mechanisms of release and implications for the design of exercise interventions." *Appl Physiol Nutr Metab* **43**(11): 1095-1104.

Wang, B., M. Shen, Y. X. Wang, Z. W. He, S. Q. Chi and Z. H. Yang (2019). "Effect of virtual reality on balance and gait ability in patients with Parkinson's disease: a systematic review and meta-analysis." *Clin Rehabil* **33**(7): 1130-1138.

Wang, D., W. J. Cui, Z. H. Hou and Y. Gao (2023). "Effectiveness of different exercises in improving postural balance among Parkinson's disease patients: a systematic review and network meta-analysis." *Front Aging Neurosci* **15**: 1215495.

Wang, J., D. Gong, H. Luo, W. Zhang, L. Zhang, H. Zhang, J. Zhou and S. Wang (2020). "Measurement of Step Angle for Quantifying the Gait Impairment of Parkinson's Disease by Wearable Sensors: Controlled Study." *JMIR Mhealth Uhealth* **8**(3): e16650.

Wang, J., Y. Yuan, T. Xie, L. Zhang, H. Xu, S. C. Lin, Y. Yang, D. Zhu and J. Zhuang (2025). "Optimal dose and type of exercise to improve motor symptoms in adults with Parkinson's disease: A network meta-analysis." *J Sci Med Sport* **28**(4): 282-291.

Wang, K., K. Li, P. Zhang, S. Ge, X. Wen, Z. Wu, X. Yao, B. Jiao, P. Sun, P. Lv and L. Lu (2021). "Mind-Body Exercises for Non-motor Symptoms of Patients With Parkinson's Disease: A Systematic Review and Meta-Analysis." *Front Aging Neurosci* **13**: 770920.

Wang, L., F. Li and L. Tang (2022). "Chronic effects of different exercise types on brain activity in healthy older adults and those with Parkinson's disease: A systematic review." *Front Physiol* **13**: 1031803.

Wang, L. L., C. J. Sun, Y. Wang, T. T. Zhan, J. Yuan, C. Y. Niu, J. Yang, S. Huang and L. Cheng (2022). "Effects of dance therapy on non-motor symptoms in patients with Parkinson's disease: a systematic review and meta-analysis." *Aging Clin Exp Res* **34**(6): 1201-1208.

Wang, R., H. Zhou, Y. C. Wang, X. L. Chang and X. Q. Wang (2022). "Benefits of Tai Chi Quan on neurodegenerative diseases: A systematic review." *Ageing Res Rev* **82**: 101741.

Wang, T. F., S. Y. Wu, B. S. Pan, S. F. Tsai and Y. M. Kuo (2022). "Inhibition of Nigral Microglial Activation Reduces Age-Related Loss of Dopaminergic Neurons and Motor Deficits." *Cells* **11**(3).

Wang, W., S. S.-I. Wong and F. H.-y. Lai (2021). "The Effect of Virtual Reality Rehabilitation on Balance in Patients with Parkinson's Disease: A Systematic Review and Meta-Analysis." *Electronics* **10**(9): 1003.

Wang, X. Q., Y. L. Pi, B. L. Chen, R. Wang, X. Li and P. J. Chen (2016). "Cognitive motor intervention for gait and balance in Parkinson's disease: systematic review and meta-analysis." *Clin Rehabil* **30**(2): 134-144.

Wang, Y., X. Sun, F. Li, Q. Li and Y. Jin (2022). "Efficacy of non-pharmacological interventions for depression in individuals with Parkinson's disease: A systematic review and network meta-analysis." *Front Aging Neurosci* **14**: 1050715.

Wang, Y., Q. Zhang, F. Li, Q. Li and Y. Jin (2022). "Effects of tai chi and Qigong on cognition in neurological disorders: A systematic review and meta-analysis." *Geriatr Nurs* **46**: 166-177.

Wang, Z., B. Song, C. Liu, H. Ma, Z. Bai, M. A. S. Carneiro, L. Youssef, C. Chen, L. Zhang and D. Wang (2025). "Effects of boxing exercise in people with Parkinson's disease: a systematic review." *Front Aging Neurosci* **17**: 1505326.

Warlo, L. S., S. El Bardai, A. de Vries, M. L. van Veelen, S. Moors, E. H. Rings, J. S. Legerstee and B. Dierckx (2024). "Game-Based eHealth Interventions for the Reduction of Fatigue in People With Chronic Diseases: Systematic Review and Meta-Analysis." *JMIR Serious Games* **12**: e55034.

Wechsler, D. (2008). "Wechsler adult intelligence scale-fourth edition (WAIS-IV)[Database record]." *APA PsycTests* **10**.

Wells, M. and F. Yang (2021). "Ballroom dance as a form of rehabilitation: a systematic review." *Biomechanics* **1**(3): 307-320.

Wen, X., Z. Liu, X. Liu, Y. Peng and H. Liu (2022). "The effects of physiotherapy treatments on dysphagia in Parkinson's disease: A systematic review of randomized controlled trials." *Brain Res Bull* **188**: 59-66.

Wild, L. B., D. B. de Lima, J. B. Balardin, L. Rizzi, B. L. Giacobbo, H. B. Oliveira, A. de Lima, II, L. A. Peyré-Tartaruga, C. R. Rieder and E. Bromberg (2013). "Characterization of cognitive and motor performance during dual-tasking in healthy older adults and patients with Parkinson's disease." *J Neurol* **260**(2): 580-589.

Willett, W. C., L. Sampson, M. J. Stampfer, B. Rosner, C. Bain, J. Witschi, C. H. Hennekens and F. E. Speizer (1985). "Reproducibility and validity of a semiquantitative food frequency questionnaire." *Am J Epidemiol* **122**(1): 51-65.

Winser, S. J., W. W. Tsang, K. Krishnamurthy and P. Kannan (2018). "Does Tai Chi improve balance and reduce falls incidence in neurological disorders? A systematic review and meta-analysis." *Clin Rehabil* **32**(9): 1157-1168.

Wong, P. L., S. J. Cheng, Y. R. Yang and R. Y. Wang (2023). "Effects of Dual Task Training on Dual Task Gait Performance and Cognitive Function in Individuals With Parkinson Disease: A Meta-analysis and Meta-regression." *Arch Phys Med Rehabil* **104**(6): 950-964.

Wrann, C. D., J. P. White, J. Salogiannnis, D. Laznik-Bogoslavski, J. Wu, D. Ma, J. D. Lin, M. E. Greenberg and B. M. Spiegelman (2013). "Exercise induces hippocampal BDNF through a PGC-1 α /FNDC5 pathway." *Cell Metab* **18**(5): 649-659.

Wrann, C. D., J. P. White, J. Salogiannnis, D. Laznik-Bogoslavski, J. Wu, D. Ma, J. D. Lin, M. E. Greenberg and B. M. Spiegelman (2013). "Exercise induces hippocampal BDNF through a PGC-1 α /FNDC5 pathway." *Cell Metab* **18**(5): 649-659.

Wu, C., Y. Xu, Z. Chen, Y. Cao, K. Yu and C. Huang (2021). "The Effect of Intensity, Frequency, Duration and Volume of Physical Activity in Children and Adolescents on Skeletal Muscle Fitness: A Systematic Review and Meta-Analysis of Randomized Controlled Trials." *Int J Environ Res Public Health* **18**(18).

Wu, C., Y. Xu, H. Guo, C. Tang, D. Chen and M. Zhu (2021). "Effects of Aerobic Exercise and Mind-Body Exercise in Parkinson's Disease: A Mixed-Treatment Comparison Analysis." *Front Aging Neurosci* **13**: 739115.

Wu, C. C., H. Y. Xiong, J. J. Zheng and X. Q. Wang (2022). "Dance movement therapy for neurodegenerative diseases: A systematic review." *Front Aging Neurosci* **14**: 975711.

Wu, J., H. Zhang, Z. Chen, R. Fu, H. Yang, H. Zeng and Z. Ren (2022). "Benefits of Virtual Reality Balance Training for Patients With Parkinson Disease: Systematic Review, Meta-analysis, and Meta-Regression of a Randomized Controlled Trial." *JMIR Serious Games* **10**(1): e30882.

- Wu, M., Q. Tang, L. Wang, M. Zhang, W. Song, L. Teng and L. Zhu (2022). "Efficacy of Traditional Chinese Exercise in Improving Gait and Balance in Cases of Parkinson's Disease: A Systematic Review and Meta-analysis." *Front Aging Neurosci* **14**: 927315.
- Wu, P. L., M. Lee and T. T. Huang (2017). "Effectiveness of physical activity on patients with depression and Parkinson's disease: A systematic review." *PLoS One* **12**(7): e0181515.
- Wu, S. Y., T. F. Wang, L. Yu, C. J. Jen, J. I. Chuang, F. S. Wu, C. W. Wu and Y. M. Kuo (2011). "Running exercise protects the substantia nigra dopaminergic neurons against inflammation-induced degeneration via the activation of BDNF signaling pathway." *Brain Behav Immun* **25**(1): 135-146.
- Wu, T. and M. Hallett (2005). "A functional MRI study of automatic movements in patients with Parkinson's disease." *Brain* **128**(Pt 10): 2250-2259.
- Wu, T., M. Hallett and P. Chan (2015). "Motor automaticity in Parkinson's disease." *Neurobiol Dis* **82**: 226-234.
- Wu, Y. and J. Ye (2020). "Adults with Parkinson's disease undergoes exergaming training to improve balance: a systematic review." *IIJET* **10**(2): 146-153.
- Xie, S., Y. Yuan, J. Wang, Y. Bai, T. Wang, B. Qiu, Y. Yang and S. C. Lin (2025). "Optimal dose and type of exercise improve walking velocity in adults with Parkinson's disease: a systematic review and Bayesian network meta-analysis." *Sci Rep* **15**(1): 2239.
- Xu, F., K. G. Soh, Y. M. Chan, X. R. Bai, F. Qi and N. Deng (2023). "Effects of tai chi on postural balance and quality of life among the elderly with gait disorders: A systematic review." *PLoS One* **18**(9): e0287035.
- Xu, H., A. Merryweather, K. B. Foreman, J. Zhao and M. Hunt (2018). "Dual-task interference during gait on irregular terrain in people with Parkinson's disease." *Gait Posture* **63**: 17-22.
- Xu, X., Z. Fu and W. Le (2019). "Exercise and Parkinson's disease." *Int Rev Neurobiol* **147**: 45-74.
- Xu, Y., C. Geng, T. Tang, J. Huang and Y. Hou (2023). "How to prevent cognitive overload in the walking-arithmetic dual task among patients with Parkinson's disease." *BMC Neurol* **23**(1): 205.
- Xue, X., X. Yang and Z. Deng (2023). "Efficacy of rehabilitation robot-assisted gait training on lower extremity dyskinesia in patients with Parkinson's disease: A systematic review and meta-analysis." *Ageing Res Rev* **85**: 101837.
- Yang, C. L., J. P. Huang, T. T. Wang, Y. C. Tan, Y. Chen, Z. Q. Zhao, C. H. Qu and Y. Qu (2022). "Effects and parameters of community-based exercise on motor symptoms in Parkinson's disease: a meta-analysis." *BMC Neurol* **22**(1): 505.
- Yang, F., Y. Trolle Lagerros, R. Bellocco, H. O. Adami, F. Fang, N. L. Pedersen and K. Wirdefeldt (2015). "Physical activity and risk of Parkinson's disease in the Swedish National March Cohort." *Brain* **138**(Pt 2): 269-275.
- Yang, J. L., Y. T. Lin, P. C. Chuang, V. A. Bohr and M. P. Mattson (2014). "BDNF and exercise enhance neuronal DNA repair by stimulating CREB-mediated production of apurinic/apyrimidinic endonuclease 1." *Neuromolecular Med* **16**(1): 161-174.
- Yang, X. and Z. Wang (2023). "Effectiveness of Progressive Resistance Training in Parkinson's Disease: A Systematic Review and Meta-Analysis." *Eur Neurol* **86**(1): 25-33.
- Yang, Y., X. Fu, H. Zhang, G. Ouyang and S. C. Lin (2023). "The effect of home-based exercise on motor symptoms, quality of life and functional performance in Parkinson's disease: a systematic review and meta-analysis." *BMC Geriatr* **23**(1): 873.
- Yang, Y., X. Y. Li, L. Gong, Y. L. Zhu and Y. L. Hao (2014). "Tai Chi for improvement of motor function, balance and gait in Parkinson's disease: a systematic review and meta-analysis." *PLoS One* **9**(7): e102942.
- Yang, Y., W. Q. Qiu, Y. L. Hao, Z. Y. Lv, S. J. Jiao and J. F. Teng (2015). "The efficacy of traditional Chinese Medical Exercise for Parkinson's disease: a systematic review and meta-analysis." *PLoS One* **10**(4): e0122469.
- Yang, Y., G. Wang, S. Zhang, H. Wang, W. Zhou, F. Ren, H. Liang, D. Wu, X. Ji, M. Hashimoto and J. Wei (2022). "Efficacy and evaluation of therapeutic exercises on adults with Parkinson's disease: a systematic review and network meta-analysis." *BMC Geriatr* **22**(1): 813.
- Yang, Y., Y. Wang, T. Gao, A. Reyila, J. Liu and H. Han (2023). "Effect of Physiotherapy Interventions on Motor Symptoms in People With Parkinson's Disease: A Systematic Review and Meta-Analysis." *Biol Res Nurs* **25**(4): 586-605.

- Yau, C. E., E. C. K. Ho, N. Y. Ong, C. J. K. Loh, A. S. Mai and E. K. Tan (2024). "Innovative technology-based interventions in Parkinson's disease: A systematic review and meta-analysis." Ann Clin Transl Neurol **11**(10): 2548-2562.
- Yin, J., Y. Liu, W. Lyu and Y. Fan (2023). "Tai Ji on Cognitive Function Improvement in Parkinson's Disease: A Meta- Analysis." J Integr Neurosci **22**(5): 123.
- Ying, Y., R. Sun, C. Hu, Y. Wang and L. Zhou (2024). "Effectiveness of exercise on sleep quality in patients with Parkinson's disease: a Meta-analysis 运动锻炼对帕金森病患者睡眠质量影响的Meta分析." Chinese Journal of Nursing (4): ID is 04.015.
- Yitayeh, A. and A. Teshome (2016). "The effectiveness of physiotherapy treatment on balance dysfunction and postural instability in persons with Parkinson's disease: a systematic review and meta-analysis." BMC Sports Sci Med Rehabil **8**: 17.
- Yogev, G., N. Giladi, C. Peretz, S. Springer, E. S. Simon and J. M. Hausdorff (2005). "Dual tasking, gait rhythmicity, and Parkinson's disease: which aspects of gait are attention demanding?" Eur J Neurosci **22**(5): 1248-1256.
- Yogev, G., M. Plotnik, C. Peretz, N. Giladi and J. M. Hausdorff (2007). "Gait asymmetry in patients with Parkinson's disease and elderly fallers: when does the bilateral coordination of gait require attention?" Exp Brain Res **177**(3): 336-346.
- Yogev-Seligmann, G., N. Giladi, L. Gruendlinger and J. M. Hausdorff (2013). "The contribution of postural control and bilateral coordination to the impact of dual tasking on gait." Exp Brain Res **226**(1): 81-93.
- Yogev-Seligmann, G., J. M. Hausdorff and N. Giladi (2008). "The role of executive function and attention in gait." Mov Disord **23**(3): 329-342; quiz 472.
- Yogev-Seligmann, G., Y. Rotem-Galili, R. Dickstein, N. Giladi and J. M. Hausdorff (2012). "Effects of explicit prioritization on dual task walking in patients with Parkinson's disease." Gait Posture **35**(4): 641-646.
- Yu, J., J. Wu, J. Lu, X. Wei, K. Zheng, B. Liu, W. Xiao, Q. Shi, L. Xiong and Z. Ren (2023). "Efficacy of virtual reality training on motor performance, activity of daily living, and quality of life in patients with Parkinson's disease: an umbrella review comprising meta-analyses of randomized controlled trials." J Neuroeng Rehabil **20**(1): 133.
- Yu, X., X. Wu, G. Hou, P. Han, L. Jiang and Q. Guo (2021). "The Impact of Tai Chi on Motor Function, Balance, and Quality of Life in Parkinson's Disease: A Systematic Review and Meta-Analysis." Evid Based Complement Alternat Med **2021**: 6637612.
- Yuan, Y., J. Wang, G. Wang, T. Wang, H. Zhang, X. Fu, L. Wu, X. Chen, R. Xia, L. Zhang, S. C. Lin and Y. Yang (2024). "Optimal dosage ranges of various exercise types for enhancing timed up and go performance in Parkinson's disease patients: a systematic review and Bayesian network meta-analysis." Front Aging Neurosci **16**: 1399175.
- Zanatta, F., N. Z. Farhane-Medina, R. Adorni, P. Steca, A. Giardini, M. D'Addario and A. Pierobon (2023). "Combining robot-assisted therapy with virtual reality or using it alone? A systematic review on health-related quality of life in neurological patients." Health Qual Life Outcomes **21**(1): 18.
- Zanuso, S., M. Bergamin, A. Jimenez, G. Pugliese, V. D'Errico, A. Nicolucci, A. Ermolao and S. Balducci (2016). "Determination of metabolic equivalents during low- and high-intensity resistance exercise in healthy young subjects and patients with type 2 diabetes." Biol Sport **33**(1): 77-82.
- Zhang, J., Y. Luximon, M. Y. C. Pang and H. Wang (2022). "Effectiveness of exergaming-based interventions for mobility and balance performance in older adults with Parkinson's disease: systematic review and meta-analysis of randomised controlled trials." Age Ageing **51**(8).
- Zhang, M., F. Li, D. Wang, X. Ba and Z. Liu (2023). "Exercise sustains motor function in Parkinson's disease: Evidence from 109 randomized controlled trials on over 4,600 patients." Front Aging Neurosci **15**: 1071803.
- Zhang, Q., J. Hu, L. Wei, Y. Jia and Y. Jin (2019). "Effects of dance therapy on cognitive and mood symptoms in people with Parkinson's disease: A systematic review and meta-analysis." Complement Ther Clin Pract **36**: 12-17.

Zhang, S., D. Liu, D. Ye, H. Li and F. Chen (2017). "Can music-based movement therapy improve motor dysfunction in patients with Parkinson's disease? Systematic review and meta-analysis." Neurol Sci **38**(9): 1629-1636.

Zhang, S. K., M. L. Gu, H. Xu, W. S. Zhou, S. J. Mao and Y. Yang (2023). "Effects of Different Exercise Modes on Gait Performance of Parkinson's Disease Patients: A Systematic Review and Network Meta-Analysis." Percept Mot Skills **130**(4): 1524-1561.

Zhang, Y., S. Liu, K. Xu, Y. Zhou, Y. Shen, Z. Liu, Y. Bai and S. Wang (2024). "Non-pharmacological therapies for treating non-motor symptoms in patients with Parkinson's disease: a systematic review and meta-analysis." Front Aging Neurosci **16**: 1363115.

Zhao, H., L. Zhang, J. Yang, W. Guo, C. Sun, R. Shi and Z. Wang (2024). "Parkinson's disease motor intervention patterns: a network meta-analysis based on patient motor function." Front Neurol **15**: 1432256.

Zhao, Y. G., W. Lv, H. Q. Huo, J. R. Wu, W. W. Cheng and S. Wang (2023). "Meta-analysis of the effect of whole-body vibration training on the improvement of limb function in patients with Parkinson's disease." Eur Rev Med Pharmacol Sci **27**(15): 6985-6995.

Zhen, K., S. Zhang, X. Tao, G. Li, Y. Lv and L. Yu (2022). "A systematic review and meta-analysis on effects of aerobic exercise in people with Parkinson's disease." NPJ Parkinsons Dis **8**(1): 146.

Zhou, B., Z. Wang, L. Zhu, G. Huang, B. Li, C. Chen, J. Huang, F. Ma and T. C. Liu (2022). "Effects of different physical activities on brain-derived neurotrophic factor: A systematic review and bayesian network meta-analysis." Front Aging Neurosci **14**: 981002.

Zhou, J., T. Yin, Q. Gao and X. C. Yang (2015). "A Meta-Analysis on the Efficacy of Tai Chi in Patients with Parkinson's Disease between 2008 and 2014." Evid Based Complement Alternat Med **2015**: 593263.

Zhou, X., P. Zhao, X. Guo, J. Wang and R. Wang (2022). "Effectiveness of aerobic and resistance training on the motor symptoms in Parkinson's disease: Systematic review and network meta-analysis." Front Aging Neurosci **14**: 935176.

Zhou, Z., R. Zhou, W. Wei, R. Luan and K. Li (2021). "Effects of music-based movement therapy on motor function, balance, gait, mental health, and quality of life for patients with Parkinson's disease: A systematic review and meta-analysis." Clin Rehabil **35**(7): 937-951.

Zhu, P. A., Q. Q. Lu, Z. L. Li, R. L. Hu, S. Xu, L. Brodersen, Y. X. Liu, H. Liu and X. Bao (2023). "Efficacy of Tai Chi on lower limb function of Parkinson's disease patients: A systematic review and meta-analysis." Front Aging Neurosci **15**: 1096417.

Zirek, E., B. Ersoz Huseyinsinoglu, Z. Tufekcioglu, B. Bilgic and H. Hanagasi (2018). "Which cognitive dual-task walking causes most interference on the Timed Up and Go test in Parkinson's disease: a controlled study." Neurol Sci **39**(12): 2151-2157.

Zoladz, J. A., J. Majerczak, E. Zeligowska, J. Mencil, A. Jaskolski, A. Jaskolska and J. Marusiak (2014). "Moderate-intensity interval training increases serum brain-derived neurotrophic factor level and decreases inflammation in Parkinson's disease patients." J Physiol Pharmacol **65**(3): 441-448.

Zotaj, A., R. Millosi, S. Sokoli and H. Doci (2024). "Effectiveness of physiotherapy rehabilitation approaches for Parkinson's disease: A Durres case study." Physiother Res Int **29**(4): e2124.

Zuccato, C. and E. Cattaneo (2009). "Brain-derived neurotrophic factor in neurodegenerative diseases." Nat Rev Neurol **5**(6): 311-322.

Álvarez, I., J. Latorre, M. Aguilar, P. Pastor and R. Llorens (2020). "Validity and sensitivity of instrumented postural and gait assessment using low-cost devices in Parkinson's disease." J Neuroeng Rehabil **17**(1): 149.

Appendix

PAPER 1

Supplementary File 1. Search strategies

Pubmed

Search: ((Parkinson*[Title/Abstract] OR PD[Title/Abstract]) AND (exercise[Title/Abstract] OR "physical activity"[Title/Abstract] OR training[Title/Abstract] OR sport*[Title/Abstract] OR rehabilit*[Title/Abstract] OR "physical therapy"[Title/Abstract] OR physiotherapy[Title/Abstract]) AND (BDNF[Title/Abstract] OR plastic*[Title/Abstract] OR synap*[Title/Abstract] OR neuro*[Title/Abstract] OR cognit*[Title/Abstract] OR biomarker*[Title/Abstract])) NOT ((rat[Title] OR animal[Title] OR mouse[Title] OR mice[Title]) NOT review[Title]) Filters: from 2003/1/1 - 2022/12/31 Sort by: Most Recent

Scopus

(TITLE ((parkinson* OR pd) AND (exercise OR "physical activity" OR training OR sport* OR rehabilit* OR "physical therapy" OR physiotherapy) AND (bdnf OR plastic* OR synap* OR neuro* OR cognit* OR biomarker*)) OR ABS ((parkinson* OR pd) AND (exercise OR "physical activity" OR training OR sport* OR rehabilit* OR "physical therapy" OR physiotherapy) AND (bdnf OR plastic* OR synap* OR neuro* OR cognit* OR biomarker*)) AND NOT TITLE ((rat OR animal OR mouse OR mice) not AND review)) AND PUBYEAR > 2002 AND PUBYEAR < 2023

Web of Science

(Parkinson* OR PD) AND (exercise OR "physical activity" OR training OR sport* OR rehabilit* OR "physical therapy" OR physiotherapy) AND (BDNF OR plastic* OR synap* OR neuro* OR cognit* OR biomarker*) (Title) or (Parkinson* OR PD) AND (exercise OR "physical activity" OR training OR sport* OR rehabilit* OR "physical therapy" OR physiotherapy) AND (BDNF OR plastic* OR synap* OR neuro* OR cognit* OR biomarker*) (Abstract) not (rat OR animal OR mouse OR mice) NOT review (Title)

ClinicalTrial.gov

(Parkinson* OR PD) AND (exercise OR "physical activity" OR training OR sport* OR rehabilit* OR "physical therapy" OR physiotherapy) AND (BDNF OR plastic* OR synap* OR neuro* OR cognit* OR biomarker*) in Record Title OR (Parkinson* OR PD) AND (exercise OR "physical activity" OR training OR sport* OR rehabilit* OR "physical therapy" OR physiotherapy) AND (BDNF OR plastic* OR synap* OR neuro* OR cognit* OR biomarker*) in Abstract NOT (rat OR animal OR mouse OR mice) NOT review in Record Title - (Word variations have been searched)

Embase

(Parkinson* OR PD) AND (exercise OR "physical activity" OR training OR sport* OR rehabilit* OR "physical therapy" OR physiotherapy) AND (BDNF OR plastic* OR synap* OR neuro* OR cognit* OR biomarker*) in Record Title OR (Parkinson* OR PD) AND (exercise OR "physical activity" OR training OR sport* OR rehabilit* OR "physical therapy" OR physiotherapy) AND (BDNF OR plastic* OR synap* OR neuro* OR cognit* OR biomarker*) in Abstract NOT (rat OR animal OR mouse OR mice) NOT review in Record Title - (Word variations have been searched)

CINHAL

(Parkinson* OR PD) AND (exercise OR "physical activity" OR training OR sport* OR rehabilit* OR "physical therapy" OR physiotherapy) AND (BDNF OR plastic* OR synap* OR neuro* OR cognit* OR biomarker*) in Record Title OR (Parkinson* OR PD) AND (exercise OR "physical activity" OR training OR sport* OR rehabilit* OR "physical therapy" OR physiotherapy) AND (BDNF OR plastic* OR synap* OR neuro* OR cognit* OR biomarker*) in Abstract NOT (rat OR animal OR mouse OR mice) NOT review in Record Title - (Word variations have been searched)

Supplementary File 2. Measurement of BDNF by study

Author and year	Sample	Unit	Timing of post-exercise BDNF measurement
Angelucci et al. 2016	Serum	pg/mL	At 8:00-9:00 a.m.
Da Silva Germanos et al. 2019	Plasma	pg/ml	Not specified
De Oliveira et al. 2020	Plasma	ng/mg	At 10-11 a.m.
Frazzitta et al. 2014	Serum	ng/mL	At 7:00 am, away from exercise
Freidle et al. 2022	Serum	pg/mL	Within 2-3 weeks after the end of the intervention*
Harro et al. 2022	Serum	ng/mL	On a non-exercise day*
Landers et al. 2019	Plasma	pg/mL	Between 48 and 72 hours from active participation in the trial*
O'Callaghan et al. 2019	Serum	ng/ml	Not specified
Pondé et al. 2019	Serum	pg/mL	Not specified
Sajatovic et al. 2017	Serum	pg/mL	Not specified
Schaeffer et al. 2022	Serum	ng/mL	Away from the exercise*
Segura et al. 2020	Plasma	pg/mL	Not specified
Soke et al. 2021	Serum	pg/ml	At 8-9 am, the day after the end of the intervention
Stuckenschneider et al. 2021	Serum	ng/mL	Not on exercise days*
Szymura et al. 2020	Serum	ng/mL	At 8-10 a.m., 2 days after the completion of the programme
Zoladz et al. 2014	Serum	pg/mL	One week after the end of the training*

*Personal communication from the authors

Supplementary File 3. Studies not included in this review and reason for exclusion

Authors, year	Reason for exclusion
Angelucci et al., 2015 (Angelucci, Peppe et al. 2015)	Not physical training
Angelucci et al., 2015 (Angelucci, Peppe et al. 2015)	Abstract (duplicate)
Azevedo et al., 2022 (Azevedo, Pereira et al. 2022)	Observational study
Bastioli et al., 2022 (Bastioli, Arnold et al. 2022)	Animals
Bekinschtein et al., 2020 (Miranda, Morici et al. 2019)	Review
Biagioni et al., 2018 (Migdadi, Wang et al. 2018)	Abstract
Campos et al., 2016 (Campos, Rocha et al. 2016)	Review
Dias Belchior et al., 2017 (Belchior, Tomaz et al. 2017)	Not BDNF measures
Farshbaf et al., 2016 (Farshbaf, Ghaedi et al. 2016)	Review
Farshbaf et al., 2016 (Farshbaf, Ghaedi et al. 2016)	Review (duplicate)
Ferreira et al., 2018 (Ferreira, de Miranda et al. 2018)	Review
Fontanesi et al., 2016 (Fontanesi, Kvint et al. 2016)	Not BDNF measures
Franzén et al., 2018 (Franzen, Johansson et al. 2018)	Protocol
Franzén et al., 2019 (Franzen, Johansson et al. 2018)	Protocol

Goldberg et al., 2015 (Goldberg, Curtis et al. 2015)	Review
Harper et al., 2019 (Harper, Dowdell et al. 2019)	Not BDNF measures
Harpham et al., 2023 (Harpham, Gunn et al. 2023)	Not BDNF measures
Hirsch et al., 2016 (Hirsch, Iyer et al. 2016)	Review
Hooper et al., 2016 (Hooper, Durham et al. 2016)	Animals
HU et al., 2005 (Hu, Liang et al. 2005)	Not physical training
Karim et al., 2022 (Karim, Iqbal et al. 2022)	Measure of BDNF <12h (5-60 min)
Khalil et al., 2017 (Khalil, Alomari et al. 2017)	Cross-sectional
Marusiak et al., 2015 (Marusiak, Zeligowska et al. 2015)	Not BDNF measures
Mattson et al., 2004 (Mattson, Duan et al. 2004)	Animals
Migdadi et al., 2018 (Migdadi, Wang et al. 2018)	Abstract
Monteiro-Junior et al., 2015 (Monteiro-Junior, Cevada et al. 2015)	Review
Norwitz et al., 2020 (Norwitz, Dearlove et al. 2020)	Not BDNF measures
Pagnussat et al., 2018 (Pagnussat, Kleiner et al. 2018)	Not physical training
Patterson et al., 2022 (Patterson, Joslin et al. 2022)	Protocol

Radak et al., 2007 (Radak, Kumagai et al. 2007)	Review
Rothman et al., 2012 (Rothman, Griffioen et al. 2012)	Review
Szymura et al., 2019 (2019)	Abstract
Tuon et al., 2014 (Tuon, Valvassori et al. 2014)	Animals
van Wegen et al., 2020 (van Wegen, Hirsch et al. 2020)	Protocol
Wang et al., 2022 (Wang, Wu et al. 2022)	Animals
Wu et al., 2011 (Wu, Wang et al. 2011)	Animals
Yang et al., 2014 (Yang, Lin et al. 2014)	Animals

Supplementary File 4. Type, intensity, frequency and duration of exercise components by study arm

Author and year	Study arm*	Activity	Type of activity	MET	Sessions week	Min session
Angelucci et al. 2016	Multimodal	Relaxation, breathing	Others	1.5	5	10
		Flexibility	Others	2.0	5	15
		Mobility	Others	2.3	5	20
		Postural	Others	2.5	5	20
		Treadmill	Aerobic	3.0	5	20
		Stationary bike	Aerobic	3.0	5	20
		Wii Fit Balance Board	Balance	2.3	5	20
		Coordination	Others	2.5	5	25
Da Silva Germanos et al. 2019	Multimodal	Aquatic exercises: stretching, mobility	Others	2.5	2	10
		Aquatic exercises: strengthening, gait, balance, proprioception	Resistance	5.0	2	20
		Aquatic exercises: dual task	Aerobic	3.0	2	20
De Oliveira et al. 2020	Multimodal	Mobility, coordination	Others	2.5	2	8
		Deep water running (endurance)	Aerobic	5.0	2	35
		Coordination	Balance	3.0	2	13
		Stretching, relaxation	Others	2.0	2	8
Frazzitta et al. 2014	Multimodal	Cardiovascular exercises	Aerobic	2.5	5	15
		Stretching, mobility	Others	2.3	5	15

Freidle et al. 2022	Multimodal	Postural	Others	2.5	5	15
		Stabilometric platform with a visual cue	Balance	2.5	5	15
		Treadmill training with both a visual and an auditory cue	Aerobic	2.8	5	30
		Occupational therapy	Others	2.0	5	40
		HiBalance: sensory integration, motor agility, anticipatory postural adjustments and stability limits	Balance	3.0	2	50
		Functional aerobic (home exercises)	Aerobic	3.5	1	20
		Strength exercises (home exercises)	Resistance	3.5	1	20
Harro et al. 2022	Speech and communication	HiCommunication: voice sound level, articulatory precision, word retrieval, memory	Others	1.3	2	50
		Voice, speech function (home exercises)	Others	1.3	1	30
	Endurance	Warm up (nordic walking)	Aerobic	2.5	2	10
Landers et al. 2019	Multimodal (High intensity)	Nordic walking	Aerobic	5.0	2	43
		Cool down (nordic walking)	Aerobic	2.5	2	10
		Treadmill, overground walking on the indoor track, stair climber, bike, recumbent bike, rowing machine	Aerobic	4.5	4	30
		Strengthening the major muscle groups of the trunk and upper/lower extremities	Resistance	4.5	4	30
		Postural, dynamic gait, sensory orientation	Balance	3.0	4	15
		Stretching	Others	2.3	4	15
		Home exercise (same exercises)	Aerobic	4.0	2	18
		Home exercise (same exercises)	Resistance	4.0	2	18
		Home exercise (same exercises)	Balance	3.0	2	9
		Home exercise (same exercises)	Others	2.3	2	9

	Multimodal (Low intensity)	Treadmill, overground walking on the indoor track, stair climber, bike, recumbent bike, rowing machine	Aerobic	2.7	4	15
		Strengthening the major muscle groups of the trunk and upper/lower extremities	Resistance	3.0	4	15
		Step touch task	Balance	2.5	4	10
		Stretching	Others	2.3	4	10
		Home exercise (same exercises)	Aerobic	3.0	2	11
		Home exercise (same exercises)	Resistance	3.0	2	11
		Home exercise (same exercises)	Balance	2.5	2	8
		Home exercise (same exercises)	Others	2.3	2	8
O'Callaghan et al. 2019	Aerobic + Resistance	Warm up	Aerobic	2.5	3	8
		Stretching	Others	2.3	3	2
		12 stations in a circuit	Aerobic	4.0	3	27
		Resistance stations	Resistance	4.0	3	12
		Cool down	Aerobic	2.5	3	8
		Stretching	Others	2.3	3	2
	High-Intensity Interval Training	Warm up	Resistance	3.0	3	10
		Power clean and press, step and press, squat, pull-down to squat, high pull, bent over row	Resistance	7.0	3	20
		Cool down	Resistance	3.0	3	5
Pondé et al. 2019	Aerobic	Treadmill	Aerobic	3.0	2	40
		Motor imagery	Others	1.1	2	14
Sajatovic et al. 2017	Aerobic + Resistance (peer support)	Warm up	Aerobic	2.5	3	5

	Aerobic + Resistance	EXCEED: fast-paced, low-resistance cycling	Aerobic	4.0	3	20
		EXCEED: progressive sequence of resistance bands	Resistance	3.5	3	20
		Cool down	Aerobic	2.5	3	5
		Warm up	Aerobic	2.5	3	5
		SGE: fast-paced, low-resistance cycling	Aerobic	4.0	3	20
		SGE: progressive sequence of resistance bands	Resistance	3.5	3	20
		Cool down	Aerobic	2.5	3	5
		Exergaming	Aerobic	4.0	3	45
Schaeffer et al. 2022	Aerobic					
Segura et al. 2020	Aerobic	Warm up	Aerobic	2.5	3	10
Soke et al. 2021	Aerobic + Resistance	Stationary tandem bicycle	Aerobic	6.0	3	20
		Cool down	Aerobic	2.5	3	5
		Stretching	Others	2.3	3	10
		Warm up	Aerobic	2.5	3	5
		Treadmill	Aerobic	4.5	3	20
	Aerobic	Cool down	Aerobic	2.5	3	5
		Task-oriented training (TOT): circuit with a series of workstations	Resistance	4.0	3	33
		Warm up	Aerobic	2.5	3	5
		Treadmill	Aerobic	4.5	3	20
		Cool down	Aerobic	2.5	3	5
Stuckenschneider et al. 2021	Multimodal	Coordination	Balance	2.5	2	20
		Wall pushups, holding medicine balls with outstretched arms, squats, or crunches	Resistance	4.1	2	20

Szymura et al. 2020	Aerobic	Walking or running exercises	Aerobic	4.1	2	20
		Warm up	Aerobic	2.5	3	5
		Wii Fit Balance Board	Balance	3.3	3	50
Zoladz et al. 2014	Aerobic	Cool down	Aerobic	2.5	3	5
		Warm up	Aerobic	2.5	3	10
		Interval training	Aerobic	3.5	3	40
		Cool down	Aerobic	2.5	3	10

*Definition of exercise intervention according Zhou B et al. in Aging Neurosci 2022 (Zhou, Wang et al. 2022)

Abbreviations: MET, Metabolic Equivalent of Task.

Supplementary File 5. Pre-post exercise BDNF levels of experimental and comparison group in controlled studies only

Author and year	Study arm*	BDNF before the exercise**	BDNF after the exercise**	SMD* **	(95% CI)
Frazzitta et al. 2014	Multimodal	21.6 (3.4)	24.8 (6.4)	0.64	(-0.16 1.45)
	Control	22.9 (4.0)	22.6 (4.3)		
Freidle et al. 2022	Multimodal	38010.8 (7956.7)	37169.4 (5928.3)	0.14	(-0.26 0.54)
	Speech and communication	37805.3 (8044.6)	35945.8 (6208.5)		
Landers et al. 2019	Multimodal (high intensity)	1960.2 (1529.5)	2580.7 (1411.2)	-0.07	(-0.85 0.70)
	Multimodal (low intensity)	960.3 (1482.9)	1697.5 (1368.1)		
O'Callaghan et al. 2019	Aerobic + Resistance	1300.1	1338.0	0.32	(-0.42 1.06)
	Control	1470.3	861.4		
	High-Intensity Interval Training	685.0	783.9		
	Control	699.9	627.9		
Sajatovic et al. 2017	Aerobic + Resistance (peer support)			0.54	(-0.24 1.32)
	Aerobic + Resistance				
Segura et al. 2020	Aerobic	20.6 (120.0)	207.1 (120.0)	1.85	(0.61 3.09)
	Control	260.0 (150.0)	149.6 (150.0)		
Soke et al. 2021	Aerobic + Resistance	1397.0	1507.5	0.03	(-0.68 0.74)
	Aerobic	1487.6	1411.2		

Szymura et al. 2020	Aerobic	21.2 (8.4)	30.4 (6.3)	1.45	(0.64	2.25)
	Control	30.1 (8.0)	25.8 (11.7)			

*Definition of exercise intervention according Zhou B et al. in Aging Neurosci 2022 (Zhou, Wang et al. 2022); **Mean (Standard deviation). For O'Callaghan et al. 2019, Soke et al. 2021 (O'Callaghan, Harvey et al. 2020, Soke, Kocer et al. 2021) the median is reported; ***Standardized Mean Difference (Hedges' g); for the studies by O'Callaghan et al. 2019, Sajatovic et al. 2017, Soke et al. 2021 (Sajatovic, Ridgel et al. 2017, O'Callaghan, Harvey et al. 2020, Soke, Kocer et al. 2021) data was derived from Jiecheng et al. 2023 (Li, Loevaas et al. 2023)

Supplementary File 6. Pre-post exercise BDNF levels separately by study arm in controlled and non-controlled studies

Author and year	Study arm*	BDNF before the exercise**	BDNF after the exercise**	SMD***	(95% CI)	
Angelucci et al. 2016	Multimodal	2188.4 (1718.8)	2356.5 (1666.7)	0.10	(-0.83	1.02)
Da Silva Germanos et al. 2019	Multimodal	493.9	933.3	-		
De Oliveira et al. 2020	Multimodal	0.2 (0.1)	0.4 (0.3)	1.00	(0.02	1.98)
Frazzitta et al. 2014	Multimodal	21.6 (3.4)	24.8 (6.4)	0.61	(-0.15	1.37)
	Control	22.9 (4.0)	22.6 (4.3)	-0.07	(-0.95	0.81)
Freidle et al. 2022	Multimodal	38010.8 (7956.7)	37169.4 (5928.3)	-0.12	(-0.52	0.28)
	Speech and communication	37805.3 (8044.6)	35945.8 (6208.5)	-0.26	(-0.66	0.15)
Harro et al. 2022	Endurance	34.8	32.3	-		
Landers et al. 2019	Multimodal (high intensity)	1960.2 (1529.5)	2580.7 (1411.2)	0.42	(-0.36	1.20)
	Multimodal (low intensity)	960.3 (1482.9)	1697.5 (1368.1)	0.52	(-0.33	1.37)
O'Callaghan et al. 2019	Aerobic + Resistance	1300.1	1338.0	-		
	Control	1470.3	861.4	-		
	High-Intensity Interval Training	685.0	783.9	-		
	Control	699.9	627.9	-		
Pondé et al. 2019	Aerobic	88.8 (111.8)	202.6 (183.4)	0.75	(-0.26	1.76)
Sajatovic et al. 2017	Aerobic + Resistance (peer support)	26.8 (15.6)	90.0 (166.4)	0.53	(-0.25	1.32)

	Aerobic + Resistance	26.8 (15.6)	90.0 (166.4)	0.53	(-0.19	1.26)
Schaeffer et al. 2022	Aerobic	23.9 (7.5)	25.2 (7.3)	0.18	(-0.50	0.85)
Segura et al. 2020	Aerobic	20.6 (120.0)	207.1 (120.0)	1.55	(0.26	2.85)
	Control	260.0 (150.0)	149.6 (150.0)	-0.74	(-1.82	0.35)
Soke et al. 2021	Aerobic + Resistance	1397.0	1507.5	-		
	Aerobic	1487.6	1411.2	-		
Stuckenschneider et al. 2021	Multimodal	33.6 (9.7)	34.3 (11.8)	0.07	(-0.91	1.05)
Szymura et al. 2020	Aerobic	21.2 (8.4)	30.4 (6.3)	1.24	(0.48	1.99)
	Control	30.1 (8.0)	25.8 (11.7)	-0.43	(-1.21	0.35)
Zoladz et al. 2014	Aerobic	10977.0 (2618.9)	14206.0 (4350.9)	0.90	(0.06	1.74)

*Definition of exercise intervention according Zhou B et al. in Aging Neurosci 2022 (Zhou, Wang et al. 2022); **Mean (Standard deviation). For the studies by Da Silva Germanos et al. 2019, Harro et al. 2022, O'Callaghan et al. 2019, Soke et al. 2021 (da Silva Germanos, Vieira et al. 2019, Soke, Kocer et al. 2021, Harro, Shoemaker et al. 2022) the median is reported. ***Standardized Mean Difference (Cohen's d)

Supplementary File 7. Sensitivity analysis

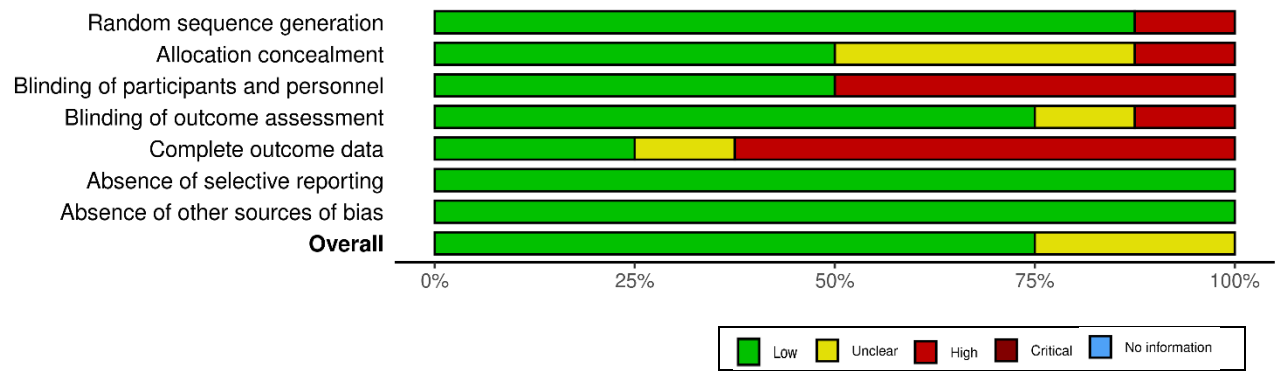
Meta-regression of between-group differences in intensity, volume and type of exercise on changes in BDNF levels (controlled studies only)

	5 studies				9 studies			
	Coefficient	(95% CI)		P value	Coefficient	(95% CI)		P value
Δ Time-weighted average of MET	0.41	(0.02	0.81)	0.042	0.14	(-0.04	0.32)	0.124
Δ Total MET-hours (x100)	-0.26	(-2.23	1.71)	0.797	-0.04	(-0.94	0.87)	0.934
Type								
Identical (Aerobic + Resistance)	Reference				Reference			
Aerobic	1.25	(-0.93	3.43)	0.262	0.58	(-0.64	1.79)	0.350
Balance	0.81	(-1.29	2.91)	0.449	0.45	(-0.80	1.70)	0.476
Resistance					0.00	(-1.31	1.31)	0.999

Linear regression of intensity, volume and type of exercise on change in BDNF (study arms of controlled and non-controlled studies)

	Coefficient	(95% CI)		P value
Time-weighted average of MET	0.26	(0.15	0.38)	0.000
Total MET-hours (x100)	0.52	(-0.02	1.06)	0.059
Type				
Aerobic	1.10	(0.50	1.70)	0.002
Balance	0.93	(0.10	1.77)	0.031
Aerobic + Resistance	0.79	(0.14	1.43)	0.020

Supplementary File 8. Risk of bias assessment using Cochrane risk of bias tool (RoB)

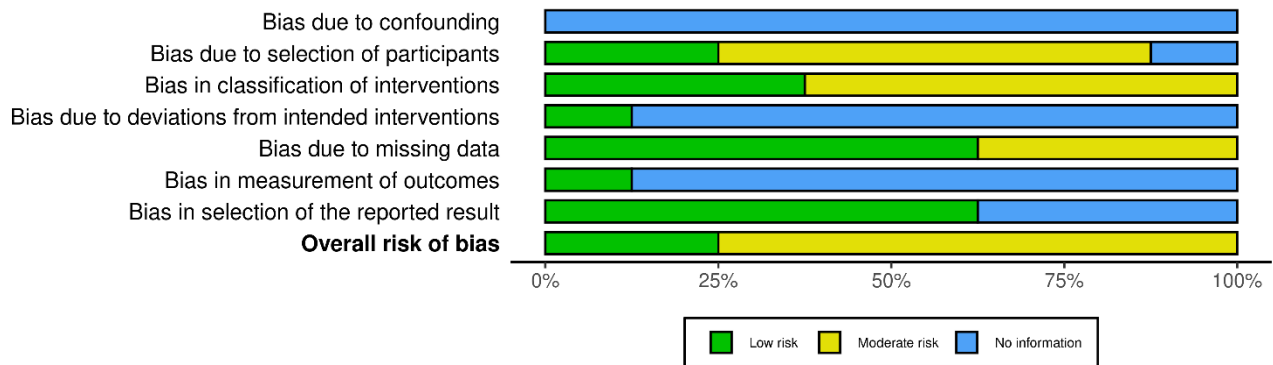


		Risk of bias							
		D1	D2	D3	D4	D5	D6	D7	Overall
Study	Frazzitta et al. 2014	+	+	X	+	X	+	+	+
	Freidle et al. 2022	+	+	+	+	+	+	+	+
	Landers et al. 2019	+	+	+	+	X	+	+	+
	O'Callaghan et al. 2019	+	+	X	+	X	+	+	+
	Sajatovic et al. 2017	+	-	+	+	X	+	+	+
	Segura et al. 2020	X	-	+	+	+	+	+	+
	Soke et al. 2021	+	X	X	X	X	+	+	-
	Szymura et al. 2020	+	-	X	-	-	+	+	-

D1: Random sequence generation
D2: Allocation concealment
D3: Blinding of participants and personnel
D4: Blinding of outcome assessment
D5: Complete outcome data
D6: Absence of selective reporting
D7: Absence of other sources of bias

Judgement
X High
- Unclear
+ Low

Supplementary File 9. Risk Of Bias In Non-randomized Studies-of Interventions (ROBINS-I)



		Risk of bias domains						
		D1	D2	D3	D4	D5	D6	D7
Study	Angelucci et al. 2016	?	?	+	+	+	?	?
	da Silva Germanos et al. 2019	?	+	+	?	+	?	?
	De Oliveira et al. 2020	?	-	-	?	-	+	+
	Harro et al. 2022	?	-	-	?	+	?	+
	Pondé et al. 2019	?	-	-	?	-	?	?
	Schaeffer et al. 2022	?	-	-	?	+	?	+
	Stuckenschneider et al. 2021	?	-	-	?	-	?	+
	Zoladz et al. 2014	?	+	+	?	+	?	+

Domains:
D1: Bias due to confounding.
D2: Bias due to selection of participants.
D3: Bias in classification of interventions.
D4: Bias due to deviations from intended interventions.
D5: Bias due to missing data.
D6: Bias in measurement of outcomes.
D7: Bias in selection of the reported result.

Judgement
- Moderate
+ Low
? No information

PAPER 3

Supplementary File 1. Search strategies

String PubMed [220 results]

(Parkinson Disease[MeSH Terms] OR Parkinson Disease*)

AND (Dual-Task* OR Double-task*)

AND (Gait[MeSH Terms] OR Neurologic Gait Disorder [MeSH Terms] OR Gait Analysis[MeSH Terms] OR Walking[MeSH Terms] OR Walking Speed[MeSH Terms] OR Biomechanical Phenomena[MeSH Terms] OR Locomotion[MeSH Terms] OR Biomechanic* OR Gait OR Walking OR Step OR Kinematic OR Spatiotemporal Parameter OR Walking Speed OR Stride Length OR Stride Frequency OR Cadence OR Step Width OR Double Support Duration OR Single Support Duration OR Swing Time OR Range of Motion OR Joint Angles)

AND (Control Group OR Healthy Control* OR Age-Matched Control*)

NOT (Meta-Analysis[Title/Abstract] OR Systematic Review [Title/Abstract])

String Scopus [821 results]

TITLE-ABS-KEY("Parkinson Disease*")

AND (ALL("Dual-Task*" OR "Double-task*" OR "Cognitive-Motor Interference"))

AND (ALL("Gait" OR "Neurologic Gait Disorder" OR "Walking" OR "Biomechanic*" OR "Locomotion" OR "Step*" OR "Kinematic" OR "Spatiotemporal Parameter" OR "Stride Length" OR "Stride Frequency" OR "Cadence" OR "Step Width" OR "Double Support Duration" OR "Single Support Duration" OR "Swing Time" OR "Range of Motion" OR "Joint Angle"))

AND (ALL("Control Group" OR "Healthy Control*" OR "Age-Matched Control*"))

AND NOT (TITLE-ABS-KEY("Meta-Analysis" OR "Systematic Review"))

String EBSCO [305 results]

((TX "Parkinson Disease" OR (MH "Parkinson Disease")))

AND ((TX "Dual-Task*" OR TX "Double-task*"))

AND ((TX "Gait" OR (MH "Gait")) OR TX "Neurologic Gait Disorder" OR (MH "Gait Disorders, Neurologic") OR (MH "Gait Analysis") OR TX "Walking" OR (MH "Walking") OR (MH "Walking Speed") OR (MH "Biomechanics") OR TX "Locomotion" OR (MH "Locomotion") OR TX "Step" OR

TX "Kinematic" OR TX "Spatiotemporal Parameter" OR TX "Stride Length" OR TX "Stride Frequency" OR TX "Cadence" OR TX "Step Width" OR TX "Double Support Duration" OR TX "Single Support Duration" OR TX "Swing Time" OR TX "Range of Motion" OR TX "Joint Angle"))
 AND ((TX "Control Group" OR TX "Healthy Control*" OR TX "Age-Matched Control*"))
 NOT ((TI "Meta-Analysis" OR AB "Meta-Analysis" OR TI "Systematic Review" OR AB "Systematic Review"))

Cochrane Library [220 results]

(Parkinson Disease OR Parkinson Disease)

AND (Dual-Task OR Double-task)

AND (Gait OR Neurologic Gait Disorder OR Gait Analysis OR Walking OR Walking Speed OR Biomechanical Phenomena OR Locomotion OR Biomechanic OR Gait OR Walking OR Step OR Kinematic OR Spatiotemporal Parameter OR Walking Speed OR Stride Length OR Stride Frequency OR Cadence OR Step Width OR Double Support Duration OR Single Support Duration OR Swing Time OR Range of Motion OR Joint Angles)

AND (Control Group OR Healthy Control OR Age-Matched Control)

NOT (Meta-Analysis OR Systematic Review)

WEB OF SCIENCE (394 results)

(Parkinson Disease[MeSH Terms] OR Parkinson Disease*) AND (Dual-Task* OR Double-task*)
 AND (Gait[MeSH Terms] OR Neurologic Gait Disorder [MeSH Terms] OR Gait Analysis[MeSH Terms] OR Walking[MeSH Terms] OR Walking Speed[MeSH Terms] OR Biomechanical Phenomena[MeSH Terms] OR Locomotion[MeSH Terms] OR Biomechanic* OR Gait OR Walking OR Step OR Kinematic OR Spatiotemporal Parameter OR Walking Speed OR Stride Length OR Stride Frequency OR Cadence OR Step Width OR Double Support Duration OR Single Support Duration OR Swing Time OR Range of Motion OR Joint Angles) AND (Control Group OR Healthy Control* OR Age-Matched Control*) NOT (Meta-Analysis[Title/Abstract] OR Systematic Review [Title/Abstract])

Table 1. Participant and Clinical Characteristics

Study	Type of study	Number of participants	Mean Age (years)	Height (m)	Mass (kg)	Sex (m/f; n)	Global cognition: MMSE (/30) or MoCA	H&Y disease stage	Motor phenotype (n)	Disease duration (years)	UPDRS motor score
Alcock et al. 2016 (Alcock, Galna et al. 2016)	Observational, cross-sectional	PD: 76, HC: 81	PD: 67.5 ± 10.0, HC: 69.7 ± 7.5	PD: 1.70 ± 0.1, HC: 1.69 ± 0.1	PD: 78.2 ± 15.1, HC: 76.0 ± 14.2	PD: 50M/26F, HC: 39M/42F	PD: 28.6 ± 1.3, HC: 29.2 ± 1.1	PD: Stage I (n=18), II (n=45), III (n=13)	PIGD n = 20, ID n = 2, TD n = 18	PD: 0.56 ± 0.42 (6.7 ± 5.0 months)	Not reported
Álvarez et al. 2020 (Álvarez, Latorre et al. 2020)	Observational, cross-sectional	PD: 54, HC: 43	PD: 68.7 ± 10.2, HC: 67.8 ± [Not reported]	PD = 1.62–1.70; HC = Not reported	PD = 72.1–79.3; HC = Not reported	PD = 30M/24F; HC = 18M/25F	PD = 24.5–27.2; HC = Not reported	I–II.5	TD n = 27; AR n = 10; MX n = 17	3.8–8.9	Not reported
Baker et al. 2008 (Baker, Rochester et al. 2008)	Experimental, within-subjects, repeated-measures	PD: 14, HC: 12	PD: 69.3 ± 3.4, HC: 71.5 ± 2.6	PD: 1.66 ± 0.11, HC: 1.65 ± 0.08	Not reported	PD: 5M/9F, HC: 5M/7F	PD: 27.71 ± 2.16, HC: 28.58 ± 1.83	PD: Median H&Y = 3 (range: 2–3)	Freezers: 9, Non-freezers: 5	PD: 6.64 ± 3.25	PD: 22.86 ± 9.26 (ON medication)
Bartmann Wild et al. 2012 (Wild, de Lima et al. 2013)	Observational, cross-sectional	PD: 18, HC: 18	PD: 69.33 ± 2.65, HC: 69.44 ± 1.41	Not reported	Not reported	PD: 8M/10F, HC: 8M/10F	PD: 26.39 ± 0.46, HC: 27.06 ± 0.31	1.97 ± 0.36 (Stage I-II)	Not specified	8.39 ± 2.85	16.22 ± 7.88 (Part III)
Brown et al. 2009 (Brown,	Experimental, counterbalance	PD: 10, HC: 10	PD: 66.6 ± 6.5,	Not reported	Not reported	PD: 5M/5F, HC: 2M/8F	PD: ≥26; HC: Not reported	PD: Stage II-III (mild	Not specified	PD: 1-13 years (mean not reported)	PD: 24-30 (on medication)

de Bruin et al. 2009)	d repeated-measures		HC: 65.4 ± 6.3					to moderate)			
Corradini et al. 2022 (Corradini, Silveira-Ciola et al. 2022)	Experimental, repeated-measures	PD: 15, HC: 15	PD: 68 ± 5, HC: 65 ± 9	PD: 1.60 ± 0.06, HC: 1.59 ± 0.08	PD: 69.1 ± 10.1, HC: 69.4 ± 15.7	PD: 5M/10F, HC: Matched (exact ratio not specified)	PD: 28.0 ± 2.5, HC: 27.2 ± 1.4	PD: 1.97 ± 0.67 (Stage I-III)	Idiopathic PD (side asymmetry: 10 left-most affected, 5 right-most affected)	PD: 6.0 ± 2.0 (72 ± 24 months)	PD: 24.7 ± 11.8 (on medication)
Dragasevic-Miskovica et al. 2021 (Dragasevic-Miskovic, Bobic et al. 2021)	Observational, Cross-sectional	PD: 30 (14 PD-NonDep, 16 PD-Dep), HC: 15	PD-NonDep: 65.9 ± 7.9, PD-Dep: 63.9 ± 6.9, HC: 62.5 ± 6.9	Not reported	Not reported	Not specified	MMSE ≥26 (exclusion criterion for dementia)	Not reported	Not specified	PD-NonDep: 8.3 ± 7.6, PD-Dep: 9.6 ± 4.2	PD-NonDep: 39.6 ± 15.2, PD-Dep: 43.7 ± 16.6
Ehgoetz Martens et al. 2018 (Ehgoetz Martens, Silveira et al. 2018)	Observational, Cross-sectional,	HA-PD: 21, LA-PD: 22, HC: 18	HA-PD: 71.8 ± 8.4, LA-PD: 67.5 ± 8.4, HC: 70 ± 8.7	Not reported	Not reported	Not specified	MoCA: HA-PD: 23.7 ± 4.1, LA-PD: 25.7 ± 4.2, HC: 26.1 ± 3.5	HA-PD: 2.2 ± 0.51, LA-PD: 2.0 ± 0.38	Not specified	Not reported	HA-PD: 26.9 ± 7.7, LA-PD: 22.8 ± 7.9
Fernandez-Lago et al. 2015 (Fernandez-Lago, Bello et al. 2015)	Observational, cross-sectional	PD: 19, HC: 19	PD: 59.68 ± 12.81, HC: 59.53 ± 12.10	PD: 1.65 ± 0.072, HC: 1.65 ± 0.08	PD: 79.91 ± 14.66, HC: 73.63 ± 8.6	PD: 11M/8F, HC: 11M/8F	PD: 29.38 ± 1.02, HC: 29.52 ± 0.89	PD: Stage 1 (n=4), 1.5 (n=3), 2 (n=6), 2.5 (n=6)	Idiopathic PD (n=19)	5.08 ± 3.83	PD: 21.06 ± 10.69
Galletly and Brauer 2005	Observational, cross-sectional	PD: 16, HC: 16	PD: 65 ± 9.5, HC: 65 ± 9.6	PD: 1.70, HC: 1.73	Not reported	PD: 9M/7F, HC: 9M/7F	PD: 28 ± 3, HC: 30 ± 1	Not reported	Idiopathic PD (n=16)	9.1 ± 4.5	PD: 14.4 ± 6.1 (UPDRS-III)

(Galletly and Brauer 2005)											
Galna et al. 2012 (Galna, Lord et al. 2012)	Observational, cross-sectional	PD: 21, HC: 12	PD: 67.6 ± 9.9, HC: 67.4 ± 8.7	Not reported	Not reported	PD: 14M/7F, HC: 5M/7F	PD: 24.8 ± 4.9, HC: 26.8 ± 2.8	PD: Stage I (1), II (13), III (7)	Not specified	PD: 46.3 ± 50.9 months (~3.9 years)	PD: 31.8 ± 9.7 (ON state)
Graham et al. 2023 (Graham, Armitage et al. 2023)	Cross-sectional interventional	PD: 43 (22 with FOG, 21 without FOG), HC: 17	PD: 68.9 ± 6.6, HC: 69.2 ± 8.0	PD: 1.73 ± 0.11, HC: 1.70 ± 0.10	PD: 81.9 ± 18.6, HC: 75.2 ± 13.5	PD: 27M/16F, HC: 9M/8F	PD: 27.3 ± 2.5, HC: 27.7 ± 1.7	PD: Stage II (39), III (4); FOG subgroup had higher H&Y scores	Freezers (FOG) vs. non-freezers (non-FOG) based on self-report	PD: 7.8 ± 5.7; FOG subgroup had longer duration	PD: 31.9 ± 14.3; FOG subgroup had higher scores
Ivaniski-Mello et al. 2023 (Ivaniski-Mello, Müller et al. 2023)	Observational, cross-sectional	PD: 24, HC: 24	PD: 67 ± 11, HC: 68 ± 9	PD: 1.62 ± 0.10, HC: 1.65 ± 0.11	PD: 70.9 ± 12, HC: 83.4 ± 19.5	PD: 13M/11F, HC: 13M/11F	PD: 27.1 ± 2.5, HC: 27.8 ± 2.2 (MMSE)	PD: H&Y 2.1 ± 1.0 (range II–IV)	Not specified	Not reported	UPDRS-III: 23.5 ± 11.9
Karan Veer and Pahuja 2022 (Veer and Pahuja 2022)	Observational, cross-sectional	PD: 25, HC: 14	PD: M = 70.94, F = 68.71	PD: M = 1.74, F = 1.60	PD: M = 80.16, F = 62.95	PD: 18M/7F	Not reported	2 (n=14), 2.5 (n=6), 3 (n=5)	Not reported	Not explicitly given	UPDRS: M = 36.16, F = 31.14
Koçer et al. 2023 (Kocer, Gulsen et al. 2023)	Observational, cross-sectional	PD: 31, HC: 31	PD: 66.03 ± 7.39	Not reported	BMI: 27.96 ± 5.22	PD: 21M/10F	MMSE: 28.06 ± 1.69	1 (n=7), 2 (n=16), 3 (n=8)	Not reported	9.58 ± 7.28	18.42 ± 12.25

Krupička et al. 2024 (Krupička, Malá et al. 2024)	Observational, cross-sectional	PD: 64, HC: 47	PD: 58.2 ± 12.3, HC: 60.4 ± 9.2	Not reported	BMI: 27.96 ± 5.22 (implied)	PD: 34M/30F	MoCA: 26.5 ± 1.75 (range 24–30)	Not reported	Not reported	1.7 ± 1.3 (range 0.1–5.3)	28.0 ± 12.6 (range 6–70)
LaPointe et al. 2010 (LaPointe, Stierwalt et al. 2010)	Observational, cross-sectional	PD: 25, HC: 13	PD: 67.44, HC: 68.07	Not reported	Not reported	PD: 19M/6F, HC: Not specified (matched to PD)	PD: DRS-2 score 136.27 ± 7.45, HC: 136.94 ± 5.72	PD: H&Y II (18), III (4), IV (3)	Not specified	Not reported	Not reported
Lin et al. 2023 (Lin, Lin et al. 2023)	Observational, case-control	PD: 16, HC: 16 (15 analyzed)	PD: 63.13 ± 5.75, HC: 60.93 ± 2.87	PD: 1.64 ± 0.08, HC: 1.64 ± 0.08	PD: 64.34 ± 9.86, HC: 66.23 ± 10.85	PD: 11M/5F, HC: 11M/4F	PD: 27.81 ± 1.28, HC: 27.80 ± 1.42	1–3 (mild to moderate)	PIGD (16)	5.25 (average)	Not reported
Lohnes et al. 2011 (Lohnes and Earhart 2011)	Observational, case-control	PD: 11, HC: 11 Age-matched	PD: 70.27 ± 6.80, HC-age: 70.82 ± 10.44	Not reported	Not reported	PD: 4M/7F, HC-age: 4M/7F	Not reported	PD: 2 = 7, 2.5 = 3, 3 = 1	Not specified	9.09 ± 5.39	21.55 ± 6.71
Mak 2013b (Mak 2013)	Observational, cross-sectional	PD: 13, HC: 15	PD: 63.9 ± 7.2, HC: 61.8 ± 6.0	PD: 1.58 ± 0.08, HC: 1.59 ± 0.07	PD: 57.7 ± 7.6, HC: 63.0 ± 7.3	PD: 7F/6M, HC: 8F/7M	PD: MMSE ≥ 23, HC: Not reported	2.4 ± 0.4	Not specified	8.0 ± 5.3	22.8 ± 6.1
Mak et al. 2013a (Mak, Yu et al. 2013)	Observational, cross-sectional	PD: 15, HC: 13	PD: 63.0 ± 4.9, HC: 60.0 ± 7.1	PD: 1.58 ± 0.07, HC: 1.57 ± 0.07	PD: 58.5 ± 11.3, HC: 56.8 ± 8.0	PD: 8M/7F, HC: 4M/9F	PD: 27.5 ± 1.7, HC: 28.4 ± 1.2	2.1 ± 0.4	Freezers (13)	7.7 ± 4.3	14.7 ± 3.8
Micó-Amigo et al. 2019a (Micó-Amigo,	Observational, longitudinal cohort	Early-stage PD: 22, Middle-stage PD: 27, HC: 25	Early-PD: 61.2, Mid-PD: 65.3, HC: 63.6	Overall means: ~1.73 m	Overall means: ~78.5 kg (PD groups)	Early-PD: 13M/9F, Mid-PD: 17M/10F, HC: 15M/10F	Early-PD: 28.3, Mid-PD: 28.4, HC: 28.9	Early-PD: 1.7, Mid-PD: 2.4	PIGD: 7 (Early-PD), 15 (Mid-PD), Tremor dominant: 12	Early-PD: 1.2 (since diagnosis), 2.0 (since symptoms),	Early-PD: 21.5, Mid-PD: 35.8, HC: 1

Kingma et al. 2019)					and 76.0 kg (HC)				(Early-PD), 12 (Mid-PD)	Mid-PD: 7.1 (since diagnosis), 8.0 (since symptoms)	
Nardello et al. 2020a (Nardello, Bertoli et al. 2020)	Observational, cross-sectional	PD: 9, HC: 9	PD: 68.2 ± 5.95, HC: 67.2 ± 3.45	PD: 1.70 ± 0.10, HC: 1.68 ± 0.08	PD: 74.2 ± 11.8, HC: 72.6 ± 13.1	PD: 6M/3F, HC: 5M/4F	PD: 27.2 ± 1.85, HC: 28.1 ± 1.66	PD: Ranged from 1 to 3 (mild to moderate)	Not specified	PD: Ranged from 1 to 9 years (mean not provided)	PD: Ranged from 23 to 37 (individual scores in Table 1)
Nardello et al. 2020b (Nardello, Bombieri et al. 2020)	Observational case-control	PD: 10, HC: 10	PD: 66.9 ± 7.00, HC: 66.9 ± 3.21	PD: 1.69 ± 0.10, HC: 1.67 ± 0.09	PD: 74.7 ± 11.2, HC: 71.4 ± 12.9	PD: 6M/4F, HC: 5M/5F	PD: 26.8 ± 2.30, HC: 28.1 ± 1.66	1.10 ± 0.88	Not specified	4.80 ± 2.57	22.1 ± 0.40
O'Shea et al. 2002 (O'Shea, Morris et al. 2002)	Observational, case-control	PD: 15, HC: 15	PD: 68.33 ± 6.59, HC: 67.73 ± 6.97	Not reported (matched for height)	Not reported	PD: 12M/3F, HC: Matched	STMS: >20/38 (PD and HC)	Not specified	Gait hypokinesia (PD)	Not reported	Modified Webster Scale ≤20/36
Ohara et al. 2023 (Ohara, Hirata et al. 2023)	Observational, prospective cohort	PD: 19, HC: 21	PD: 67.9 ± 8.7, HC: 65.6 ± 8.5	Not reported	Not reported	PD: 10M/9F, HC: 9M/12F	PD: 23.7 ± 3.1, HC: 26.3 ± 2.5 (MoCA-J)	1.8 ± 1.2 (PD)	Right-side dominant: 11, Left-side dominant: 8	1.9 ± 1.4	MDS-UPDRS-III: 29.4 ± 10.8 (baseline), 15.8 ± 8.6 (6 months)
Orcioli-Silva et al. 2020 (Orcioli-Silva, Vitória et al. 2020)	Observational, case-control	PD: 20, HC: 30	PD: 69.8 ± 5.9, HC: 68.0 ± 5.6	PD: 1.66 ± 0.10, HC: 1.63 ± 0.09	PD: 74.5 ± 11.0, HC: 76.7 ± 13.9	PD: 15M/5F, HC: 15M/15F	PD: 26.9 ± 1.8, HC: 27.7 ± 1.6 (MMSE)	(H&Y 1/1.5/2/2.5), On: 3/11/6/0	Right-side affected: 8, Left-side affected: 12	5.6 ± 3.1	MDS-UPDRS-III: 27.7 ± 11.4 (On)
Pieruccini-Faria et al. 2014	Observational, cross-sectional	PD: 18, HC: 15	PD: 71.5 ± 7, HC: 69.5 ± 6	PD: 1.74 ± 0.04,	Not reported	PD: 4F; HC: 9F	3MS: PD: 98.1 ± 3, HC: 97.6 ± 2	PD: H&Y 1.5 (n=3), 2 (n=7),	Not specified	Not reported	PD: 25.0 ± 6, HC: Not applicable

(Pieruccini-Faria, Ehgoetz Martens et al. 2014)				HC: 1.71 ± 0.05				2.5 (n=3), 3 (n=5)				
Plotnik et al. 2009 (Plotnik, Giladi et al. 2009)	Observational, cross-sectional	PD: 21, HC: 13	PD: 71.9 ± 7.3, HC: 68.4 ± 4	Not reported	Not reported	PD: 15M/6F, HC: 6M/7F	MMSE: Not explicitly reported	Not specified (excluded freezing of gait)	Not specified	Not reported	Not reported	Not reported
Ranchet et al. 2020 (Ranchet, Hoang et al. 2020)	Observational, cross-sectional	PD: 18, HC: 18	PD: Not explicitly reported, HC: Matched	Not reported	Not reported	PD: Not specified, HC: Matched	MoCA: Excluded if ≤15 (PD group)	PD: H&Y 1 (n=3), 2 (n=13), 3 (n=2)	Subtypes: PIGD (n=3), Tremor (n=8), Rigidity (n=7)	Not reported	Not explicitly reported	Not explicitly reported
Rochester et al. 2005 (Rochester, Hetherington et al. 2005)	Experimental, repeated-measures	PD: 20, HC: 10	PD: 64.6 ± 7.96, HC: 63.5 ± 7.03	PD: 1.68 ± 0.095, HC: 1.72 ± 0.09	PD: 69.70 ± 8.20, HC: 71.96 ± 16.81	PD: 12M/8F, HC: 6M/4F	PD: 27.15 ± 1.98, HC: 28.90 (all ≥26, no dementia)	Median: 2.5 (range: 1.5–4)	Not specified	10.0 ± 1.6	Not reported	Not reported
Rochester et al. 2014 (Rochester, Galna et al. 2014)	Experimental	PD: 121, HC: 189	PD: 67.0 ± 10.4, HC: 69.4 ± 7.7	Not reported	Not reported	PD: 81M/40F, HC: 78M/106F	PD: 28.6 ± 1.3, HC: 29.2 ± 1.0 (all ≥24, no dementia)	HY I: 28; HY II: 72; HY III: 21 (median severity: mild to moderate)	Not specified	Early PD (within 4 months of diagnosis)	MDS-UPDRS III: 25.5 ± 10.4	

Salazar et al. 2017 (Salazar, Ren et al. 2017)	Experimental	PD: 19, HC: 13	PD: 66.3 ± 5.6, HC: 63.2 ± 4.5	Not reported	Not reported	PD: 11M/8F, HC: 5M/8F	Not explicitly reported (excluded dementia; mild- moderate PD cohort)	Median: 2 (range: 1–3; mild- moderate PD)	Not specified	4.9 ± 4.2	20.6 ± 10.1
San Martín Valenzuela et al. 2020 (San Martín Valenzuela, Duenas Moscardo et al. 2020) Souza	Observational, cross-sectional	PD: 40, HC: 43	PD: 66.72 ± 7.5, HC: 66.60 ± 8.75	PD: 1.61 ± 0.07, HC: 1.58 ± 0.08	PD: 70.45 ± 12.13, HC: 68.43 ± 12.15	PD: 17M/23F, HC: 15M/28F	MMSE > 25 (adapted for PD)	PD: I (n=4), II (n=9), III (n=27)	Not specified	5.78 ± 4.67	Not reported
Speciali et al. 2013 (Speciali, de Oliveira et al. 2013) Souza	Observational, cross-sectional	PD: 14, HC: 9	PD: 67.5 ± 5.6, HC: 65.1 ± 5.1	PD: ~1.63, HC: ~1.65	PD: ~68.1, HC: ~68.1	PD: 7M/7F, HC: 4M/5F	PD: ~27.1, HC: ~28.1 (MMSE)	PD: 2-3 (H&Y)	Not specified	Not specified	Not specified
Speciali et al. 2014 (Speciali, Oliveira et al. 2014)	Observational, cross-sectional	PD: 14, HC: 9	PD: 67.5 ± 5.6, HC: 65.1 ± 5.3	PD: ~1.66, HC: ~1.64	PD: 68.5 ± 15.2, HC: 68.1 ± 10.5	PD: 7M/7F, HC: 4M/5F	PD: 27.6 ± 1.9, HC: 28.1 ± 2.1 (MMSE)	PD: 2 (n=4), 2.5 (n=8), 3 (n=2)	Not specified	Not specified	Not specified
Stuart et al. 2017 (Stuart, Galna et al. 2017)	Observational, cross-sectional	PD: 60, HC: 40	PD: 67.9 ± 7.8, HC: 66.9 ± 10.9	Not reported	PD: 82.6 ± 19.8, HC: 72.3 ± 12.6	PD: 37M/19F, HC: 17M/23F	PD: 26.7 ± 2.2 (MoCA), HC: 28.5 ± 1.3 (MoCA)	PD: H&Y 1 (n=21), 2 (n=30), 3 (n=5)	Not specified	Median: 5 years (range: 0.3–37)	UPDRS-III: 36.8 ± 14.1

Stuart et al. 2018 (Stuart, Lord et al. 2018)	Observational, cross-sectional	PD: 55, HC: 32	PD: 67.93 ± 7.86, HC: 67.03 ± 10.80	PD: 1.71 ± 0.09, HC: 1.68 ± 0.10	PD: 82.98 ± 10.78, HC: 73.98 ± 12.70	PD: 36M/19F, HC: 15M/17F	PD: 26.71 ± 2.18, HC: 28.41 ± 1.24	PD: Stage I (20), II (30), III (5)	Not specified	Median: 5 years (IQR: 2– 7.5)	36.80 ± 14.22
Toda et al. 2019 (Toda, Iijima et al. 2019)	Observational, cross-sectional	PD: 64, HC: 20	PD: 67.9 ± 8.6, HC: 71.0 ± 7.1	PD: 1.62 ± 0.08, HC: 1.60 ± 0.09	PD: 58.5 ± 10.2, HC: 59.3 ± 12.8	PD: 37M/27F, HC: 11M/9F	PD: 28.9 ± 1.4 (range 24– 30), HC: Not specified	PD: Stage I (10), II (44), III (10)	Not specified (excluded vascular parkinsonism)	6.5 ± 4.2 (range 1–20)	11.1 ± 8.1 (range 0– 49)
Tseng et al. 2012 (Tseng, Jeng et al. 2012)	Observational, cross-sectional	PD: 22, HC: 42	PD: 70.5 ± 8.8, HC: 69.6 ± 8.5	Not reported	PD: BMI 23.0 ± 4.3, HC: BMI 24.2 ± 2.6	PD: 11M/11F, HC: 22M/20F	PD: 26.8 ± 3.1, HC: 29.5 ± 0.6	PD: Stage I (50%), II (50%)	Not specified (excluded atypical parkinsonism)	5.1 ± 4.9	Not reported
Yogev et al. 2005 (Yogev, Giladi et al. 2005)	Observational, cross-sectional	PD: 30, HC: 28	PD: 70.9 ± 7.9, HC: 69.8 ± 6.3	PD: 1.68 ± 0.11, HC: 1.69 ± 0.07	PD: 73.9 ± 16.0, HC: 72.7 ± 12.5	PD: Not specified, HC: Not specified	PD: 28.1 ± 1.6, HC: 29.1 ± 1.1	PD: 2.3 ± 0.4 (Stage II-III)	Not specified	Not reported	PD: 17.5 ± 8.3 (UPDRS-III)
Yogev et al. 2007 (Yogev, Plotnik et al. 2007)	Observational, cross-sectional	PD: 21, Fallers: 15, HC: 11	PD: 71.9 ± 7.3, Fallers: 76.3 ± 4.9, HC: 67.5 ± 3.5	Not reported	Not reported	PD: 81% male, Fallers: 47% male, HC: 55% male	PD: 28.3 ± 1.3, Fallers: 28.3 ± 1.4, HC: 29.5 ± 0.7	PD: H&Y 2- 3	Not specified	Not specified	PD: 20.4 ± 7.9, Fallers: 2.9 ± 1.9, HC: 0.2 ± 0.6
Yogev- Seligmann et al. 2012 (Yogev- Seligmann, Rotem-Galili et al. 2012)	Observational, cross-sectional (comparative)	PD: 20, HC: 20	PD: 70.3 ± 6.6, HC: 70.9 ± 7.0	PD: 1.68 ± 0.1, HC: 1.67 ± 0.1	PD: 69.9 ± 13.9, HC: 67.7 ± 10.6	PD: 40% female, HC: 50% female	PD: 26.4 ± 2.8, HC: 26.4 ± 1.9	PD: 2.3 ± 0.5	Not specified	PD: 7.4 ± 4.6	PD: 20.7 ± 8.9, HC: 1.7 ± 2.4

Yogev-Seligmann et al. 2013 (Yogev-Seligmann, Giladi et al. 2013)	Observational, cross-sectional (comparative)	PD: 18, HC: 15	PD: 68.7 ± 4.7, HC: 75.4 ± 5.4	PD: 1.7 ± 0.1, HC: 1.6 ± 0.1	PD: 74.5 ± 10.6, HC: 67.7 ± 8.9	PD: 11% female, HC: 60% female	PD: 25.6 ± 1.7, HC: 27 ± 1.7	PD: 2–3	Not specified	Not specified	PD: 23.3 ± 9.1; Older: 2.9 ± 3.3

Legend. **AR**, Akinetic-Rigid; **BMI**, Body Mass Index; **CoM**, Center of Mass; **CoP**, Center of Pressure; **CV**, Coefficient of Variation; **DLPFC**, Dorsolateral Prefrontal Cortex; **DRS-2**, Dementia Rating Scale-2; **EMA**, Effective Mechanical Advantage; **F8WT**, Figure-8 Walk Test; **FAB**, Frontal Assessment Battery; **FOG**, Freezing of Gait; **fNIRS**, functional Near-Infrared Spectroscopy; **GDI**, Gait Deviation Index; **GPS**, Gait Profile Score; **GRF**, Ground Reaction Force; **GVS**, Gait Variable Scores; **H&Y**, Hoehn and Yahr; **HA-PD**, High Anxiety–Parkinson’s Disease; **HC**, Healthy Controls; **IMU**, Inertial Measurement Unit; **LA-PD**, Low Anxiety–Parkinson’s Disease; **LOS**, Limits of Stability; **LRI**, Locomotor Rehabilitation Index; **MAP**, Movement Analysis Profile; **MCI+**, Mild Cognitive Impairment positive; **MCI–**, Mild Cognitive Impairment negative; **MDS-UPDRS**, Movement Disorder Society-sponsored UPDRS; **MMSE**, Mini-Mental State Examination; **MoCA**, Montreal Cognitive Assessment; **MX**, Mixed Phenotype; **PCI**, Phase Coordination Index; **PD**, Parkinson’s Disease; **PFC**, Prefrontal Cortex; **PIGD**, Postural Instability/Gait Difficulty; **RMS**, Root Mean Square; **RoM**, Range of Motion; **SSWS**, Self-Selected Walking Speed; **SSWS-DT**, Self-Selected Walking Speed under Dual-Task; **TD**, Tremor-Dominant; **3MBWT**, 3-Meter Backward Walk Test; **3MS**, Modified Mini-Mental State Examination; **TMT-A**, Trail Making Test Part A; **TUG**, Timed Up and Go Test; **UPDRS**, Unified Parkinson’s Disease Rating Scale; **VAM**, Vitaport Activity Monitor; **WCST**, Wisconsin Card Sorting Test; **WML**, White Matter Lesions; **10MWT**, 10-Meter Walk Test. Values are presented as mean ± standard deviation for both the Parkinson’s disease group and the control group, respectively.

Table 2. Protocol and Measurements

Study	Type of study	Measurements	Device	Distance (m)
Alcock et al. 2016 (Alcock, Galna et al. 2016)	Observational, cross-sectional	Foot clearance (toe/heel trajectories), temporal-spatial gait parameters	CATRite® walkway, Vicon® motion capture	25-m circuit
Álvarez et al. 2020 (Álvarez, Latorre et al. 2020)	Observational, cross-sectional	Postural control (sway, LOS), spatiotemporal gait parameters (speed, cadence, stride length/width/time, dual-task effects)	Wii Balance Board, Kinect v2	6-m walking test
Baker et al. 2008 (Baker, Rochester et al. 2008)	Experimental, within-subjects, repeated-measures	Gait variability (step time CV, double limb support time CV) under single- and dual-task conditions with auditory, attentional, and combined cues	GAITRite electronic walkway	8-meter walkway
Bartmann Wild et al. 2012 (Wild, de Lima et al. 2013)	Observational, cross-sectional	Cognitive tasks (Stroop, WCST), gait parameters (speed, swing time, stance time)	Kinometry with JVC GR-DVL 9800 camera, Dvideow system, Labview 85 software	9-meter corridor
Brown et al. 2009 (Brown, de Bruin et al. 2009)	Experimental, counterbalanced repeated-measures	Gait velocity (m/s), stride length (m), double-limb support (% gait cycle), cognitive task errors	6-camera 3D motion analysis system (Peak Performance Technologies/Vicon), iPod Nano for music	10-meter walkway

Corradini et al. 2022 (Corradini, Silveira-Ciola et al. 2022)	Experimental, repeated-measures	Spatial-temporal gait parameters (stride length, width, duration, velocity, double support time) Trajectory deviations (medial-lateral, horizontal) Obstacle circumvention strategy (lead-in/lead-out) Gaze behavior (fixations, duration) Dual-task cognitive performance (serial subtractions)	8-camera Vicon Motion System (100 Hz) ASL Eye Tracking Mobile System (60 Hz)	8.5 m walkway (obstacle at 5 m)
Dragasevic-Miskovica et al. 2021 (Dragasevic-Miskovic, Bobic et al. 2021)	Observational, Cross-sectional	Gait variability (stride length, stride duration, swing time) under single-task and dual-task conditions	Wireless sensor system (SENSY) with IMUs and shoe insoles (FSR)	15-meter hallway
Ehgoetz Martens et al. 2018 (Ehgoetz Martens, Silveira et al. 2018)	Observational, Cross-sectional,	Gait parameters (velocity, step length, step time, step width, and variability) under single-task and dual-task conditions	Proto-Kinetics Zeno Walkway System	10-meter walkway
Fernandez-Lago et al. 2015 (Fernandez-Lago, Bello et al. 2015)	Observational, cross-sectional	Gait speed, stride length, stride frequency, CV of stride length/frequency, cognitive performance (phoneme monitoring)	OptoGait system, treadmill (SportsArt 6300)	8-m walkway for overground walking
Galletly and Brauer 2005 (Galletly and Brauer 2005)	Observational, cross-sectional	Gait velocity, stride length, cadence, concurrent task performance (calculation, language, motor tasks)	Clinical Stride Analyzer (B&L Engineering)	10-m walkway for overground walking

Galna et al. 2012 (Galna, Lord et al. 2012)	Observational, cross-sectional	Saccadic frequency/timing during walking (straight, turning, dual-task); gait duration; correlations with cognition (MoCA, attention), vision (acuity, contrast sensitivity), and motor severity (UPDRS-III)	Electrooculography (EOG; Zerowire) synchronized with 3D motion analysis (VICON Mx3+)	2.5 m analyzed (total walking path: 5 m)
Graham et al. 2023 (Graham, Armitage et al. 2023)	Cross-sectional interventional	Gait (speed, stride length, foot strike angle, variability) and visual exploration (saccade frequency/duration/velocity, fixation duration) during single/dual-task walking with/without visual cues	Mobile eye-tracking (Tobii Pro Glasses 2, >100 Hz) and inertial sensors (APDM Mobility Lab, 128 Hz)	9 m straight path with 180° turns (2-minute walking trials)
Ivaniski-Mello et al. 2023 (Ivaniski-Mello, Müller et al. 2023)	Observational, cross-sectional	Gait speed (SSWS, SSWS-DT), DT-interference effect, LRI, TUG, sit-to-stand 30s	Stopwatch, standard chair	10-meter walk (14m path)
Karan Veer and Pahuja 2022 (Veer and Pahuja 2022)	Observational, cross-sectional	Gait: stance time, swing time, stride time, and their variability under dual-task	Pressure sensors in footwear, data sampled at 100 Hz	~Timed 2 min walk
Koçer et al. 2023 (Kocer, Gulsen et al. 2023)	Observational, cross-sectional	10MWT, TUG, F8WT, 3MBWT in both single-task and dual-task conditions	Stopwatch	10MWT (10m), TUG (6m), F8WT (~1.5m loop), 3MBWT (3m)
Krupička et al. 2024 (Krupička, Malá et al. 2024)	Observational, cross-sectional	Gait speed, stride length, cadence under single-task and dual-task (counting) conditions	GAITRite® pressure walkway system	5.15 m of timed walkway in 10 m TUG

LaPointe et al. 2010 (LaPointe, Stierwalt et al. 2010)	Observational, cross-sectional	Stride length, gait velocity, double-support time, speech rate, task accuracy	GAITRite® Portable Walkway System	4.27 m (14 ft)
Lin et al. 2023 (Lin, Lin et al. 2023)	Observational, case-control	Walking speed, step length, step time, CV of step length and time, response accuracy, reaction time, composite score	GAITRite pressure mat	3.66
Lohnes et al. 2011 (Lohnes and Earhart 2011)	Observational, case-control	Gait velocity, stride length, cadence, cognitive performance	GAITRite walkway	5
Mak 2013b (Mak 2013)	Observational, cross-sectional	Step length, step length variability, cadence, cognitive task accuracy	Zebris treadmill (FDM-T system)	Treadmill (fixed speed)
Mak et al. 2013a (Mak, Yu et al. 2013)	Observational, cross-sectional	Stride length, cadence, gait velocity, cognitive task accuracy	GAITRite walkway mat	3.66 (active area) + 1m beyond
Micó-Amigo et al. 2019a (Micó-Amigo, Kingma et al. 2019)	Observational, longitudinal cohort	Single-task: Circular walking (3 rounds, 1.2 m diameter) Dual-task: Walking while marking crosses or subtracting serial 7 digits	DynaPort® Hybrid (triaxial accelerometer and gyroscope)	Circular path diameter: 1.2 m
Nardello et al. 2020a (Nardello, Bertoli et al. 2020)	Observational, cross-sectional	Spatiotemporal gait parameters (stance time, swing time, stride time, cadence, stride length, walking speed) Dual-task performance (repeating days of the week backwards) Turning tasks (60° and 120°)	Eight-camera motion capture system (Vicon MX Ultramet)	10 m walkway (straight and turning conditions)

Nardello et al. 2020b (Nardello, Bombieri et al. 2020)	Observational case-control	Kinetic (GRF, joint moments), kinematic (speed), leverage (moment arms), EMA	Vicon motion capture system, AMTI force platform	8
O'Shea et al. 2002 (O'Shea, Morris et al. 2002)	Observational, case-control	Spatiotemporal gait variables (speed, stride length, cadence, double support)	Clinical Stride Analyzer (CSA), video camera	14 (middle 10m analyzed)
Ohara et al. 2023 (Ohara, Hirata et al. 2023)	Observational, prospective cohort	Stride length, velocity, sequence effect (SE) under single/dual-task and straight/circular walking	Wearable inertial sensors (WALK-MATE Viewer®)	15 (straight), ~9.42 (circular, 3 laps)
Orcioli-Silva et al. 2020 (Orcioli-Silva, Vitório et al. 2020)	Observational, case-control	PFC activation (HbO ₂), gait parameters (step length, velocity, variability)	Mobile fNIRS (OctaMon), GAITRite system	26.8 (circuit), 7 (straight segments)
Pieruccini-Faria et al. 2014 (Pieruccini-Faria, Ehgoetz Martens et al. 2014)	Observational, cross-sectional	Gait velocity, step time/length variability, obstacle contacts, dual-task performance	Optotrak® cameras	~6.5 m (obstacle position)
Plotnik et al. 2009 (Plotnik, Giladi et al. 2009)	Observational, cross-sectional	Bilateral coordination (PCI), gait speed, stride/swing time variability, gait asymmetry	Force-sensitive footswitches	25 m corridor (2 min walking)
Ranchet et al. 2020 (Ranchet, Hoang et al. 2020)	Observational, cross-sectional	DLPFC activity (Δ HbO ₂ / Δ HbR), gait parameters (speed, cadence, stride length, variability), cognitive performance	fNIRS (NIRSport), wearable gait sensors (Physiolog®)	Oval path (dimensions not specified; 30s trials)
Rochester et al. 2005 (Rochester, Hetherington et al. 2005)	Experimental, repeated-measures	Walking speed, mean step length, step frequency; dual-task performance	Vitaport Activity Monitor (VAM) with accelerometers	Mean: 6.60 $\pm$ 1.51 (range: 4.2–10.4; distance varied per home environment)
Rochester et al. 2014 (Rochester, Galna et al. 2014)	Experimental	Gait characteristics (pace, variability, rhythm, postural control, asymmetry) under	GAITRite instrumented walkway (7m $\times$ 0.6m)	25-m oval walking circuit (gait sampled repeatedly over GAITRite mat)

		single- and dual-task (digit span recall) conditions		
		Cognition: Set-shifting (Oral Trail Making Test-B)		
Salazar et al. 2017 (Salazar, Ren et al. 2017)	Experimental	Gait: Speed, stride length, stride frequency Intertrial variability for both cognition and gait	OptoTrak/3020 System (infrared markers for 3D kinematic analysis)	10.4-m walkway (middle strides analyzed)
San Martín Valenzuela et al. 2020 (San Martín Valenzuela, Duenas Moscardo et al. 2020)	Observational, cross-sectional	Spatiotemporal, kinematic, and kinetic gait outcomes under single-task and dual-task conditions	3D photogrammetry (12 smart cams, Kinescan/IBV software) and 2 force platforms (Dinascan/IBV)	10
Souza Speciali et al. 2013 (Speciali, de Oliveira et al. 2013)	Observational, cross-sectional	Gait Deviation Index (GDI), spatiotemporal variables	8 optic-electronic cameras (Motion Analysis Corporation)	6.0
Souza Speciali et al. 2014 (Speciali, Oliveira et al. 2014)	Observational, cross-sectional	Gait Profile Score (GPS), Movement Analysis Profile (MAP), Gait Variable Scores (GVS)	8-camera motion analysis system (Motion Analysis Corporation)	6.0
Stuart et al. 2017 (Stuart, Galna et al. 2017)	Observational, cross-sectional	Saccade frequency, gait velocity, step length, double support time	Mobile eye-tracker (Dikablis), Vicon 3D motion capture	~7.0
Stuart et al. 2018 (Stuart, Lord et al. 2018)	Observational, cross-sectional	Saccade frequency, gait characteristics (velocity, step length, double support time)	Mobile infrared eye-tracker (Dikablis), electrooculography	~7 m straight walk

Toda et al. 2019 (Toda, Iijima et al. 2019)	Observational, cross-sectional	Gait parameters (speed, stride, cycle, variability), WML (PVH/WMH on MRI), frontal function (FAB)	(EOG), 3D motion capture system (Vicon) Portable gait rhythmogram (LSI Medicine Corp.), MRI (Scheltens' criteria for WML)	10 m (with 2-m acceleration/deceleration zones)
Tseng et al. 2012 (Tseng, Jeng et al. 2012)	Observational, cross-sectional	Spatiotemporal gait parameters (velocity, cadence, swing, stride), attention capability (dual-task performance)	GAITRite® walkway system	5.0 m (forward/backward)
Yogev et al. 2005 (Yogev, Giladi et al. 2005)	Observational, cross-sectional	Gait speed, stride time, swing time, stride/swing time variability, cognitive task performance	Computerized gait analysis system (force-sensitive insoles)	25-meter corridor (2-min walking)
Yogev et al. 2007 (Yogev, Plotnik et al. 2007)	Observational, cross-sectional	Gait asymmetry (swing time), gait speed, stride variability	Computerized force-sensitive system (pressure-sensor shoes)	25 (2-minute walk)
Yogev-Seligmann et al. 2012 (Yogev-Seligmann, Rotem-Galili et al. 2012)	Observational, cross-sectional (comparative)	Gait speed, stride time, swing time, stride variability, swing variability	Ambulatory recorder with footswitches (Bai Engineering)	30 (1-minute walk with turns)
Yogev-Seligmann et al. 2013 (Yogev-Seligmann, Giladi et al. 2013)	Observational, cross-sectional (comparative)	Gait speed, stride time, stride variability, cycling time, postural sway	Ambulatory recorder with footswitches (B&L Engineering), force plate (AMTI ACCUSWAYPLUS), triaxial accelerometer	30 (1-minute walk with turns)

Table 3. Quality assessment of the included studies

Study	Study Design	AXIS Total (/20)	STROBE ✓/✗	DT Checklist* (0–5)	GRADE Level	Notes
Alcock et al. 2016 (Alcock, Galna et al. 2016)	Observational, cross sectional	17	✓	3/5	Moderate	Strengths: Large sample size (N=157), 3D motion capture, counterbalanced task order. Limitations: No cognitive load measurement (e.g., NASA-TLX), no mention of familiarization.
Álvarez et al. 2020 (Álvarez, Latorre et al. 2020)	Observational, cross-sectional	16	✓	4/5	Moderate–High	Strengths: Large sample (n=97); validated low-cost devices (Kinect/Wii); dual-task paradigm. Limitations: No cognitive load measurement; Kinect v2 discontinued; treadmill not used (ecological validity).
Baker et al. 2008 (Baker, Rochester et al. 2008)	Experimental, within-subjects, repeated-measures	13	✓	4/5	Moderate	Strengths: Counterbalanced design, ecologically valid dual-task (tray carrying). Limitations: Small sample (n=14 PD, n=12 controls), no cognitive load measurement, limited gait variability analysis (single stride).
Bartmann Wild et al. 2012 (Wild, de Lima et al. 2013)	Observational, cross-sectional	14	✓	4/5	Moderate	Strengths: Robust neuropsychological and gait analysis, multiple task complexities. Limitations: Small sample (n=18 per group), no cognitive load measurement, single-stride gait analysis.
Brown et al. 2009 (Brown,	RCT (counterbalanced)	14	✓	4/5	Moderate	Strengths: Randomized design, ecological validity (self-selected music). Limitations: Small sample size (n=10 per group), no

de Bruin et al. 2009)						cognitive load measurement (NASA-TLX), potential bias from unblinded assessors.
Corradini et al. 2022 (Corradini, Silveira-Ciola et al. 2022)	Observational, cross-sectional	14	✓	4/5	Moderate	Strengths: Robust neuropsychological and gait analysis, multiple task complexities. Limitations: Small sample (n=18 per group), no cognitive load measurement, single-stride gait analysis.
Dragasevic-Miskovica et al. 2021 (Dragasevic-Miskovic, Bobic et al. 2021)	Cross-sectional	14	✓	4/5	Moderate	Strengths: Clear methodology, robust statistical analysis, dual-task conditions well-defined. Weaknesses: No blinding, small sample size, cognitive load not directly measured.
Ehgoetz Martens et al. 2018 (Ehgoetz Martens, Silveira et al. 2018)	Cross-sectional	17	✓	4/5	Moderate-High	Strengths: Matched groups for motor severity, clear DT protocol, ecological validity. Weaknesses: No cognitive load measurement, small HC group.
Fernandez-Lago et al. 2015 (Fernandez-Lago, Bello et al. 2015)	Cross-over	14	✓	4/5	Moderate	Strengths: Rigorous design, clear DT protocol, treadmill vs. overground comparison. Weaknesses: No cognitive load measurement, small sample, handrail use may confound results.
Galletly and Brauer 2005 (Galletly and Brauer 2005)	Cross-sectional	14	✓	4/5	Moderate	Strengths: Clear comparison of task types (cognitive vs. motor), use of visual cues, standardized gait analysis. Limitations: Small sample (n=16 per group), no

Galna et al. 2012 (Galna, Lord et al. 2012)	Observational, cross-sectional	15	✓	4/5	Moderate	cognitive load measurement (e.g., NASA-TLX), no long-term follow-up. Strengths: Robust eye-tracking methodology, ecological validity (complex environments), cognitive correlates analyzed. Limitations: Small sample (n=21 PD, n=12 controls), no cognitive load measurement (e.g., NASA-TLX), EOG limitations (lateral saccades only).
Graham et al. 2023 (Graham, Armitage et al. 2023)	Cross-sectional	17	✓	4/5	Moderate–High	Strengths: Comprehensive eye-tracking (100Hz), robust dual-task design, subgroup analysis (FOG vs. non-FOG). Limitations: Small HC group (n=17), no kinematic joint analysis.
Ivaniski-Mello et al. 2023 (Ivaniski-Mello, Müller et al. 2023)	Cross-sectional	15	✓	4/5	Moderate–High	Strengths: Standardized dual-task (arithmetic), locomotor index. Limitations: No cognitive load measurement, small sample (n=48).
Karan Veer and Pahuja 2022 (Veer and Pahuja 2022)	Cross-sectional	14	✓	3/5	Moderate	Strengths: Gender-specific analysis, high classification accuracy (100%). Limitations: Small sample (n=39), no cognitive load measurement.
Koçer et al. 2023 (Kocer, Gulsen et al. 2023)	Cross-sectional	13	✓	3/5	Moderate	Strengths: Clear methodology, counterbalanced task order, robust statistical analysis. Weaknesses: No blinding, cognitive load not directly measured (only serial subtraction), no familiarization phase.

Krupička et al. 2024 (Krupička, Malá et al. 2024)	Cross-sectional	15	✓	4/5	Moderate–High	Strengths: Rigorous MRI analysis, drug-naïve PD cohort, clear subgroup stratification. Weaknesses: No cognitive task performance data, small iTDC subgroup, potential motivational bias.
LaPointe et al. 2010 (LaPointe, Stierwalt et al. 2010)	Cross-sectional	13	✓	3/5	Moderate	Strengths: Clinically relevant cognitive-linguistic tasks, clear fall-risk implications. Weaknesses: No blinding, small PD subgroup (H&Y 3–4), cognitive task performance not quantified.
Lin et al. 2023 (Lin, Lin et al. 2023)	Observational	14	✓	4/5	Moderate–High	Strengths: Focus on executive-function tasks, composite scoring, task prioritization analysis. Weaknesses: Small sample size (n=16 PD), no cognitive load measurement, PIGD subtype bias.
Lohnes et al. 2011 (Lohnes and Earhart 2011)	Quasi-experimental	13	X	3/5	Moderate	Small sample size (n=11 per group), no blinding, but robust cueing protocol and counterbalanced design.
Mak 2013b (Mak 2013)	Cross-sectional	14	✓	3/5	Moderate	Small sample (n=13 PD, n=15 controls), but rigorous treadmill protocol and matched walking speed.
Mak et al. 2013a (Mak, Yu et al. 2013)	Cross-sectional	15	✓	4/5	Moderate	Novel audio-visual cueing (traffic lights) showed immediate benefits for PD gait, but lacks long-term follow-up.
Micó-Amigo et al. 2019a (Micó-Amigo, Kingma et al. 2019)	Observational, longitudinal cohort	16	✓	3/5	Moderate	Strengths: Long follow-up (5 years), standardized protocols. Weaknesses: No cognitive load measurement, attrition bias.

Nardello et al. 2020a (Nardello, Bertoli et al. 2020)	Cross-sectional	13	✓	3/5	Moderate	Strengths: Standardized dual-task protocol, kinematic analysis. Weaknesses: Small sample size (n=9 PD), no cognitive load measurement.
Nardello et al. 2020b (Nardello, Bombieri et al. 2020)	Cross-sectional	13	✓	3/5	Moderate	Strengths: Clear comparison of PD vs. controls, detailed biomechanical analysis. Limitations: Small sample size (n=10 per group), no cognitive load measurement (e.g., NASA-TLX), no blinding.
O'Shea et al. 2002 (O'Shea, Morris et al. 2002)	Cross-sectional	14	✓	3/5	Moderate	Strengths: Clear methodology, controlled speed, detailed leverage analysis. Weaknesses: Small sample size (n=10 per group), no cognitive load measurement, no familiarization phase.
Ohara et al. 2023 (Ohara, Hirata et al. 2023)	Cross-sectional	13	✓	3/5	Moderate	Strengths: Matched controls, standardized tasks, clear gait metrics. Weaknesses: Small sample (n=15 per group), no cognitive load measurement, no familiarization.
Orcioli-Silva et al. 2020 (Orcioli-Silva, Vitório et al. 2020)	Experimental, within-subject cross-over (on/off medication)	17	✓	4/5	High	Strengths: fNIRS for PFC activation, controlled medication states, ecological gait task. Weaknesses: No cognitive load measurement, small sample (n=20 PD).
Pieruccini-Faria et al. 2014 (Pieruccini-Faria, Ehgoetz Martens et al. 2014)	Cross-sectional	15	✓	4/5	Moderate	Strengths: Clear protocol, counterbalanced design, robust gait analysis. Weaknesses: No NASA-TLX, small sample size (n=33).

Plotnik et al. 2009 (Plotnik, Giladi et al. 2009)	Cross-sectional	14	✓	3/5	Moderate	Strengths: Clear bilateral coordination metric (PCI), robust cognitive task. Weaknesses: No NASA-TLX, small sample (n=34).
Ranchet et al. 2020 (Ranchet, Hoang et al. 2020)	Cross-sectional	15	✓	4/5	Moderate	Strengths: fNIRS with short-separation channels, robust gait analysis. Weaknesses: No NASA-TLX, small sample (n=36).
Rochester et al. 2005 (Rochester, Hetherington et al. 2005)	Repeated-measures (quasi-experimental)	13	X	3/5	Moderate	Strengths: Home-based testing (ecological validity), clear protocol. Limitations: Small sample (n=20 PD), no blinding, no cognitive load measurement.
Rochester et al. 2014 (Rochester, Galna et al. 2014)	Cross-sectional (observational)	17	✓	4/5	High	Strengths: Large sample (n=121 PD + 189 controls), controlled baseline task demand, robust gait analysis. Limitations: No cognitive load measurement (e.g., NASA-TLX), no blinding.
Salazar et al. 2017 (Salazar, Ren et al. 2017)	Cross-sectional	13	✓	3/5	Moderate	Strengths: Clear methodology, controlled walking conditions. Limitations: No blinding, cognitive load not directly measured, no familiarization phase.
San Martín Valenzuela et al. 2020 (San Martín Valenzuela, Duenas Moscardo et al. 2020)	Observational, cross- sectional	15	✓	4/5	Moderate	Strengths: Comprehensive biomechanical analysis, multiple functional DT conditions. Limitations: No cognitive load measurement, lack of familiarization phase.

Souza Speciali et al. 2013 (Speciali, de Oliveira et al. 2013)	Observational, cross-sectional	13	✓	3/5	Moderate	Strengths: Detailed 3D gait analysis, use of GDI for PD assessment. Weaknesses: Small sample size, no cognitive load measurement (e.g., NASA-TLX).
Souza Speciali et al. 2014 (Speciali, Oliveira et al. 2014)	Observational, cross-sectional	14	✓	4/5	Moderate	Strengths: Robust 3D gait analysis, use of GPS/MAP for dual-task assessment. Weaknesses: Small sample size, no cognitive load measurement (e.g., NASA-TLX).
Stuart et al. 2017 (Stuart, Galna et al. 2017)	Observational, cross-sectional	16	✓	3/5	Moderate	Strengths: Large sample (60 PD + 40 controls), robust eye-tracking and gait analysis. Limitations: No cognitive load measurement (e.g., NASA-TLX), no blinding, task order not fully randomized.
Stuart et al. 2018 (Stuart, Lord et al. 2018)	Observational, cross-sectional	16	✓	4/5	Moderate-High	Strengths: Large sample (55 PD + 32 controls), robust eye-tracking and gait analysis. Limitations: No cognitive load measurement (e.g., NASA-TLX), no blinding, fixed visual cue distance (not individualized).
Toda et al. 2019 (Toda, Iijima et al. 2019)	Observational, cross-sectional	13	✓	3/5	Moderate	Strengths: Clear methodology, quantitative gait analysis, dual-task paradigm. Weaknesses: No blinding, cognitive load not directly measured, no task familiarization mentioned.
Tseng et al. 2012 (Tseng, Jeng et al. 2012)	Observational, cross-sectional	13	✓	3/5	Moderate	Strengths: Clear dual-task paradigm, quantitative gait analysis (GAITRite®), attention capability stratification. Weaknesses: No blinding, cognitive load

Yogev et al. 2005 (Yogev, Giladi et al. 2005)	Observational, cross- sectional	16	✓	4/5	Moderate–High	not directly measured, small PD sample size (n=22). Strengths: Large sample (30 PD, 28 HC), robust gait analysis (stride/swing variability), clear cognitive task differentiation. Weaknesses: No NASA- TLX for cognitive load, no familiarization phase, potential order effects (fixed task sequence).
Yogev et al. 2007 (Yogev, Plotnik et al. 2007)	Observational, cross- sectional	15	✓	4/5	Moderate	Strengths: Focus on gait asymmetry (GA), clear dual-task paradigm (serial 7s), robust gait analysis (swing time variability). Weaknesses: No NASA-TLX, small control group (n=11), potential age/sex confounds (PD group 81% male).
Yogev- Seligmann et al. 2012 (Yogev- Seligmann, Rotem-Galili et al. 2012)	Observational, cross- sectional (comparative)	14	✓	4/5	Moderate	Strengths: Clear methodology, detailed cognitive assessment, explicit prioritization instructions. Weaknesses: No blinding, small sample size (n=20 per group), cognitive load not directly measured.
Yogev- Seligmann et al. 2013 (Yogev- Seligmann, Giladi et al. 2013)	Observational, cross- sectional (comparative)	14	✓	4/5	Moderate	Strengths: Clear isolation of postural vs. bilateral coordination demands, robust cognitive/motor assessments, randomized task order. Weaknesses: Small sample size (n=15–21 per group), no cognitive load measurement, stance task not uniform across groups.

*DT Standardization, Cognitive Load Measurement, Ecological Validity, Familiarization, Task Order Randomization

Legend. RCT, Randomized Controlled Trial; PD, Parkinson's Disease; HC, Healthy Controls; MCI, Mild Cognitive Impairment; DT, Dual Task; FOG, Freezing of Gait; PIGD, Postural Instability and Gait Disorder subtype; AXIS, Appraisal tool for Cross-Sectional Studies; PEDro, Physiotherapy Evidence Database scale; Cochrane RoB 2.0, Cochrane Risk of Bias tool, version 2.0; GRADE, Grading of

Recommendations Assessment, Development and Evaluation; **STROBE**, Strengthening the Reporting of Observational Studies in Epidemiology; **DT Checklist**, Dual-Task Checklist; **NASA-TLX**, NASA Task Load Index; **fNIRS**, Functional Near-Infrared Spectroscopy; **PCI**, Phase Coordination Index; **EOG**, Electrooculography; **IMU**, Inertial Measurement Unit; **GDI**, Gait Deviation Index; **GPS**, Gait Profile Score; **MAP**, Movement Analysis Profile; **GA**, Gait Asymmetry; **GAITRite®**, Commercial gait analysis system.

Supplementary Table S1: Detailed AXIS Tool Assessment. This table reports the study-level responses for each of the 20 AXIS items. Each item is scored as "Yes" (Y), "No" (N), or "Unclear" (U), with a total score of 20 for each study. Higher scores indicate better methodological quality.

Study	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	Total (/20)
Alcock et al. 2016	Y	Y	Y	Y	Y	Y	Y	Y	U	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	17
Álvarez et al. 2020	Y	Y	Y	Y	Y	Y	Y	Y	U	N	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	16
Baker et al. 2008	Y	Y	Y	U	N	Y	Y	Y	U	N	Y	Y	Y	Y	Y	U	U	Y	Y	Y	13
Bartmann Wild et al. 2012	Y	Y	Y	U	N	Y	Y	Y	U	N	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	14
Brown et al. 2009	Y	Y	Y	U	N	Y	Y	Y	U	N	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	14
Corradini et al. 2022	Y	Y	Y	U	N	Y	Y	Y	U	N	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	14
Dragasevic-Miskovica et al. 2021	Y	Y	Y	U	N	Y	Y	Y	U	N	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	14

Ehgoetz																					
Martens et al. 2018	Y	Y	Y	Y	Y	Y	Y	Y	U	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	17
Fernandez-Lago et al. 2015	Y	Y	Y	U	N	Y	Y	Y	U	N	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	14
Galletly and Brauer 2005	Y	Y	Y	U	N	Y	Y	Y	U	N	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	14
Galna et al. 2012	Y	Y	Y	Y	U	Y	Y	Y	U	N	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	15
Graham et al. 2023	Y	Y	Y	Y	Y	Y	Y	Y	U	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	17
Ivaniski-Mello et al. 2023	Y	Y	Y	Y	U	Y	Y	Y	U	N	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	15
Karan Veer and Pahuja 2022	Y	Y	Y	U	N	Y	Y	Y	U	N	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	14
Koçer et al. 2023	Y	Y	Y	U	N	Y	Y	Y	U	N	Y	Y	Y	Y	Y	U	U	Y	Y	Y	13
Krupička et al. 2024	Y	Y	Y	Y	U	Y	Y	Y	U	N	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	15
LaPointe et al. 2010	Y	Y	Y	U	N	Y	Y	Y	U	N	Y	Y	Y	Y	Y	U	U	Y	Y	Y	13
Lin et al. 2023	Y	Y	Y	U	N	Y	Y	Y	U	N	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	14

Lohnes et al. 2011	Y	Y	Y	U	N	Y	Y	Y	U	N	Y	Y	Y	Y	Y	U	U	Y	Y	Y	13
Mak 2013b	Y	Y	Y	U	N	Y	Y	Y	U	N	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	14
Mak et al. 2013a	Y	Y	Y	Y	U	Y	Y	Y	U	N	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	15
Micó-Amigo et al. 2019a	Y	Y	Y	Y	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	16
Nardello et al. 2020a	Y	Y	Y	U	N	Y	Y	Y	U	N	Y	Y	Y	Y	Y	U	U	Y	Y	Y	13
Nardello et al. 2020b	Y	Y	Y	U	N	Y	Y	Y	U	N	Y	Y	Y	Y	Y	U	U	Y	Y	Y	13
O'Shea et al. 2002	Y	Y	Y	U	N	Y	Y	Y	U	N	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	14
Ohara et al. 2023	Y	Y	Y	U	N	Y	Y	Y	U	N	Y	Y	Y	Y	Y	U	U	Y	Y	Y	13
Orcioli-Silva et al. 2020	Y	Y	Y	Y	Y	Y	Y	Y	U	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	17
Pieruccini-Faria et al. 2014	Y	Y	Y	Y	U	Y	Y	Y	U	N	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	15
Plotnik et al. 2008	Y	Y	Y	Y	U	Y	Y	Y	U	N	Y	Y	Y	Y	Y	U	U	Y	Y	Y	14
Ranchet et al. 2020	Y	Y	Y	Y	U	Y	Y	Y	U	N	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	15
Rochester et al. 2005	Y	Y	Y	U	N	Y	Y	Y	U	N	Y	Y	Y	Y	Y	U	U	Y	Y	Y	13

Rochester et al. 2014	Y	Y	Y	Y	Y	Y	Y	Y	U	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	17
Salazar et al. 2017	Y	Y	Y	U	N	Y	Y	Y	U	N	Y	Y	Y	Y	Y	U	U	Y	Y	Y	13
San Martín Valenzuela et al. 2020	Y	Y	Y	Y	U	Y	Y	Y	U	N	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	15
Souza Speciali et al. 2013	Y	Y	Y	U	N	Y	Y	Y	U	N	Y	Y	Y	Y	Y	U	U	Y	Y	Y	13
Souza Speciali et al. 2014	Y	Y	Y	U	N	Y	Y	Y	U	N	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	14
Stuart et al. 2017	Y	Y	Y	Y	Y	Y	Y	Y	U	N	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	16
Stuart et al. 2018	Y	Y	Y	Y	Y	Y	Y	Y	U	N	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	16
Toda et al. 2019	Y	Y	Y	U	N	Y	Y	Y	U	N	Y	Y	Y	Y	Y	U	U	Y	Y	Y	13
Tseng et al. 2012	Y	Y	Y	U	N	Y	Y	Y	U	N	Y	Y	Y	Y	Y	U	U	Y	Y	Y	13
Yogev et al. 2005	Y	Y	Y	Y	Y	Y	Y	Y	U	N	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	16
Yogev et al. 2007	Y	Y	Y	Y	U	Y	Y	Y	U	N	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	15
Yogev-Seligmann et al. 2012	Y	Y	Y	U	N	Y	Y	Y	U	N	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	14

Yogev-																						
Seligmann	Y	Y	Y	U	N	Y	Y	Y	U	N	Y	Y	Y	Y	Y	Y	U	Y	Y	Y		14
et al. 2013																						

Legend: Y = Yes (criterion fully met); N = No (criterion not met); U = Unclear / Not reported; AXIS = Appraisal Tool for Cross-Sectional Studies (Downes et al., 2016).

AXIS Items:

1. Were the aims/objectives of the study clear?
2. Was the study design appropriate for the stated aim(s)?
3. Was the sample size justified?
4. Was the target/reference population clearly defined? (Is the context/setting clearly described?)
5. Was the sample frame taken from an appropriate population base so that it closely represented the target/reference population under investigation?
6. Was the selection process likely to select subjects/participants that were representative of the target/reference population under investigation?
7. Were measures undertaken to address and categorise non-responders?
8. Were the risk factor and outcome variables measured appropriate to the aims of the study?
9. Were the risk factor and outcome variables measured correctly using methods/measurements that had been trialled, piloted or published previously?
10. Is it clear what was used to determine disease status (measurement, self-report, etc.)?
11. Were the methods (including statistical methods) sufficiently described to enable them to be repeated?
12. Were the basic data adequately described?
13. Does the response rate raise concerns about non-response bias?
14. If appropriate, was information about non-responders described?
15. Were the results internally consistent?
16. Were the results for the analyses described in the methods, presented?
17. Were the authors' discussions and conclusions justified by the results?
18. Were the limitations of the study discussed?
19. Were there any funding sources or conflicts of interest that may affect the authors' interpretation of the results?
20. Was ethical approval or consent of participants attained?

Supplementary Table S2. List of excluded studies with reasons

Study	Study Design	Title	Reason
Alharthi 2024 (Alharthi 2024)	Machine learning analysis	Interpretable machine learning comprehensive human gait deterioration analysis	Wrong outcome, wrong population, wrong study design
Al-Yahya et al. 2018 (Al-Yahya, Mahmoud et al. 2018)	Cross-sectional	Neural Substrates of Cognitive Motor Interference During Walking; Peripheral and Central Mechanisms	Outcomes of interest not reported
Amboni et al. 2012 (Amboni, Barone et al. 2012)	Cross-sectional	Gait patterns in parkinsonian patients with or without mild cognitive impairment	Outcomes of interest not reported
Barbieri et al. 2017 (Barbieri, Simieli et al. 2018)	Cross-sectional	Obstacle Avoidance Increases Asymmetry of Crossing Step in Individuals With Parkinson's Disease and Neurologically Healthy Individuals.	Wrong outcome, wrong population, wrong study design
Calabrò et al. 2020 (Calabro, Naro et al. 2020)	Intervention study	Improving motor performance in Parkinson's disease: a preliminary study on the promising use of the computer assisted virtual reality environment (CAREN).	Wrong outcome, wrong population, wrong study design
Carlson et al. 2024 (Carlson, Chiu et al. 2024)	Cross-sectional	Dual-Task Performance and Brain Morphologic Characteristics in Parkinson's Disease	Wrong outcome, wrong population, wrong study design

de Lima Gomes et al. 2018 (Gomes, Miranda et al. 2018)	Cross-sectional	Analysis of functional profile and mobility in Parkinson's disease: a cross sectional study.	Wrong outcome, wrong population, wrong study design
DRKS00003290 (Drks 2011)	Pilot study	Morphometric correlates and predictors of impaired gait and balance in Parkinson's Disease-a pilot study	Wrong outcome, wrong population, wrong study design
Erra et al. 2019 (Erra, Mileti et al. 2019)	Intervention study	Immediate effects of rhythmic auditory stimulation on gait kinematics in Parkinson's disease ON/OFF medication	Wrong outcome, wrong population, wrong study design
Fernandes et al. 2015 (Fernandes, Coelho et al. 2015)	Cross-sectional	Standing balance in individuals with Parkinson's disease during single and dual-task conditions.	Wrong outcome, wrong population, wrong study design
Fernandes et al. 2016 (Fernandes, Sousa et al. 2016)	Cross-sectional	Parkinson's Disease and Cognitive-Motor Dual-Task: Is Motor Prioritization Possible in the Early Stages of the Disease?	Outcomes of interest not reported
Ginis et al. 2017 (Ginis, Pirani et al. 2017)	Observational pilot study	Focusing on heel strike improves toe clearance in people with Parkinson's disease: an observational pilot study	Outcomes of interest not reported
Gomez et al. 2022 (Gomez, Foreman et al. 2022)	Cross-sectional	Upper-extremity kinematics and interlimb movement correlation in persons with Parkinson Disease on irregular terrain, cross-slope, and under dual-task condition	Wrong outcome, wrong population, wrong study design

Harrison et al. 2018 (Harrison, Horin et al. 2018)	Randomized controlled trial	Internal cueing improves gait more than external cueing in healthy adults and people with Parkinson disease	Outcomes of interest not reported
Harro et al. 2024 (Harro, Alderink et al. 2024)	Cross-sectional	Dynamic Measures of Balance during Obstacle-Crossing in Self-Selected Gait in Individuals with Mild-to-Moderate Parkinson's Disease	Wrong outcome, wrong population, wrong study design
Hua et al. 2022 (Hua, Nguyen et al. 2022)	Cross-sectional	Insole-Based Falling Risk Evaluation for Patients With Parkinson's Disease Through Walking While Holding a Cup of Water	Outcomes of interest not reported
Kim et al. 2022 (Kim, Kim et al. 2022)	Randomized controlled trial	Robot-assisted gait training with auditory and visual cues in Parkinson's disease: a randomized controlled trial	Wrong outcome, wrong population, wrong study design
Lee et al. 2020 (Lee, Youm et al. 2020)	Cross-sectional	Gait characteristics under imposed challenge speed conditions in patients with parkinson's disease during overground walking	Wrong outcome, wrong population, wrong study design
Maidan et al. 2016 (Maidan, Nieuwhof et al. 2016)	Cross-sectional (fNIRS study)	The Role of the Frontal Lobe in Complex Walking Among Patients With Parkinson's Disease and Healthy Older Adults: An fNIRS Study	Wrong outcome, wrong population, wrong study design
Micó-Amigo et al. 2019b (Mico-Amigo, Kingma et al. 2019)	Longitudinal study	Potential markers of progression in idiopathic Parkinson's disease derived from assessment of circular gait with a single body-fixed-sensor: A 5 year longitudinal study	Wrong outcome, wrong population, wrong study design

Nishida et al. 2020 (Nishida, Kanbe et al. 2020)	Review/foreign language	Relationship between gait and cognition in Parkinson's disease	Foreign language and wrong publication type
Ozcan Gulsen et al. 2023 (Ozcan Gulsen and Tunca Yilmaz 2023)	Cross-sectional	Dual task effect on upper and lower extremity skills in different stages of Parkinson's disease	Wrong outcome, wrong population, wrong study design
Picelli et al. 2010 (Picelli, Camin et al. 2010)	Preliminary investigation	Three-dimensional motion analysis of the effects of auditory cueing on gait pattern in patients with Parkinson's disease: a preliminary investigation	Wrong outcome, wrong population, wrong study design
Pilgram et al. 2016 (Pilgram, Earhart et al. 2016)	Cross-sectional	Impact of limiting visual input on gait: Individuals with Parkinson disease, age-matched controls, and healthy young participants	Wrong outcome, wrong population, wrong study design
Pompeu et al. 2011 (Pompeu, Okamoto et al. 2011)	Cross-sectional	Dual-task performance assessment: motor performance of gait, balance, posture and manual skill in dual-tasks	Wrong outcome, wrong population, wrong study design
Sarbaz and Pourakbari 2019 (Sarbaz and Pourakbari 2019)	Experimental study	The effects of counting the stride numbers on the Parkinsonian gait: Suggesting a possible reason for dual task interference	Wrong outcome, wrong population, wrong study design
Seuthe et al. 2024 (Seuthe, Hermanns et al. 2024)	Cross-sectional	Gait asymmetry and symptom laterality in Parkinson's disease: two of a kind?	Outcomes of interest not reported
Sousani et al. 2025 (Sousani, Fernandez Rojas et al. 2025)	Cross-sectional	Exploring Brain-Body Interactions in Parkinson's Disease: A Study on Dual-Task Performance	Outcomes of interest not reported

Stegemoller et al. 2014 (Stegemoller, Wilson et al. 2014)	Cross-sectional	Associations Between Cognitive and Gait Performance During Single- and Dual-Task Walking in People With Parkinson Disease.	Wrong outcome, wrong population, wrong study design
Thorson et al. 2022 (Thorson, Hogan et al. 2022)	Retrospective analysis	Aquatic Therapy Intervention, Including the 4-Walls Drill, for Persons With Hoehn and Yahr Stage IV Parkinson's Disease: A Retrospective Data Analysis.	Wrong outcome, wrong population, wrong study design
Uribe et al. 2022 (Uribe, Fuentes et al. 2022)	Cross-sectional	Differentiation of the motor cost associated with cognitive tasks in Parkinson's disease: A dual-task study.	Wrong outcome, wrong population, wrong study design
Wang et al. 2020 (Wang, Gong et al. 2020)	Controlled study	Measurement of Step Angle for Quantifying the Gait Impairment of Parkinson's Disease by Wearable Sensors: Controlled Study	Outcomes of interest not reported
Xu et al. 2018 (Xu, Merryweather et al. 2018)	Cross-sectional	Dual-task interference during gait on irregular terrain in people with Parkinson's disease	Outcomes of interest not reported
Xu et al. 2023 (Xu, Geng et al. 2023)	Experimental study	How to prevent cognitive overload in the walking-arithmetic dual task among patients with Parkinson's disease	Outcomes of interest not reported
Zirek et al. 2018 (Zirek, Ersoz Huseyinsinoglu et al. 2018)	Controlled study	Which cognitive dual-task walking causes most interference on the Timed Up and Go test in Parkinson's disease: a controlled study.	Wrong outcome, wrong population, wrong study design

PRISMA CHECKLIST 2020

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	p. 1, Title page
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	p. 1, Structured abstract
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	p. 2, Introduction, first paragraph
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	p. 3, Introduction, last paragraph
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	p. 3, Methods (“Eligibility criteria”)
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	p. 7, Methods (“Information sources”)
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	p. 8, Methods (“Search strategy”) + Supplementary File 1
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	p. 9, Methods (“Study selection”)
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	p. 9, Methods (“Data extraction”)
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	p. 10, Methods (“Outcomes”)

Section and Topic	Item #	Checklist item	Location where item is reported
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	p. 10, Methods (“Outcomes”)
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	p. 4, Methods (“Risk of bias assessment”)
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	pp. 12–13, Methods (“Data synthesis”)
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Page 12, Methods – Data synthesis
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 12, Methods – Data synthesis
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Pages 12–13, Methods – Data presentation
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page 13, Methods – Data synthesis
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Page 13, Methods – Subgroup analyses
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Page 13, Methods – Sensitivity analyses
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	p. 13, Methods (“Publication bias”)
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	p. 13, Methods (“GRADE assessment”)
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	p. 6, Results + Figure 1 (PRISMA flow diagram)
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	p. 6, Figure 1 (PRISMA flow diagram)
Study characteristics	17	Cite each included study and present its characteristics.	pp. 6–20, Results + Table 1

Section and Topic	Item #	Checklist item	Location where item is reported
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	pp. 24-34, Results + Table 2
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	pp. 6-20, Results + Table 1
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	pp. 17-20, Results + Table 1
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	NA
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	NA
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	NA
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	NA
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	pp. 24-34, Results + Table 2 (GRADE summary)
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	p. 34, Discussion (first paragraph)
	23b	Discuss any limitations of the evidence included in the review.	pp. 34-35, Discussion
	23c	Discuss any limitations of the review processes used.	p. 35, Discussion
	23d	Discuss implications of the results for practice, policy, and future research.	p. 35, Discussion (last paragraph)
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	p. 6, Methods ("Protocol and registration")
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	p. 6, Methods ("Protocol and registration")
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	p. 6, Methods ("Protocol and registration")

Section and Topic	Item #	Checklist item	Location where item is reported
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	p. 37, Acknowledgements/Funding
Competing interests	26	Declare any competing interests of review authors.	p. 37, Declarations
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	p. 37, Data availability statement

PAPER 4

Appendix Table 1. Characteristics of participants, interventions and outcomes

First author, year	Study design	included studies	Participants	Type of meta-analysis	Intervention category	Population (age, H&Y)	Outcomes assessed	Motor outcomes	Non-motor outcomes	Duration / Frequency / Intensity	Control	Notes / Comments
Ernst et al. 2024 (Ernst, Folkerts et al. 2024)	Systematic review & network meta-analysis	154 RCTs	7837	NMA	Physical exercise (dance, gait/balance, endurance, resistance, mind-body, aqua, LSVT BIG, flexibility) Pharmacological (rasagiline, levodopa, modafinil, caffeine, doxepin, methylphenidate, memantine) + exercise	Adults with PD, mostly mild-moderate, age 60–74	Motor signs, QoL, adverse events	Dance, gait/balance, functional training effective (UPDRS-M improvement)	QoL improved with aqua, mind-body, multi-domain	Variable (short-term ≤6 weeks)	Passive controls, active comparators	Largest synthesis; interventions relatively safe, effects comparable across exercise types
Elbers et al. 2015 (Elbers, Verhoef et al. 2015)	Systematic review & meta-analysis	11 RCTs	1817	Pairwise		Adults with PD; some with clinically relevant fatigue	Subjective fatigue (FSS, MFI), ADL, adverse events	No consistent motor outcomes	Rasagiline effective (reduced fatigue); doxepin low-quality positive effect; no benefit from other drugs or exercise	Variable	Placebo / usual care	No clear treatment recommendation; only rasagiline shows consistent effect
Sitja Rabert et al. 2012 (Sitja Rabert, Rigau Comas et al. 2012)	SR	10	—	Narrative	MC (WBV)	PD: 6 studies, MS: 4 studies; middle-aged/older	Functional performance (ADL), gait, balance, muscle, QoL, AEs	Gait, balance	QoL	Short-term; single sessions mostly; long-term unclear	Passive / other active therapy	Evidence insufficient; small number of studies; method quality limited; appears safe; WBV may improve gait short-term in PD but no clear effect on other outcomes

Foster Vander Elst et al. 2023 (Foster Vander Elst, Foster et al. 2023)	SR	—	—	Narrative	MC (dance / mind-body)	Adults; not specified for PD	Cognitive, emotional, social, neural	Motor coordination, rhythm	Emotion, social interaction, motivation, eudaimonia	Varied; not standardized	Not applicable	Conceptual + SR; focuses on neuroscience of dance; mostly narrative; minimal PD-specific data
Akrama et al. 2023 (Akrama, Sitzmann et al. 2023)	SR	12 (6 RCTs, 6 cohort)	413	Narrative	HYB (exergaming / mind-body)	H&Y I–III; age NR	Balance (BBS, DGI), QoL (PDQ-39)	Balance	QoL	Not standardized; mostly supervised	Usual care / other interventions	Positive effects on balance and QoL; preliminary evidence; home-based exergaming needs further studies
Burrai et al. 2024 (Burrai, Apuzzo et al. 2024)	SR	5	209	Meta-analysis	MC (Rhythmic Auditory Stimulation)	PD; age ≥ 65; H&Y NR	Gait (speed, stride, cadence)	Gait speed, stride length, cadence	—	Short-term; not fully specified	Usual care / control	Beneficial effect on gait speed and stride; low-quality; risk of bias (no blinding); no adverse events; further studies needed
Mahmoud et al. 2023 (Mahmoud, Al-Turkistani et al. 2023)	SR	9	263	Meta-analysis	MC (dance / mind-body)	PD; H&Y NR; age NR	FOG, balance, UPDRS-3	Balance, UPDRS-3, FOG	—	Not specified	Usual care / control	Dance improves balance and UPDRS; small effect on FOG; PEDro quality mostly high; GRADE low–very low; further high-quality studies recommended
Costa et al. 2025 (Costa, de Oliveira Barreto Suassuna et al. 2025)	SR + MA	10 (for MA)	157	Random-effects	PE (various, incl. aerobic)	PD; age NR; H&Y NR	Cognition (general, executive)	—	General cognition, exec function	Not reported	Non-exercise control	Small–moderate effects on cognitive symptoms; aerobic near-significant effect; supports exercise for cognition in PD; quality and trends discussed

Ain et al. 2025 (Ain, Parveen et al. 2025)	SR + MA	18	NR	Meta- analysis	MC / HYB (VR, tele- rehab)	PD; age NR; H&Y NR	Balance, gait, functional activities	Balance, gait (DGI, TUG)	—	Not reported	Traditional exercise (TE)	VR improved balance more than TE; gait similar VR/TR vs TE; TR feasible, clinically beneficial; highlights tele- & VR- rehabilitation potential Small but consistent benefits for motor and QoL; mixed exercise most effective; dose- response identified; safe; high methodological quality (Cochrane RoB2.0); supports home-based interventions
Gao et al. 2024 (Gao, Zhang et al. 2024)	Systema tic review + NMA (RCTs)	30 RCTs	2264	Network meta- analysis	Physical exercise (home-based, mixed, aerobic, etc.)	PD; age not specified ; H&Y not specified	Motor symptoms, QoL, walking speed, balance, finger dexterity	UPDRS motor (SMD -0.28), walking speed, balance, dexterity	QoL (SMD 0.15)	≥18 weeks, ≥850 METs- min/week needed for significant effect; varied modalities	Usual care / other exercise	Moderate-quality evidence; boxing improves both motor & non-motor symptoms; safe with high adherence; further homogeneous RCTs needed
Wang et al. 2025 (Wang, Song et al. 2025)	Systema tic review	13 (mostly RCTs + pre- post)	402	None (narrativ e synthesi s)	Physical exercise (boxing)	PD; 53- 89 yrs; ~72% male; H&Y not consiste ntly reported PD with cognitiv e	Strength (LE), balance, mobility, gait, disease severity, QoL, depression, safety, adherence	LE strength, gait, mobility, balance	QoL, depression, adherence, safety	6-96 weeks; community/g ym-based; varied frequency/int ensity	Not specified (pre-post comparisons , some usual care)	Very low-quality evidence; feasibility demonstrated; no significant effect on QoL, function, wellbeing; interventions diverse; small underpowered
Pigott et al. 2024 (Pigott, Armstrong et al. 2024)	Systema tic review + meta- analysis	14 (11 RCTs, 3 non- controll ed)	Not report ed (across includ ed studie s)	Random -effects meta- analysis (REML) for RCTs	Motor- cognitive / cognitive interventions (training, stimulation, rehab, combined physical-	impairm ent (PD- MCI & PD- dementi a); age	QoL (HrQoL), function (ADL), wellbeing	—	QoL, function, wellbeing	Not standardized; various interventions (from short- term cognitive training to	Usual care or active comparators (varied)	

					cognitive, psychoeducational, psychological)	variable ; H&Y not specified				broader rehab programs)		studies; promising but inconclusive
Lorenzo-García et al. 2023 (Lorenzo-Garcia, Nunez de Arenas-Arroyo et al. 2023)	Systematic review + network meta-analysis	48 RCTs	2977	NMA (network + standard meta-analysis)	PE (resistance, endurance, alternative, dance, sensorimotor)	PD patients; age not specified ; H&Y not reported	QoL (primary)	—	QoL	Not standardized; varied across studies	Usual care / control	Alternative exercise, dance, and sensorimotor interventions showed significant positive effects on QoL vs control; evidence supports PE for QoL but heterogeneity remains; more research needed on which type works best at which disease stage RAGT improves some motor outcomes, high-to-low quality evidence; no clear superiority over control; further RCTs needed VR improves manual dexterity; most studies high risk of bias; immersive VR seems more effective; feasible for telerehabilitation; methodological rigor needed
Alwardat et al. 2018 (Alwardat, Etoom et al. 2018)	Systematic review + meta-analysis	7 RCTs	NR	Meta-analysis	Motor / motor-cognitive (RAGT)	PD; age NR; H&Y NR	Motor impairments (UPDRS-III, gait, balance)	UPDRS-III, stride length, gait speed, balance	—	Not fully specified; interventions varied	Conventional therapy / control	VR improves manual dexterity; most studies high risk of bias; immersive VR seems more effective; feasible for telerehabilitation; methodological rigor needed
Lahude et al. 2023 (Lahude, Souza Correa et al. 2023)	Systematic review	8	NR	Narrative synthesis	Motor / motor-cognitive (VR)	PD; age NR; H&Y NR	Manual dexterity	Box and Blocks Test, 9-Hole Peg Test, Purdue Pegboard	—	Protocols heterogeneous; intervention details varied	Not specified / varies	Balance, dance, alternative exercises, BWS, resistance, and
Lorenzo-García et al. 2024	Systematic review +	86	4,693	Network meta-analysis	Physical exercise	PD; age NR;	Balance, postural	ABC scale, BBS,	—	Varied; 8 exercise categories;	Control groups /	

(Lorenzo-Garcia, Cavero-Redondo et al. 2024)	network meta-analysis					H&Y NR	stability, general mobility	MiniBEST est, TUG		protocols heterogeneous	other exercise	sensorimotor effective; interventions improve mobility and postural stability; highlights variety of effective physical exercise modalities
De Freitas et al. 2020 (De Freitas Tb Ms, Leite et al. 2020)	Systematic review	7	7 studies: 3 clinical trials, 1 uncontrolled, 3 pilot studies	Narrative synthesis	Motor / motor-cognitive	PD; mild-moderate; age NR	Gait and balance outcomes	Gait speed, step length, cadence, mediolateral and anteroposterior balance	—	Varied; dual-task training vs single-task or no intervention	Single-task or no intervention	Dual-task gait and balance training may improve gait and balance in mild-moderate PD; studies small and poor quality; further RCTs needed
Braz de Oliveira et al. 2024 (Braz de Oliveira, Rigo Lima et al. 2024)	Systematic review + meta-analysis	12	380	Meta-analysis	Motor / motor-cognitive (aquatic exercise)	PD; mild-moderate; age NR	Body structure & function, activity, participation	Postural balance (improved with AEP alone)	Muscle strength, depressive symptoms, mobility, QoL (no significant improvement)	Avg 50 min/session, 3x/week, 7 weeks; included postural balance, gait, single/double training, aerobic, trunk mobility, Ai Chi	Active control	AEP improves postural balance; no significant effect on other outcomes; GRADE quality applied; recommended as adjunct therapy; ICF framework suggested for rehab planning
Wu et al. 2022 (Wu, Zhang et al. 2022)	Systematic review +	583	PD	Meta-analysis	MM (VR balance training)	Not reported	Balance	Balance	—	0–20 min/session, 4–6x/week, 3–5 weeks, >30	Usual care / control	VR balance training significantly improved balance with large effect sizes; dose-

meta-analysis										sessions, 201–300 min/week			response relationships preliminarily analyzed; methodological quality 5–8/10.
Ishaq et al. 2025 (Ishaq, Shah et al. 2025)	Systematic review (animal studies)	9 studies	PD animal models (MPTP or 6-OHDA mice/rats)	Narrative synthesis	PE	Animal models	Nigrostriatal glutamatergic pathway markers, motor function	Balance, coordination, gait	Glutamate, GLT-1, GS, Gln, mGluR2/3, VGULT1, mGluR5, AMPA/NMDA receptor modulation	4 weeks, 5x/week, treadmill or voluntary wheel running	PD model untreated	Exercise training modulated glutamatergic excitatory balance, neuroprotective effects, improved motor function; CAMARADES 4–6/10.	
Braz de Oliveira et al. 2021 (de Oliveira, Lobato et al. 2021)	Systematic review	270 (10 studies)	Individuals with PD, mild to moderate	Narrative synthesis	Resistance exercise (RE)	Human, mild-moderate PD	Body structure/function, activity, participation	Upper limb muscle strength, postural balance, gait, cardiorespiratory fitness	Quality of life	Varies per study	Active or usual care	Low to very low level of evidence; RE improved body structure/function and gait, but not participation (QoL)	
Patel and Mans 2022 (Patel and Mans 2022)	Systematic review	25 studies	Individuals with PD	Narrative synthesis	Supplemental activities (dance, yoga, martial arts)	Human, PD	Motor and non-motor outcomes	Motor symptoms	Non-motor symptoms	Varies per study	Usual care or none	Supplemental activities improved both motor and non-motor symptoms; PEDro used for quality assessment; interventions nontraditional movement-based	
Mansfield 2015 (Mansfield,	Systematic review	8 studies, 404	Older adults and	Meta-analysis	Perturbation-based balance training	Human, PD and	Falls, fallers, risk ratios	Reduced risk of falls	Not specifically reported	Varies per study	Usual care or non-	PBT reduced fall risk (RR=0.71), fewer falls (rate ratio=0.54);	

Wong et al. 2015)	& meta-analysis of RCTs	participants	individuals with neurological conditions (including PD)			older adults					perturbation training	heterogeneity in study designs; PEDro used for quality assessment
Zhou et al. 2022 (Zhou, Zhao et al. 2022)	Systematic review & network meta-analysis	20 trials, 719 patients	Patients with Parkinson's disease	Network meta-analysis (frequentist approach)	Aerobic and resistance training of varying intensity and cycles	Human, mild to moderate PD	UPDRS III, 6MWT, 10MWT, TUG, PDQ-39	Significant improvements with short-period high-intensity resistance training (SMD=-0.95) and variable improvements for aerobic/resistance interventions	Quality of life (PDQ-39)	Varies by study; high-intensity short-period resistance most effective	Usual care or other exercise	Short-period high-intensity resistance training may provide optimal motor benefit; further high-quality RCTs needed
Perry et al. 2019 (Perry, Nelissen et al. 2019)	Systematic review & meta-analysis	10 studies	Patients with Parkinson's disease	Meta-analysis with meta-regression	Functional-task training	Human, PD, mild to moderate	UPDRS ADL	Positive effect on ADL scores directly after intervention	-	Intensity (minutes/week) positively correlated with effect size	No intervention or placebo	Moderate quality of evidence; intensity should be maximized within patient capability

								n (UPDRS=-2.62) and at first follow-up (UPDRS=-4.0) Tai Chi, resistance training, dance improved motor symptoms ; Tai Chi and dance improved balance; walking capacity improved after dance			
Li et al. 2022 (Li, Gao et al. 2022)	Systematic review & meta-analysis	26 RCTs, 1243 participants	Patients with Parkinson's disease	Meta-analysis	Long-term exercise therapy (Tai Chi, resistance training, dance)	Human, PD, mild to moderate	Motor symptoms, balance, walking capacity	-	≥12 weeks; higher frequency (2x/wk) and longer duration per session increased effect size	Control interventions (varied)	Long-term exercise effective for motor symptoms; dance may be ideal; dose-response relationships noted
Doucet et al. 2021 (Doucet, Franc et al. 2021)	Systematic review	45 studies (10 Level 1b, 27 Level 2b, 8 Level 3b)	Adults with Parkinson's disease	Narrative synthesis	Occupational therapy interventions (MIRT, outpatient OT, resistance exercise, multimodal/targeted exercise, alternative	Human, PD, adults	ADLs, rest, sleep	MIRT and multimodal/targeted exercise improve ADLs; resistance exercise low evidence	Sleep: MIRT moderate evidence; CBT and alternative therapies low- moderate evidence	Control varied (standard care or no intervention)	Provides evidence- based guidance for OT interventions on ADLs and sleep; supports use of MIRT and targeted programs

Author(s)	Study Design	Number of Studies / Participants	Population	Analysis Type	Interventions		Outcomes	Adverse Effects	Quality of Evidence	Limitations	Conclusions	
					Therapies	CBT						
Du et al. 2023 (Du, Ma et al. 2023)	Systematic review and meta-analysis	7 RCTs, n = 406	Patients with Parkinson's disease	Meta-analysis	Dual-task (DT) gait and balance training	therapies, CBT)	Gait velocity, cadence, TUG, Mini-BESTest	Gait velocity ↑, cadence ↑, TUG ↓, Mini-BESTest ↑	Not reported	Varied by study	Control groups per individual RCTs	Evidence suggests DT training improves motor and balance abilities; recommends further research to optimize DT protocols based on disease severity
Braz et al. 2018 (Braz, Dutra et al. 2018)	Systematic Review	7	Individuals with Parkinson's disease	Narrative synthesis (no meta-analysis)	Nintendo Wii-based exergames	Adults and elderly; age not specified; H&Y not specified	Functional and health outcomes	Balance, mobility, motor performance, independence	Risk of falls	Variable across studies; intensity, frequency, and duration not standardized	Various controls depending on included studies	Most studies were quasi-experimental; 57% had low methodological quality; more consistent improvement in balance; standardization needed for games, intensity, and frequency
McDermott et al. 2021 (McDermott, Haberlin et al. 2021)	Systematic Review	4	652 participants with Parkinson's disease	Narrative synthesis (no meta-analysis)	eHealth interventions (web and mobile applications)	Adults with PD; age not specified; H&Y not specified	Physical activity levels	Physical activity-related motor tasks	Adverse effects, enjoyment, attrition	Variable; intervention specifics differed across studies	Various controls depending on included studies	Improvements in PA reported in 3 studies but not consistent for all participants; safe and feasible; high enjoyment; low attrition (~12.5%); effectiveness unclear due to heterogeneity
Cugusi et al. 2017 (Cugusi, Manca et al. 2017)	Systematic Review	6 RCTs	221 participants with Parkinson's	Narrative synthesis (no meta-analysis)	Nordic Walking	Adults with PD; age not specified; H&Y not specified	Functional and clinical outcomes	Walking performance, balance, mobility	Not specifically reported	Variable across studies; specifics of NW sessions	Compared with treadmill, free walking,	NW feasible and likely effective; high heterogeneity and methodological differences prevent

			son's disease	meta- analysis)		not specified				not standardized	LSVT BIG, or home exercise programs	firm conclusions; further standardized studies needed
Lina et al., 2020 (Lina, Guoen et al. 2020)	Systematic Review and Meta-Analysis	12 RCTs	360 patients with Parkinson's disease	Quantitative meta-analysis	Virtual Reality rehabilitation	Middle-aged and elderly; age ranges 45+; H&Y not specified	Balance, motor function, gait, activities of daily living	Balance (Berg Balance Scale), motor function (Timed Up and Go), gait (10- Meter Walk Test) Motor symptoms (UPDRS III), functional mobility (Timed Up and Go), endurance (6MWT), gait parameters (GAITRite), freezing of gait (FOG_Q)	Activities of daily living (modified Barthel Index)	Variable across studies; specifics of VR sessions differed	Various controls depending on included studies	VR rehabilitation improves balance, motor function, gait, and ADLs; significant effect sizes reported; interventions heterogeneous
dos Santos Delabary et al. 2018 (Dos Santos Delabary, Komerowski et al. 2018)	Systematic Review with Meta-Analysis	5 RCTs	159 patients with Parkinson's disease	Quantitative meta-analysis	Dance practice	Adults with PD; age not specifically reported ; H&Y not specified	Functional mobility, motor symptoms, quality of life		Quality of life (PDQ-39)	Variable across studies; specifics of dance sessions differed	Compared to other exercise types or no intervention	Dance improved motor outcomes and functional mobility; significant benefits vs both other exercise and no intervention; intervention protocols heterogeneous
Pritchard et al. 2019 (Pritchard,	Systematic Review	10	Individuals with	Narrative synthesis	Aquatic therapy	Adults with PD; age not	Balance, gait, quality of life	Balance, gait	Quality of life	Variable across studies;	Compared with other therapeutic	Aquatic therapy may improve balance, gait, and QoL; large effects

Laster et al. 2019)			Parkin son's diseas e	s (no meta- analysis)		specifica lly reported ; H&Y not specified			frequency, duration, and intensity not standardized	exercise or no exercise	observed; current evidence heterogeneous and definitive conclusions limited	
Marotta et al. 2022 (Marotta, Calafiore et al. 2022)	Systema tic Review and Networ k Meta- Analysis	7 RCTs	236 partici pants with Parkin son's diseas e	Network meta- analysis	Commercial exergames (Nintendo Wii™, Xbox Kinect™)	Adults with PD; age not specified ; H&Y not specified	Functional locomotion	Functional locomotio n measures (standardi zed mean difference)	Not specifically reported	Variable across studies; specifics not standardized	Compared with control or other exergame platform	Wii demonstrated the greatest improvement in functional locomotion compared with Kinect and controls; immediate positive effects observed; Wii may be preferable for PD patients, especially with cognitive issues or freezing
Chen et al. 2020 (Chen, Tan et al. 2020)	Systema tic Review and Meta- Analysis	20 RCTs	1,143 partici pants with Parkin son's diseas e	Quantita tive meta- analysis	Exercise interventions (aerobic, dance, Tai Chi, martial arts, anaerobic, combined)	Adults with PD; age not specified ; H&Y not specified	Quality of life	Some motor- related functional domains indirectly via exercise	Overall QoL and different QoL domains	Interventions ≥12 weeks showed significant improvement s; type and frequency varied	Compared with no intervention	Exercise improved QoL significantly; aerobic, dance, and Tai Chi most effective; interventions <12 weeks less effective
Radder et al. 2020 (Radder, Lígia Silva de Lima et al. 2020)	Systema tic Review and Meta- Analysis	191 RCTs	7,998 partici pants with Parkin son's diseas e	Quantita tive meta- analysis	Multiple physiotherapy interventions (conventional, resistance training, treadmill, strategy training,	Adults with PD; age not specified ; H&Y not specified	Motor symptoms, balance, gait, quality of life	Motor symptoms , gait, balance	Quality of life	Variable across studies; specifics differ by intervention	Compared with no intervention or sham treatment	Provides comprehensive overview of physiotherapy effectiveness; different modalities benefit motor, gait, balance, or QoL differently; dual- tasking not effective;

					dance, martial arts, aerobic, hydrotherapy, balance & gait, dual tasking, exergaming, Nordic walking)							assists evidence-based decision-making
McDonnell et al. 2018 (McDonnell, Rischbieth et al. 2018)	Systematic Review and Meta-Analysis	4 studies (3 RCTs)	84 participants with mild Parkinson's disease	Quantitative meta-analysis	LSVT-BIG (amplitude-oriented training)	Mild PD; age not specified ; H&Y mild	Functional mobility and motor function	Motor function (UPDRS III), Timed Up and Go, 10-metre walk test	Not reported	16 sessions over 4 weeks delivered by certified instructor	Compared with general physiotherapy exercises or shorter LSVT-BIG protocol	LSVT-BIG more effective than shorter or standard physiotherapy in improving motor function; preliminary moderate-quality evidence; amplitude-oriented training reduces motor impairments
Aras et al. 2022 (Aras, Seyyar et al. 2022)	Systematic Review and Meta-Analysis of Systematic Reviews	16 systematic reviews /meta-analyses	Not specified (aggregated from included reviews)	Quantitative meta-analysis	Tai Chi	Adults with PD; age and H&Y not specified	Functional mobility, balance, falls	Functional mobility, balance	Falls (incidence/risk)	Variable across included studies; specifics not standardized	Compared with control or other interventions as per included reviews	Tai Chi significantly improves balance, functional mobility, and reduces falls in PD; effect sizes reported for all outcomes; evidence aggregated from multiple systematic reviews
Monteiro Mazzarin et al. 2017 (Mazzarin, Valderramas et al. 2017)	Systematic Review and Meta-Analysis	9 controlled trials (randomized, nonran	Not specified	Quantitative meta-analysis	Dance and Tai Chi	Adults with PD; age and H&Y not specified	Functional mobility, balance, agility	Functional mobility, balance, agility	Not specifically reported	2 weeks to 12 months; intervention type and intensity varied	Compared with other therapies or no intervention	Tai Chi improved functional mobility compared with other therapies; no significant differences in balance or agility

			domize d, semiran domize d)										between dance and Tai Chi; interventions heterogeneous
Li et al. 2021 (Li, Zhang et al. 2021)	Systema tic Review and Meta- Regressi on Analysis	22 RCTs	836 patien ts with Parkin son's diseas e	Quantita tive meta- analysis with meta- regressi on	Virtual reality- based rehabilitation	Adults with PD; age not specified ; H&Y not specified	Balance, quality of life, activities of daily living, depressive symptoms	Balance (g = 0.66), activities of daily living (g = 0.62)	Quality of life (g = 0.28), depressive symptoms (g = 0.67)	Variable across studies; session number and frequency impacted outcomes; video game consoles recommende d	Compared with control	VR rehabilitation significantly improved balance, ADLs, QoL, and depressive symptoms; high methodological quality for individual trials; overall evidence rated very low to low	
Coelho et al. 2022 (Coelho, de Oliveira et al. 2022)	Systema tic Review	11 interven tion studies	Not specifi ed	Qualitati ve systemat ic review	Perturbation- based balance training (PBT)	Adults with PD; age and H&Y not specified	Postural control, gait, falls	Postural control, gait	Falls reduction, PD severity	Variable across studies; specifics not standardized	Compared with conventiona l physiothera py or no intervention	PBT can improve postural control, gait, and reduce falls; evidence limited by methodological quality and publication bias; promising adjunct to physiotherapy Home-based active video games improve motor function (gait, balance); no definitive conclusions on cognition or QoL; interventions feasible, safe, and enjoyable; optimal dose, supervision, and	
Gallou- Guyot et al. 2022 (Gallou- Guyot, Nuic et al. 2022)	Systema tic Review	9 studies	412 adults with Parkin son's diseas e	Qualitati ve systemat ic review	Home-based active video games	Adults with PD; age not specified ; H&Y not specified	Motor function, cognitive function, quality of life	Gait, balance	Cognition, quality of life	Variable across studies; specifics not standardized	Compared with usual care or conventiona l therapy		

Dominguez Ferraz et al. 2017 (Ferraz, Trippo et al.)	Systematic Review	12 studies (3 RCTs)	Adults with Parkinson's disease	Qualitative systematic review	Nintendo Wii-based rehabilitation	Adults with PD, H&Y I-III; age not specified	Postural balance, mobility	Balance, mobility	Not reported	Variable across studies; specifics not standardized	Compared with conventional therapy or no intervention	retention of benefits not established Some evidence of improvement in balance and mobility; results limited due to low methodological quality and heterogeneity; caution advised in interpreting effectiveness
Zhao et al. 2024 (Zhao, Zhang et al. 2024)	Systematic Review and Network Meta-Analysis	71 RCTs (87 interventions, 27 distinct interventions)	3,732 participants	Network Meta-Analysis	Exercise interventions (archery, cycling, binary rhythm dance, others)	Adults with PD; age not specified; H&Y stages not specified	Motor function (MDS-UPDRS III)	MDS-UPDRS III score changes	Not reported	Variable across studies; specifics not standardized	Compared across multiple exercise interventions and with control groups	Archery, cycling, and binary rhythm dance showed the highest SUCRA rankings for motor improvement; most interventions showed some efficacy; study provides ranking of exercise interventions for motor outcomes
Lima et al. 2013 (Lima, Scianni et al. 2013)	Systematic Review with Meta-Analysis	4 (quasi-) RCTs	People with mild to moderate Parkinson's disease	Meta-analysis for pooled data	Progressive resistance exercise	Mild to moderate PD; age not specified; H&Y stages not detailed	Muscle strength, physical performance	Increased muscle strength (SMD = 0.50, 95% CI 0.05–0.95); improved walking capacity (mean difference	Most other physical performance measures showed no clinically worthwhile improvement	Progressive resistance training; progression of load based on participant ability; specifics variable across studies	Standard care, usual care, or non-exercising control	Exercise effective for strength and walking capacity but not for all physical performance measures; recommended for PD rehabilitation with focus on walking.

96 m, 95%
CI 40–152)

McMahon et al. 2021 (McMahon, Blake et al. 2021)	Systematic Review with Meta-Analysis	Not specified (RCTs and non-RCTs)	Individuals with Parkinson's disease	Meta-analysis for pooled data	Nonpharmacological interventions targeting respiratory function (functional training, generalised strength training, respiratory muscle training, aerobic exercise, qigong, yoga, breath stacking, incentive spirometry, singing)	PD; age and H&Y not specified	Respiratory outcomes: inspiratory and expiratory muscle strength, peak expiratory flow, peak cough flow, dyspnoea perception	Not applicable	Improved inspiratory muscle strength (MD 19.68; CI 8.49–30.87), expiratory muscle strength (MD 18.97; CI 7.79–30.14), peak expiratory flow (MD 72.21; CI 31.19–113.24), peak cough flow and perceived dyspnoea	Variable by intervention; details heterogeneous	Standard care or non-intervention controls	Evidence supports respiratory muscle training and other interventions for improving respiratory outcomes; no studies on respiratory rate or morbidity/mortality; methodological quality variable.
Cano Molina and Calvo Muñoz, 2019 (Molina and Muñoz 2019)	Systematic Review	8 RCTs	People with Parkinson's disease (sample size not specified)	Narrative synthesis	External rhythmic cueing (auditory or visual)	Age and H&Y not specified	Gait performance: stride length, gait velocity, cadence, and other gait parameters	Statistically significant improvements in one or more gait variables in all studies	Not reported	Protocols varied across studies; not standardized	Standard care or no intervention	External cueing improves gait performance in PD; further research needed to define optimal cue modality and protocol

Song et al. 2017 (Song, Grabowska et al. 2017)	Systematic review and meta-analysis	21 studies (15 RCTs)	735 participants with PD	Meta-analysis of RCTs	Tai Chi / Qigong	Not reported (PD patients)	Motor function, non-motor function, quality of life	UPDRS III, balance, Timed-Up-and-Go, 6-Minute Walk, falls	Depression, cognition, quality of life	2–6 months	No treatment (47%), active interventions (53%)	Methodological bias: low in 6, moderate in 7, high in 2; TCQ improved motor function, depression, and QOL, but not cognition; some publication bias noted
Guo and Tang 2024 (Guo and Tang 2024)	Systematic review and meta-analysis	21 studies (9 healthy older adults, 12 PD)	Health y older adults and PD patients	Random -effects meta-analysis	Tai Chi, yoga, resistance training	PD: not specified ; Healthy older adults: ≥65 yrs	Balance, motor function	Berg Balance Scale, Timed Up and Go, UPDRS III	Not reported	12 weeks; 3–4 times/week; 50–60 min per session	Control groups (unspecified)	Tai Chi most effective for PD balance; resistance training best for healthy older adults; all interventions improved balance; heterogeneity assessed with I ²
Emmanouilidis et al. 2021 (Emmanouilidis, Hackney et al. 2021)	Systematic review	38 studies (RCTs and other quantitative trials)	People with PD (number not reported)	Narrative synthesis; some quantitative data	Dance (face-to-face, digital, virtual)	Not reported	Feasibility, gait, balance, quality of life, disability	Gait, balance	Quality of life, disability	Not specified; modes included digital and in-person	Control groups (varied)	7 high risk of bias, 20 moderate, 11 low; dance beneficial for balance, gait, QOL, disability; good adherence to digital interventions; accessible form of exercise
Fernández-González et al. 2023 (Fernandez-Gonzalez, Rodriguez-Costa et al. 2023)	Systematic review	7 RCTs	Patients with PD (number not specified)	Narrative synthesis	Virtual reality	Not specified	Upper limb motor control	Fine motor dexterity, gross motor dexterity, strength, tremor, functionality, speed	Not reported	Not specified	Not reported	VR interventions showed positive effects on all measures of upper limb motor control

Wang et al. 2016 (Wang, Pi et al. 2016)	Systematic review and meta-analysis	9 trials (4 RCTs, 5 single-group interventions)	181 participants with PD	Hedge's g meta-analysis	Cognitive motor intervention (CMI)	Not specified	Gait and balance	Gait speed, stride time, Berg Balance Scale, Unipedal Stance Test	Not reported	Not specified	RCTs and non-RCTs included	CMI improved gait speed, stride time, balance; limited by quality of included trials
Mandelbaum and Lo 2014 (Mandelbaum and Lo 2014)	Systematic review	10 studies	People with PD	Narrative synthesis	Dance	Not reported	Mobility, gait, balance, upper extremity function, disability, falls, QOL	Walking speed, balance, gait, falls, upper extremity function	Disability, quality of life, safety, tolerability	Variable (class-based interventions)	5 studies had control groups (3 active)	Dance is safe, enjoyable, alternative intervention; limitations include small samples, design issues, inconsistent outcome measures
Zhou et al. 2021 (Zhou, Zhou et al. 2021)	Systematic review & meta-analysis	17 RCTs	598	Quantitative meta-analysis	Music-based movement therapy	PD patients (mean age not specified; H&Y not systematically reported)	Motor function (UPDRS III, TUG), balance (BBS, Mini-BEST), gait (velocity, cadence, stride length, freezing of gait), mental health, quality of life	Significant improvement in UPDRS III, TUG, BBS, Mini-BEST, walking velocity, freezing of gait	Significant improvement in mental health; no significant change in quality of life	Varied across studies; interventions typically structured as regular sessions (details differ per trial)	Mixed: some active, some passive controls	Publication bias checked (Egger, funnel plot, trim-and-fill). Effects robust for motor and mental outcomes; quality of life effects less consistent.
Choi et al. 2020 (Choi, Cho et al. 2020)	Systematic review & meta-analysis	18 RCTs	1,144	Quantitative meta-analysis	Exercise therapies (various modalities: aerobic, balance, functional training, etc.)	PD patients (mean age not specified; H&Y stages not	UPDRS total, Berg Balance Scale, preferred walking speed, TUG	Significant improvement in UPDRS total, UPDRS II & III, balance,	Not specifically reported (focus on motor outcomes; safety mentioned)	Varied across included RCTs (not standardized)	Compared to non-exercise therapy or regular activity	Exercise therapies considered relatively safe. Methodological quality of included studies low → limits strength of conclusions. Further high-quality RCTs needed.

Kwok et al. 2016 (Kwok, Choi et al. 2016)	Systematic review & meta-analysis of RCTs	10 studies (9 in meta-analysis : 5 Tai Chi, 2 Yoga, 2 Dance)	Not specified in abstract (mild-moderate PD)	Pooled meta-analysis (RevMan 5.3)	Mind-body exercises (Tai Chi, Yoga, Dance)	consistently reported)	Motor symptoms, postural instability, functional mobility, psychosocial well-being	walking speed, TUG	Psychosocial outcomes not consistently assessed; limited data	Variable (different per study; not standardized across trials)	Non-exercise controls	Strong evidence for immediate moderate-to-large effects on motor function, postural instability, functional mobility. Psychosocial benefits understudied, esp. for yoga. Methodological quality: 1 strong, 5 moderate, 4 weak.
						Mild to moderate PD (age: middle-aged and older adults; H&Y not specified)		Significant improvements in UPDRS III (SMD = -0.91), Berg Balance Scale (SMD = 1.48), TUG (SMD = -0.97), 6MWT (SMD = 0.78). Subgroup: Yoga showed strongest effect on UPDRS III				
Delgado-Alvarado, 2020 (Delgado-Alvarado, Marano et al. 2020)	Systematic review	35 studies (past 5 years)	Not specified in abstract (PD with freezing of gait)	Narrative synthesis (qualitative evaluation, no pooled MA)	Nonpharmacological, nonsurgical treatments for freezing of gait (FOG): active therapies (cognitive/physical training),	PD patients with FOG (details NR in abstract)	Freezing of gait, mobility, quality of life	Promising results with active training programs and cueing strategies; neuromod	QOL mentioned as secondary, but not consistently assessed	Variable, heterogeneous across studies	Variable (active control, usual care, or no control depending on study)	Identifies two main categories: long-lasting (active/passive) vs. transient (cueing). No meta-analysis due to heterogeneity. Suggests nonpharmacological therapies are promising but evidence quality limited.

					passive therapies (TMS, tDCS), transient effect therapies (visual, auditory, proprioceptive cues)			ulation (TMS/tDCS) also studied				
Ramírez-Nieto et al. 2018 (Ramírez-Nieto, Ortiz-Gutiérrez et al. 2018)	Systematic review	12 articles + 2 posters	276	Narrative	Commercial video games	Adults with PD	Balance, gait, QoL	Improved balance, postural control, step length, cadence, walking speed Gait	QoL improved	Variable across studies	Conventional therapy	Low methodological quality; effects not proven superior to conventional treatment
Freitag et al. 2019 (Freitag, Brucki et al. 2019)	Systematic review	19 studies	NR	Narrative	Virtual reality for dual-task gait training	Adults with PD	Gait, motor function, cognition	improvement reported in all studies	Cognition assessed variably	Variable across studies	Conventional or usual care	Effective for dual-task gait, but heterogeneity in protocols; no standardized guidelines yet
Flynn et al. 2019 (Flynn, Allen et al. 2019)	Systematic review + meta-analysis	16 RCTs	NR	Meta-analysis	Home-based prescribed exercise	Adults with idiopathic PD	Balance-related activities, gait speed, quality of life	Improved balance-related activities (SMD 0.21) and gait speed (SMD 0.30) vs control	No improvement in quality of life	Minimum 2/3 of exercise at home; details variable across studies	Control (usual care, sham, or no physiotherapy); centre-based exercise for comparison	Home-based exercise as effective as centre-based; safe and feasible

Sharififar et al. 2014 (Sharififar, Coronado et al. 2014)	Systematic review	6 RCTs	NR	Narrative synthesis	Whole Body Vibration (WBV)	Patients with PD, no cognitive impairment	Mobility, balance	Mixed results; some studies show improvement, not superior to active control Moderate-quality evidence for improvement in balance (BBS) and functional mobility (TUG)	Not reported	Variable across studies: duration, frequency, sessions, rest	Placebo or active control	Promising for mobility and balance, but heterogeneity limits conclusions; more research needed on equipment types and dosage
Pinto et al. 2019 (Pinto, Salazar et al. 2019)	Systematic review & meta-analysis	19 (8 RCTs, 3 non-RCTs, 8 pre-post)	484	Meta-analysis	Hydrotherapy (alone or combined with land-based therapy)	PD patients, age 54–78, disease duration 3–10 yrs	Balance, functional mobility, motor status, QOL		Low-quality evidence for no effect on motor status (UPDRS-III) and QOL (PDQ, SF-36)	Variable across studies	Land-based therapy or usual care	Hydrotherapy can improve balance and functional mobility; effects on QOL and motor status less clear; low risk of bias in included RCTs
De Santis and Kaplan 2020 (De Santis and Kaplan 2020)	Systematic review	13 (5 RCTs, 8 observational)	318	Narrative synthesis	Nordic Walking	Early-stage PD, low-moderate severity	Motor & non-motor outcomes	Improved symptom severity, walking speed, gait pattern (4–24 weeks)	Less consistent; maintenance requires regular training	4–24 weeks; supervised training recommended	Baseline or any control	NW is well accepted and safe; benefits evident mainly during ON-phases of medication; training must be regular to maintain effects; study quality poor to moderate
Liu et al. 2019 (Liu, Yeh et al. 2019)	Meta-analysis	5 RCTs	355	Meta-analysis	Tai Chi	PD patients, not specified	Falls, balance, functional mobility	Decreased fall rates (OR=0.47, p=0.001); improved	Not assessed	Not specified	No intervention or other physical training	Moderate- to high-quality evidence; Tai Chi effective in reducing falls and

								BBS (MD=3.47) , FR (MD=3.55 cm), TUG (MD=-1.06 s) Improved motor function (SMD -0.70), balance (SMD 0.89), walking capacity (SMD -1.24), gait velocity (SMD 0.48); no improvement in endurance , step length, cadence				improving balance and mobility
Zhu et al. 2023 (Zhu, Lu et al. 2023)	Meta- analysis	10 RCTs	532	Meta- analysis	Tai Chi	PD patients, not specified	Motor function, balance, functional walking capacity, gait velocity, endurance, step length, cadence		Not assessed	Not specified	Compared to control groups	Tai Chi beneficial for motor and gait-related outcomes, but not for endurance or gait parameters like step length and cadence; heterogeneity variable across outcomes
Stein Jr. and Maidanchen 2016 (Stein Jr and Maidanchen 2016)	Systema- tic review	5	Not specifi- ed	Not a meta- analysis	Dance as physiotherapy	PD patients, not specified	Disease severity, mobility, posture, static and dynamic balance, coordination, gait, freezing of	Improved mobility, posture, balance, coordination, gait,	Improved mood, cognition, social interaction, treatment adherence, quality of life	Not specified	Not specified	Dance shows cognitive, motor, and social benefits; considered a safe, enjoyable, and effective physiotherapeutic strategy for PD

							gait, mood, spatial cognition, social interaction, treatment adherence, quality of life	freezing of gait					
Cosentino et al. 2020 (Cosentino, Baccini et al. 2020)	Systematic review and meta-analysis	19	913	Meta-analysis	Physiotherapy	PD patients, not specified	Freezing of gait (FoG) questionnaire	Improvement in short-term and follow-up FoG; tailored physiotherapy particularly effective	Not specifically assessed	Variable across studies	No treatment or control interventions	Physiotherapy shows short- and long-term effectiveness in improving FoG; further RCTs needed to determine optimal type and duration of interventions	
Comparan 2018 (Comparan 2018)	Meta-analysis	8 (4 DTT, 4 AT)	Patients with PD	Quantitative meta-analysis	Dual-task training (DTT), Aerobic training (AT)	Age 30–88, H&Y 1–3	Gait parameters	Gait speed, Step length	Cognitive aspects (implicit in DTT), Fall risk	Varies across included studies; not specified in abstract	AT and DTT	Effect size for gait speed ES=0.09, step length ES=0.33; DTT comparable to AT but more economical; PEDro scores 4–8 (fair to high quality)	
Shen et al. 2016 (Shen, Wong-Yu et al. 2016)	Meta-analysis	25 RCTs	Patients with PD	Quantitative meta-analysis	Exercise training (various: balance, gait, Tai Chi, etc.)	Not specified in abstract	Balance, gait ability, falls	Balance performance, Gait performance	Fall incidence	Short-term (up to 12 months), facility-based training more effective; frequency/intensity varied across studies	No intervention or placebo	Hedges' g = 0.303 (short-term), 0.419 (long-term) for balance/gait; rate ratio for falls 0.485 (short-term), 0.413 (long-term); moderate methodological quality	

Kearney et al. 2019 (Kearney, Shellikeri et al. 2019)	Systematic review	18 (8 single-group, 10 RCTs)	Patients with PD	Systematic review	Augmented visual feedback-based interventions	Not specified in abstract	Motor rehabilitation outcomes	Impairment, activity, participation, global motor function	Not specified	High intensity, large amounts of treatment; gamified feedback; 100% real-time performance feedback	Traditional rehabilitation / education programs	AVF interventions often superior to traditional programs; effect sizes small to large; high-quality rigorous studies limited
Chung et al. 2016 (Chung, Thilarajah et al. 2016)	Systematic review and meta-analysis	7 RCTs	401 participants with PD	Quantitative meta-analysis	Resistance training	Early to advanced PD, H&Y 1–4	Muscle strength, physical function, balance, motor symptoms	Muscle strength, balance, parkinsonian motor symptoms	Gait, balance confidence, quality of life (no significant improvement)	Moderate intensity, 2–3 times/week, 8–10 weeks	Non-resistance training or no intervention	SMD: strength 0.61, balance 0.36, motor symptoms 0.48; PEDro median score 6/10; improves strength, balance, motor symptoms but not gait or QoL
Flynn et al. 2019 (Flynn, Allen et al. 2019)	Systematic review and meta-analysis	17 trials vs usual care/placebo; 4 trials vs centre-based	Adults with mild to moderate PD	Quantitative meta-analysis	Home-based exercise	Mild to moderate PD, H&Y not specified	Balance-related activities, gait speed, QOL	Balance-related activities, gait speed	Quality of life (QOL)	High dose ≥150 min/week for ≥6 weeks; supervision varied (≤33% minimally supervised, 100% fully supervised)	Usual care, placebo, or centre-based exercise	SMD 0.3–0.5 for balance/gait; home-based as effective as centre-based; uncertainty remains for low-dose and fully supervised sessions; quality of evidence good; long-term retention unclear; cost/adherence not assessed
Winser et al. 2018 (Winser, Tsang et al. 2018)	Systematic review and	10 RCTs	720 participants (7 PD,	Quantitative meta-analysis	Tai Chi	Parkinson's disease and stroke;	Balance, falls incidence	Timed Up and Go Test, Berg Balance Scale	Falls incidence	Not specified in abstract	Active treatment or no treatment	Tai Chi significantly reduced falls in PD (OR 0.47) and stroke (OR 0.21); improved balance vs no

	meta-analysis		3 stroke)			H&Y not specified						treatment in PD; no significant difference vs active treatment; 7 studies high quality, 3 low quality; limited evidence for other neurological disorders
Gomes Neto et al. 2020 (Gomes Neto, Pontes et al. 2020)	Systematic review and meta-analysis	15 RCTs	435 participants with PD	Quantitative meta-analysis	Water-based exercise	Parkinson's disease; H&Y not specified	Balance, mobility, functional independence, functional performance, fear of falling, quality of life	Balance, mobility, functional performance	Fear of falling, quality of life	Not specified in abstract	Usual care or land-based exercise	Water-based exercise improved balance, mobility, and QoL vs land-based/usual care; land-based improved fear of falling; MD for balance, mobility, QoL reported; heterogeneity assessed with I ²
Li and Chen 2021 (Li and Chen 2021)	Network meta-analysis	32 RCTs	1,352 PD patients	Network meta-analysis	Multiple exercise interventions: Tai Chi, balance training, resistance training, robot-assisted gait, Nordic walking, Argentine tango, VR training, vestibular rehab, treadmill, waltz	Adults with PD, H&Y not specified	Balance function	Balance measures	Not reported	Varied by included studies; not standardized	Conventional rehab	Vestibular rehabilitation ranked highest for improving balance; all interventions improved balance vs. usual care; conclusions limited by study heterogeneity and quality of included trials

Wu, 2022 (Wu, Tang et al. 2022)	Systematic review and meta-analysis	15 RCTs	873 participants with PD	Quantitative meta-analysis	Traditional Chinese exercise (TCE)	PD; H&Y not specified	Balance, gait, motor symptoms	Berg Balance Scale (BBS), Timed Up and Go (TUG), one-legged blind balance test, gait velocity, 6MWT, stride length, UPDRS-III	Not specified	High-intensity long sessions; number of sessions and session duration moderated effects	Control group type varied	Significant improvements in balance, gait velocity, stride length, 6MWT, UPDRS-III; cadence and step length not significantly affected; PEDro score, exercise type, control group type, number of sessions moderated effects
Baglio et al. 2022 (Baglio, Pirastru et al. 2022)	Systematic review	14	PD patients (elderly, exact N not reported)	Systematic review (no quantitative meta-analysis)	Motor rehabilitation	Age: elderly; H&Y: not specified	MRI markers (structural and functional), clinical outcomes	Improvements in movement automaticity, cortico-subcortical pathway strengthening	Activation of compensatory networks (fronto-parietal), quality of life	Not specified	Not specified	Limited number of heterogeneous studies; highlights dual mechanism of rehabilitation; calls for advanced quantitative MRI methods
Toh 2013 (Toh 2013)	Systematic review	8 (4 RCTs, 2 single-arm, 2 case reports)	Individuals with PD (small sample sizes; exact	Systematic review (no quantitative meta-analysis)	Tai Chi exercise	Not specified; H&Y: not reported	Motor and non-motor performance	Inconclusive evidence for improvement	Inconclusive evidence for improvement	Varied among studies; not consistently reported	Varied (RCTs had control groups; single-arm and case reports did not)	Evidence inconsistent; methodological quality of trials limited; cannot draw firm conclusions on efficacy; recommends further research with rigorous design

Rodríguez et al. 2020 (Rodríguez, Crespo et al. 2020)	Systematic review of RCTs	3 RCTs (total 111 patients)	N not specified) Patients with Parkinson's disease	Systematic review (no quantitative meta-analysis)	Respiratory muscle training (inspiratory, expiratory, or both)	Middle-aged and elderly; H&Y not specified	Respiratory muscle strength, swallowing function, phonatory measures, dyspnoea, spirometric indices	Improved maximal inspiratory and expiratory pressures	Improved swallowing function, phonatory measures, perception of dyspnoea	Varied by study; specific durations/frequencies not consistently reported	Control groups in RCTs (details varied)	Positive effects on respiratory strength and swallowing/phonatory function; limited number of studies; evidence not robust
Spaulding et al. 2013 (Spaulding, Barber et al. 2013)	Meta-analysis	25 studies	Individuals with Parkinson's disease	Quantitative meta-analysis	Cueing (auditory vs visual)	Not specified ; H&Y not reported	Gait parameters: cadence, stride length, velocity	Auditory cueing: improved cadence, stride length, velocity; Visual cueing: improved stride length only	Not reported	Varied by included studies; not consistently reported	Control conditions varied across studies	Auditory cueing more effective than visual; highlights need for optimized cueing strategies; studies heterogeneous
Lee et al., 2018 (Lee, Kim et al. 2018)	Systematic review	8 studies	People with Parkinson's disease	Systematic review (no quantitative meta-analysis)	Non-pharmacological therapies (physical exercise, cognitive behavioural, complementary interventions)	Not specified ; H&Y not reported	Sleep quality, UPDRS	Limited/in direct impact	Sleep quality improvement in some studies	Varied by study; not consistently reported	Control groups varied by study	Heterogeneous interventions and outcomes; inconsistent effects on sleep; further research needed to identify optimal therapies

de Goede et al. 2001 (de Goede, Keus et al. 2001)	Systematic review and meta-analysis	Not specified (included studies from 1966–1999; true or quasi-experiments)	Patients with Parkinson's disease	Quantitative meta-analysis	Physical therapy	Not specified; H&Y not reported	ADLs, stride length, walking speed, neurologic signs	Improvements in stride length and walking speed; mixed results for neurologic signs	ADLs improved (SES .40)	Varied by study; specifics not consistently reported	Control conditions varied across studies	Supports benefit of PT added to standard medication; limited by small number of studies and methodological quality issues
Ćwiekała-Lewis et al., 2017 (Cwiekała-Lewis, Gallek et al. 2017)	Systematic review	11 studies (7 RCTs, 4 quasi-experimental)	548 PD participants	Systematic review (no quantitative meta-analysis)	Tai Chi exercise	Mean age 68; 50% women; H&Y not specified	Physical function (balance) and well-being	Improved balance	Some improvements in well-being; mixed results	Varied across studies; not consistently reported	Control groups varied by study	Overall positive effects on balance; evidence on well-being mixed; further research needed with larger samples and standardized interventions
Barnish and Barran, 2020 (Barnish and Barran 2020)	Systematic review	56 studies (reported in 67 publications)	1531 PD participants	Systematic review (no quantitative meta-analysis)	Active group-based performing arts (dance, singing, music therapy, theatre)	Not specified; H&Y not reported	Quality of life, functional communication, speech, motor function, cognitive status	Positive effects observed in motor function (varied by intervention)	Improvements in quality of life, communication, speech, cognition (varied by modality)	Varied by study; not consistently reported	Control groups varied; details heterogeneous	Dance most studied (38 studies); evidence supports therapeutic benefit of performing arts; heterogeneity prevents determination of which modality is best for which outcome
Ferreira et al. 2021 (Ferreira, Binda et al. 2021)	Systematic review	78 animal studies	Parkinson's disease animal	Systematic review (no quantitative)	Treadmill exercise	Animal models; age/H&Y not applicable	Dopaminergic system, behavior, neuroplasticity, neuroinflammation,	Improvements in behavior and motor-	Effects on neuroplasticity, neuroinflammation, mitochondria	Varied by study; specifics often not reported	Control groups varied across studies	High risk of bias in included studies; methodological details often lacking; provides guidance for future

			model s	meta- analysis)			mitochondria, musculoskeletal systems	related outcomes				preclinical studies on treadmill exercise
Allen et al. 2012 (Allen, Sherrington et al. 2012)	Systema tic review	53 trials (90 interven tions)	People with Parkin son's diseas e	Systema tic review (no quantita tive meta- analysis)	Exercise and motor training	Not specified ; H&Y not reported	Participant characteristics, intervention delivery, retention, adherence, adverse events	Not primary focus; interventio ns targeted motor outcomes Improved motor status	Not primary focus; reported inconsistently	Average duration 8.3 ± 4.2 weeks; mostly fully supervised (74%) at facilities (79%)	Control groups varied by trial	High retention rates; sparse reporting of adherence and adverse events; interventions labor-intensive, highlighting challenges for clinical translation
Ban et al. 2021 (Ban, Yue et al. 2021)	Meta- analysis of RCTs	10 studies	359 PD partici pants	Quantita tive meta- analysis	Yoga	Not specified ; H&Y not reported	Motor function, balance, functional mobility, anxiety, depression, quality of life	(UPDRS- III), balance (BBS, BESTest), functional mobility (TUG) Exercise subgroup may impact motor function indirectly	Reduced anxiety (HADS, BAI), reduced depression (HADS, BDI), improved QoL (PDQ-39, PDQ-8)	Varied by study; specifics not consistently reported	Control groups varied by study	Yoga showed beneficial effects on motor and non-motor outcomes as well as quality of life in PD patients
Lee et al. 2017 (Lee, Choi et al. 2017)	Meta- analysis	18 studies	People with Parkin son's diseas e	Quantita tive meta- analysis	Non- pharmacologic al interventions (including exercise programs)	Not specified ; H&Y not reported	Health-related quality of life (HRQOL)		HRQOL improved; exercise programs particularly effective	Varied by study; specifics not consistently reported	Control groups varied by study	Non-pharmacological interventions, especially exercise, improve HRQOL in PD; overall positive effect size -4.17
Garcia- Agundez et al. 2019 (Garcia- Agundez,	Systema tic review	64 publicat ions (clinical trials, pilot	People with Parkin son's diseas e	Systema tic review (narrativ e synthesi	Exergame- based therapy (Microsoft Kinect, Wii Balance Board)	Not specified ; H&Y not reported	Motor function, balance, gait, cognitive function (attention, working	Improvem ents in TUG, BBS; motor function similar or	Cognitive improvements in attention, alertness, working memory, executive function	Varied by study; feasibility for home and clinical settings	Traditional rehabilitatio n or regular exercise	Exergame-based therapy is feasible, safe, and effective; further studies needed on standardized outcomes, follow-up,

Folkerts et al. 2019)		studies, technical papers, previous reviews)		s; includes meta-analyses)		memory, executive function)	better than traditional rehab					and linking game parameters with UPDRS
de Dreu et al. 2012 (de Dreu, van der Wilk et al. 2012)	Meta-analysis of RCTs	6 studies	168 PD participants	Quantitative meta-analysis	Music-based movement therapy (individual rhythmic music training, partnered dance classes)	Not specified ; H&Y not reported	Walking ability, balance, quality of life	Improvements in BBS, TUG, stride length; gait-related MbM improved walking velocity	No significant effects on UPDRS-motor score, Freezing of Gait, or QoL	Varied by study; specifics not consistently reported	Control groups varied by study	MbM-therapy shows promise for gait and balance improvements; larger studies and long-term follow-up needed
Reyes et al. 2013 (Reyes, Ziman et al. 2013)	Systematic review	10 studies	Patients with neurodegenerative disorders (including Parkinson's disease and multiple	Systematic review	Respiratory muscle training (IMT and EMT)	Not specified ; H&Y not reported	Respiratory function parameters	Not primary outcome	Improvement in respiratory function measures	Varied by study; specifics not consistently reported	Control groups varied by study	Some evidence for benefit in PD and MS, but limited number and quality of studies; cannot definitively conclude effectiveness

Wu et al. 2021 (Wu, Xu et al. 2021)	Network meta-analysis	52 trials	1971 patients with Parkinson's disease	Network meta-analysis (frequentist)	Aerobic exercise, mind-body exercise (yoga, walking, others)	Not specified; H&Y not reported	Motor function (UPDRS-III, TUG, BBS), non-motor symptoms (depression, cognition, ADLs)	UPDRS-motor, TUG, BBS	Depression, cognition, activities of daily living	Yoga: 60-min sessions, 2x/week; others varied	Control groups varied per study	Yoga ranked highest for motor function, TUG, depression, cognition, and ADLs; walking best for BBS; evidence supports specific dosing for yoga
de Oliveira et al. 2021 (de Oliveira, Lobato et al. 2021)	Systematic review of RCTs	10 RCTs	411 individuals with Parkinson's disease	Systematic review (no pooled meta-analysis)	Aerobic exercise (treadmill, walking)	Mild to moderate PD; age not specified; H&Y not reported	Functional capacity, gait, mobility, muscle strength, postural balance, quality of life	Gait: walking speed & stride length improved; mobility improved; lower limb strength improved; cadence & upper limb strength not improved; postural balance no effect	Quality of life: no significant improvement	Interventions varied; treadmill or walking; frequency/intensity varied per study	Control groups varied per study	Evidence level low to very low (GRADE); AE effective for gait, mobility, lower limb strength, but not for balance or QoL
Lei et al. 2022 (Lei, Ma et al. 2022)	Network meta-analysis of RCTs	20 RCTs	996 participants with Parkinson	Network meta-analysis	Tai Chi (24-form simplified, 8-form Yang style, 8-form	Elderly patients with PD; age not specified	Motor function (UPDRS III), balance (BBS)	UPDRS III: 24-form Tai Chi and Tai Chi	Not assessed	Varied by study; not consistently reported	Control groups varied (usual care or no	24-form Tai Chi and Tai Chi exercise programs most efficacious; provides

			son's diseas e		Chen style, Tai Chi exercise program)	; H&Y not reported		exercise program most effective; BBS: TCEP and 24- form Tai Chi ranked highest			intervention)	guidance for clinical exercise prescription
Wu et al. 2022 (Wu, Xiong et al. 2022)	Systema tic review	33 PD, 16 MCI, 4 AD	People with neuro degen erative diseas es (PD, MCI, AD)	Systema tic review (no quantita tive meta- analysis reported)	Dance movement therapy (DMT)	PD, MCI, AD; age not specified , H&Y for PD not specified	Motor function, cognitive deficits, mood, quality of life	Balance, gait, general disease condition	Global cognitive function, memory, executive function, mood, quality of life	Not specified	Non-dance / usual care	Evidence stronger for PD and MCI; insufficient evidence for AD; effects on mood and quality of life controversial
Dibble et al. 2009 (Dibble, Addison et al. 2009)	Systema tic review	Not specifie d (systema tic review of exercise studies)	People with Parkin son's diseas e	Systema tic review (no quantita tive meta- analysis reported)	Exercise interventions	PD; age not specified ; H&Y not specified	Balance outcomes, postural stability, QOL, falls	Postural instability, balance task performan ce	Quality of life, fall events	Not specified; dosing and exercise components not clearly defined	Non- exercise / usual care	Evidence moderate for postural stability and balance tasks; limited for QOL/falls; need for longer-term follow-up and clearer intervention protocols
Li et al. 2022 (Li, Guo et al. 2022)	Meta- analysis	7 studies	97 indivi duals with Parkin	ALE (activati on likelihoo d	Exercise interventions	PD; age and H&Y not specified	Brain activation patterns, motor improvements	Indirect (via brain activation)	Cognitive/motor coordination (via brain activation)	Not specified	Not specified	Exercise enhanced activation in cerebellum, occipital, parietal, frontal lobes; improvements likely

			son's disease	estimation) meta-analysis								due to coordinated brain region changes, not single area
Mrówczyński 2019 (Mrowczynski 2019)	Systematic review	Not specified	Humans (general population and PD patients) 835 (intervention) + 837 (control); mean age 60.8– 78.5; 807 M / 469 F	Systematic review	Endurance training	PD and general population; age and H&Y not specified	Motor performance, metabolic health, neuroplasticity	Reduction of motor deficits in PD, enhancement of motoneuron function	BDNF/TrkB levels, dopamine release, hormone modulation, metabolic outcomes (weight, glucose, blood pressure)	Not specified	Not specified	Endurance training increases BDNF/TrkB, modulates motor and metabolic adaptations; pleiotropic effects on nervous system and metabolic health
Kamieniarz et al. 2020 (Kamieniarz, Milert et al. 2021)	Systematic review	N/A		N/A	Tai Chi, Qigong	PD stages I– IV (mostly I–III)	Motor and non- motor function, QOL, sleep, depression, gait, balance	UPDRS III, BBS, FRT, TUG, GAITRite, 6MWT, COP measures	PDQ-39/8, BMLSS, PDSS-2, MMSE, MoCA-BJ, BDI, GDS, HAMD, NMSS	Tai Chi: 5–24 weeks, 30–90 min/session, 1–5x/week; Qigong: 6–72 sessions, 30– 60 min/session, 1–5x/week	No treatment, resistance training, stretching, aerobic, dance, multimodal	Most effective Tai Chi: Yang-style 24 form, 12– 16 weeks, 1 h/session, 1–3x/week; most effective Qigong: 12–16 weeks, 1 h/session, 1x/week; generally safe, low adverse events; heterogeneity in studies; small sample sizes in some studies
del Pozo- Cruz et al. 2012 (del Pozo-Cruz, Adsuar et al. 2012)	Systematic review	13 studies included: 5 PD, 2 cerebral palsy, 3 MS, 3 stroke	n not aggregated; age varied ; gender not	N/A	Whole-Body Vibration (WBV)	PD, CP, MS, stroke	Gait, balance, proprioception, strength, health- related QOL	Gait, balance, strength, proprioception	Health-related quality of life	Intervention details varied; WBV frequency, duration, and intensity not consistently reported; short-term: 1	Usual care, no intervention, other exercise	Moderate evidence for short-term strength improvement; weak evidence for proprioception and QOL; long-term minor evidence for improvements in strength, balance, gait,

			report ed							session; long- term: variable		proprioception; methodological quality varied; further research needed
Johansson et al. 2020 (Johansson, Hagstromer et al. 2020)	Systema tic review & metasyn thesis	N/A	Huma ns with Parkin son's diseas e; n not aggreg ated; age and gende r varied adults with Parkin son's diseas e; n and gende r varied ; mild to moder ate PD	N/A	Physical exercise	Parkinso n's disease	Neuroplasticity markers, brain structure and function, neurochemical adaptations	Possible changes in brain function related to motor control	Neurochemical, cognitive, structural brain changes	Exercise interventions varied across studies; duration, frequency, and intensity not consistently reported	Not consistently reported; varied by included studies	Narrative synthesis indicates positive changes in brain function and structure; meta-analysis of neurochemical adaptations inconclusive; GRADE analysis: very low overall quality of evidence; need for more rigorous human studies
Lamotte et al. 2015 (Lamotte, Rafferty et al. 2015)	Systema tic review + meta- analysis	8 RCTs	Standar d meta- analysis on UPDRS motor scores		Endurance / aerobic exercise training	Mild to moderat e PD	Motor and non- motor features, functional outcomes, cardiorespirator y fitness, VO ₂ max, gait, balance, mobility, depression, fatigue, QoL	Gait improved; UPDRS motor signs not consistentl y improved	Depression, fatigue, quality of life, cardiorespiratory function	Intensity: moderate to vigorous (mean HR 69.7% HRmax); duration and frequency varied across studies	Varied across included studies	Endurance training improves physical conditioning and cardiorespiratory capacity; evidence insufficient to support as specific treatment for PD; need for larger well-designed RCTs

Kwakkel et al. 2007 (Kwakkel, de Goede et al. 2007)	Systematic review	23 RCTs	adults with PD; n and gender varied	N/A	Physical therapy (transfer, posture, balance, reaching/grasping, gait, physical condition)	PD; mild to moderate	Motor and functional outcomes, task-specific performance, gait, postural control	Improvements task-specific; gait improved mainly with external rhythmic cues	Not reported	Varied across studies; dosage and treatment contrast often insufficient	Varied across studies	Effects of PT are task- and context-specific; improvements may not generalize; decline after treatment suggests need for chronic therapy; methodological quality improved over last 5 years; need for responsive measurement instruments
Mehrholz et al. 2010 (Mehrholz, Friis et al. 2010)	Systematic review, Cochrane	18 RCTs	adults with PD; n varied	Standard meta-analysis	Treadmill training	PD; H&Y stage not consistently reported	Gait parameters (speed, stride length, distance, cadence), dropout, safety	Gait speed ↑ (MD 0.09 m/s, moderate quality), stride length ↑ (MD 0.05 m, low quality); walking distance and cadence not significantly improved	Not reported	Varied across studies; details of duration/frequency/intensity heterogeneous	No treadmill / usual care	Improvements mainly in gait speed and stride length; small-to-moderate clinical relevance; heterogeneity across trials; long-term effects unknown; some studies high risk of bias due to no-intervention controls
Šumec et al. 2015 (Šumec, Filip et al. 2015)	Systematic review	N/A	PD patients; n not	N/A	Nonpharmacological balance interventions (exercise, Tai	PD; H&Y stage not	Balance, quality of life, depression,	Balance ↑ (various methods)	Quality of life ↑, depression ↓, motivation ↑	Varied across interventions; details	Usual care / no intervention	Evidence suggests balance interventions have psychological benefits as well as

			specific; adults		Chi, Qi Gong, Yoga, dance, boxing, robotic- assisted, VR- based, neurofeedback)	consiste ntly reported	motivation, enjoyment			heterogeneou s		physical; heterogeneity in study designs and intervention types; emphasizes practical and creative approaches for PD
Deane et al. 2001 (Deane, Jones et al. 2001)	Systema tic review of RCTs	43 trials, 1,673 particip ants	Patien ts with Parkin son's diseas e	Narrativ e synthesi s (no quantita tive meta- analysis possible)	Physiotherapy : general physiotherapy , exercise, treadmill training, cueing, dance, martial arts	Not specified ; PD patients	Motor: gait speed, Timed Up and Go, UPDRS motor subscale; Non- motor: PDQ-39, falls	Gait speed (19 trials), Timed Up and Go (15 trials), UPDRS motor subscale (22 trials)	PDQ-39 (13 trials), falls (5 trials)	Variable across trials; not specified uniformly	Comparator physiothera py intervention	Small sample sizes (avg. 39 participants per trial); Randomization/allocati on concealment poor or not reported; Blinded assessors ~50%; Only 10 trials used intention- to-treat analysis; High heterogeneity prevented meta- analysis; Insufficient evidence to favor one physiotherapy approach over another; Need for more rigorous trials with standardized interventions and outcomes
Römbling et al. 2025 (Römbling, Brixius et al. 2025)	Systema tic review	13 studies (2000– 2024)	Indivi duals with Parkin son's diseas e	Narrativ e synthesi s; no quantita tive meta-	Boxing training	Not specified	Motor: balance, motor symptoms; Cognitive: cognitive function;	Improvem ents in motor symptoms and balance	Improvements in cognitive function, psychosocial well- being	Not standardized; variations in intensity, frequency, session	Not specified / varied	Methodological inconsistencies; small sample sizes; lack of standardized boxing protocols; need for individualized

				analysis due to heteroge neity Narrativ e			Psychosocial: well-being			duration across studies		programs and longitudinal studies
Narayanasett i et al. 2025 (Narayanaset ti, Bansal et al. 2025)	Systema tic review	7 studies	Parkin son's diseas e (sampl e sizes 10–79)	synthesi s; no quantita tive meta- analysis due to heteroge neity	Physiotherapy : standard exercises, technological interventions	Not specified	Tremor reduction, motor function	Positive effects on tremor and motor function	Not specified	Varied across studies; not standardized	Not specified / varied	Heterogeneity in PD classification, outcome measures, and intervention duration; evidence shows temporary benefits; limited number of studies
Shruthi and Krishnaprasa d 2021 (Shruthi and Krishnaprasa d 2021)	Systema tic review	Systema tic reviews and RCTs from the last 5 years	Patien ts with Parkin son's diseas e	Narrativ e synthesi s; no quantita tive meta- analysis	Fall- prevention interventions: exercise-based programs, Tai Chi	Not specified	Falls, balance	Improvem ent in balance and fall reduction	Not specified	Not standardized across studies	Comparator: usual care or no intervention	Evidence supports exercise-based programs and Tai Chi for fall prevention; some negative results due to disease progression; high-level evidence from recent reviews and RCTs Small sample sizes, heterogeneous intervention durations;
Giorgi et al. 2025 (Giorgi, Platano et al. 2025)	Systema tic review of RCTs	5 RCTs	Patien ts with Parkin son's diseas e (sampl e sizes 10–62)	Narrativ e synthesi s; no pooled meta- analysis	Argentine Tango (AT)	Not specified	Balance, gait, functional mobility, psychological outcomes	Improved balance (Mini- BESTest, BBS, FRT), gait performan ce (6MWT, TUG), mobility	Some studies: reduced depressive symptoms, increased balance confidence	10 weeks to 24 months; varied across studies	Usual care or conventiona l exercise	FoG outcomes inconclusive; preliminary evidence of psychological benefits; need for larger standardized trials

Somaa and Asghar 2021 (Somaa and Asghar 2021)	Systematic review	17 RCTs	Patients with Parkinson's disease	Narrative synthesis; no quantitative meta-analysis due to heterogeneity	Paramedical therapies: physiotherapy, speech and language therapy, occupational therapy	Not specified	Motor function, balance, gait, postural stability, risk of falls, quality of life	Improvement in all motor aspects, gait speed, balance	Quality of life; speech outcomes (dysarthria)	Variable; heterogeneous across studies	Comparator: usual care or other paramedical interventions	Evidence supports benefit of multidisciplinary physiotherapy and speech therapy; heterogeneity prevents determination of superior modality; need for standardized intensity, duration, and outcome measures in future trials
Quirosa-Galán et al. 2024 (Quirosa-Galán, García-Bravo et al. 2024)	Systematic review	Not specified (various studies on VR/video games)	Patients with Parkinson's disease	Narrative synthesis; no quantitative meta-analysis reported	Virtual reality / video games	Not specified	Motor function, balance, gait	Improvements in gait, balance, overall motor function	Cognitive function improvements noted	Variable; details not standardized across studies	Comparator: usual care or conventional therapy	Small sample sizes, some studies lacked control groups; methodological limitations; evidence suggests VR/video games enhance motor function and balance
DÁVILA-MORÁN, MONTENEGRO et al. 2024 (DÁVILA-MORÁN, MONTENEGRO et al.)	Systematic review	21 studies (2014–2024)	Patients requiring physical rehabilitation, including Parkinson's	Narrative synthesis; no pooled meta-analysis	Virtual reality: immersive and non-immersive VR	Not specified	Balance, gait, motor function, quality of life	Immersive VR showed greater improvements in balance and gait	Quality of life improved, especially with immersive VR	Variable across studies; not standardized	Comparator: conventional rehab or non-immersive VR	Heterogeneity in technologies and populations; immersive VR led to greater adherence; larger controlled studies needed; promising for home rehabilitation

			disease		Non-pharmacological interventions: physical exercises, balneotherapy, manual therapy, acupuncture, botanical preparations, body-psychological practices, multiprotection care								Low-to-moderate evidence; mostly favorable results; active physical activities more effective than passive; minor transient adverse events reported; need for more robust methodology and detailed reporting
Huissoud et al. 2024 (Huissoud, Boussac et al. 2024)	Systematic review	18 RCTs (2004–2021)	976 patients with Parkinson's disease	Narrative synthesis; no pooled meta-analysis		Not specified	Pain management, motor function, quality of life	Physical exercises improved motor outcomes	Pain reduction, some NPIs improved quality of life	Variable; dependent on intervention type	Comparator: usual care or other NPI		
Stickdorn et al. 2018 (Stickdorn, Marks et al. 2018)	Systematic review	3 RCTs (2005–2017)	Patients with idiopathic Parkinson's disease (Hoehn & Yahr I–IV)	Narrative synthesis; no quantitative meta-analysis	LSVT-BIG exercise intervention	Mildly to severely affected PD patients	Motor functioning	Two studies: no advantage over other exercise interventions; One study: LSVT-BIG superior with different training doses	Not specified	Training doses varied; details differ across studies	Comparator: other exercise interventions		Small number of studies; moderate methodological quality (PEDro 5–6/10); dose-response relationship unclear; more high-quality studies needed
Quan et al. 2024 (Quan,	Systematic	60	— (vario	Narrative	Virtual Reality (immersive,	Patients with	Cognitive function,	Improvement in	Cognitive function, memory, attention,	Variable — depends on	Conventional cognitive		Review introducing MD-VRCRTM model;

Liu et al. 2024)	review (PRISMA)		us neurological conditions)	synthesis (no meta-analysis)	semi-immersive; non-immersive; single & multiplayer)	neurological disorders (stroke, PD, AD, TBI, ASD)	attention, memory, motor function, social skills	motor function (especially in PD and stroke populations)	social skills, cognitive stimulation	condition and VR modality	rehab / non-immersive training	categorization of VR rehab types. No pooled effect sizes. VR shown as promising adjunct to conventional rehab; emphasis on personalization by condition. Very low certainty of evidence (GRADE). Some studies included PD. Benefits in HRQOL and function; moderate mental health effect. Adverse events: mostly mild (fatigue, pain, falls); some serious (hospitalization, pneumonia). Heterogeneity alta. Necessità di RCT di alta qualità.
Ahler et al. 2024 (Ahler, Busk et al. 2024)	Systematic review + meta-analysis (GRADE)	20 (19 RCT + 1 cohort)	1,759	Random-effects meta-analysis	Structured outdoor physical activity (nature-based exercise)	or mental diseases (including PD, OA, stroke, depression, etc.)	HRQOL, physical function, pain, mental health, adverse events	↑ Physical function (SMD = 0.39, 95% CI 0.13–0.64)	↑ HRQOL (SMD = 0.45), ↑ mental health outcomes (SMD = -0.52, favoring intervention)	Interventions varied (outdoor PA, structured sessions, duration/frequency heterogeneity studies)	No intervention, usual care, indoor PA, or outdoor without exercise	
Lozano and Pizarro 2024 (Lozano and Pizarro 2024)	Systematic review (PRISMA)	5 RCTs	327 PD patients	Narrative synthesis (no pooled meta-analysis)	Aquatic therapy	PD, no specific age/H&Y reported	Motor symptoms, functional mobility, disability	↑ Gait, posture, balance, functional mobility; ↓ bradykinesia, tremor, rigidity	Not reported	30–45 min/session; 2–5 times/week; 6–11 sessions total	Usual care or non-aquatic therapy	Focus on motor symptom improvement in PD. Small number of studies. No meta-analysis conducted. Good short-term effects, but long-term outcomes unclear.
Lee et al. 2024 (Lee, Lee et al. 2024)	Systematic review +	7	Patients with neurological	Meta-analysis (SMD,	Core-based exercises (core stability, yoga)	Stroke, PD, chorea;	Proprioception (joint position sense, kinesthesia)	↑ Joint position sense (SMD=	Not reported	Variable per study; type: core stability vs yoga	Usual care or non-core exercise	Core-based exercises improve proprioception, particularly core

	meta-analysis		disorders (stroke, PD, chorea)	Hedges' g)		age not reported		1.33), ↑ kinesthesia (SMD=-0.33); beneficial mainly in stroke					stability exercises in stroke patients. No significant effect in PD or chorea. High methodological quality; low heterogeneity (I ² mostly 0%). Yoga not effective.
Ying et al. 2024 (Ying, Sun et al. 2024)	Systematic review + meta-analysis	13 RCTs	874 PD patients	Random-effects meta-analysis (SMD)	Exercise interventions (mainly Traditional Chinese Exercise, others unspecified)	Parkinson's disease; age/H&Y not reported	Sleep quality	Not reported	↑ Sleep quality (SMD=-0.54 overall)	40–55 min/session; 4–5 times/week; 12-week intervention; light intensity; type: TCE most effective	Usual care / non-exercise	Subgroup analyses suggest best effect: light-intensity, 4–5×/week, 40–55 min/session, 12 weeks, TCE. Small-moderate effect; meta-analysis shows statistically significant improvement in sleep quality.	
Mai et al. 2024 (Mai, Lee et al. 2024)	Bayesian network meta-analysis	19 RCTs	2,372 PD patients	Network meta-analysis (SMD, 95% CrI)	Pharmacotherapy, exercise, supplements, brain stimulation	Parkinson's disease; age/H&Y not reported	Apathy (reduction in apathy scores)	Not reported	↓ Apathy (most effective: pharmacotherapy, SMD -0.43 to -0.66 vs others)	Variable per study	Placebo or usual care	Pharmacotherapy most efficacious (dopamine agonists similar efficacy to other medications). Exercise, supplements, and brain stimulation less effective. Focus on non-motor symptom: apathy.	
Hodgson et al. 2024 (Hodgson, Jordan et al. 2024)	Systematic review + meta-analysis	40 studies for review; 27 for	1,211 PD patients	Meta-regression analysis	Observational/physical assessments (no intervention)	Parkinson's disease; age/H&Y not reported	Physical function (mobility, balance), psychological	↓ Mobility (TUG), ↓ Balance (BBS) moderated	↑ Depression, anxiety; depression worsens motor outcomes	Not applicable	Observational/standard assessments	Symptoms of depression significantly modulate mobility and balance. Only one study	

	regression	meta-regression				Y not reported	symptoms (depression, anxiety)	by depression severity				examined direct physical-psychological relationships. Highlights interaction between motor and non-motor symptoms in PD. Useful for understanding holistic patient management.
Sánchez-Lozano, 2024 (Lozano and Pizarro 2024)	Systematic review (PRISMA, GRADE)	6 RCTs	165 PD patients	Narrative synthesis	Hydrotherapy / water-based therapy	Mild-moderate PD; age not reported	Balance, mobility, gait, functional capacity, pain, disability	↑ Balance, ↑ mobility, ↑ gait, ↑ functional capacity	↓ Pain, ↓ disability	40–60 min/session; 2–3×/week; 6–12 weeks total	Usual care / non-water therapy	Safe and well tolerated; all studies showed improvements in motor outcomes; small sample size; early-stage PD.
Donida et al. 2023 (Donida, dos Santos Delabary et al. 2023)	Systematic review + meta-analysis	3 RCTs	126 PD patients	Meta-analysis	Dance interventions (Tango, Irish dance)	Parkinson's disease; age/H&Y not reported	Balance (dynamic and static)	↑ Dynamic balance (Tango); no effect (Irish dance)	Not reported	Variable per study; Tango classes (frequency/intensity not specified)	Non-intervention or other physical training	Tango improves dynamic balance in PD; Irish dance did not show significant effect. Small sample; heterogeneity due to dance type. Relevant for motor outcomes (balance).
Dincher 2023 (Dincher 2023)	Systematic review + meta-analysis	16 studies (3 excluded from qualitative analysis)	PD patients; not specified	Meta-analysis (SMD, 95% CI)	Whole Body Vibration (single vs multiple sessions)	Parkinson's disease; age/H&Y not reported	Motor and functional outcomes	Mixed effects; some parameters improved, some no effect	Not clearly reported	Variable per study; frequencies, session durations differ	Control groups varied or absent	Effects heterogeneous; no clear conclusion on optimal frequency/duration; need for further studies. Relevant for motor outcomes and rehabilitation planning.

Tao et al. 2024 (Tao, Shao et al. 2024)	Systematic review	Not specified	PD patients; sample sizes vary	Narrative synthesis (no pooled effect sizes reported)	Exercise interventions (Tai Ji, balance training, progressive resistance, cognitive gait dual task)	Mild-moderate Parkinson's; age/H&Y not reported	Fall incidence, balance	↓ Falls with Tai Ji; improved balance with Tai Ji and balance training	Not reported	Variable by intervention type; Tai Ji, balance and dual-task training frequency/intensity not consistently reported	Usual care or non-intervention	Tai Ji most effective in reducing falls; progressive resistance less effective; cognitive gait dual-task promising; heterogeneity across studies; relevant for motor outcomes (fall prevention).
De Vitis et al. 2023 (De Vitis, Battaglino et al. 2023)	Literature review	6 studies	Independent PD patients (n not pooled)	Narrative synthesis	Telemedicine / telerehabilitation	Mild-moderate PD; independent; age not reported	Postural stability	Improved balance, mobility, functional rehabilitation	Not reported	Home-based, technologically assisted; session frequency/intensity variable	Usual care or non-intervention	≥50% of studies positive
Aldana-Benítez et al. 2023 (Aldana-Benitez, Caicedo-Pareja et al. 2023)	Systematic review	25 clinical trials	Neurological disorders, PD n=61	Narrative synthesis	Dance / rhythmic auditory stimulation	PD participants: age 66–68; men & women	Motor function, balance, gait, mental functions, disease impact, ADLs	Improved gait, balance, mobility	Cognitive flexibility, processing speed, social support, HRQoL	60 min/session, 10 weeks; tango; comparisons: waltz, foxtrot, Tai chi, no intervention	Other dance styles / Tai chi / no intervention	Tango improved mobility, social support, PDQ-39 SI; other interventions mostly non-significant
Xue et al. 2023 (Xue, Yang et al. 2023)	Systematic review and meta-analysis	14 RCTs	572 PD patients	Meta-analysis	Robot-assisted gait training (RAGT)	PD patients, mild-moderate (H&Y not specified)	Motor function, balance	10MWT, 6MWT, TUG, UPDRS III improved	–	Intervention specifics vary per study; session frequency/duration not specified	Conventional gait training	RAGT significantly improved motor and balance outcomes vs control

Corrales Gómez et al. 2023 (Corrales Gómez, Torres Naranjo et al. 2023)	Systematic review	16 studies	PD patients (sample not pooled)	Narrative synthesis	Exercise / Physical activity (physiotherapy, boxing, Tai Chi, aquatherapy, other trainings) Physical therapy (hydrotherapy, PT exercises, gait training with body weight support, electroacupuncture, massage)	PD patients, mild-moderate (H&Y not specified)	Quality of life, motor and cognitive symptoms	Motor improvements reported	Cognitive and mental well-being, QoL	Intervention durations 6–12 weeks; intensity varied per study	Usual care or non-intervention	Exercise generally improved QoL and motor/cognitive outcomes
Henemann et al. 2023 (Henemann, Truchem et al. 2023)	Systematic review	9 clinical trials	242 PD patients	Narrative synthesis		PD patients, H&Y 1–4	Pain levels, functional improvements	Some improvement in gait and mobility reported	Pain reduction, improved comfort	Duration varied per study; 1–12 weeks typical; frequency/intensity varied	Usual care or non-intervention	All PT modalities showed positive effects on pain
Le Sant et al. 2023 (Le Sant, Lecharte et al. 2023)	Systematic review + meta-analyses	10 RCTs	Adults with neurological conditions (including PD)	Meta-analyses for strength/power; narrative for others	Eccentric resistance training	Neurological patients (PD, stroke, MS); adults	Strength, power, motor capacities, balance, fatigue, fall risk, QoL	Significant improvements in strength and power; mixed effects on motor capacities	Mixed effects on balance, fatigue, QoL	Varied per study; interventions followed ACSM ET guidelines	Conventional rehab or no intervention	Evidence mainly supports strength/power improvements
Pedro et al. 2023 (Pedro, de Oliveira et al. 2023)	Systematic review	7 RCTs	206 PD patients	Qualitative + SMD/MD	MOTomed® movement therapy	PD patients (moderate)	Motor function, MDS-UPDRS, gait, tremor, balance, PDQ-8	Significant improvements in MDS-UPDRS III,	PDQ-8 (QoL, depression), balance (CTSIB1)	High-cadence cycling, 1 session to multiple, varied	Standard rehab or no intervention	Studies moderate quality; measured multiple motor outcomes

Study		Study design		Study population		Intervention		Comparison		Outcomes		Quality of evidence	
Author(s)	Year	Design	Participants	Intervention	Comparison	Primary	Secondary	Primary	Secondary	Primary	Secondary		
Cardoso et al. 2022 (Cardoso, Sa-Caputo et al. 2022)	2022	Systematic review (animal studies)	20 experimental studies	Rats (75%), mice (20%), pigs 5%	Qualitative	Whole-body vibration exercise	Male 16 studies, female 4 studies	Motor function, coordination, behavioral control, neuronal plasticity, synapse function	Improved motor performance and coordination	Behavioral control, neuronal plasticity, synapse function	Varied WBV protocols (heterogeneous); exact frequencies/durations differ across studies	Standard conditions / no intervention	SYRCLE Risk of Bias tool: none fulfilled all methodological criteria
Wang et al. 2022 (Wang, Sun et al. 2022)	2022	Systematic review & network meta-analysis	62 RCTs	3,050 participants	Network meta-analysis	Non-pharmacological interventions (35 types, including dance, LSVT-BIG, CBT, Tai Chi, yoga, VR, bright light therapy)	Adults with Parkinson's, varied H&Y stages	Depression (primary), quality of life	Some interventions (LSVT-BIG, dance) may improve motor indirectly	Depression, mood, QoL	Varied by intervention (sessions/frequency heterogeneous)	Standard care / waitlist / usual treatment	Dance ranked highest (SUCRA 82.3%), followed by LSVT-BIG (77.4%) and CBT (73.6%)
Hao et al. 2022 (Hao, Zhang et al. 2022)	2022	Systematic review & network meta-analysis	60 RCTs	2,859 participants	Network meta-analysis	10 exercise interventions: dance, yoga, resistance training, aquatic	Adults with PD, varied H&Y stages	Motor function (BBS, UPDRS, TUG)	Dance improved BBS (SUCRA 78.4%), UPDRS	Not primary focus	Varied by intervention; RCTs heterogeneous	Standard care / usual treatment	Dance, yoga, VR, resistance training ranked highest for motor outcomes

	meta-analysis				training, Taiji Qigong, treadmill, virtual reality, walking, cycling, Baduanjin Qigong			(SUCRA 72.3%); Yoga improved TUG (SUCRA 78%)				
Sklivas et al. 2022 (Sklivas, Robinson et al. 2022)	Systematic review & meta-analysis	14 RCTs	Adults with frailty, chronic or acute disease	Meta-analysis	Power training (high-velocity concentric movements)	Age >18, prefrail/frail or chronic disease; mixed populations	Physical function (e.g., mobility, SPPB, TUG)	Improved physical function vs control (ES 0.41); similar to conventional resistance training (ES 0.10)	Not primary focus	Varied; high-velocity, lower work per session	Conventional resistance training or control activities	Power training effective, especially for functional improvements with less work per session
Wang et al. 2022 (Wang, Zhang et al. 2022)	Systematic review & meta-analysis	40 RCTs	2,754 participants	Meta-analysis	Tai Chi / Qigong	Neurological disorders: PD, stroke, MCI, dementia, TBI	Cognition: global cognitive function, executive function, memory, visuospatial ability, cognitive processing speed	Some motor improvements reported, not primary	Improved cognitive outcomes (P<0.05)	Varied by study; standardized tai chi/Qigong programs	Active or non-active control	Effective for cognition across multiple neurological disorders; no RCTs for other neurological diseases
Liu et al. 2022 (Liu, Tung et al. 2022)	Systematic review	45 studies	Not specified	Narrative synthesis	Fall prevention & management interventions	Patients with Parkinson's disease	Falls, fear of falling	Balance, gait, fall incidence	Fear of falling, cognition	Varied by study; multifactorial interventions	Standard care or no intervention	Constructed a fall prevention model based on physical, cognitive, environmental, and medical factors

Palheta de Lima et al. 2022 (de Lima, da Silva et al. 2022)	Systematic review	10 studies	556 participants	Narrative synthesis	Resistance training	Older adults with Parkinson's disease	Balance, postural control, strength, quality of life	BESTest, FOG-Q, MDS-UPDRS motor scores	Quality of life	30–45 min/session, 8–12 weeks	Standard care or no intervention	Most interventions were 8–12 weeks; majority of measures focused on motor and balance outcomes
Barclay et al. 2022 (Barclay, Gray et al. 2022)	Systematic review	12 studies	423 participants (52% male)	Narrative with some meta-analysis	Lower limb active passive trainer cycling (with/without FES)	Neurological conditions: stroke, MS, SCI, Parkinson's disease	Spasticity, cardiovascular fitness, walking, QoL	6-Minute Walk Test (stroke studies), spasticity measures	Quality of life (1 study), cardiovascular fitness	Heterogeneous; intervention details varied; some with FES	Standard care or no intervention	Most studies heterogeneous in design, outcomes, and populations
Cabeleira et al. 2022 (Cabeleira, da Campo et al. 2022)	Systematic review & meta-analysis	4 RCTs	Not specified	Meta-analysis	Home-based exercises with minimal oversight (HBEMO)	Parkinson's disease	Motor function, quality of life	UPDRS-III	PDQ-39	Heterogeneous; minimal supervision	Conventional therapies / usual care	Small number of studies
Wells and Yang 2021 (Wells and Yang 2021)	Systematic review	12 studies	Not specified (various neurological/medical conditions)	Narrative (no meta-analysis)	Ballroom dance	PD, MS, SCI, stroke, dementia, cancer, diabetes	Motor function, gait, balance, quality of life	Gait, balance	QoL	Variable; combination of smooth & rhythm dances	Not always specified	Safe, low attrition (7.7%)
He et al. 2020 (He, Su et al. 2020)	Systematic review	7 RCTs	196 PD patients	Quantitative meta-analysis	Whole-body vibration (WBV)	PD, age not specified, H&Y	Motor function, balance, walking	UPDRS-III, TUG, functional reach,	None reported	Not consistently reported	No vibration or conventional PT	WBV not superior to control for most outcomes; small benefit

	& meta-analysis					not specified		Berg Balance, Tinetti				on sit-to-stand / turning
de Oliveira et al. 2021 (de Oliveira, Mendes et al. 2021)	Systematic review	38 studies	Not specified (total 169 initially identified)	Narrative synthesis	Serious games / exergames	PD patients; age not consistently reported; H&Y not consistently reported CNS disorders (MS, PD, stroke, dementia, epilepsy, brain tumor); age not consistently reported; H&Y for PD not consistently reported	Motor symptoms (bradykinesia, gait), usability, adherence	Gait, bradykinesia, balance	Not consistently reported	Variable; protocols depended on study	Not always reported	Mostly VR-based; devices: Leap Motion, Kinect; therapist involvement common
Lenoir dit Caron et al. 2021 (Lenoir Dit Caron, Coquart et al. 2021)	Systematic review	16 studies	Not consistently reported; subset for PD = 5	Narrative synthesis	Yoga		Health-related quality of life (HRQoL)	Not consistently reported	HRQoL questionnaires	Variable; dependent on study; not always reported	No intervention, usual care, or active control	Evidence quality: low–moderate; heterogeneous questionnaires limit comparability

Ismail et al. 2021 (Ismail, Lee et al. 2021)	Systematic review + meta-analysis	20 RCTs	723 participants	Quantitative syntheses (RevMan)	Dance (Tango, Ballroom, Irish, Waltz-Foxtrot, Folk, Turo, mixed, PD-tailored)	PD; age not consistently reported; H&Y not always reported	Disease severity, balance, gait, agility, cognition, mood, QoL, adverse events	Improved motor severity (MDS-UPDRS III) MD -6.01; balance (MiniBest Test) MD 4.47; no consistent gait/agility improvements Dynamic balance: improved BBS score (SMD 0.52, 95% CI 0.31–0.73); TUG: no significant difference (SMD -0.26, 95% CI -0.62–0.1)	Cognition, mood, QoL: inconsistent/no clear improvement	Variable across studies; not consistently reported	Standard care / other physical therapy	Small samples, methodological limitations; heterogeneity
Wang et al. 2021 (Wang, Wong et al. 2021)	Systematic review + meta-analysis	15 RCTs	Not consistently reported	Quantitative syntheses (meta-analysis)	Virtual reality (VR) rehabilitation	PD; age not always reported; H&Y not always reported	Balance (dynamic and static), balance confidence, quality of life	Balance confidence, quality of life: improved	Balance confidence, quality of life: improved	Variable across studies; not consistently reported	Traditional exercise / standard care	Risk of bias assessed via Cochrane Handbook; PEDro scale used
Oh and Lee 2021 (Oh and Lee 2021)	Systematic review + meta-analysis	8	Not consistently reported	Quantitative syntheses	Aquatic exercise	Neurological disorders (Parkinson's,	Balance, gait, pain, physical function, quality of life	Improved balance and gait	QOL (physical health, mental health, vitality) improved; pain decreased	Variable across studies; not consistently reported	Standard care / usual therapy	PEDro scale used for quality assessment

						MS, cerebral palsy, hemiplegia, fibromyalgia); age not consistently reported						
Molina Palomino et al. 2021 (Molina Palomino, López López et al. 2021)	Systematic review	10	Not consistently reported; mixed PD	Qualitative syntheses	High-speed cycling, endurance exercise	Mild-moderate PD	Bradykinesia	Improved bradykinesia in most studies; high-speed cycling showed effects in 1–5 weeks, endurance exercise from 9 weeks	Not assessed	High-speed cycling: 1–5 weeks; Endurance exercise: 9 weeks–24 months; intensity high for cycling, variable for endurance	Standard care / usual therapy	PEDro scale used for quality assessment
Cugusi et al. 2021 (Cugusi, Prosperini et al. 2021)	Systematic review and meta-analysis	34 trials	1594	Meta-analysis	Exergaming	Chronic diseases (including neurological disorders, rheumatologic,	HRQoL	Not primary focus	Improved HRQoL (small effect size SMD 0.24; neurological disorders SMD 0.22)	Variable across studies; health care setting interventions more effective; home-based	Standard care / usual therapy	PEDro scale for risk of bias; GRADE used

						cardiorespirator y, metabolic; PD included)				interventions less effective		
Magdi et al. 2021 (Magdi, Sayed Ahmed et al. 2021)	Systematic review and meta- analysis	8 RCTs	239	Meta- analysis	Cueing techniques (auditory, visual, proprioceptive)	Parkinson's Disease	Gait, gait-related mobility, functional activities, freezing of gait	Gait: medium effect (non- cueing techniques showed more improvement); Functional activities: significant improvement	Balance: small, non-significant improvement	Variable across studies; not specified	Non-cueing or usual therapy	Freezing of gait not quantitatively analyzed; combination with other treatments may enhance gait outcomes
Huang et al. 2021 (Huang, Wang et al. 2021)	Systematic review	139 RCTs	Varied across studies	None (systematic review only)	Tai Chi	Diseased and healthy populations; including PD, musculoskeletal, circulatory, nervous	Motor function, balance, quality of life, disease- specific outcomes	Improvement in balance, mobility, physical function in multiple populations	HRQoL, mental health, disease- specific symptoms	Most common: 12– 24 weeks, 2–3 times/week, 60 min/session, moderate intensity, Yang style 24- form	Usual care or no intervention	Evidence summarized for exercise prescription principles; large heterogeneity

Systematic review											
Author(s)	Study type	Number of studies	Number of participants	Quality of evidence	Intervention	Comparison	Outcomes	Effect size	Duration	Control groups	Notes
da Costa et al. 2020 (da Costa Daniele, de Bruin et al. 2020)	Systematic review	11	925 (545 intervention, 380 control)	None (systematic review only)	Physical exercise (strength, balance, mixed)	Parkinson's disease	Balance, motor symptoms	Improved UPDRS-III, PDQ-39; strength training/balance most effective	Not reported	≥8 weeks; type varied; strength and balance emphasized	Positive effect on motor symptoms and balance; strength/balance modalities highlighted
Hidalgo-Agudo et al. 2020 (Hidalgo-Agudo, Lucena-Anton et al. 2020)	Systematic review & meta-analysis	11 (5 in meta-analysis)	Not specified (from included RCTs)	Meta-analysis for selected outcomes	Dance-based therapy, aquatic therapy	Parkinson's disease	Balance, gait, functional outcomes	Dance improved TUG (SMD = -1.16), BBS (SMD = 4.05); aquatic improved ABC scale (SMD = 10.10)	Not reported	Not consistently specified	Highlights benefit of dance-based therapy on functional balance; aquatic interventions on balance confidence
Wu et al. 2020 (Wu and Ye 2020)	Systematic review	11 studies	1–76 per study	Narrative synthesis	Exergaming (Wii, Xbox)	Parkinson's disease	Balance, gait, postural instability, fatigue	Improved balance, gait, postural stability	Reduced fatigue	20–60 min, 1–3x/week, 6–12 weeks	Exergaming recommended as postural stability treatment; variation in study designs
Toneti, et al. 2020 (Toneti, Barbosa et al. 2020)	Systematic review	28 studies	Adults and elderly	Narrative synthesis	Qigong (integrative, complementary practice)	Adults and elderly; including Parkinson's,	Balance, mobility, fatigue, pain, depression, QoL	Improved balance in PD and other conditions	Reduced fatigue, pain, depression; improved QoL	Medium- to long-term interventions; details vary by study	High risk of bias in blinding reported

						cancer, COPD, fibromyalgia, etc.						
Bluett et al. 2019 (Bluett, Bayram et al. 2019)	Systematic review	12 studies	Not specified (VR studies on PD-FOG) Adults with neurological gait/balance impairments (stroke, PD, MS, HAM/TSP) Older adults; neurological patients (TBI, MS, PSP)	Narrative synthesis	Virtual reality (VR) paradigms	Parkinson's patients with freezing of gait	Freezing of gait episodes, cortical-subcortical connectivity	Reproduction of FOG in VR; insight into gait deficits	Dysfunctional brain connectivity during FOG	VR paradigms varied; some MRI-compatible	Not specified	VR used to safely study FOG pathophysiology
Libório et al. 2019 (Libório, de Oliveira Santana et al. 2019)	Systematic review with meta-analysis	Clinical trials on home-based exercise (HBE)	Older adults; neurological patients (stroke, PD, MS, HAM/TSP) Older adults; neurological patients (TBI, MS, PSP)	Meta-analysis (weighted mean differences)	Home-based exercise programs	Stroke, Parkinson's disease, Multiple sclerosis, HAM/TSP	Walking activity, balance, mobility, functionality	Gait speed, walking distance, balance	Functional independence, cardiorespiratory capacity	6–12 weeks; variable frequency/intensity depending on study	Control groups as per primary studies	HBE effective on walking, mobility, performance; PEDro scale for quality; suggested WHODAS use
Bevilacqua et al. 2019 (Bevilacqua, Maranesi et al. 2019)	Systematic review	10 RCTs (8 RCTs, 2 other designs)	Older adults; neurological patients (TBI, MS, PSP)	Narrative synthesis	Non-immersive virtual reality	Stroke, MS, PSP, TBI, geriatric populations	Motor and cognitive rehabilitation	Motor abilities, gait, balance	Cognitive abilities, emotional state, compliance	Variable depending on study; typically short-term sessions	Control groups as per primary studies	PEDro scores 4–9; clinical heterogeneity

Chiong et al. 2019 (Chiong, Patel et al. 2019)	Systematic review	Recent clinical trials (past 5 years, human studies)	PD patients (older adults, 45+ yrs)	Narrative synthesis	Physical exercise: aquatherapy, resistance training	Parkinson's disease	Motor symptoms (gait, balance)	Gait, balance, postural control	QoL, functional mobility	Variable depending on study; typically moderate-intensity sessions	Control groups as per primary studies	Focus on recent exercise interventions for motor improvement
Ramírez-Nieto et al. 2018 (Ramírez-Nieto, Ortiz-Gutiérrez et al. 2018)	Systematic review	12 articles + 2 posters	276 PD patients	Narrative synthesis	Commercial video games	Parkinson's disease	Balance, gait	Step length, cadence, walking speed, postural control	QoL	Variable across studies; typically short interventions	Conventional therapy or other interventions	Evidence suggests benefits in balance and gait, but not superior to conventional therapy
Mooventhana and Nivethitha 2017 (Mooventhana and Nivethitha 2017)	Systematic review	94 studies	Variable across studies	Narrative synthesis	Yoga	Neurological disorders (MS, stroke, epilepsy, PD, dementia, cerebrovascular, neuropathy, myelopathy, Guillain-Barre)	Motor and non-motor outcomes depending on disorder	Gait, balance, strength, coordination (varies)	Cognition, QoL, psychological well-being, fatigue, depression	Variable across studies; heterogeneous protocols	Usual care or no intervention	Yoga appears beneficial as adjuvant therapy for neurological disorders
Skórkowska-Telichowska et al. 2016 (Skórkowska)	Systematic review	27 analyzed studies	Older adults, mean age	Narrative synthesis	Nordic walking	Elderly adults, including early	Physical fitness, exercise capacity,	Endurance, gait, walking	Depression, quality of life	Variable across studies; protocols	Standard care, usual physical activity	Nordic walking safe and effective for older adults; potential

- Telichowska, Kropielnicka et al. 2016)		(from 74 identified)	~65 years			PD, cardiovascular, COPD, metabolic syndrome Elderly adults; included some with chronic diseases such as PD, stroke, T2DM, hypertension	mobility, depression	performance		heterogeneous		adjuvant therapy for early PD
Tan and Wu 2017 (Tan and Wu 2017)	Systematic review	Literature search 1998– 2015; no clear # of included studies	Older adults >60 years	Narrative syntheses	Whole body vibration (WBV)		Low extremity function, balance, walking ability, muscle strength, chronic disease indices	Muscle strength, balance, walking ability, neuromuscular function	Muscle stiffness, amyostasia, some disease indices	Variable; protocols heterogeneous	Standard therapy / usual care	WBV is safe and feasible; improves strength, balance, mobility
Aguiar et al. 2016 (Aguiar, da Rocha et al. 2016)	Systematic review	7 studies (RCTs, quasi- RCTs, case series)	People with mild to moderate PD	Narrative syntheses	Therapeutic dance	PD patients	Walking, freezing of gait, quality of life, feasibility, safety	Walking, freezing of gait, mobility	Quality of life, feasibility, safety	Variable; heterogeneous protocols across studies	Standard care / non- dance interventions	Dance therapy is feasible and safe
McNeely et al. 2015 (McNeely, Duncan et al. 2015)	Systematic review	Not specified (literature review)	Older adults and people with PD	Narrative syntheses	Dance interventions	Older adults, PD patients	Balance, gait, physical function, cardiovascular health, muscle strength, body composition,	Balance, gait, endurance , muscle strength	Cardiovascular health, body composition, flexibility, proprioception	Variable; heterogeneous protocols across studies	Standard care / non- dance interventions	Dance shows wide- ranging benefits, but standardized outcome measures lacking

		of dance studies)					flexibility, proprioception					
Soares et al. 2014 (Soares, Dos Viana Santos et al. 2014)	Systematic review	10 studies	Patients with neurological disorders (stroke, PD, cerebral palsy)	Narrative synthesis	Wii-based rehabilitation	Stroke, Parkinson's disease, cerebral palsy	Motor impairments, functional outcomes	Balance, gait, motor performance	Not specified	Variable; heterogeneous protocols (games, duration, frequency)	Standard physiotherapy / no intervention	Wii rehabilitation effective for motor improvement
Ayán Pérez and Cancela 2014 (Ayán Pérez and Cancela 2014)	Systematic review	12 studies	Patients with Parkinson's disease	Narrative synthesis	Water-based exercise	Parkinson's disease	Motor symptoms, functional mobility, quality of life	Gait, balance, functional mobility	Quality of life	Heterogeneous protocols; short-term interventions	Conventional physiotherapy or no intervention	Only 3 studies scored >10/15 on methodological quality
Zhou et al. 2015 (Zhou, Yin et al. 2015)	Systematic review & meta-analysis	9 studies	Patients with Parkinson's disease	Meta-analysis (random-effects)	Tai Chi	Parkinson's disease	Motor function, balance, gait, quality of life	Motor function improved (P=0.002); balance improved (P<0.00001); no significant change in gait velocity or stride length	Quality of life not significantly improved	Protocols heterogeneous; follow-up data insufficient	Conventional physiotherapy or no intervention	PEDro scores varied; methodological flaws noted

Aman et al. 2015 (Aman, Elangovan et al. 2014)	Systematic review	51 studies	Various neurological and musculoskeletal conditions (mostly post-stroke; some Parkinson's, dystonia)	Narrative synthesis	Proprioceptive training	Mixed neurological and musculoskeletal patients	Proprioceptive function, sensorimotor outcomes	Motor function improved; joint position sense up to 109%; muscle vibration training up to 60% improvement	Somatosensory function	Protocols heterogeneous; both passive & active movements; with/without visual feedback; vibration >30 Hz beneficial	Standard therapy or no intervention	Training consistently improved joint position sense and sensorimotor function
O'Connor and Kini 2011 (O'Connor and Kini 2011)	Systematic review	N/A (primary studies up to Nov 2010)	Humans with tremor (various neurological conditions including Parkinson's)	Narrative synthesis	Non-pharmacological, non-surgical interventions	Tremor patients	Tremor severity, functional activities	Tremor reduced with neuromuscular physiotherapy, strength training, functional electrical stimulation; mixed results for orthoses, vibration therapy	Functional improvements in ADLs	Heterogeneous protocols; limb cooling task-specific; orthoses and vibration need further evaluation	Standard therapy or no intervention	Evidence base is limited; many interventions promising but not yet robustly tested

Kiepe et al. 2012 (Kiepe, Stöckigt et al. 2012)	Systematic review	11 RCTs	Adults with various physical and mental illnesses (breast cancer, dementia, PD, heart failure, type 2 diabetes, depression, fibromyalgia)	Narrative synthesis	Dance therapy / Ballroom dance	PD, breast cancer, depression, diabetes, heart failure, dementia, fibromyalgia	Quality of life, balance, coordination, ROM, psychological distress	Improved balance and coordination in PD; improved shoulder ROM in breast cancer	Reduced psychological distress in depression; improved QoL in breast cancer, heart failure	Varied interventions across studies; generally short-term programs, specifics heterogeneous	Standard care / other interventions	Small sample sizes; mostly US and Scandinavian studies
Du et al. 2025 (Du, Wei et al. 2025)	Systematic review & meta-analysis	21 RCTs	1051 participants	Random-effects meta-analysis	VR-based interventions (cognitive rehab, exergames, telerehabilitation, music attention, immersive cognitive	Neuropsychiatric disorders (schizophrenia, MCI, PD, brain	Cognitive function	Not primary	Cognitive outcomes: memory, attention, problem-solving, social functioning	Varied by study; mostly multiple sessions over weeks	Standard care / sham interventions	Subgroup analysis: cognitive rehab, exergame, telerehab effective; others not

					training, vocational/problem-solving)	injuries, stroke)						
Crizzle and Newhouse 2006 (Crizzle and Newhouse 2006)	Systematic review	7 studies	Patients with Parkinson's disease	Narrative syntheses	Physical / therapeutic exercise	Parkinson's disease	Mortality, strength, balance, mobility, ADL	Axial rotation, functional reach, flexibility, balance, muscle strength, short-step gait, mobility	ADL	Varied by study; not standardized; short- and medium-term interventions	Standard care / usual activity	Included RCTs (3), open trial (1), self-assessment (3)
Keus et al. 2007 (Keus, Bloem et al. 2007)	Evidence-based review	6 systematic reviews, 23 RCTs	Patients with Parkinson's disease	Narrative syntheses	Physical therapy	Parkinson's disease	Transfers, posture, reaching & grasping, balance, gait, physical capacity	Gait, balance, transfers, joint mobility, muscle power	Not specified	Varied; moderate methodological quality; treatment recommendations based on ≥2 controlled trials	Standard care / usual activity	Identified 6 core areas of physical therapy; 4 evidence-based treatment recommendations
Luna et al. 2025 (Luna, Pardo-Cocuy et al. 2025)	Systematic review & meta-analysis	6 SRs, 5 in meta-analysis	Patients with Parkinson's disease	Meta-analysis of RCTs	LSVT®BIG	Parkinson's disease	Motor function, gait, quality of life	Walking speed (10-MWT), UPDRS-III, motor function	QoL (PDQ-39)	Varied per study; moderate intensity LSVT®BIG program	General exercise / usual care	Comprehensive search up to Oct 2024; Cochrane RoB and GRADE applied
Lheureux et al. 2025 (Lheureux, Lejeune et al. 2025)	Systematic review & meta-analysis	28 RCTs	1151 participants, H&Y 1.4–3.4	Meta-analysis	Virtual reality (VR), exergaming	Parkinson's disease	Balance, mobility	Balance (SMD 0.42 vs CT), mobility (SMD 0.18 vs CT)	–	Mean treatment 18.8 h qualitative, 23 h quantitative	Conventional therapy (CT)	VR more effective than CT for balance; mobility similar; specific vs non-specific VR no difference

Barnish et al. 2025 (Barnish, Reynolds et al. 2025)	Systematic review & meta-analysis	94 studies	2453 participants, mean age 68, 55% male, 18 countries	Meta-analysis + narrative synthesis	Active group-based performing arts (dance, singing, tango)	Parkinson's disease	Motor function, QoL, speech, cognitive status	Dance improved motor function (50/54 studies), tango UPDRS-III MD -9.89	Dance QoL PDQ-39 MD -7.81, singing improved speech	Not specified	Usual care or other comparators	Evidence supports benefit for certain performing arts; limitations include heterogeneity, comparator differences, male underrepresentation
De Natale et al. 2025 (De Natale, Qorri et al. 2025)	Systematic review & meta-analysis	11 RCTs	67.3, 67.95 % male	Random-effects meta-analysis	Virtual Reality (immersive and non-immersive)	Parkinson's disease	Balance, mobility	BBS improved (SMD 0.58, 95% CI 0.07–1.09, p=0.03), 6MWT not significant	–	Not consistently reported	Conventional therapy	Substantial heterogeneity for BBS (I ² =77%); moderate for 6MWT (I ² =41%)
Duñabeitia et al. 2025 (Dunabeitia, Gonzalez-Devesa et al. 2025)	Systematic review of RCTs	12 RCTs	Not specified	Narrative synthesis	Stretching	Parkinson's disease	Motor symptoms, functional mobility, balance, gait, strength, cardiorespiratory fitness, mental health, neurocognitive function, sleep quality, fatigue	Motor symptoms and functional mobility improved; less pronounced than Tai Chi or WuQinXi Qigong	Limited to no improvements	4 weeks – 6 months	Not specified	Benefits smaller than other exercise interventions
Kim et al. 2025 (Kim, Kang et al. 2025)	Systematic review	28 RCTs	Not specified	Meta-analysis	Aerobic exercise / Aerobic-based	Parkinson's disease	Motor function	Aerobic-based combined exercise >	Not assessed	<60 vs. ≥60 min per session; <4 vs. ≥4	Not specified	Moderator analyses performed

	& meta-analysis				combined exercise			aerobic alone; ≥60 min/session more effective; frequency, period, intensity not significant	sessions/week ; <12 vs. ≥12 weeks; low-to-moderate vs. moderate-to-high intensity			
Alcantara Garcia Meliani et al. 2025 (Meliani, Lima et al. 2025)	Systematic review & meta-analysis	7 RCTs	Not specified	Meta-analysis	Dance & Yoga	Parkinson's disease	Anxiety, depressive symptoms, cognition, self-esteem, fecal and urinary incontinence	Not primary focus	Anxiety (Yoga effective), depressive symptoms (both beneficial), cognition (Dance positive effect)	Not specified	Not specified	High heterogeneity ($I^2 = 75\text{--}97\%$)
Li et al. 2025 (Li, Huang et al. 2025)	Systematic review & network meta-analysis	68 RCTs	3,114	Network meta-analysis	Various exercise types (DE, WE, HE, OE, TR, FAE, RAGT, etc.)	Parkinson's disease	Gait performance (velocity, step length, 6MWT)	Significant improvements in gait speed and step length; DE best for gait velocity & step length; FAE & RAGT best for 6MWT	Not assessed	Not consistently specified	CON (control) and other exercise types	29 exercise interventions compared
Lou et al. 2025 (Lou, Xiang et al. 2025)	Systematic review	18 studies (16 in meta-	963	Meta-analysis	Tai Chi	Parkinson's disease	Balance, mobility, gait (speed,	Balance: improved; Mobility: improved;	Not assessed	4–16 weeks (varied), frequency not	Conventional medication or other exercises	Compared to conventional medication and other exercises; some

	& meta-analysis	analysis)				endurance, amplitude)	Gait speed: improved; Gait endurance /amplitude: no significant improvement Multi-modal & sensory-motor: more balance components; Exergaming: intensity well-reported	specified in abstract	outcomes superior to other exercises		
Wallin et al. 2025 (Wallin, Franzén et al. 2025)	Systematic mapping review	114 studies (126 interventions)	5335	Mapping review	Balance training (exergaming, multi-modal, sensory-motor, task-oriented)	Parkinson's disease	Balance control, training components	Dual-task cognitive-motor aspects included in some interventions	FITT-VP principles extracted; intensity strategies better reported in exergaming	Categorized balance components (motor, sensory, cognitive); intensity strategies varied by intervention type	
de Almeida et al. 2025 (de Almeida, Tavares Sobreira et al. 2025)	Systematic review & meta-analysis	4 RCTs	Not specified (small sample)	Meta-analysis	Power training	Parkinson's disease	Physical functional performance	TUG, PWS, FWS, SLS, BBA	Intervention details varied; intensity/volume possibly suboptimal	Control or other PA interventions	No significant improvements vs control or alternative PA
Wang et al. 2025 (Wang, Yuan et al. 2025)	Systematic review & network	81 RCTs	4596	Network meta-analysis	12 exercise types (dance, aerobic, resistance, BWS, sensory, etc.)	Parkinson's disease	Motor symptoms	UPDRS-III (overall motor)	Dose-response: optimal 1300 MET-min/week; dance most	Usual care or other exercises	MI changes achieved at 670 MET-min/week overall; lower for specific types

	meta-analysis										effective at 850 MET-min/week; improvements also at 60–100 MET-min/week for specific exercises		
Palm et al. 2025 (Palm, Swarowsky et al. 2025)	Systematic review and meta-analysis	13 RCTs	Not reported (all adult PD patients) Animal models (MPTP, 6-OHDA, PFF- α -synuclein); not specified; age not specified; gender not specified	Standard meta-analysis	Group exercise (GE)	Adults with PD	Quality of life (QoL)	Not reported	QoL		Not standardized across studies; total volume varied	Individual exercise (IE), Usual care (UC)	GE showed similar effect as IE, but small statistically significant improvement vs UC; evidence quality low to moderate.
Ishaq et al. 2024 (Ishaq, Shah et al. 2024)	Systematic review	16 preclinical studies		Systematic review	Exercise training (various regimens)	Animal models of PD	Nigrostriatal neuroprotection, motor function	Improved motor function in PD animal models		Molecular markers: α -synuclein aggregation, TLR/MyD88/I κ B α /NF- κ B pathway, pro- and anti-inflammatory cytokines, BAX/Bcl-2 ratio, caspase proteins, BDNF/GDNF, TH, DAT, PSD-95, synaptophysin	5 days/week for 6.5 weeks	PD animal models without exercise	Neuroprotective effects mediated via anti-inflammatory, anti-apoptotic, neurotrophic, and dopaminergic signaling pathways; CAMARADES checklist scores 4–6/10; registered in PROSPERO (CRD42024484537)

Tan et al. 2025 (Tan, Pan et al. 2025)	Systematic review and meta-analysis	18 RCTs	Not specified; age not specified; gender not specified	Meta-analysis of RCTs	Traditional Chinese exercises (TCEs)	PD patients	Neuropsychiatric symptoms (NPSs), cognition, quality of life	Not specifically reported	Improved depression, anxiety, sleep quality, cognition, and quality of life; no significant effect on fatigue	Interventions up to 12 weeks showed greater anti-depression/anxiety effects; >12 weeks improved sleep and cognition	Standard care or conventional medications; TCEs alone or combined with medications	Some methodological limitations: incomplete randomization, limited blinding, risk of selection/performance/detection bias; GRADE: mostly low or very low; PROSPERO registration CRD42024540164
Fan et al. 2025 (Fan, Soh et al. 2025)	Systematic review	14 studies	Older adults with functional impairments; age not specified; male/female	Systematic review	Tai Chi (Yang-style, Sun-style, Chen-style, simplified-style)	Older adults with MCI, NS-LBP, preclinical disabilities, chronic diseases, poor balance, OA, PD, sarcopenia, fall risk	Motor function, balance, gait, mobility, strength, fall rates	Improved balance, gait, mobility, strength, and reduced fall risk	Not specifically reported	12 weeks; 2–5 times/week; 60 min per session	Not specified	Yang-style most effective; assessment via SL, 6MWT, TUGT, CST, FES; PRISMA guidelines followed
González-Devesa et al. 2024 (Gonzalez-	Systematic review and	13 studies	PD patients; age not	Meta-analysis	Boxing training	PD patients	Motor function, balance, gait, cardiorespirator	No significant improvements in	Trend toward improved quality of life (non-significant)	Not specified	Control groups from original studies	Evidence uncertain; boxing shows no substantial impact on physical or mental

Devesa, Ayan et al. 2024)	meta-analysis		specified; gender not specified				y fitness, quality of life	mobility, balance, gait, or motor symptoms				health outcomes; methodological quality assessed with PEDro and MINORS scales
Xie et al. 2025 (Xie, Yuan et al. 2025)	Systematic review and Bayesian network meta-analysis	54 studies	2,828 PD patients; age not specified; gender not specified	Network meta-analysis	Aerobic Exercise (AE), Multicomponent Exercise (Mul), Sensory Exercise (SE), Resistance Training (RT), Mind-Body Exercise (MBE)	PD patients	Walking velocity	AE most effective at 1,400 METs-min/week; Mul at 1,000 METs-min/week; SE at 1,000 METs-min/week; RT at 750 METs-min/week; MBE at 500 METs-min/week	Not specifically reported	Dose-specific protocols per exercise type	Control groups from original studies	ROB2 used for bias assessment; PROSPERO registration CRD42024506919; provides guidance for optimal exercise prescription in PD
Asgharzadeh Chamleh et al. 2025 (Asgharzadeh Chamleh, Afkanpour et al. 2025)	Systematic review	31 studies	Patients with stroke, PD, and MS; age/gender not specified	Systematic review	Game-based telerehabilitation, virtual reality, serious games	Neurological patients including PD	Physical function, rehabilitation adherence, usability, engagement	Improved home-based motor rehabilitation (varies per study)	Challenges: motivation, usability, exercise adherence; opportunities: engagement, affordability	Not specifically reported	Control groups from original studies	Wii console most used; emphasizes tailored remote rehab, long-term adherence; highlights technological barriers and facilitators

Song et al. 2025 (Song, Ge et al. 2025)	Systematic review and meta-analysis	15 RCTs	792 older adults with PD; age/gender not specified	Meta-analysis	Aerobic training (AT), Resistance training (RT)	Older adults with PD	Walking and balance abilities (UPDRS-III, Gait Velocity, Mini-BESTest, TUG)	AT improved UPDRS-III, gait velocity, TUG; RT improved Mini-BESTest	Not specifically reported	Not specified; interventions per original studies	Standard care or control groups from RCTs	AT superior for UPDRS-III, gait, TUG; RT best for Mini-BESTest; I ² heterogeneity varied across outcomes
Li et al. 2024 (Li, Wang et al. 2024)	Systematic review and network meta-analysis	27 RCTs	1,219 older adults; age not specified; gender not specified	Network meta-analysis	Dance interventions (Creative Dance, Folk Dance, Ballroom Dance)	Older adults, including PD patients	Fall risk, balance, mobility	Creative Dance improved Berg Balance Scale; Folk Dance and Ballroom Dance improved TUG and Berg Balance Scale in PD patients	Not specifically reported	Not specified; interventions per original studies	Control groups from RCTs	Creative Dance best for balance in healthy older adults; Folk Dance best for TUG and balance in PD; PROSPERO registration CRD42022323426
Peng et al. 2024 (Peng, Zhao et al. 2024)	Systematic review and meta-analysis	30 controlled trials	2,029 PD patients; age/gender not specified	Meta-analysis	Oriental Exercises (OEs)	PD patients	Non-motor symptoms, quality of life	Not specifically reported	Improved cognition (MoCA, FAB, SCWT), neuropsychiatric symptoms (HAMD, HAMA, SCL-90), QOL (PDQ, NMSQ)	Not specified	Control groups from original studies	Customization of OE regimens recommended; evidence supports benefit on NMS and QOL; emphasizes need for large-scale rigorous studies

Lazzarini et al. 2024 (Lazzarini, Mosconi et al. 2024)	Systematic review and meta-analysis	15 RCTs	629 adults with PD; age/gender not specified	Meta-analysis	Robot-assisted training (RAT)	PD adults	Motor impairment, balance, mobility, freezing of gait, falls, adverse events	No clear improvements; effectiveness uncertain	Not specifically reported	Not specified; interventions per original studies	Comparators included treadmill, overground gait, conventional therapy, or no treatment	Very low certainty of evidence; risk of bias, small sample sizes, and inconsistency across studies; PROSPERO registration CRD42022371124
Gil et al. 2024 (Gil, Moratelli et al. 2024)	Systematic review and meta-analysis	11 studies	Not specified in abstract	Meta-analysis	Dance interventions (various styles: samba, tango, folk, dance-physiotherapy, etc.)	People with Parkinson's disease	Cognitive function (MoCA, other tools)	Not reported	Cognitive outcomes (MoCA, other tests) improved; high heterogeneity ($I^2=90\%$)	Not specified	Usual care or other exercise interventions (depending on study)	Registered in PROSPERO (CRD42023474696); cognitive measures heterogeneous; potential publication bias; some studies with low/moderate RoB
Cui et al. 2024 (Cui, Hu et al. 2024)	Systematic review and meta-analysis	29 RCTs (17 high ACSM compliance, 12 low; alt. 11 high vs 19 low with stricter criterion)	Not specified in abstract	Meta-analysis	Aerobic exercise (dose classified per ACSM guidelines)	Patients with Parkinson's disease	Motor function (UPDRS-III), Balance (BBS), Mobility (TUG), Quality of life (QOL)	Improved with high-dose AE: UPDRS-III, BBS, TUG	Improved QOL (trend stronger in high-dose AE)	Classified as high vs low ACSM compliance ($\geq 4/6$ or $\geq 5/6$ criteria); dose variable across studies	Lower-dose aerobic interventions, or usual care depending on study	PROSPERO CRD42024517548; preliminary support for high-dose aerobic exercise; heterogeneity; more RCTs needed
Chartier et al. 2024 (Chartier, Godard et al. 2024)	Systematic review	21 RCTs and controlled trials	940 participants with Parkinson	Systematic review (no	Combined physical + cognitive training (sequential,	Patients with subcortical neurode	Motor, cognitive, behavioral outcomes	Reported improvements in physical function	Reported improvements in cognitive and behavioral outcomes	Variable across studies; heterogeneity;	Usual care / exercise only / cognitive training	Evidence inconsistent due to heterogeneity of tests, disease progression, targeted functions; lack of

			son's diseas e (other subcor tical NDs also screen ed) Patien ts with chroni c diseas es (MS=1 0, cancer =3, renal diseas e=2, stroke =1, PD=1); n not fully specifi ed in abstra ct	meta- analysis)	dual task, synergic)	generati ve diseases (mostly PD); stages not specified		(varied results)	(discrepant findings)	not standardized	only depending on trial	follow-up data; more studies needed
Warlo et al. 2024 (Warlo, El Bardai et al. 2024)	Systema tic review and meta- analysis	17 studies	n=588; mean age	Random -effects meta- analysis	Game-based eHealth interventions (mainly exergaming; some balance- based)	Adults with chronic diseases (includi ng Parkinso n's disease)	Fatigue (primary), QoL	Balance- based exergamin g showed motor benefits (fatigue reduction linked to physical activity)	Fatigue reduction, QoL improvement	Variable across studies; not standardized	Conventiona l care or no care	Significant moderate effect (SMD -0.65); high heterogeneity (I ² =85.87%); subgroup analysis: MS trend positive, cancer NS; most studies exergaming-focused
Barbieri et al. 2025 (Barbieri,	Systema tic review	13 RCTs	n=588; mean age	Random -effects	Aerobic exercise	PD patients; H&Y	Functional capacity,	↓ UPDRS motor	Improved functional capacity, ↑ VO ₂ max	6–70 weeks; mostly 10–12 wks; 2–3	Usual care or non- aerobic	Aerobic training effective in improving cardiorespiratory

Barbieri et al. 2025)	and meta-analysis (RCTs)		66.2y (range 57–73); gender not specified	meta-analysis	(varied intensities)	not reported ; older adults (57–73y)	VO ₂ max, UPDRS-III	score (MD -2.48)		sessions/week ; ~47 min/session; low to high intensity	control interventions	fitness and functional outcomes; consistent reductions in UPDRS; GRADE assessment performed
Jiang Y, 2024 (Jiang, Zhang et al. 2024)	Systematic review and meta-analysis (observational studies: cohort + case-control)	21 studies (13 cohort, 8 case-control)	not specified in abstract; mixed genders; age varies across studies	Random -effects meta-analysis, dose-response	Physical activity (all types)	General population; not specific to H&Y (prevention, not PD patients)	Risk of developing PD (incidence); subgroup and dose-response analyses	Not applicable (focus on incidence, not symptoms)	PD risk reduction; gender differences; BMI and ethnicity subgroups	PA dose: protective effect per 10 MET-h/week ↑; duration/intensity varied across studies	Low/no PA exposure groups	PA associated with ↓ PD risk (RR=0.77); 9% risk reduction per 10 MET-h/week; protective across genders; less clear effect in high BMI or Asian populations
Zhao et al. 2024 (Zhao, Zhang et al. 2024)	Systematic review and network meta-analysis (RCTs)	111 RCTs	5,358 participants; age not specified in abstract;	Network meta-analysis (NMA) with SUCRA ranking	Multiple motor interventions (archery, high-intensity agility training, dance, Tai Chi, etc.)	PD patients: disease stage not specified in abstract	Motor function: UPDRS-III, TUG, BBS, Mini-BESTest, 6MWT	Archery: best for UPDRS-III; High-intensity agility: best for TUG; Dance &	Not reported	Interventions varied widely: most studies 6–12 weeks, 2–3 sessions/week ; intensity ranged (low–high)	Routine care or low-activity comparators	Archery, Tai Chi, dance, and high-intensity agility training ranked highest in motor improvements; very large NMA, high heterogeneity expected

			mixed gende rs					Tai Chi: improved balance (BBS, Mini- BEST); Dance: improved walking (6MWT)					
Cardoso et al. 2024 (Cardoso, Fernandes et al. 2024)	Systema tic review	9 RCTs/pi lot studies	Adults >18 yrs with neurol ogical condit ions (stroke , PD, AD, MCI); n not specifi ed in abstra ct; mixed gende rs	Systema tic review (no meta- analysis)	Aerobic exercise (moderate to high intensity)	Neurolo gical conditio ns includin g PD; adults	Peripheral BDNF levels, neuroplasticity, functional gains	Functional capacity (reported as gains linked to exercise)	Neuroplasticity, peripheral BDNF increase	≥30 min per session, 3x/week, ≥4 weeks, moderate– high intensity	Comparator s varied (usual care, conventiona l therapy, lower intensity exercise)	Evidence supports AE for increasing BDNF and inducing neuroplasticity; PD included among broader neurological conditions; clinical relevance highlighted	
Bevilacqua et al. 2024 (Bevilacqua, Benadduci et al. 2024)	Systema tic review	14 RCTs	Older adults with PD (≥65	Systema tic review (no	Technology- assisted interventions (mainly VR exergames)	PD, ≥65 years	Gait, balance, physical performance, cognition	Gait, balance, mobility	Cognitive function	Variable across included RCTs; interventions	Conventiona l/Traditional rehabilitatio n	Technology-assisted rehab outperformed traditional approaches for gait and balance; VR exergames were the	

			yrs), n not specified in abstract	meta-analysis)							involved technological rehabilitation training (often VR exergames)	most common; effects on both motor and cognitive domains
Yau et al. 2024 (Yau, Ho et al. 2024)	Systematic review + Bayesian network meta-analysis	51 RCTs	2095 PD patients (age not specified in abstract)	Network meta-analysis (Bayesian)	Technology-based interventions (VR training, robotic assistance, biofeedback, proprioceptive, internet-based, exercise comparators)	PD patients (varied, age not specified)	UPDRS-III/MDS-UPDRS-III, stride length, 10MWT, TUG, balance scales, QoL	UPDRS-III, stride length, TUG, 10MWT, balance	Quality of life	Variable across RCTs	Conventional interventions, exercise, internet-based, usual care	VR most effective for TUG, balance, and QoL; Proprioceptive best for stride length; All interventions similar for UPDRS; VR outperformed robotic and exercise
Zotaj A, 2024 (Zotaj, Millosi et al. 2024)	Case study + systematic review	n.a. (clinical data + literature review)	407 PD patients, age 30-100, both sexes (male predominance)	Systematic review	Physiotherapy rehabilitation	PD patients, 30-100 years	Motor function, posture, balance, bradykinesia, tremor	Improved posture, balance, bradykinesia, tremor	n.s.	Variable physiotherapy protocols; short- and long-term interventions	European Union standards	Effectiveness declines with age; advanced methods in Italy yielded better outcomes; emphasizes tailored programs, standardization, and long-term monitoring
Still et al. 2024 (Still, Hale et al. 2024)	Systematic review + meta-analysis	14 observational studies	People with Parkinson's (n not specified)	Meta-analysis	Physical activity under free-living conditions	Free-living, unsupervised PA	Cognition, anxiety, apathy, depression, sleep quality, fatigue, pain	n.s.	Improved cognition (β 0.12–0.28), less affective disorders (β -0.20), better sleep, less chronic pain	Varied PA levels (unsupervised, home/community)	n.s.	Higher PA levels linked to better cognition and reduced affective symptoms; overall high methodological quality

			ed for each study)									
			adults, both sexes									
			PD patients									
Hussain et al. 2024 (Hussain, Farooqui et al. 2024)	Meta-analysis, Systematic review	12 RCTs	aged 18–85 years, both sexes, n not specified per study	Meta-analysis	Non-immersive virtual reality (NIVR) using Wii-Fit	Adults with PD	Balance, cognition	Improved balance (Berg Balance Scale SMD 0.61, 95% CI 0.28–0.95; I2 = 53%)	No significant effect on cognition (SMD 0.15, 95% CI -0.21–0.51; I2 = 0%)	Varied, NIVR sessions (not standardized)	Control groups per individual study	Effective for balance rehabilitation; ineffective for cognitive improvement; moderate heterogeneity for balance, low for cognition
			PD patients,									
Bispo et al. 2024 (Bispo, Lins et al. 2024)	Systematic review	15 studies	adults (n not specified), both sexes	Systematic review	Physical activity (various forms)	Adults with PD	Quality of life, motor and non-motor symptoms	Improvements in motor symptoms in 9 studies	Improvements in non-motor symptoms in 7 studies	Varied interventions across studies	Not applicable / varied per study	Physical activity generally yielded positive effects on QoL, motor and non-motor symptoms; heterogeneity in interventions and assessments
States et al. 2025 (States, Dewan et al. 2025)	Systematic review with meta-analysis	27 RCTs (30 reports)	1200 participants, adults with PD,	Meta-analysis	Group exercise (balance-focused)	People with PD	Clinical balance measures	Improved Timed Up & Go (MD -2.29; 95% CI -3.56 to -1.02), Mini-BEST	Not assessed	Varied per study; regular group exercise	Control: no-exercise, comparison: individual exercise	Group exercise more effective than no-exercise on some balance measures; similar effectiveness to individual exercise; supports patient

Vasu et al. 2024 (Vasu, Hui Lim et al. 2024)	Systematic review	11 RCTs	647 participants with PD	Systematic review	Physiotherapeutic interventions targeting hand dexterity	Adults with PD, not specified H&Y stage	Hand dexterity, activities of daily living (ADL), upper limb motor performance, quality of life	8/11 studies showed improvements in hand dexterity; 4/7 studies showed improvements in upper limb motor performance	2/3 studies reported positive effects on ADL; 2 studies reported benefits in QoL	Intervention periods ranged from a single session to 12 weeks	Usual care or other PD treatments	High risk of performance bias, unclear risk of selection bias; home-based dexterity rehabilitation appears promising; limited evidence to declare one intervention superior
Alanazi 2024 (Alanazi 2024)	Systematic review	19 interventional studies	1673 older adults with neurodegenerative diseases (including PD and dementia)	Systematic review	Nursing-based physical activity interventions (aerobic, resistance, Tai Chi, yoga)	Older adults with neurodegenerative diseases; specific H&Y stage not reported	Cognitive function, mobility, balance, activities of daily living (ADL), quality of life	Improvements in mobility, balance, and ADL reported	Improvements in cognitive performance and overall QoL	Varies across studies; type, intensity, and duration of activity differed	Usual care or no intervention	Benefits were consistent but varied with type, intensity, and duration; small sample sizes, heterogeneity, and short-term follow-ups limit generalizability
Sarasso et al. 2024 (Sarasso, et al. 2024)	Systematic review and meta-analysis	14 RCTs	548 patients with Parkinson's disease	Meta-analysis	Dual-task gait training vs. single-task gait training	Not specified; adult pwPD	Dual-task gait speed, stride length, cadence, dual-task costs, quality of life	Dual-task gait speed (SMD 0.48), balance confidence	Quality of life improved; balance confidence not significantly changed	Variable across studies; 12 weeks	Single-task gait training	Evidence certainty: low to very low; supports dual-task gait training for improving gait

Parente et al. 2024)	meta- analysis		son's diseas e			balance confidence, quality of life	stride length (MD 0.09 m), cadence (MD 5.45 steps/min) improved with dual- task training	significantly affected	details not fully specified		spatiotemporal gait parameters
Park and Lee 2024 (Park and Lee 2024)	Systema tic review	17 studies	Older adults and indivi duals with neurol ogical condit ions (inclu ding Parkin son's diseas e, stroke, MS); n not consist ently report ed; age	Systema tic review	Interactive telerehabilitati on with remote monitoring/gu idance	Older adults and neurolo gical populati ons	Balance and gait improved across all studies	Not reported	≥4 weeks; interventions delivered via VR, smartphone/t ablet apps, or videoconferen cing	Usual care or baseline comparison	Supports effectiveness of telerehabilitation for improving balance and gait; applicable to PD among other neurological conditions

Steendam- Oldekamp and van Laar 2024 (Steendam- Oldekamp and van Laar 2024)	Systematic review	22 studies (13 inpatient multidisciplinary rehab [MR], 9 inpatient non-MR)	not specified People with Parkinson's disease; not consistently reported; age not specified People with Parkinson's disease; not specified; age not specified	Systematic review	Inpatient multidisciplinary rehabilitation (MR) and non-MR rehabilitation	PwPD (H&Y stage not specified)	Motor, functional, cognitive performance, ADLs, QoL	Improvements in motor and functional outcomes reported across studies	Improvements in cognitive performance and QoL reported	Duration/frequency varied across studies; inpatient setting	Usual care or baseline comparison	Confirms effectiveness of inpatient rehab (MR and non-MR) for PD; highlights need for improved study designs, use of AI, wearables, new biomarkers
Chrysagiset al. 2024 (Chrysagis, Trompouki et al. 2024)	Systematic review	3 studies	not specified; age not specified	Systematic review	Boxing exercise	PwPD	Functionality, disease severity, mobility, physical activity, balance, QoL	Improvements in balance reported	Improvements in QoL reported	Duration/frequency varied across studies	Baseline or standard care	Positive effects of boxing on balance and QoL; results mixed for other functional outcomes; all included studies were high quality (PEDro)
do Amaral et al. 2024 (do Amaral, de	Systematic review and	3 RCTs	n = 130; age not	Meta- analysis	Vestibular rehabilitation	PwPD, all stages	Postural balance	Improvement in Berg Balance Scale (MD	Not reported	Duration/frequency varied across studies	Standard care / control	Evidence quality very low (GRADE); risk of bias "some concern" in all studies; effect

Almeida et al. 2024)	meta-analysis		specific; gender not specified n = 2,158; age not specified; gender not specified					= 5.35, 95% CI = 2.39–8.31, P < 0.001)					promising but needs confirmation in larger studies
Zhang et al. 2024 (Zhang, Liu et al. 2024)	Systematic review and meta-analysis	36 studies	specific; gender not specified	Meta-analysis	Non-pharmacological interventions (exercise, CBT, rTMS, acupuncture)	PwPD, all stages	Sleep, depression, anxiety, cognition, constipation, QoL	Not reported	Significant improvement in PDSS, HAMD, BDI, HAMA, MMSE, MoCA, PDQ-39	Varied interventions across studies	Standard care / control		No serious adverse events; subgroup effects varied and should be interpreted with caution; PROSPERO registration CRD42023486897
Lin et al. 2024 (Lin, Zhang et al. 2024)	Systematic review	5 RCTs (6 articles)	not specified; gender not specified	Systematic review	Dual-task (DT) vs single-task (ST) training	PwPD, all stages	Walking, balance, cognitive functions	Slight improvement in double support time and stride time variability; lab balance measures improved (Hedges' g 0.18–1.25)	No significant improvement in cognitive function	Training details varied across studies	Single-task training		Limited number of studies; inconclusive results; firm conclusions cannot be drawn; larger, high-quality studies needed
Kaagman et al. 2024 (Kaagman, van Wegen et al. 2024)	Systematic review and	5 RCTs	n = 216; age not specified	Systematic review and	Exercise therapy (motorized treadmill, Speedflex	PwPD, all stages	BDNF levels, UPDRS, 6MWT, BBS	Improvement in UPDRS, UPDRS-	BDNF increase (neuroplasticity marker)	Intervention duration varied across studies	UC / usual care / sham / no intervention		Methodological quality: 3 good, 1 fair, 1 poor; exercise increases serum BDNF and

	meta-analysis		ed; gender not specified n = 236	meta-analysis	machine, rowing, unspecified)			III, 6MWT, BBS				alleviates motor symptoms
Folkerts et al. 2024 (Folkerts, Ernst et al. 2024)	Systematic review and meta-analysis	17 studies (9 included in meta-analysis)	(meta-analysis); age not specified; gender not specified n = 1,477;	Systematic review and meta-analysis	Physical exercise interventions (varied types)	PwPD, all stages	Global cognition	Not reported	Small-to-medium improvement in global cognition (SMD 0.33 overall; SMD 0.72 vs active CG)	Varied across studies	Passive or active control groups	Effect size small-to-medium; evidence very uncertain; further large RCTs needed; type of exercise most effective for cognition not determined
Tang et al. 2024 (Tang, Gong et al. 2024)	Systematic review and network meta-analysis	29 studies	age not specified; gender not specified n = 728	Network meta-analysis	Non-pharmacological interventions for sleep (massage, music therapy, treadmill, etc.)	PwPD	Sleep quality	Not reported	Significant improvement in sleep quality for massage (SUCRA 97.3%), music therapy (94.2%), treadmill training (85.7%)	Varied across studies	Sham, usual care, or other interventions	SUCRA ranking identifies massage therapy as most effective; limited quantity/quality of studies; further high-quality trials needed
Costa et al. 2024 (Costa, Prati et al. 2024)	Systematic review and meta-analysis	17 studies	(depression), n = 241 (anxiety)	Meta-analysis	Physical exercise (aerobic, resistance, mind-body)	PwPD	Depression, anxiety	Not reported	Moderate to large improvement in depression (SMD -0.71); small to moderate improvement in	Varied across studies	Non-exercise control	Subgroup analyses: aerobic, resistance, mind-body effective for depression; resistance and mind-body effective for anxiety;

			y); age not specified; gender not specified n = 16						anxiety (SMD - 0.39)			methodological limitations noted
Paterno et al. 2024 (Paterno, Polsinelli et al. 2024)	Systematic review	16 studies (8 two-arm trials, 8 single-arm trials)	age not specified; gender not specified	Systematic review with meta-analysis	Exercise (aerobic, resistance, balance, others)	PwPD	Brain-derived neurotrophic factor (BDNF)	Not reported	Not reported	Varied; intensity measured via MET; volume calculated as MET × duration	Control or usual care in two-arm trials	Exercise significantly increased BDNF levels (Hedges' g = 0.70); intensity positively associated with BDNF change; no effect of exercise type; high heterogeneity (I ² = 76%)
Navas-Otero et al. 2024 (Navas-Otero, Pineda-Nogueras et al. 2024)	Systematic review with meta-analysis	8 RCTs	n not specified; age not specified; gender not specified	Systematic review with meta-analysis	Tai Chi	People with neurodegenerative diseases (Parkinson's disease n=6, cognitive decline n=2)	Health-related quality of life (HRQoL)	Not reported	HRQoL	8–24 weeks	Active interventions or usual care	Tai Chi significantly improved HRQoL (SMD = 0.41; 95% CI 0.21–0.60; p<0.001); low heterogeneity (I ² = 4%); further studies needed due to heterogeneity across interventions
Palm et al. 2024 (Palm, Swarowsky et al. 2024)	Systematic review with	23 RCTs	n not specified; age	Systematic review with	Group exercise	People with Parkinson	Motor function, mobility	Motor function and mobility	Not reported	Not reported	Individual exercise (IE) or usual care (UC)	Group exercise showed no difference compared to IE; improved motor

	meta-analysis		not specified; gender not specified	meta-analysis		n's disease						function and mobility compared to UC (9/11 meta-analyses); evidence quality low to moderate; supports group exercise as adjunct for adherence and socialization
							Psychological and cognitive outcomes, quality of life, depression, anxiety, motivation, memory, social cognition, stress, self-efficacy, language fluency		Psychological outcomes: QoL, anxiety, depressive symptoms, motivation, memory, social cognition, stress, self-efficacy, language fluency			Dance interventions generally equally effective as other structured exercise; preliminary evidence suggests superiority for motivation, memory, social cognition; inferior for stress, self-efficacy, language fluency; supports dance as cognitive and psychological therapy adjunct
Fong Yan A, 2024 (Fong Yan, Nicholson et al. 2024)	Systematic review with meta-analysis	27 studies	1392 (944 F, 418 M, 30 unreported)	Systematic review with meta-analysis	Dance interventions	Across lifespan; includes people with PD		Not reported specifically		≥4 weeks; structured dance interventions	Structured exercise comparison groups	
Jönsson et al. 2024 (Jönsson, Krogh et al. 2024)	Systematic review	16 studies	Not uniformly reported; includes ND populations (SCI, sIBM, MS,	Systematic review	Blood flow restriction exercise (BFRE)	Neurological disorders, including Parkinson's disease	Safety (adverse events), efficacy (muscle size, strength, functional performance)	Muscle strength, physical function	Pain, fatigue, autonomic responses	Variable across studies; BFRE protocols	Control conditions varied; some RCTs	BFRE appears potentially safe and effective; safety concerns include fatigue, soreness, autonomic dysreflexia; limited quality and heterogeneity of studies; small sample sizes; interpret with caution

			PD, stroke)									
Cheng et al. 2024 (Cheng, Quan et al. 2024)	Systema tic review, three- level meta- analysis	13 trials (11 in statistic al analysis)	496 partici pants	Meta- analysis / Systema tic review	Dance interventions	Parkinso n's disease	Quality of life, mental health	Not primary outcome	Mental health, QoL	Variable across studies; lower total dosage and non- partnered dance more effective	Passive control groups	Dance interventions improve mental health (g=0.43) and QoL (g=0.46); theoretical framework links neurological, social, physical, and psychological effects TR improves QoL in neurological patients; for PD and MS results comparable to in- person care; high heterogeneity limits interpretation
Federico et al. 2024 (Federico, Cacciante et al. 2024)	Systema tic review, meta- analysis	28 studies (16 in meta- analysis)	Not specifi ed	Systema tic review / Meta- analysis	Telerehabilitat ion (TR)	Stroke, Parkinso n's disease, Multiple sclerosis	Quality of life, satisfaction, technology acceptance	Not primary outcome	QoL, satisfaction, acceptance	Variable across studies	In-person treatment / usual care	Hydrotherapy shows positive long-term effects on balance; continuous effects on motor function, mobility, and QoL less clear; sensitivity analysis showed improvement in mobility
Liu et al. 2023 (Liu, Huang et al. 2023)	Systema tic review, meta- analysis	5 RCTs	135 PD patien ts	Systema tic review / Meta- analysis	Hydrotherapy	Parkinso n's disease	Balance, mobility, motor function, quality of life	Balance improved long-term; motor function no significant effect	QoL no significant long-term effect	Variable across studies; long- term follow- up	Usual care / control	Home-based exercise is effective for motor and functional outcomes, especially when minimum dose is met; useful during limited physical activity periods
Yang et al. 2023 (Yang, Fu et al. 2023)	Systema tic review, meta- analysis	20 studies	1885 PD patien ts	Systema tic review / Meta- analysis	Home-based exercise	Parkinso n's disease	Motor symptoms, quality of life, functional performance	Walking speed, balance, finger dexterity improved; overall motor	QoL improved; fear of falling decreased	≥8 weeks and ≥30 sessions recommende d for effectiveness	Usual care / control	

Proud et al. 2024 (Proud, Miller et al. 2024)	Systematic review, meta-analysis	18 RCTs	704 PD patients	Systematic review / Meta-analysis	Upper limb exercise / training	Parkinson's disease	Hand dexterity, self-reported hand function, handwriting	symptoms small effect Small positive effect on within-hand dexterity (SMD=0.26)	Nonsignificant effect on self-reported hand function; low-quality evidence for handwriting	Variable across studies; task-related approaches recommended	Usual care / control	Moderate certainty for dexterity; unclear for self-reported function and handwriting; optimal dose and intervention components need further research
Huang et al. 2024 (Huang, Dong et al. 2024)	Meta-analysis	38 studies	1486 PD patients	Meta-analysis	Rhythmically cued exercise interventions	Early to middle stages of PD	Motor function, cognition, mental state	Improvement in motor examination (SMD=-0.61), TUG (MD=-0.91), ADL (SMD=-0.49), balance (SMD=0.59), walking velocity, step length, stride length; no improvement in freezing of gait or cadence	No significant improvements in cognition and mental state	≥10 weeks intervention associated with better motor outcomes	Exercise therapy without rhythm	Safe and well tolerated; treatment duration positively associated with motor improvements; large-scale trials needed

								Improvement in BBS (MD=2.80), ABC (MD=7.30), 10-MWT (MD=0.06), gait speed (MD=3.67), stride length (MD=5.53), cadence (MD=4.52), UPDRS III (MD=-2.16), 6MWT (MD=13.87); no improvement in TUG (MD=-0.56)				
Jiang et al. 2024 (Jiang, Zhou et al. 2024)	Meta-analysis	17 studies	670 PD patients (335 RAGT, 335 control)	Meta-analysis	Robot-assisted gait training (RAGT)	PD patients with motor dysfunction	Balance, gait, walking function, UPDRS III, TUG	Improvement in dominant hand fine dexterity (SMD=0.34), non-dominant hand fine	Not assessed	Not specified in abstract	Control group (conventional therapy)	Safe and well tolerated; improves several gait and balance outcomes but insufficient evidence for all lower limb motor functions
Malwanage et al. 2024 (Malwanage, Dissanayaka et al. 2024)	Meta-analysis	8 RCTs	344 PD patients	Meta-analysis	Proprioceptive training	PD patients with upper limb deficits	Hand dexterity, upper limb function, QoL		No evidence of improvement in QoL	2-8 weeks	No intervention or other active interventions	Very low certainty of evidence; small sample sizes; short-term effects only; longer-duration studies needed

dexterity (SMD=0.36), dominant hand gross manual dexterity (SMD=1.73); no improvement in non-dominant hand gross dexterity or overall upper limb function
Improvement in disease severity (MD=-4.80), motor function, functional mobility, QoL, VO₂ max
Not primary focus

Improvement in QoL (MD=-0.54), maximum oxygen consumption (MD=1.81)
HIIT interventions vs moderate-intensity, usual care, or control; duration varied across studies
Moderate-intensity exercise, usual care, or control
Feasible and beneficial for motor function; heterogeneity between studies; high-intensity vs moderate-intensity comparisons limited; evidence certainty varies by outcome (high for disease severity, moderate for QoL, very low for VO₂ max)
Physical exercise interventions are effective for global

Sena et al. 2023 (Sena, Costa et al. 2023)	Meta-analysis	15 RCTs	654 PD patients, mean age 65.4 yrs	Meta-analysis	High-intensity interval training (HIIT)	Adults with PD	Disease severity, motor function, functional mobility, QoL, VO ₂ max
Kim et al. 2023 (Kim,	Meta-analysis	21 RCTs	761 PD	Meta-analysis	Physical exercise (aerobic,	Adults with PD	Global cognitive function, executive

Lee et al. 2023)			patients		strength, flexibility, combined)		function, attention/working memory, language, memory, visuospatial function		executive function (SMD=0.94); no effect on attention/working memory, language, memory, visuospatial function		min per session; any frequency/period; combined exercise programs most effective		cognition and executive function; combined exercise programs recommended; aerobic, strength, and flexibility alone did not show significant benefits; informs non-pharmacological cognitive therapy in PD
Rotondo et al. 2023 (Rotondo, Proietti et al. 2023)	Systematic review and meta-analysis	18 studies (6 included in meta-analyses)	PD patients (not pooled; adults)	Meta-analysis and systematic review	Physical activity interventions (aerobic, moderate intensity)	Adults with PD	Neurotrophic factors (BDNF, IGF-1), motor and non-motor symptoms	Not primary focus	Potential improvements in quality of life; neuroplasticity markers (BDNF, IGF-1)		Moderate intensity aerobic exercise; duration/intensity varied; standardized in some studies	Control / usual care	Physical activity may increase serum BDNF (MD 5.99 ng/mL) and IGF-1 (MD 33.47 ng/mL); preliminary evidence supports moderate-intensity aerobic exercise; limited sample size and heterogeneity; calls for standardized RCTs to confirm NF changes
Tao et al. 2024 (Tao, Luo et al. 2024)	Systematic review and meta-analysis	21 studies	787 PD patients	Meta-analysis and systematic review	Robot-assisted rehabilitation (upper and lower limb)	Adults with PD	Motor function, fatigue, balance, upper limb function	UPDRS III (lower limb), BBS, some gait measures	Fatigue (PFS)		Protocols varied; robotics often combined with virtual reality	Control / usual care	Robotics improved lower limb function, balance, and fatigue; no significant effect on upper limb outcomes; best results observed when combined with VR; heterogeneity in intervention types and doses

Tobar et al. 2023 (Tobar, Jaramillo et al. 2023)	Systematic literature review	10 studies	Not specified	Systematic review	Physical rehabilitation approaches including VR, exercise programs, yoga	Adults with PD	Physical function, gait, endurance, performance, mental health	Endurance, gait capacity, performance, independence in daily life activities	Anxiety, depression, mental health	Protocols varied across studies	Usual care / passive control	Most interventions used advanced technologies like VR combined with exercise; yoga used for mental health; significant improvements in motor and non-motor outcomes reported; further research needed to determine optimal rehabilitation strategies
Costa et al. 2023 (Costa, Suassuna et al. 2023)	Systematic review and meta-analysis	23 clinical trials	327 across studies; age and gender varied	Systematic review & meta-analysis	Multimodal exercise, aerobic, resistance, dance, conventional physical therapy, others	Adults with PD	Non-motor symptoms assessed by general PD scales	Not primary focus	Non-motor symptoms (general NMS)	Varied by intervention type	Non-exercise, cognitive/leisure approaches, conventional exercise	Aerobic exercise showed significant improvement over conventional exercise; multimodal exercise trends favored cognitive approaches; overall exercise trends toward improvement in NMS; risk of bias varied across studies
Okemuo et al. 2023 (Okemuo, Gallagher et al. 2023)	Systematic review and meta-analysis	5 RCTs	130 participants; age 31.3–58 years; 72% male,	Meta-analysis	Rebound exercise	In-patient adults with neurological disorders (stroke,	Balance, mobility	Mobility improved (TUG: -6.08 s over 3–8 weeks; pooled SMD = -0.53, p = 0.01)	No significant effect	3–8 weeks; frequency/intensity varied	Usual care or no exercise	Balance outcomes not significantly improved; limited number of studies; moderate-to-high methodological quality; only partial PD representation (15%)

			28% female			MS, PD, SCI)						
He et al. 2023 (He, Fang et al. 2023)	Network meta-analysis	58 studies	2,227 participants; age NR; gender NR	Bayesian network meta-analysis	Mindfulness-based therapy (qigong, yoga, Tai Chi), dance, exercise, music, acupuncture	PD patients	Motor function (TUG, UPDRS I/II), QoL (PDQ-39)	Qigong superior in TUG (-5.54 s vs non-intervention; superior to dance, Tai Chi, acupuncture, music, exercise) Walking speed (SMD 0.42), stride length (SMD 0.69), cadence (SMD 0.41), functional balance (SMD 1.15), dynamic balance (SMD -0.5), motor impairments (SMD -0.86)	UPDRS-I/II: mixed results; PDQ-39: no significant differences	Intervention details varied; multi-modal	Non-intervention or other interventions	Mindfulness-based therapies (qigong, Tai Chi, yoga) recommended as preferred non-pharmacological rehabilitation; network meta-analysis allows ranking of interventions
García-López et al. 2023 (Garcia-Lopez, de Los Angeles Castillo-Pintor et al. 2023)	Systematic review with meta-analysis	17 RCTs	826 participants; mean PEDro score 6.59±1; age NR; gender NR	Meta-analysis	Dual-task training (DTT)	PD patients	Gait (speed, step & stride length, cadence, steps/day), balance (functional & dynamic), motor impairments, ADLs, QoL		ADLs, QoL (improvements reported, SMD not specified)	Intervention details varied across studies	Single-task training or usual care	DTT is effective and safe; no adverse effects reported; improves gait, balance, and motor function

Xu et al. 2023 (Xu, Soh et al. 2023)	Systematic review	16 RCTs	Older adults; age NR; mostly female	Systematic review	Tai Chi (Yang, Sun, Taoist, Health Qigong)	Elderly with gait disorders, including PD, mild cognitive impairment, chronic stroke, sedentary, fear of falling	Postural balance, gait, UPDRS III, mobility, lower body strength, falls, QoL	Postural stability and balance, gait, mobility, lower body strength, UPDRS III, falls	Quality of life (limited evidence, only 2 studies)	12-week intervention most common; 60 min per session; 1–2 sessions/week	No exercise / usual care	Yang Style most commonly used; benefits balance; more studies needed in male populations
Yin et al. 2023 (Yin, Liu et al. 2023)	Meta-analysis	6 RCTs	PD patients; age NR; gender NR	Meta-analysis	Tai Ji (Tai Chi)	PD patients	Cognitive function (global cognition, executive function, cognitive motor)	Not significant	Improvement in global cognition (p < 0.05) and trend for executive function (p = 0.09)	45–60 min per session, 2 times/week, ≤12 weeks	Usual care / control	No significant effect on cognitive motor; effect may reduce with disease progression; TJ recommended as cognitive intervention
Malmir et al. 2023 (Malmir and Ashrafganjooie 2023)	Systematic review & Meta-analysis	6 studies (3 in meta-analysis : 2 RCTs + 1 multicenter trial)	PD patients; age NR; gender NR	Meta-analysis	HiBalance training program	Idiopathic PD	Physical function, self-reported function	Improvement in gait velocity; moderate effect on Mini-BESTest	No changes in self-reported function	NR; intervention duration NR; follow-up 6–12 months	Control/usual care	Gains in gait velocity waned at follow-up; highlights need for post-HiBalance maintenance programs

Qian et al. 2023 (Qian, Fu et al. 2023)	Systematic review & Network meta-analysis	199 RCTs	9,523 PD patients; age NR; gender NR	Network meta-analysis	24 types of exercise interventions	Adults with PD	Postural balance: BBS, static/dynamic balance, proactive/reactive balance	BWS treadmill: best for BBS & dSSB; Aquatic exercise: best for sSSB; Pilates: best for proactive balance; BGT_ECA & RA_GT: best for reactive balance TUG: SMD -0.55; 6MW: SMD 1.11; stride length: 0.45; gait velocity: 0.42; UPDRS-III: -0.76; BBS: 0.88	NR	NR	Control/usual care	Evidence quality often low; effects dependent on specific outcome measure
Li et al. 2024 (Li, Cao et al. 2024)	Systematic review & Meta-analysis	15 RCTs	Early-to mid-stage PD; n NR; age NR; gender NR	Meta-analysis	Self-directed physical activity (SDPA)	Early- to mid-stage PD	Motor function, mobility, balance, QoL	PDQ-39: 0.04 (NS)		NR	Control / usual care	SDPA improved motor outcomes and balance; no significant effect on freezing of gait or QoL
Zhao et al. 2023 (Zhao, Lv et al. 2023)	Systematic review & Meta-analysis	9 RCTs	n=346 (WBV =172; control=174);	Meta-analysis	Whole-body vibration (WBV)	Patients with PD	Limb function, gait, balance, daily living	UPDRS-III: MD -2.39; Walking	Balance: MD -0.06 (NS); ADL: MD 0.03 (NS)	NR	Conventional therapy / usual care	WBV improves motor function and gait stability; no significant effects on balance or

			age NR; gender NR					stability: MD -1.96				daily living; more high- quality studies needed
Rodríguez- Mansilla et al. 2023 (Rodríguez- Mansilla, Bedmar- Vargas et al. 2023)	Systema- tic review	20 studies	n=480; age NR; gender NR	Systema- tic review	Virtual reality (VR)	Patients with PD	Balance, gait, adherence, motivation, cognitive and sensory stimulation	Improved balance and gait (general)	Cognitive and sensory stimulation	NR	Various (controlled and non- controlled trials)	VR provides good adherence, motivation, feedback, and can be used for home rehabilitation; devices included Nintendo Wii + Balance Board and Microsoft Kinect
Hussain et al. 2023 (Hussain, Farooqui et al. 2023)	Meta- analysis	21 trials	n NR; age NR; gender NR	Meta- analysis	Exercise-based management (exergaming, gamepad, VR, gait, core training)	Patients with PD	Balance, freezing of gait, motor symptoms	Significant improvement in balance (BBS SMD=0.60; Mini- BESTest SMD=0.87) ; trend for FOG improvement (SMD=0.21 , p=0.06)	NR	NR	NR	Exercise-based therapies improve balance and FOG; interventions include VR, exergaming, gait and core training
Feng et al. 2023 (Feng, Xu et al. 2023)	Meta- analysis	64 RCTs	13,241 participants; age NR; gender NR	Meta- analysis	Exercise (balance, combined)	Neurode- generative diseases (PD, dementia, stroke)	Falls, fractures, fall-related injuries	Reduced falls in PD (RaR=0.49) , dementia (0.64), stroke (0.40)	NR	Short-, moderate-, long-term interventions; low injury rate (0.007% per	Non- exercise	Exercise effective for fall and injury prevention; good compliance (74.8%); safe intervention

Cui et al. 2023 (Cui, Li et al. 2023)	Systematic review & meta-analysis of RCTs	32 studies (from 26 articles)	Patients with Parkinson's disease	Dose-response meta-analysis based on ACSM compliance	Exercise interventions (high ACSM compliance vs low/uncertain ACSM compliance)	Not specified in abstract; PD patients, mixed H&Y stages	Motor function, balance, mobility, quality of life	UPDRS-III, Timed Up and Go (TUG), Berg Balance Scale (BBS)	PDQ-39 (quality of life)	Variable per study; classified as high or low ACSM compliance	Low or uncertain ACSM compliance exercise interventions	High ACSM compliance interventions improved motor function, mobility, and QoL more than low/uncertain compliance; effect on balance less pronounced
Wang et al. 2023 (Wang, Cui et al. 2023)	Systematic review & network meta-analysis of RCTs	60 RCTs	3,537 patients with Parkinson's disease	Network meta-analysis	Exergaming, Dance, Rhythmical auditory exercise, and other exercise types	Not specified in abstract; PD patients, mixed H&Y stages	Postural balance	Timed Up and Go (TUG), Berg Balance Scale (BBS), Mini-Balance Evaluation Systems Test (Mini-BESTest)	Not reported	Variable across studies	Other types of exercises	Exergaming, Dance, and rhythmical auditory exercise were most effective in improving postural balance; risk of bias: 35 low, 21 medium, 4 high
Kossi et al. 2024 (Kossi, Raats et al. 2024)	Systematic review of RCTs	28 RCTs	Patients with neurological conditions (MS, spinal cord)	Qualitative synthesis	Rehabilitation interventions	Not specified; includes PD, MS, stroke, SCI, TBI	Participation outcomes	Not specifically reported	Participation (primary in 15 studies)	Variable per study	Control groups as per individual RCTs	Limited evidence for improving participation; only a few studies included PD patients; 4 studies showed significant pre-post improvements

				injury, stroke, TBI); few PD patients								
				Meta-analysis comparing nonstandard PT vs standard PT and standard PT vs no intervention	Physical therapy (PT) interventions, including nonstandard (aquatic, others) and standard PT	Mean age 61–77 years; mixed H&Y stages	Gait, balance, UPDRS score, quality of life, cognition	Gait (14 trials), balance (10 trials), UPDRS (various)	Quality of life (3 trials), cognition (1 trial)	PT regimen 2–12 weeks (mostly 30–60 min sessions), 2–3 times/week	Standard PT or no intervention	Wide variety of PT types tested; durability reported in ~48% of trials; meta-analysis showed no significant difference in main outcomes; long-term effectiveness unclear
El Hayek et al. 2023 (El Hayek, Lobo Jofili Lopes et al. 2023)	Systematic review & meta-analysis of RCTs	46 trials	3,905 patients with Parkinson's disease									
				Meta-analysis comparing VR-based rehabilitation vs conventional treatment	Virtual reality (VR)-based rehabilitation	Not specified; PD patients, mixed H&Y stages	Balance function, gait, activities of daily living, motor function, quality of life	Balance: Berg Balance Scale (BBS), Activities-specific Balance Confidence; gait and motor function not significant	ADL, quality of life	Variable across studies; not specified in abstract	Conventional rehabilitation	VR-based rehab improved balance but not gait, ADL, motor function, or QoL; more recent studies show greater balance improvement; long-term follow-up needed
Kwon et al. 2023 (Kwon, Park et al. 2023)	Systematic review & meta-analysis of RCTs	14 RCTs	524 patients with Parkinson's disease									

ly improved												
Folkerts et al. 2023 (Folkerts, Nielsen et al. 2023)	Systematic review & meta-analysis of RCTs	30 RCTs (14 pharmacological, 16 non-pharmacological)	Patients with Parkinson's disease	Meta-analysis of pharmacological (modafinil) and non-pharmacological (exercise, acupuncture) interventions	Physical exercise, acupuncture, pharmacological (modafinil)	Not specified; PD patients, mixed H&Y stages	Fatigue	Not specifically reported	Fatigue (physical and mental)	Variable across studies; exercise interventions unspecified in abstract	Passive or placebo control groups	Physical exercise showed small significant improvement in fatigue; pharmacological (modafinil) and acupuncture not significant; further research needed on holistic fatigue management
Tonkin et al. 2023 (Tonkin, Miller et al. 2023)	Systematic review & network meta-analysis of RCTs	5 RCTs	218 patients with Parkinson's disease	Network meta-analysis	Exercise interventions: Tango, mixed-treadmill training (TT), body-weight resistance training	Early-to-mid stage PD; age not specified	Non-motor experiences of daily living (NMeDL)	Not specifically reported	MDS-UPDRS Part I scores	Variable per study; exercise modality specific	Control (usual care or no intervention)	Tango and mixed-TT most effective for improving NMeDL; evidence low confidence; early exercise adoption recommended
Zhang et al. 2023 (Zhang, Gu et al. 2023)	Systematic review & network meta-analysis of RCTs	159 RCTs	Patients with Parkinson's disease	Network meta-analysis	24 exercise interventions including Pilates, body weight support treadmill training, resistance	Not specified; PD patients, mixed H&Y stages	Gait performance	Timed Up and Go (TUG), stride length, stride cadence, 6-Minute Walking	Not reported	Variable per study; exercise modality specific	Control (usual care or no intervention)	Exercise interventions improved gait indexes; efficacy varied by exercise type and specific gait outcome; Pilates, BWSTT, resistance training, multidisciplinary exercise ranked highest

					training, multidisciplin ary exercise			Test (6MWT)				
				Meta- analyses where								
Li et al. 2023 (Li, Loevaas et al. 2023)	Systema tic review & meta- analysis of RCTs	49 RCTs	2,104 patien ts with Parkin son's diseas e	≥3 trials reported same outcome ; narrativ e synthesi s for others Meta- analysis	Exercise interventions (various types and doses)	Not specified ; PD patients, mixed H&Y stages	PD progression markers (UPDRS "off" motor scores, BDNF levels, neuroplasticity indicators)	"Off" UPDRS motor scores improved (Hedge's g -0.39)	BDNF concentration improved (Hedge's g 0.54); other neuroplasticity measures	Variable per study; exercise type and dose not standardized	Control (no or sham exercise)	Limited evidence that exercise may attenuate PD progression; further large RCTs needed; low to very low certainty of evidence
Lin et al. 2023 (Lin, Tam et al. 2023)	Systema tic review & meta- analysis of RCTs	8 trials (9 articles)	337 patien ts with Parkin son's diseas e	compari ng mindful ness/me ditation therapie s vs control Meta- analysis	Mindfulness and meditation therapies	Not specified ; PD patients, mixed H&Y stages	UPDRS-III, cognitive function, gait, QoL, ADL, depression, anxiety, pain, sleep disturbance	UPDRS-III improved (MD - 6.31); gait not significant ly changed	Cognitive function improved (SMD 0.62); other non- motor outcomes not significantly changed	Variable per study; not specified	Control treatments (usual care, waitlist, or sham)	Mindfulness/meditatio n may serve as complementary therapy; improvements mainly in motor score and cognition; no significant effect on ADL, mood, or sleep
Yang et al., 2023 (Yang, Wang et al. 2023)	Systema tic review & meta- analysis of RCTs	42 RCTs	2,530 patien ts with Parkin son's diseas e	compari ng different physioth erapy interven tions Meta- analysis	Physiotherapy : strength training, mind-body exercise, aerobic exercise, non- invasive brain stimulation	Not specified ; PD patients, mixed H&Y stages	Motor symptoms, balance, gait, functional mobility	UPDRS / MDS- UPDRS motor scores; clinically meaningful improvement	Balance, gait, functional mobility	Variable per study; intervention- specific	Control groups as per individual RCTs	Mind-body exercise most effective overall; NiBS also beneficial for motor symptoms; BGT and acupuncture less effective; promotes mind-body exercise for clinical use

					(NiBS), balance and gait training (BGT), acupuncture			ents for mind- body exercise and NiBS				
Abuoaf et al. 2023 (Abuoaf, AlKaabi et al. 2023)	Systema tic review of RCTs	5 RCTs	328 patien ts with Parkin son's diseas e	Qualitati ve synthesi s	Physical exercise interventions	Early to moderat e PD; disease duration 2.9–8.0 years; majority male	Anxiety	Not reported	Anxiety	Variable per study; not specified	Control groups per individual RCTs	Insufficient evidence to support or refute effect of exercise on anxiety; studies limited by small sample sizes and methodological issues; high-quality RCTs needed
Zhang et al. 2023 (Zhang, Li et al. 2023)	Systema tic review & network meta- analysis	109 RCTs	4,631 patien ts with Parkin son's diseas e	Network meta- analyses and meta- regressi on	Physical exercise: dancing, Nordic walking, Qigong, yoga, multimodal training, aquatic training, exercise gaming	Not specified ; PD patients, mixed H&Y stages	Motor function, mobility, balance, hand function	General motor symptoms , mobility, balance, hand function	Not reported	Variable per study; exercise type specific	Non- exercise or usual care control	Chronic exercise sustains motor function and delays PD progression; dancing best for general motor symptoms, Nordic walking for mobility/balance, Qigong for hand function; provides evidence for multiple effective exercise modalities
Omar Ahmad et al., 2023 (Omar Ahmad, Longhurst et al. 2023)	Systema tic review & meta- analysis	25 articles	Not specifi ed	Meta- analysis	Exercise interventions (endurance and non- endurance)	Not specified ; PD patients	UPDRS, overall PD symptoms	UPDRS motor scores improved	Non-motor symptoms qualitatively assessed	4–26 weeks	Control groups per individual studies	Overall positive effect of exercise on PD symptoms; no significant difference between aerobic and non-aerobic exercise

López-Liria et al. 2023 (Lopez-Liria, Vega-Tirado et al. 2023)	Systematic review & meta-analysis	9 RCTs	240 patients with idiopathic Parkinson's disease	Meta-analysis	Trunk-specific and balance exercises	Not specified; PD patients, mixed H&Y stages	Balance, postural stability	Static and dynamic balance; Berg Balance Scale improved significantly in subjective measures	Not reported	Variable per study; trunk-specific exercise or balance combined with muscle strengthening	Control groups per individual studies	Trunk-specific exercises may complement pharmacological treatment; modest improvements in balance; some outcomes not statistically significant
Johansson et al. 2023 (Johansson, Folkerts et al. 2023)	Systematic review & meta-analysis	11 studies	597 patients with Parkinson's disease	Meta-analysis	Motor-cognitive training (dual-task)	Mean age 68.9 years; mean PD duration 6.8 years	Dual-task performance	Dual-task gait speed, cadence, stride length, gait speed cost improved	Cognitive dual-task performance	Not specified; variable per study	Control groups per individual studies	Motor-cognitive training improves dual-task performance in PD; high-certainty evidence
Dai et al. 2023 (Dai, Yuan et al. 2023)	Systematic review & meta-analysis	10 RCTs	Not specified	Meta-analysis	Aquatic exercise	Not specified	Balance, walking ability, motor function, quality of life	Walking ability improved; motor function not significantly improved	Quality of life improved	Not specified	Conventional rehabilitation therapy	Aquatic exercise improves balance, walking ability, and QoL in PD; no significant effect on overall motor function; limited by number and quality of studies
Zanatta et al. 2023 (Zanatta, Farhane-Medina et al. 2023)	Systematic review	70 studies	Not specified	Descriptive syntheses	Robot-assisted therapy (RAT) alone or RAT + virtual reality (VR)	Stroke, multiple sclerosis, spinal cord injury, Parkinson's	Health-related quality of life (HRQoL), cognitive and psychological outcomes	Upper and lower limb impairment outcomes described, but	Cognitive (memory, attention, executive function) and psychological (mood, motivation, self-efficacy, well-	Interventions heterogeneous; longitudinal follow-up up to 36 months	Various comparators, depending on study	Promising evidence for RAT and RAT+VR improving HRQoL; heterogeneity across studies; more targeted short- and long-term research recommended

						n's disease		heterogen	being, fear of falling, satisfaction, device usability)	in some studies		
Martín-Núñez et al. 2023 (Martín-Núñez, Calvache-Mateo et al. 2023)	Systematic review with meta-analysis	6 RCTs	1,251 persons with PD	Meta-analysis	Exercise-based interventions: balance, strength, aerobic, multimodal	Not specified	Physical activity levels	Indirectly measured via PA levels	Quality of life mentioned as context	Heterogeneous interventions; details vary per study	Various comparators depending on study	Exercise interventions showed a positive effect on PA (SMD 0.50, 95% CI -0.02, 1.00; P = .06); limited studies and heterogeneity prevent definitive conclusions
Shahhar et al. 2022 (Shahhar, Qasheesh et al. 2022)	Systematic review	10 studies (4 RCTs)	Not specified	Narrative synthesis	Nintendo Wii Fit / exergaming	People with Parkinson's Disease; age not specified, H&Y stage not specified	Balance, life outcomes	Balance	Quality of life	≥5 weeks of Wii Fit exercises; frequency not specified	Some studies used conventional exercises as control	Wii Fit improves balance; combination with conventional exercises produces better results; evidence still limited and heterogeneous
Harpham et al. 2023 (Harpham, Gunn et al. 2023)	Systematic review and meta-analysis	11 studies (7 controlled/comparator, 4 single group)	117 HIIT participants	Meta-analysis for VO ₂ peak/max; narrative for other outcomes	High-Intensity Interval Training (HIIT)	People with Parkinson's Disease, mild-to-moderate severity; age not specified, H&Y stage	Feasibility, safety, VO ₂ peak/max, motor symptoms, BDNF	Motor symptoms	BDNF	6 weeks – 24 months; supervised; HIIT protocols; majority ≤12 weeks	Moderate-intensity continuous exercise (MICE) or usual care	HIIT is feasible and safe for mild-to-moderate PD; improves cardiorespiratory fitness and motor symptoms; increases BDNF; adverse events rare; long-term adherence requires further study

						mild-to-moderate						
Yang et al. 2022 (Yang, Huang et al. 2022)	Systematic review and meta-analysis	22 studies	809 participants	Meta-analysis	Community-based exercise (dance, Chinese martial arts, Nordic walking, home-based exercise)	People with Parkinson's Disease; age variable; H&Y stage not specified	Motor function, balance, walking ability	UPDRS-III, Timed Up and Go test, UPDRS, 6-Minute Walk Test, Berg Balance Scale	Not reported	Most common: 60 min twice a week; duration and weekly frequency influenced effects; modality dependent (tango, tai chi)	Usual care	Community-based exercise improves motor function in PD; heterogeneity high; age, treatment duration, and weekly frequency may influence outcomes
Wong et al. 2023 (Wong, Cheng et al. 2023)	Systematic review and meta-analysis	10 RCTs	466 participants	Meta-analysis and meta-regression	Dual task (DT) training	Individuals with Parkinson's Disease; age not specified ; H&Y stage not specified	DT gait performance, cognitive function	DT gait speed, DT step and stride length	Attention, executive function (Trail Making Tests A & B)	Not specified; intervention effects related to baseline gait speed	Usual care or conventional exercise	DT training improves DT gait speed, step and stride length, attention, and executive function; effect on TMT-A maintained at follow-up; participants with slower initial gait speed showed greater improvement
Wang et al. 2022 (L, F et al. 2022)	Systematic review	29 studies (5 PD, 24 healthy older adults)	Not specified	Systematic review	Tai Chi, treadmill training, dancing	Healthy older adults and people with PD; age not specified	Brain activity, cognitive function, memory, emotion	Not specified	Cognitive function, memory, emotion	Chronic / long-term interventions; exact duration/frequency not specified	Not specified	Treadmill training showed inverse functional connectivity changes in PD; Tai Chi and dancing increased brain activity in healthy older adults;

						; H&Y stage not specified						evidence limited and heterogeneous
Simpkins and Yang 2023 (Simpkins and Yang 2023)	Systematic review with meta-analysis	14 RCTs	612 PwPD	Meta-analysis	Dance-based interventions	People with PD; age not specified ; H&Y stage not specified	Balance	Balance (postural control)	Not reported	12+ week interventions showed greatest benefit; 60-90 min per session; various dance styles	Control group (usual care or no intervention)	Medium overall effect size (ES=0.57); dance styles ES ranged 0.40–2.00; longer interventions (≥12 weeks) more effective; informs balance training and fall prevention programs
Navarro-Lozano et al. 2022 (Navarro-Lozano, Kiper et al. 2022)	Systematic review with meta-analysis	5 studies (3 in meta-analysis)	Not specified	Meta-analysis	Non-immersive virtual reality / video games	People with Parkinson's disease; age and H&Y stage not specified	Walking speed, gait parameters, balance, quality of life	Walking speed and other spatio-temporal gait parameters	Balance, quality of life	Face-to-face sessions; VR or video games	Control group (usual care or no intervention)	Inconclusive findings on walking speed, balance, QoL; more studies needed; differentiation between rehab-specific vs commercial VR/video games suggested
Lai et al. 2022 (Lai, Cai et al. 2022)	Systematic review with meta-analysis	10 RCTs	804 participants	Meta-analysis	Baduanjin (Qigong)	Parkinson's disease; age and H&Y stage not specified	Motor function, balance, gait	UPDRS-III, Fugl-Meyer Assessment of Lower Extremity	Berg Balance Scale, 6-min walk distance	Intervention durations varied; heterogeneity noted due to disease severity and duration differences	Control group (usual care or no intervention)	Baduanjin significantly improved motor function, balance, and gait; more high-quality multicentre RCTs needed
Zhen et al. 2022 (Zhen,	Systematic review	20 studies	Not specified	Meta-analysis	Aerobic exercise	Parkinson's disease;	Balance, gait, motor function, quality of life	Timed Up and Go, Berg	PDQ-39 (quality of life)	Duration/frequency varied across studies	Control group (usual care or no	Aerobic exercise improved balance, gait (velocity and

Zhang et al. 2022)	with meta-analysis					age and H&Y stage not specified		Balance Scale, stride/step length, gait velocity, UPDRS-III, 6-minute walk test		intervention)	stride/step length), and motor function, but not step cadence or quality of life	
Yang et al. 2022 (Yang, Wang et al. 2022)	Systematic review and network meta-analysis	250 RCTs	13,011	Network meta-analysis	24 exercise types (Power training, BWS treadmill training, robotic-assisted gait training, Dance, Yoga, Resistance training, etc.)	Adults ≥50 years with PD	Motor function, balance, gait, freezing of gait, depression, anxiety, sleep, cognition, muscle strength, fear of falling	Motor symptoms, balance, gait velocity, walking distance, freezing of gait, muscle strength	Depression, anxiety, sleep quality, cognition, fear of falling	Varied across studies	Control group (usual care or no exercise)	PT best for motor symptoms, BWS_TT best for balance and gait, RA_GT best for freezing of gait, Dance best for depression, Yoga reduced anxiety, RT improved sleep and cognition; low quality evidence overall
Yang and Wang 2023 (Yang and Wang 2023)	Systematic review and meta-analysis	14 RCTs	761	Meta-analysis	Progressive Resistance Training (PRT)	Adults with PD	Freezing of gait, muscular strength, gait velocity, stride length, TUG, balance, quality of life	Freezing of gait, muscle strength	Quality of life	Varied across studies	Balance training, modified fitness, or usual care	PRT improved freezing of gait, muscular strength, and quality of life; no significant effect on gait velocity, stride length, TUG, or Berg Balance Scale
Chuang et al. 2022 (Chuang, Chen et al. 2022)	Network meta-analysis (RCTs)	23	949	Network meta-analysis	Exergames and Virtual Technology-Assisted Rehabilitation (VTAR)	Adults with PD	Gait, balance, acceptability, depressive symptoms	Gait, balance	Depressive symptoms (no significant effect), acceptability (drop-out rates)	Varied across RCTs	Usual treatment, other active rehabilitation	Exergames and VTAR improved gait and balance more than usual treatment or other active controls; adequately tolerated; evidence quality rated

												low–moderate (GRADE); small samples and heterogeneity noted
Wang et al. 2021 (Wang, Li et al. 2021)	Systematic review & meta-analysis	14 RCTs	404 PD patients	Between-group effect sizes	Mind-body exercises (e.g., Tai Chi, Qigong, Yoga)	PD; mild to moderate; age not specified	Global cognitive function (MoCA), QoL (PDQ-39), fatigue (PFS-16), depression (BDI), sleep quality (PDSS-2)	Not specifically reported	↑ Global cognitive function (MD=1.68, P=0.0008); sleep quality & QoL improved; low to moderate doses and 6–10 or >15 weeks duration showed significant benefits	60–200 min/week; 6–10 or >15 weeks	Passive control / usual care	Low to moderate dose and appropriate duration are most effective; 57% of included studies were high quality.
Wang et al. 2022 (Wang, Zhou et al. 2022)	Systematic review	58 (28 PD, 21 cognitive impairments, 9 MS)	N/A (varied per included study)	Systematic review	Tai Chi Quan (TCQ)	Patients with neurodegenerative diseases (PD, cognitive impairment, MS)	Motor function, balance, falls, cognition, quality of life, mood	Motor function, balance, falls	Global cognitive function, quality of life, mood	Varied across studies; not specified	Usual care or other non-TCQ interventions	TCQ improved motor function, balance, falls (especially in PD), and cognitive function (especially in cognitive impairment); evidence for QoL and mood benefits is limited; considered safe
Kim et al. 2023 (Kim, Lee et al. 2023)	Meta-analysis	19 RCTs (23 comparisons)	1,302 PD patients	Meta-analysis	Exercise (combined, aerobic, light-to-moderate, moderate-to-vigorous)	Patients with Parkinson's disease; age not specified; H&Y not specified	Depressive symptoms	Not reported	Depressive symptoms	Varied across included studies; light-to-moderate and moderate-to-vigorous intensity	Usual care or other control interventions	Exercise significantly reduced depressive symptoms in PD; combined exercise more effective than aerobic alone; effect size slightly higher for light-to-moderate intensity; exercise type

												may matter more than intensity
Shahien et al. 2023 (Shahien, Elaraby et al. 2023)	Systematic review	6 studies	Not specified	Systematic review	Physical therapy (electrical stimulation, tremor glove, eccentric exercises, weights, virtual reality, transcranial low voltage pulsed electromagnetic fields)	Patients with Parkinson's disease; age and H&Y not specified	Hand tremor measures	Tremor amplitude, UPDRS tremor score, RMS angular velocity	Not reported	Varied by intervention; specifics not consistent across studies	Usual care or other controls	Tremor glove and electrical stimulation showed largest improvements; evidence limited and heterogeneous; meta-analysis not feasible due to single-study data
Marotta et al. 2022 (Marotta, Calafiore et al. 2022)	Systematic review of RCTs	10 RCTs	Not specified	Systematic review	Virtual reality (VR) and exergaming / telerehabilitation	Patients with Parkinson's disease; age and H&Y not specified	Cognitive function	Not reported	Executive function, Trail Making Test, Digit Span backward, MoCA, MyCQ score	Varied across studies; specifics not consistently reported	Conventional rehabilitation	50% of studies used exergaming (significant improvements in cognitive scales), 50% used VR (improvement in executive functions); 40% of studies had high risk of bias
Goh et al. 2023 (Goh, Canning et al. 2023)	Systematic review with meta-analyses	65 RCTs	Not specified; total number not reported	Meta-analysis / Systematic review	Physical therapy/exercise; cognitive/behavioral therapies	People with Parkinson's disease; age and H&Y not specified	Freezing of gait (FOG)	Small effect on reducing FOG post-intervention (Hedges' g = -0.26)	Cognition, anxiety, fear of falling (mentioned as related impairments)	Varied across studies; not standardized	Control or other exercise/cognitive interventions	Very low-certainty evidence; uncertain effects when comparing exercise with cueing vs without, action observation plus strategy vs strategy alone, and dance vs multimodal exercises; personalized

												interventions recommended
Mustafaoglu et al. 2022 (Mustafaoglu, Ahmed et al. 2022)	Systematic review with network meta-analysis	60 RCTs	2037 participants	Network meta-analysis / Systematic review	Mind-body exercises (Yoga, Tai-Chi, Pilates, Qigong, Dance)	Patients with Parkinson's disease; age and H&Y not specified	Functional performance, health-related quality of life (HRQoL)	Pilates most effective for functional mobility and balance; Yoga and Dance most effective for motor function; Qigong most effective for gait speed Rhythmic cueing improved gait velocity, stride length, motor symptoms (UPDRS-III); Dance improved stride length,	Dance most effective for HRQoL	Varied across studies; not standardized	Control or other exercises	The most effective mind-body exercise varied by domain; MBE is overall effective for functional performance and HRQoL
Karpodini et al. 2022 (Karpodini, Dinas et al. 2022)	Systematic review with meta-analysis	49 studies	3767 participants	Meta-analysis / Systematic review	Rhythmic cueing, Dance, Resistance Training (RT)	Patients with Parkinson's disease; age and H&Y not specified	Motor function, functional mobility, gait, quality of life	RT improved quality of life (PDQ-39)	Varied across studies; not standardized	Control or other exercises	Positive effects confirmed for multiple outcomes; subgroup analyses supported beneficial effects; suggests holistic exercise protocols for PD	

								TUG, motor symptoms ; RT improved TUG, knee flexion, leg press				
Feller et al. 2023 (Feller, Fox et al. 2023)	Systematic review with meta- analysis	36 RCTs (14 pooled quantita- tively)	961 partici- pants (for depres- sion outco- me); 485 for QoL Huma- n PD patien- ts (14 studie- s); animal PD model s (18 studie- s)	Meta- analysis / Systematic review	Physical exercise	Patients with Parkinso- n's disease; age and H&Y not specified	Depression symptoms, quality of life, acceptability	Not specificall- y reported	Significant improvement in depressive symptoms and quality of life	Varied across studies	Usual care	Physical exercise significantly reduced depressive symptoms (SMD -0.49) and improved QoL (SMD - 0.51); most studies at high risk of bias; exercise well tolerated
Arenales Arauz et al. 2022 (Arenales Arauz, Ahuja et al. 2022)	Systematic review with meta- analysis	14 human studies + 18 animal studies		Meta- analysis / Systematic review	Whole-Body Vibration (WBV)	PD patients; age and H&Y not specified	Stability, balance, motor function, neuropathologic- al mechanisms	Small but significant improvements in stability (Hedges' g = 0.39) and balance (Hedges' g = 0.30)	Effects on neuroinflammation , neurotransmitter systems, growth factors, neurogenesis, synaptic plasticity, oxidative stress	≥3 weeks duration, ≥3 sessions/week , vibration frequency ≥20 Hz	Control conditions varied	WBV shows small positive effects on human PD motor outcomes; evidence from neuropathological mechanisms in animals supports potential benefits; high-quality studies needed
Ji et al. 2022 (Ji, Lu et al. 2022)	Meta- analysis / Systematic	Multiple RCTs (total 523 PD	PD patients with HY	Meta- analysis / Systematic	Long-term physical therapy	HY stage 1- 3; age not specified	Motor symptoms, ADL, levodopa equivalent dose (LED)	Significant improvements in MDS- UPDRS	ADL scores improved	≥6 months of physical therapy	Short-term PT, other interventions, or no treatment	Long-term PT improves motor symptoms in mild-to- moderate PD, reduces LED dose, effective

	tic review	patients)	stage 1-3	tic review				motor scores; reduced LED dose					with or without antiparkinsonian drugs
Li et al. 2022 (Li, Chen et al. 2022)	Systematic review / Meta-analysis	15 RCTs (488 participants)	Adults with neurodegenerative diseases, mean age 58.6–81.6	Systematic review / Meta-analysis	Wearable sensor-based exercise	Mean age 58.6–81.6; H&Y not specified	Balance (primary), motor symptoms, mobility, functional gait abilities, fall-associated self-efficacy, adverse events	No significant improvement in motor symptoms	No significant changes in secondary non-motor outcomes	3–12 weeks of intervention	Traditional exercise	Wearable sensor-based exercise significantly improved balance compared with traditional exercise, but evidence lacking for motor symptoms and functional mobility; low risk of bias in only 5 studies	
Kashif et al. 2022 (Kashif, Ahmad et al. 2022)	Systematic review	25 RCTs	Patients with Parkinson's disease, age not specified	Systematic review	Virtual reality (VR) interventions	Age not specified ; H&Y not reported	Balance, gait, motor function	UPDRS-III, gait parameters	Not assessed	Intervention details varied; mostly clinic-based, 1 home-based	Traditional physical therapy or other interventions	VR interventions generally improved balance, gait, and motor function; most studies rated fair or good quality; evidence supports VR as supportive rehabilitation tool in PD	
Ono et al. 2023 (Ono, Nishimoto et al. 2023)	Systematic review and meta-analysis	13 RCTs (6 included in meta-analysis)	750 participants; Parkinson's disease and older adults	Meta-analysis	Walking training with poles (pole walking)	Parkinson's disease patients and older adults; age not specified ; H&Y	Walking speed, functional mobility, walking endurance	Walking speed (SMD = 0.42, 95% CI = 0.04–0.80 for PD), functional mobility,	Not assessed	Intervention details varied across studies	Walking without poles and/or other exercise interventions	Moderate-quality evidence that pole walking improves walking speed in PD patients; no significant improvement for functional mobility in PD or walking speed in older adults	

Zhang et al. 2022 (Zhang, Luximon et al. 2022)	Systematic review and meta-analysis	19 RCTs	781 older adults with Parkinson's disease	Meta-analysis	Exergaming-based interventions (EbIs)	Older adults with PD; age not specified; H&Y not reported	Mobility and balance performance	walking endurance TUG (MD = -1.03 s), 6MWT (MD = 63.48 m), BBS (MD = 2.129), FGA (MD = 2.099); gait velocity and stride length not significantly improved	Not assessed	Intervention details varied across studies	Traditional physical training interventions (TPTIs)	EbIs statistically superior to TPTIs for TUG, 6MWT, BBS, and FGA; only 6MWT reached minimal clinically important difference; further research needed
Sivertseva et al. 2022 (Sivertseva, Anfilofeva et al. 2022)	Systematic review and meta-analysis	Not specified	Patients with neurological diseases (PD, stroke, MS, Huntington's disease, spinal cord injury)	Meta-analysis	Dance movement therapy	Age not specified; H&Y not reported	Motor and non-motor outcomes	Motor outcomes reported in PD and post-stroke rehabilitation; details not specified	Cognitive function improved in PD; no effect on depression, fatigue, apathy	Not specified	Usual care or other rehabilitation interventions	Dance therapy effective in improving cognitive impairment in PD and in rehabilitation for other neurological diseases; non-motor outcomes mixed

Chang et al. 2022 (Chang, Song et al. 2022)	Systematic review	16 studies	Elderly adults, stroke patients, Parkinson's patients	Systematic review	Augmented reality (AR)-based interventions	Age not specified; H&Y not reported	Balance, gait, muscle function, physical performance, fall efficacy	Balance, gait, muscle performance, fall efficacy; turning and timing in FOG in PD not improved	Not specified	Not specified	Standard rehabilitation without AR or other interventions	AR interventions showed favorable effects on lower limb rehabilitation, but more robust and homogeneous trials are needed, especially in Parkinson's disease
Wen et al. 2022 (Wen, Liu et al. 2022)	Systematic review of RCTs	10 RCTs	Patients with Parkinson's disease	Systematic review	Physiotherapy interventions for dysphagia: acupuncture, EMST, rTMS, VAST, electrical stimulation, SLT	Age not specified; H&Y not reported	Swallowing function / dysphagia	Not applicable	Dysphagia severity and swallowing function	Not consistently reported across studies	Usual care or sham interventions	Acupuncture, EMST, high-frequency rTMS, and VAST showed potential efficacy; insufficient evidence for electrical stimulation
Hortobágyi et al. 2022 (Hortobágyi, Vetrovsky et al. 2022)	Systematic review with meta-analysis and meta-regression	50 studies, 60 intervention arms	2283 participants	Systematic review + meta-analysis	Aerobic and resistance training (low- vs. high-intensity)	Healthy young and older adults; patients with MS, Parkinson's disease, stroke	Neuroplasticity markers, motor and cognitive function, brain activation, brain structure	Motor outcomes improved with exercise-induced neuroplasticity	Cognitive outcomes not significantly associated with neuroplasticity changes	Intensity varied: low- vs. high-intensity aerobic and resistance training	Usual care or lower-intensity interventions	Exercise intensity scaled neuroplasticity in healthy young adults, but not in older adults or neurological patients; motor improvements associated with neuroplasticity, cognition not significantly associated

Bishnoi et al. 2023 (Bishnoi, Shankar et al. 2023)	Systematic review and meta-analysis	25 RCTs	Adults ≥55 years with neurological disorders (Parkinson's disease, stroke, others)	Standard meta-analysis	Sensory stimulation (auditory, somatosensory), electrical stimulation, physical activity, conventional physical therapy	PD adults ≥55 years, stroke adults ≥55 years, H&Y not reported	Changes in spatiotemporal gait parameters (cadence, step length, step width, double limb support)	Step length, cadence, gait speed, step width, double limb support	Not reported	Variable by study; interventions included sensory stimulation, electrical stimulation, physical activity, conventional therapy; frequency/intensity varied by study	Usual care / Control groups included RCTs	Sensory and electrical stimulation most effective for PD step length and gait speed; physical activity improved cadence; conventional therapy improved step length and cadence in stroke; heterogeneity considered in analysis
Gollan et al. 2022 (Gollan, Ernst et al. 2022)	Systematic review and meta-analysis	18 RCTs	Patients with Parkinson's disease	Standard meta-analysis	Resistance training	PD adults, age not specified, H&Y stage not specified	Motor and non-motor outcomes including muscle strength, motor impairment, freezing of gait, mobility, balance, QoL, depression, cognition, adverse events	Muscle strength, motor impairment, mobility, balance, freezing of gait	Quality of life, depression, cognition	Variable by study; RT protocols differed across included studies	Passive control and physically active control groups	RT improved muscle strength, motor impairment, mobility, balance, QoL, and depression compared with passive control, but not superior to other active interventions
Tian et al. 2022 (Tian, Kang et al. 2022)	Systematic review and meta-analysis	14 RCTs	516 patients with Parkinson's disease	Standard meta-analysis	Physical activity (resistance exercise, other forms of exercise)	PD adults, age not specified, H&Y stage not specified	Depression	Not reported	Depression (primary outcome)	Resistance exercise: 60–90 min, >4 times/week, up to 12 weeks; other interventions varied	Control groups included RCTs	Physical activity significantly improved depression; subgroup analysis showed strongest effect for long-term PD patients (>5 years); further

												large-scale studies needed
Allen et al. 2022 (Allen, Canning et al. 2022)	Systematic review and meta-analysis	32 studies (25 exercise, 3 medication, 1 education, 3 exercise+education)	3370 participants with Parkinson's disease	Standard meta-analysis	Exercise interventions, exercise plus education, cholinesterase inhibitors, fall-prevention education	Mild to moderate PD adults, age not specified, H&Y not specified	Falls, fall-related fractures, quality of life, adverse events	Rate of falls, number of people falling	Health-related quality of life, adverse events	Variable by study; exercise and exercise+education interventions varied in type, frequency, and intensity; cholinesterase inhibitors per study protocols	Control interventions: usual care, sham exercise, or passive control	Exercise reduces fall rate and slightly reduces people falling; cholinesterase inhibitors may reduce fall rate but increase non-fall-related adverse events; evidence for education limited; further high-quality RCTs needed
Salse-Batán et al. 2022 (Salse-Batan, Sanchez-Lastra et al. 2022)	Systematic review and meta-analysis	12 RCTs	People with Parkinson's disease	Standard meta-analysis	Nordic walking	PD adults, age not specified, H&Y not specified	Walking ability, motor impairment, functional mobility, balance, physical fitness, quality of life	Walking ability, motor impairment, functional mobility, balance, physical fitness	Quality of life	Variable by study; NW programs adhered to well, specific duration/frequency not standardized	Control groups in included RCTs	NW improved walking ability and quality of life (latter needing further research), but no clinically significant changes in global motor impairment, functional mobility, balance, or physical fitness; some minor adverse effects reported
Carmignano et al. 2022 (Carmignano, Fundaro et al. 2022)	Systematic review	20 studies (9 RCTs, 4 uncontrolled studies,	Patients with Parkinson's disease	N/A	Robot-assisted gait training (exoskeleton and end-effector devices)	PD adults, age not specified, disease severity variable,	Gait outcomes	Gait	Not reported	Variable by study; training protocols differed by device and study	Other interventions in included studies	RAGT showed benefits on gait, no adverse events reported; not superior to other interventions except in patients with more severe or advanced PD

		2 SRs, 5 descriptive reports)				H&Y not specified						
Hvingelby et al. 2022 (Hvingelby, Glud et al. 2022)	Systematic review and network meta-analysis	148 RCTs	Patients with Parkinson's disease	Network meta-analysis	Aquatic therapy with dual task, strength and balance training, high-frequency rTMS, other gait interventions	PD adults, age not specified, H&Y not specified	Gait measures (dynamic gait, fitness, balance, freezing of gait)	Dynamic gait, fitness, balance, freezing of gait	Not reported	Variable by study; interventions differed in type, frequency, and duration	Other interventions or usual care included RCTs	Aquatic therapy and strength/balance training most effective for dynamic gait and fitness; high-frequency rTMS also effective for fitness; no interventions significantly improved freezing of gait; no superior intervention could be recommended
Bishnoi et al. 2022 (Bishnoi, Lee et al. 2022)	Systematic review & meta-analysis	32	PD & stroke	Meta-analysis	Treadmill interventions	Adults ≥55, neurological disorders	Gait parameters	↑ Step & stride length (PD & stroke); ↑ cadence (stroke)	Not specifically reported	Variable; interventions heterogeneous	Active controls (overground PT, usual care)	Sensory stimulation & body-weight support had largest effect on step length.
Truijen et al. 2022 (Truijen, Abdullahi et al. 2022)	Systematic review	25	PD patients	Narrative synthesis	Home-based exercise	Mild to moderate PD	Motor & non-motor outcomes	Improvement in balance & gait	QoL, adherence improved	Variable across studies	Usual care / no intervention	Home-based interventions feasible and safe.
de Almeida et al. 2022 (de Almeida, Santana et al. 2022)	Meta-analysis & systematic review	27 RCTs	1152 PD patients	Between-group effect sizes (Hedges' g)	Endurance training	PD; H&Y not specified	Motor signs (UPDRS-III)	ET decreases UPDRS-III scores vs. nonactive (g=-0.68) & active	Not reported	Variable; included different intensities	Nonactive & active controls	ET effective; dose-response relationship unclear.

Wang et al. 2022 (Wang, Sun et al. 2022)	Systematic review & meta-analysis	9	307 PD patients	Meta-analysis	Dance therapy	PD; age not specified	Cognition, depression, fatigue, apathy	controls (g=-0.33) ↑ Cognition (MD 1.50, 95% CI 0.52–2.48) VR as effective as conventional training; some studies show greater effect; motivation improved RT ↑ strength, ↑ functional capacity, ↑ QoL; ET ↑ cardio fitness, ↑ functional capacity; OITM feasible & safe Improvement in balance;	No significant effect on depression, fatigue, apathy	6–12 weeks; frequency varied	Passive / usual care	Dance therapy improves cognitive function; no effect on other non-motor symptoms.
Sevcenko et al. 2022 (Sevcenko and Lindgren 2022)	Systematic review	18 RCTs	PD & stroke	Descriptive syntheses	Virtual reality training	PD & stroke; age not specified	Functional ability		Usability generally well accepted	Variable; 2016–2020 RCTs	Conventional training	Disorder-specific considerations advised; high methodological quality.
Gamborg et al. 2022 (Gamborg, Hvid et al. 2022)	Systematic review & meta-analysis	33 RCTs	PD patients	Qualitative & quantitative analyses	Intensive exercise (resistance, endurance, OITM)	PD; H&Y not specified	Strength, functional capacity, UPDRS-III, cardio fitness		Depressive symptoms improved in some studies	Variable; 5–12 weeks	Control / usual care	RT & ET show solid effects; inconsistencies warrant cautious interpretation.
Vinolo Gil et al. 2021 (Vinolo Gil,	Systematic review	11	308 participants	Meta-analysis	Augmented reality +	PD & other patients	Balance, limb function		Not consistently reported	Variable; interventions	Conventional therapy	Positive effects but high heterogeneity; small sample sizes.

Gonzalez-Medina et al. 2021)	& meta-analysis			on 4 studies	conventional therapy			limb function improved		heterogeneous		
Fail et al. 2022 (Fail, Marinho et al. 2022)	Systematic review & meta-analysis	62	Healthy & chronic disease adults	Meta-analysis	Aquatic exercise	Adults; healthy & chronic disease	Strength, balance, cardiorespiratory fitness, QoL	↑ Strength, balance, cardio fitness across conditions	QoL improved in chronic disease adults	8–16 weeks; 2–3x/week, 46–65 min/session	Passive / usual care	Effective for health & fitness in both healthy & diseased adults.
Gandhi and Steele 2022 (Gandhi and Steele 2022)	Systematic review	26	PD patients with dysphagia	Narrative synthesis	Dysphagia interventions (pharmacological, neurostimulation, behavioral)	PD adults	Swallowing timing, safety, efficiency	Exercises with biofeedback & DBS improve timing; LSVT & levodopa improve efficiency	Safety improved with DBS & expiratory muscle strength training	Variable; ≥5 participants/study	Control / usual care	Studies with higher methodological rigor showed benefits; low certainty evidence overall.
García-López et al. 2021 (García-López, Obrero-Gaitan et al. 2021)	Systematic review	10	537 PD patients	Between-group effect sizes	Non-immersive VR	PD; age 55–80	Balance & falls	Balance improved; step & stride improvements; not significant in all studies	Reduced number/risk of falls	5–12 weeks; 30–75 min/session	Control / usual care	Effective in balance & fall prevention; some studies show no significant difference.
Hulzinga et al. 2021 (Hulzinga, de Rond et al. 2021)	Systematic review	209 (PD & healthy)	209 PD & healthy adults	Narrative synthesis	Repeated gait perturbation training	PD & older adults	Gait & balance	No pooled significant effect; some individual	Not specifically reported	Variable across studies	Control / usual care	Individual improvements seen; overall effect not significant.

Campo-Prieto et al. 2021 (Campo-Prieto, Santos-Garcia et al. 2021)	Systematic review	10	PD patients	Narrative synthesis	Immersive VR	PD; age not specified	Physical & functional capacity	improvements in physical and functional abilities	Not reported	Variable; feasibility confirmed	Control / usual care	Feasible and safe; small sample sizes.
Sarasso et al. 2022 (Sarasso, Gardoni et al. 2022)	Systematic review & meta-analysis	9	901 PD patients	Between-group effect sizes	VR-based balance training	PD; age not specified	Balance, mobility	↑ BBS (MD 2.09); ↑ TUG (MD 1.55 s)	Not reported	Variable; 3–5 weeks	Control / conventional physiotherapy	VR improves balance & mobility.
Salari et al. 2022 (Salari, Hayati et al. 2022)	Systematic review	1760	Stroke, PD, MS	Narrative synthesis	Exercise	Adults; age not specified	Balance	↑ Balance (0.67 ± 0.12); highest in myelomeningocele (1.66 ± 0.3)	Not reported	Variable	Control / usual care	Exercise effective in multiple populations.
Tiihonen et al. 2021 (Tiihonen, Westner et al. 2021)	Systematic review & meta-analysis	22	505 PD patients	Inverse variance-based meta-analysis	Cycling / bicycling interventions	PD; severity varied	Motor & cognitive, balance, QoL	Motor & balance improved; gait features improved	QoL improved (PDQ-39)	Variable	Control groups varied	Beneficial for motor performance & QoL; interventions heterogeneous.
Suárez-Iglesias et al. 2022 (Suarez-Iglesias, Santos et al. 2022)	Systematic review & meta-analysis	14 RCTs (meta-analysis on 5)	PD patients with mild-moderate	Between-group effect sizes (meta-analysis)	Yoga	Mild-moderate PD; age not specified	Motor & non-motor symptoms, QoL	Motor symptoms improved vs passive control; comparable	QoL & psychological benefits reported	Variable; heterogeneous protocols	Passive control / exercise interventions	Safe, feasible, well-accepted; improves motor & non-motor outcomes.

			diseases					e to other exercises				
Vellata et al. 2021 (Vellata, Belli et al. 2021)	Systematic review	15	421 PD patients	Narrative synthesis	Telerehabilitation	PD; age not specified	Motor & non-motor function, QoL, patient satisfaction	Some improvements in gait, balance, dexterity FOG severity: moderate improvement; targeted FOG ES=-0.24; interventions addressing FOG correlates ES=-0.40; generic exercise not significant Attenuated complex I deficits, cytochrome c release, ATP depletion, complexes II-V	Speech & QoL improved	Variable across studies	Control varied	Feasible; cognitive impairment not addressed; studies heterogeneous.
Gilat et al. 2021 (Gilat, Ginis et al. 2021)	Systematic review & meta-analysis	41	1838 PD patients	Between-group effect sizes (ES)	Exercise & training targeting FOG	Adults with PD; FOG status varied	FOG severity, gait function		Not reported	Variable; retention effects not seen post-training	Control varied	Targeted FOG interventions moderately effective; generic exercises ineffective.
Nhu et al. 2021 (Nhu, Cheng et al. 2021)	Systematic review (animal studies)	10 controlled trials	Animal models of PD	Narrative synthesis / qualitative meta-analysis	Treadmill exercise	Animal models	Neural mitochondrial function		Improved mitochondrial biogenesis, fusion, mitophagy	1-18 weeks; various durations	Control / sedentary animals	Suggest treadmill exercise may slow PD progression via mitochondrial mechanisms.

Elena et al. 2021 (Elena, Demetris et al. 2021)	Systematic review & meta-analysis	14	548 PD patients	Between-group effect sizes	Exergaming rehabilitation	Older adults with PD	QoL, balance, gait, UPDRS, TUG	abnormalities Balance & gait improved; UPDRS & TUG not significant	QoL improved	Not specified	Conventional physiotherapy	Exergaming shows positive effects; further research needed on mental health outcomes.
Álvarez-Bueno et al. 2023 (Álvarez-Bueno, Deeks et al. 2023)	Network meta-analysis of RCTs	56 studies	2,740 participants across 56 studies, age 57.6–77.7	Network meta-analysis	9 exercise categories: endurance, resistance, combined, balance, dance, alternative exercises, body weight supported, sensorimotor (with/without endurance)	Patients with Parkinson's disease	Motor symptoms (UPDRS-III)	Motor symptoms improvement	Not reported	Varied per study; interventions included multiple exercise modalities	Control / non-intervention groups	Most effective interventions: sensorimotor training including endurance (ES -1.09), resistance (ES -0.82), and dance (ES -0.64); highlights that complex, demanding exercises are most effective
Amirthalingam et al. 2021 (Amirthalingam, Paidi et al. 2021)	Systematic review of RCTs	13 RCTs	NR (mixed population: PD, stroke, CP)	Narrative synthesis (no pooled meta-analysis)	Virtual Reality-based rehabilitation	Adults with PD and stroke; children with CP (details vary by study; PD severity not always	Motor function (gait, balance, posture, upper limb function)	Improved gait and posture in PD; improved upper limb, gait and balance in stroke; no significant change in CP	Not assessed	Various protocols; intensity and duration varied across trials (short-to medium-term interventions)	Conventional rehabilitation	VR interventions showed significant motor improvements in PD and stroke; no effect in CP. Some studies showed sustained benefits months after intervention.

Okada et al. 2021 (Okada, Ohtsuka et al. 2021)	Systematic review + meta-analysis	10 RCTs	663 (PD)	SMD	Long-term physiotherapy (≥6 months)	PD, H&Y 1–3	Motor symptoms, levodopa-equivalent dose (LED)	↓ motor symptoms off medication (SMD -0.65), ↓ LED (SMD -0.49) ↑ Plasma BDNF levels significantly in PD and other conditions (SMD overall = 2.22, 95% CI: 1.33–3.12, p < 0.001)	Not assessed	≥6 months	No/control intervention	Subgroup: aerobic exercise improved motor symptoms; multidisciplinary rehab reduced LED; low/very low quality evidence
Ruiz-González et al. 2021 (Ruiz-Gonzalez, Hernandez-Martinez et al. 2021)	Systematic review and meta-analysis of RCTs	18 RCTs (MS, PD, MCI, AD)	NR (varied across studies)	Standardized mean difference (SMD)	Physical exercise (combined, aerobic, resistance)	Individuals with neurodegenerative disorders, including PD	Plasma BDNF levels	Improvements reported in rigidity and stiffness associated with exercise and hydrotherapy	Not assessed (no pain outcomes)	≥12 and <12 weeks; ≥150 and <150 min/week; all intensities effective	No exercise	Exercise increased BDNF regardless of type, duration or volume. Strongest evidence for MS and PD; trend for MCI.
Qureshi et al. 2021 (Qureshi, Jamal et al. 2021)	Systematic review	Not specified (narrative synthesis)	Not reported	Narrative synthesis (no pooled meta-analysis)	Non-pharmacological pain management (exercise, hydrotherapy, acupuncture, massage, neuromodulation – DBS and SCS)	Patients with Parkinson’s disease	Pain intensity (VAS), pain perception, musculoskeletal pain, dystonic pain, central pain	Significant reduction in pain perception with exercise, hydrotherapy, acupuncture, massage, and neuromodulation; DBS effective for dystonic/central pain; SCS	Duration and intensity varied widely between studies and interventions	Usual care or pharmacological treatment	Evidence supports beneficial effects of multiple non-pharmacological approaches for PD pain management. DBS and SCS showed more specific effects for certain pain types, while exercise and hydrotherapy provided broader analgesic	

Farashi et al. 2021 (Farashi, Kiani et al. 2021)	Meta-analysis	7 studies	Not reported (varied)	Meta-analysis (log OR, 95% CI)	Exercise therapy (hand movement, cycling, upper/lower/whole-body)	Patients with Parkinson's disease; mild to moderate	Tremor amplitude, tremor frequency	log(OR) for all exercise types = 2.00 (95% CI 0.88–3.12; I ² = 78%); hand movement exercise log(OR) = 1.00 (95% CI 0.24–1.77; I ² = 0.0%) — significant reduction in tremor amplitude /frequency	Not assessed	4–12 weeks; frequency and session duration varied across studies	Usual care or no intervention	improved VAS pain scores	benefits. Literature still sparse; more RCTs are needed.
								UPDRS III: MD = –4.49 at 3 months, –5.96 at 6 months, –14.58 at 12 months (all p < 0.01); significant					Exercise significantly reduced tremor in PD patients, especially hand movement exercises which had lower heterogeneity. No significant publication bias detected. Exercise is low-cost, non-invasive, and suitable as an adjunct to pharmacological treatment.
Hasan et al. 2022 (Hasan, Alshafie et al. 2022)	Systematic review and meta-analysis	14 RCTs	372	Meta-analysis of continuous outcomes (MD, 95% CI)	Dance therapy / structured dance interventions	Patients with Parkinson's disease; mild to moderate severity (Hoehn	UPDRS III, Mini-BESTest, TUG, Berg Balance Scale (BBS), functional mobility, cognition		Cognition and balance confidence improved	3–12 months; 2–3 sessions/week; 45–60 min/session	Conventional exercise or no intervention		Dance therapy produced significant improvements in motor symptoms, balance, and functional mobility. Positive effects were sustained over time (notably at 12 months). Most studies used tango, ballroom, or contemporary

Picelli et al. 2021 (Picelli, Capecchi et al. 2021)	Systematic review	18 studies (2 SRs, 9 RCTs, 4 uncontrolled, 3 case series)	Not reported (varied)	Narrative synthesis (no pooled meta-analysis)	Robot-assisted gait training (end-effector & exoskeleton)	Patients with Parkinson's disease; mild to advanced stages (Hoehn & Yahr I–IV)	Postural stability, static and dynamic balance, freezing of gait (FOG), falls, balance confidence (ABC), gait parameters related to balance	Improvement in TUG and BBS compared with exercise or no activity	Balance confidence (ABC), activities of daily living	Intervention duration varied (typically 4–8 weeks); intensity and frequency heterogeneous	Conventional gait training, usual care, or no intervention	dance. No serious adverse events reported. Moderate heterogeneity across studies.
Cortés-Pérez et al. 2021 (Cortés-Pérez, Zagalaz-Anula et al. 2021)	Systematic review and meta-analysis	5 RCTs	149	Meta-analysis of continuous outcomes (SMD)	Leap Motion Controller (LMC) video game-based therapy	Stroke; non-acute CNSD (cerebral palsy, multiple sclerosis, Parkinson's disease); mean	Upper extremity (UE) mobility, UE mobility-oriented tasks, grip strength (GS), gross motor dexterity (GMD), fine motor dexterity (FMD)	Improvement in mobility	Not reported	4–8 weeks; 2–5 sessions/week; 30–60 min/session	Conventional therapy (CT)	LMC showed moderate to large effects on UE mobility and dexterity. Evidence quality ranged from low to very low. Stronger effects when LMC combined with conventional therapy. No adverse events reported. Limited sample sizes across included RCTs.

						age ≈ 55 years		CI 0.03– 0.90); GMD 0.73 (95% CI 0.28–1.17); with CT: GMD 0.80 (95% CI 0.06–1.15), FMD 0.82 (95% CI 0.07–1.57). UPDRS total (ES = -0.35), UPDRS III (ES = - 0.35), stride length (ES = 1.00), BBS (ES = 0.65)				
Lorenzo- García et al. 2021 (Lorenzo- García, Cavero- Redondo et al. 2021)	Systema- tic review and meta- analysis	12 RCTs	419	Meta- analysis of continuo- us outcome- s	Body Weight Support (BWS) gait training	Mean age ≈ 65 years; Hoehn & Yahr I–III	UPDRS total, UPDRS III, 6MWT, gait velocity, cadence, stride length, BBS	Improved balance and gait; no significant effect on motor symptoms	None reported	4–12 weeks; 2–5 sessions/week ; session duration 20– 45 min	Conventiona- l gait training / usual care	Significant improvements in overall clinical severity, stride
Li et al. 2021 (Li, Song et al. 2021)	Systema- tic review with meta- analysis	9 RCTs	444 patien- ts with PD	Standar- d meta- analysis	Moderate aerobic exercise	PD, various stages	Balance, gait, motor symptoms, quality of life	Significant improvement in gait velocity,	Quality of life improved, especially in treadmill subgroup	Varied; treadmill- based interventions most effective for QoL	Compared to usual care or no exercise	Moderate aerobic exercise is safe and effective for balance and gait; limited effect on motor symptoms; effects on QoL depend on exercise type
Yu et al. 2021 (Yu, Wu et al. 2021)	Systema- tic review and	17 RCTs	951 PD patien- ts	Pairwise meta- analysis	Tai Chi	PD patients (age not specified	Gait velocity, UPDRS-III, Berg Balance Scale (BBS), Activities-	Significant improvement in gait velocity,	No significant effect on PDQ-39 (QoL) or TUGT	Duration/freq- uency/intensit- y varied across RCTs;	Usual care, routine exercise, or other control	Tai Chi was safe, improved motor function and balance; no clear benefit for

	meta-analysis of RCTs			(RevMan 5.3)		; H&Y not explicitly reported)	specific Balance Confidence (ABC), Timed Up and Go Test (TUGT), PDQ-39	UPDRS-III, BBS, ABC		not standardized in abstract	conditions depending on included RCTs	QoL; need for higher-quality, larger RCTs
Alexandre de Assis et al. 2020 (Alexandre de Assis, Luvizutto et al. 2020)	Systematic review and meta-analysis	6 studies (3 included in meta-analysis)	PD patients (number not specified)	Meta-analysis on gait speed, stride length, cadence	Proprioceptive Neuromuscular Facilitation (PNF)	PD patients (age and H&Y not specified)	Walking speed, stride length, cadence	Significant improvement in gait speed; stride length and cadence analyzed Significant improvements in leg strength, balance, fast gait velocity, TUG, FOG-Q; no significant change in stride length	Not reported	Duration/frequency/intensity not standardized; details not reported	Other therapies (comparators varied across studies)	PNF is similar or superior to other therapies for gait speed; limited RCTs; further high-quality studies needed
Li et al. 2020 (Li, He et al. 2020)	Systematic review and meta-analysis of RCTs	25 RCTs (31 papers)	1,239 PD patients	Pairwise meta-analysis (random/fixed effects)	Lower limb resistance training (RT)	PD patients (age and H&Y not specified)	Leg strength, balance, gait performance (fast gait velocity, TUG, FOG-Q, stride length), QoL	QoL significantly improved	QoL significantly improved	Duration/frequency/intensity varied across trials; details not standardized	Usual care or other control interventions depending on trial	RT has positive effects on motor function, balance, gait, and QoL; heterogeneity in outcome measures; further studies needed
Marquez et al. 2020 (Marquez, Aguinaga et al. 2020)	Systematic review	Systematic reviews, meta-analyses, and pooled analyses	General population and individuals with	Narrative/meta-analytic syntheses	Physical activity (PA)	Adults 18–65+ and older adults; specific ages for clinical	QoL, well-being	Not specifically assessed	QoL and well-being improved with PA in adults and some clinical populations	Duration/frequency/intensity varied; different modes and intensities of PA	Minimal or no-treatment controls	Strong evidence in adults and older adults; moderate evidence for PD and schizophrenia; limited evidence for youth and adults with depression/bipolar;

		(2006–2018)	psychiatric/neurologic conditions (including PD, schizophrenia, depression, bipolar disorder, dementia)			populations not reported						insufficient evidence for dementia; high-quality RCTs needed
Cristini et al. 2021 (Cristini, Weiss et al. 2021)	Systematic review with meta-analysis	12 studies (10 RCTs, 2 non-RCTs)	690 PD patients	Meta-analysis (SMD with 95% CI)	Exercise (various modalities)	PD patients (age and H&Y not specified)	Sleep quality (subjective and objective)	Not reported	Subjective sleep quality improved; objective sleep efficiency improved in one study	Moderate to maximal intensity exercise effective; mild to moderate intensity non-significant	Control interventions varied; minimal/no treatment or standard care	Exercise improves sleep quality in PD; higher intensity yields better outcomes; methodological quality of positive studies lower; further high-quality RCTs needed
van de Wetering-van Dongen et al. 2020 (van de Wetering-van Dongen,	Systematic review	10 studies (4 RCTs, 4 controlled trials)	PD patients (number not specified)	Narrative synthesis	Respiratory training (IMST, EMST, air stacking, breath-stacking, incentive	PD patients (age and H&Y not specified)	Respiratory muscle strength, swallowing safety, phonatory aspects, chest wall volumes	Improvements in respiratory muscle strength	Improvements in swallowing safety and phonatory function	Intervention protocols varied across studies; details not standardized	Control interventions varied depending on study	Respiratory training shows positive effects; best evidence for EMST, IMST, EMST+air stacking; future studies should standardize

Kalf et al. 2020)					spirometry, postural training)							devices and outcome measures
Rodríguez et al. 2021 (Rodriguez, Albillos-Almaraz et al. 2021)	Systematic review	6 studies (5 RCTs, 1 controlled trial)	PD patients (number not specified)	Narrative synthesis	Vigorous-intensity aerobic exercise	PD patients (age and H&Y not specified)	Disease severity, motor function, aerobic fitness	No significant improvement in motor function	No significant improvement in non-motor outcomes	Vigorous intensity defined as $\geq 77\%$ max HR, 60% HR reserve, or $\geq 64\%$ VO ₂ max; details varied by study	Moderate/low-intensity aerobic exercise	Evidence too limited to recommend vigorous aerobic exercise over moderate/low intensity; only one study showed higher aerobic fitness with vigorous exercise
Berti et al. 2020 (Berti, Pini et al. 2020)	Systematic review	21 studies (RCTs, controlled trials, case reports)	PD patients (number not specified)	Narrative synthesis	Argentine tango dance interventions	PD patients (age and H&Y not specified)	Motor function, adherence, intervention applicability	Positive effects on motor function implied; detailed outcomes varied by study	Not explicitly reported	Intervention delivery varied; dosing and procedures usually detailed; predominantly extensive programs	Control groups varied or absent depending on study	Tango programs adaptable and feasible; reporting of interventions generally adequate but could be improved; Adapted Tango is most researched modality
Aburub et al. 2020 (Aburub, Ledger et al. 2020)	Systematic review	9 studies	PD patients (number not specified)	Narrative synthesis	Aerobic exercise	Early-stage PD (age and H&Y not specified)	Cardiopulmonary function, cardiac function, pulmonary function	Not explicitly reported	Not explicitly reported	Duration/frequency/intensity varied; details not standardized	Control conditions varied or not specified	Aerobic exercise may improve cardiac function in early-stage PD; lack of studies on pulmonary function; further research needed
Carapellotti et al. 2020 (Carapellotti, Stevenson et al. 2020)	Systematic review and meta-	16 RCTs (9 included in meta-	636 PD patients	Meta-analysis on motor, non-	Dance interventions	Mild to moderate PD (age not	Motor impairments, balance, motor symptom severity, non-	Improvements in balance and motor	Effects on non-motor symptoms and QoL less clear; more research needed	Interventions >1 day; duration/frequency/intensity	Control conditions varied	Dance improves motor impairments, particularly balance; further research needed for non-motor

	analysis of RCTs	analysis)		motor, and QOL outcomes		specified)	motor symptoms, QoL	symptom severity		y varied across studies		symptoms and QoL; larger RCTs recommended
Abou et al. 2021 (Abou, Alluri et al. 2021)	Systematic review and meta-analysis	61 trials in review, 53 trials in meta-analysis	3,954 participants in review ; 3,524 in meta-analysis	Meta-analysis on fear of falling outcomes	Physical therapy interventions (gait + balance training, home-based exercise, leisure exercise)	Adults with neurologic diseases including PD, MS, stroke, SCI (age and H&Y not specified)	Fear of falling (FOF)	Gait with balance training reduced FOF in PD; home-based/leisure exercise improved FOF in MS	Not specifically reported	Duration/frequency/intensity varied by study; details not standardized	Usual care or gait training alone	Interventions effective for FOF in PD and MS; limited evidence for stroke and SCI; overall evidence quality very low to moderate; further research needed
de Almeida et al. 2021 (de Almeida, Porto et al. 2021)	Systematic review and meta-analysis	11 RCTs/quasi-RCTs	393 PD patients (211 dance, 182 control)	Meta-analysis on postural control	Dance interventions	Idiopathic PD (age and H&Y not specified)	Postural control	Dance improved postural control (SMD = 0.82)	Not reported	Intervention duration varied; short-term improvements observed	Control groups (usual care or non-dance activity)	Dance improves postural control in PD; can be effective in a short period; may help prevent falls
Chen et al. 2020 (Chen, Zhang et al. 2020)	Systematic review and meta-analysis	7 RCTs	325 PD patients (180 males, 145 females)	Meta-analysis (random-effects)	Qigong exercise	PD patients (age not specified)	Motor symptoms, walking ability, balance	Improved motor symptoms (SMD = 0.59), walking ability	Not reported	Duration/frequency/intensity varied across studies; subgroup	Active or passive controls depending on study	Qigong improves motor function, walking, and balance; effects on motor symptoms influenced by age; beneficial alternative therapy

			female s)					(SMD = 0.78), balance (SMD = 0.72) Improved gait speed (SMD = - 0.23), cadence (SMD = - 0.25), motor symptoms (SMD = 0.56), balance (SMD = - 0.44); no significant change in step or stride length Wii and Kinect improved functional locomotion; Wii may be superior Improved balance (Hedge's g		analysis performed		
Li et al. 2020 (Li, Wang et al. 2020)	Systematic review and meta-analysis	11 RCTs	322 PD patients	Meta-analysis on gait, motor symptoms, balance	Dual-task training	PD patients (age and H&Y not specified)	Gait parameters, motor symptoms, balance		Not reported	Duration/frequency/intensity varied by study; details not standardized	Non-intervention or other training forms	Dual-task training improves gait, motor symptoms, and balance relative to controls; effective in PD rehabilitation
Marotta et al. 2022 (Marotta, Calafiore et al. 2022)	Systematic review and network meta-analysis	7 RCTs	236 PD patients	Network meta-analysis	Exergames (Nintendo Wii™, Xbox Kinect™)	PD patients (age and H&Y not specified)	Functional locomotion		Not reported	Intervention duration/frequency/intensity varied; details not standardized	Control groups (usual care or no intervention)	Wii may provide better functional recovery than Kinect; useful for locomotion rehabilitation and visual cueing in patients with freezing
Prosperini et al. 2021 (Prosperini,	Systematic review	41 RCTs	1223 patients	Meta-analysis with	Exergames	Adults with neurolo	Balance function		Not reported	Intervention duration varied; higher	Alternative intervention	Exergames are effective and safe for improving balance; possible

Tomassini et al. 2021)	and meta-analysis		(various neurological conditions including PD)	meta-regression		gical disabilities (age and H&Y not specified)		= 0.43); higher session frequency → larger effect		weekly frequency associated with better effect; intensity of single session not significant	s or usual care	sustained effect; mild-moderate adverse events in few studies
Chen et al. 2020 (Chen, Gao et al. 2020)	Systematic review and meta-analysis of RCTs	14 RCTs (12 in meta-analysis)	574 PD patients (481 in meta-analysis)	Meta-analysis	Virtual reality (VR) training	PD patients (age and H&Y not specified)	Balance (Berg Balance Scale, Dynamic Gait Index, Functional Gait Assessment), gait	VR improved Berg Balance Scale, Dynamic Gait Index, Functional Gait Assessment; TUG not significant	Activities-Specific Balance Confidence not significant	Intervention duration/frequency/intensity varied across studies; details not standardized	Active interventions	VR comparable to active interventions; promising adjunct for balance rehabilitation; moderate statistical evidence; differences did not reach clinically important change threshold
Miller et al. 2020 (Miller, Suárez-Iglesias et al. 2019)	Systematic review and meta-analysis of RCTs	12 studies in qualitative synthesis; 4 RCTs in meta-analysis	PD patients with FOG (sample sizes not specified)	Meta-analysis	Physiotherapy interventions, especially with visual/auditory cueing	PD patients with FOG (age and H&Y not specified)	Freezing of gait (FOG)	interventions, particularly those with cueing, significantly improved FOG	Not reported	Duration/frequency/intensity varied across studies; details not standardized	Control groups (traditional physiotherapy or no intervention)	Cue-based physiotherapy more effective than traditional approaches; methodological quality generally good; further research needed for PD patients with cognitive impairment and objective FOG measures

Rutz and Benninger 2020 (Rutz and Benninger 2020)	Systematic review	20 RCTs	PD patients with FOG and/or gait impairments	Narrative synthesis (no pooled meta-analysis)	Physical therapy interventions: cueing (visual/auditory/tactile), treadmill walking, aquatic obstacle training, slackline, balance/coordination training	PD patients (age and H&Y not specified)	Freezing of gait (FOG), gait impairments	Cueing strategies, treadmill walking, aquatic obstacle training, supervised slackline training effective for reducing FOG; treadmill and cues also improve general gait kinematics	Not reported	Duration/frequency/intensity varied; not standardized across studies	Control groups (usual care, no intervention, or other PT interventions)	Evidence level A for visual/auditory cueing, treadmill, aquatic obstacle, slackline; tactile cues and other therapies probably effective but need further research; lack of long-term follow-up studies
da Costa et al. 2020 (da Costa Daniele, de Bruin et al. 2020)	Systematic review and meta-analysis	103 preclinical studies	1,172 mice	Meta-analysis	Exercise (primarily treadmill running)	Healthy, Alzheimer's disease, Parkinson's disease models	Learning, memory, neurogenesis, BDNF, TrkB, amyloid clearance, amyloid plaques	Not the main focus; motor behavior sometimes assessed	Cognitive outcomes (learning, memory), molecular outcomes (BDNF, TrkB, neurogenesis, amyloid)	4–8 weeks (range 24 h to 32 weeks), 60 min/day (range 8–120 min/day), 10–12 m/min (range 0.2–36 m/min)	Non-exercised controls	Exercise improved learning/memory, neurogenesis, increased BDNF/TrkB, reduced amyloid plaques; effects seen in healthy and disease models; scarce evidence on inflammation, oxidative stress, energy metabolism; limited data on acute vs chronic exercise,

												extreme training, and durability of effects
		10 studies (5 WBV included in meta-analysis, 3 localized vibration qualitative syntheses)	PD patients (number not specified)	Meta-analysis (WBV)	Vibratory stimulation (Whole Body Vibration [WBV] and localized vibration)	Parkinson's disease	Gait, balance, quality of life	Gait (Timed Up and Go test, Stand-walk-sit test improved with WBV)	Quality of life (no significant effect)	WBV: protocols varied; details per study	Conventional physiotherapy	WBV improved gait performance significantly; no significant improvements for other outcomes; localized vibration data too heterogeneous for meta-analysis; suggests vibration may modulate motor responses via proprioception
Marazzi et al. 2021 (Marazzi, Kiper et al. 2021)	Systematic review and meta-analysis											
Morris et al. 2019 (Morris, Ellis et al. 2019)	Systematic review	2 studies	37 PD participants	Narrative syntheses (no quantitative meta-analysis)	Boxing exercises	Parkinson's disease	Balance, mobility, quality of life	Balance, mobility improved	Quality of life improved	24–36 sessions over 12 weeks	Not always specified	Evidence limited due to small number of studies and participants; interventions incompletely reported; websites promoting boxing often lack verifiable evidence; safety guidelines and professional training highlighted as important
Jin et al. 2019 (Jin, Wang et al. 2019)	Systematic review	22 studies (21 RCTs)	1199 PD participants	Quantitative meta-analysis	Mind-body exercises (Tai Chi, Yoga,	Parkinson's disease; age not	Motor function, depressive symptoms, quality of life	UPDRS, Timed-Up-and-Go,	Depression improved, QoL improved	4–24 weeks, frequency not always specified	No-intervention, placebo, waiting-list,	High-quality studies (86% ≥ Pedro 6); heterogeneity high for UPDRS & depression;

	& meta-analysis				Health Qigong)	specified ; various disease severities		Balance improved			routine care, non-sport controls	subgroup analyses suggest sex, disease severity, drug use, and intervention duration influence outcomes
Carroll et al. 2020 (Carroll, Morris et al. 2020)	Systematic review & meta-analysis	14 RCTs	472 PD participants	Quantitative meta-analysis (7 studies included)	Aquatic therapy	PD, H&Y I-IV	Gait, balance, motor disability, mobility, falls, mood, cognitive function, health-related QoL	Balance, motor disability, mobility (TUG improved)	Mood, cognitive function, QoL	3–11 weeks; frequency and intensity variable	Land-based physiotherapy, no intervention	Exercise prescription highly variable and often under-dosed; aquatic therapy had comparable benefits to land-based physiotherapy; TUG showed statistically significant improvement in aquatic therapy group
Triegaardt et al. 2020 (Triegaardt, Han et al. 2020)	Systematic review & meta-analysis	10 studies in meta-analysis, 27 in systematic review	1031 PD participants (343 in meta-analysis, 688 in systematic review)	Meta-analysis and systematic review	Virtual reality (VR) rehabilitation	PD, age not specified	Gait, balance, motor function, coordination, cognitive function, mental health, QoL, ADL	Stride length improved (SMD 0.70 vs active rehab; SMD 1.27 vs passive rehab), gait speed, balance, coordination	Cognitive function, mental health, quality of life, activities of daily living	Duration and frequency varied among included studies	Active rehabilitation, passive rehabilitation	VR showed improvements over passive rehab and comparable improvements vs active rehab; may be considered for routine use in PD rehabilitation
Lei et al. 2019 (Lei, Sunzi et al. 2019)	Systematic review	16 RCTs	555 PD participants	Meta-analysis	Virtual reality (VR) rehabilitation	PD, age not specified	Gait, balance, mobility, QoL, confidence, neuropsychiatric symptoms, global motor	Step and stride length improved (SMD = 0.72),	QoL (SMD = -0.47), confidence (SMD = -0.73), neuropsychiatric symptoms (SMD = -0.96); no	Duration and frequency varied among included studies	Conventional/traditional rehabilitation	VR performed better than conventional rehab for gait, balance, and mobility; mild adverse events

							function, ADL, cognitive function	balance (SMD = 0.22), mobility (MD = -1.95); no significant effects on gait speed or dynamic gait index	significant effects on global motor function, ADL, cognitive function			reported (dizziness, vomiting)
Moritz et al. 2020 (Moritz, Snowdon et al. 2020)	Systematic review	10 controlled trials	490 participants	Narrative synthesis (meta-analysis not feasible due to heterogeneity)	Combined aquatic physiotherapy + usual care	Stroke and Parkinson's disease; age not specified, H&Y not reported	Balance, walking, mobility, ADL, neurological impairments	improvements in balance, walking, mobility, ADL in some trials; PD: no significant motor improvements	No significant effects on non-motor outcomes in PD or stroke	Varied across included studies	Usual care physiotherapy alone	Preliminary evidence supports benefit in stroke, but not in PD; heterogeneity and mixed trial quality limit conclusions
Tang et al. 2019 (Tang, Fang et al. 2019)	Network meta-analysis	19 RCTs	920 PD patients	Bayesian network meta-analysis	Exercise interventions: dance, tango, Qigong, Tai Chi, yoga, resistance training	Age not specified, H&Y not reported	Six-minute walk, gait velocity, UPDRS III, PDQ-39, TUG, BBT	Improvements in gait velocity, UPDRS III, TUG, BBT, depending on exercise type;	PDQ-39 (quality of life) improved with dance and RT	Varied across studies	Usual care or control	Tango was identified as the most effective exercise for improving functional mobility; RT also effective for some outcomes; results support individualized exercise selection

Smith et al. 2020 (Smith, Barker et al. 2020)	Systematic review	24 RCTs	Individuals with neurodegenerative diseases (mainly MS and PD)	Systematic review (no meta-analysis)	Exercise interventions: treadmill training, progressive resistance training, and other exercise types	Adults with neurodegenerative diseases; H&Y not reported	High-level mobility: HiMAT, Dynamic Gait Index, RMI, modified RMI, Functional Gait Assessment, Functional Ambulation Category	tango and RT often most effective Some benefit in treadmill training for PD and MS; resistance training may help MS; high-level mobility outcomes rarely primary	Not specified	Varied across studies	Usual care or control	High-level mobility rarely targeted in interventions; more research needed specifically on early-stage neurodegenerative disease and high-level mobility-focused interventions
Dauwan et al. 2021 (Dauwan, Begemann et al. 2021)	Systematic review and meta-analysis	122 RCTs	7,231 participants across 6 chronic brain disorders (AD, HD, MS, PD, schizophrenia, a,	Meta-analysis	Physical exercise	Adults with chronic brain disorders; H&Y not reported	QoL, depressive symptoms, cognition (attention, working memory, executive functioning, memory, psychomotor speed)	Not reported specifically for PD	QoL, depressive symptoms, cognition	Varied; meta-regression showed dose-response effect for exercise time (min/week) on depressive symptoms	Treatment as usual	Exercise was safe in most studies (69%); medium effect on QoL, large effect on mood, small but significant effects on cognition; transdiagnostic evidence including PD

			unipolar depression)									
Suárez-Iglesias et al. 2019 (Suarez-Iglesias, Miller et al. 2019)	Systematic review and meta-analysis	4 RCTs + 4 non-RCTs	Not specified (mild-to-moderate PD)	Meta-analysis on 4 RCTs	Pilates	Mild-to-moderate PD; age not specified	Fitness, balance, functional autonomy, lower limb function	Balance, lower limb function	Functional autonomy	Varied; not uniformly reported	Traditional training programs	Pilates improves fitness, balance, physical function; superior to conventional exercises for lower-body function; methodological quality poor to fair; safe for mild-to-moderate PD
Zhang et al. 2019 (Zhang, Hu et al. 2019)	Systematic review and meta-analysis	7 RCTs	Not specified	Meta-analysis	Dance therapy	PD patients; age/H&Y not specified	Executive function, global cognition, depression, apathy	Not reported	Executive function improved; no effect on global cognition, depression, apathy	Not specified	Non-dance therapy	Dance therapy benefits executive function in PD; no effect on mood or global cognition; small number of studies
Santos et al. 2019 (Santos, Scaldaferri et al. 2019)	Systematic review and meta-analysis	5 RCTs	N not fully specified (balance N=72, QoL N=56)	Meta-analysis	Nintendo Wii + traditional physiotherapy	PD patients; age/H&Y not specified	Balance, quality of life	Balance improved (WMD 1.24; 95% CI 0.2–2.3)	Quality of life improved (WMD -8.9; 95% CI -15.2 to -2.6)	Not fully specified	Traditional physiotherapy	Combined NW and traditional physiotherapy improved balance and QoL, but methodological quality of studies was low; intervention reporting incomplete
Perrochon et al. 2019 (Perrochon, Borel et al. 2019)	Systematic review and meta-analysis	11 RCTs	N not fully specified; mixed neurol	Meta-analysis	Exercise-based games (commercial or custom VR/video)	Adults with neurological disease; age not	Upper and lower limb function, adherence, safety	Limited effects on upper/lower limbs	Feasibility, compliance, minor adverse events	Home-based; details heterogeneous	Conventional therapy or usual care	EBGs at home were generally as effective as conventional therapy; higher dropout in EBG groups; minor adverse events reported;

			logical popul ations (stroke , PD, MS)		games) at home	always specified						supports home-based rehabilitation using games
Wang et al. 2019 (Wang, Shen et al. 2019)	Systema tic review and meta- analysis	12 RCTs	419 partici pants	Meta- analysis	Virtual reality interventions	Parkinso n's disease; age not specified ; H&Y not specified	Balance and gait	Significant improvm ents in Berg Balance Scale, Timed Up and Go Test, stride length; no significant effect on gait velocity or walk distance Improvem ents in gait speed, Timed Up and Go, freezing of gait questionn aire, six- minute walk test	Not reported	Details heterogeneou s across studies	Conventiona l therapy / usual care	VR improves balance in PD patients; limited or no effect on gait velocity and walking distance; PEDro median score 6.4, indicating moderate quality
Kalyani et al. 2019 (Kalyani, Sullivan et al. 2019)	Systema tic review and meta- analysis	12 studies include d in meta- analysis (from 25 retained)	Not specifi ed	Meta- analysis	Dance-based interventions	Parkinso n's disease; age not specified ; H&Y not specified	Gait, cognition, dual-tasking		Improvements in global cognition (MoCA), cognitive dual-tasking (dual- task TUG)	Details heterogeneou s; intensity, frequency, duration not clearly established	Controls (non-dance intervention s or usual care)	Dance interventions may improve gait, cognition, and dual- task performance in PD; evidence limited by moderate-to-high risk of bias and lack of RCTs

Cugusi et al. 2019 (Cugusi, Manca et al. 2019)	Systematic review and meta-analysis	7 RCTs (6 meta-analysed)	159	Meta-analysis	Aquatic exercise	Parkinson's disease; age not specified; H&Y not specified	Disease severity, motor impairments, activity performance, fear of falling, non-motor impairments, quality of life	UPDRS III improved (MD -4.6); Berg Balance Scale improved (MD 2.7); benefit maintained at follow-up	Falls Efficacy Scale improved (MD -4.0); PDQ-39 improved (MD -6.0)	Mean intervention 7.2 weeks (SD 2.2); supervised; frequency/intensity not specified	No intervention or land-based exercise	Aquatic exercise shows greater improvement than no intervention in motor impairments and slightly to moderately greater benefits than land-based exercise on balance, fear of falling, and quality of life	
Pinto et al. 2019 (Pinto, Salazar et al. 2019)	Systematic review and meta-analysis	19 studies (8 RCTs, 3 non-RCTs, 8 pre-post)	484	Meta-analysis	Hydrotherapy (alone or combined with land-based therapy)	PD patients; age 54–78 years; PD duration 3–10 years; H&Y not specified	Balance, functional mobility, motor status, quality of life	Balance Scale MD 2.00); functional mobility improved (Timed Up and Go MD -1.08)	QOL (PDQ, SF-36) not significantly improved; motor status (UPDRS III) not significantly improved	Not specified	Land-based therapy alone or usual care	Hydrotherapy improves balance and functional mobility; no clear effect on motor status or quality of life; evidence level I; low risk of bias in RCTs	
Robinson et al. 2019 (Robinson, Dennett et al. 2019)	Systematic review and meta-analysis	16 RCTs		Meta-analysis	Parkinson's disease & multiple sclerosis	Task-specific training: treadmill and over-ground walking	PD & MS; age not specified; H&Y not reported	Walking velocity, stride length, step length, walking endurance, cadence	PD: improved comfortable walking velocity (MD 0.21 m/s), stride length (MD 0.12 m), step	Not reported	Not specified	Over-ground walking	Treadmill training effective for improving mobility in PD and MS; over-ground walking effectiveness uncertain; sample sizes small; findings should be interpreted with caution; PROSPERO CRD42016047334

De Keersmaecker et al. 2019 (De Keersmaecker, Lefeber et al. 2019)	Systematic review and meta- analysis	18 studies	337 patients (stroke n=12, MS n=4, PD n=1, TBI n=1)	Meta- analysis	VR-enhanced gait training	CNS movement disorder ; age not specified ; H&Y not reported for PD	Gait spatiotemporal parameters, functional and kinematic/kinetic outcomes	length (MD 0.12 m); no effect on cadence or endurance ; MS: improved walking velocity (MD 0.36 m/s), endurance (MD 26.53 m) Significant improvements in spatiotemporal and functional gait parameters in each population; VR superior to conventional gait training only in post-stroke patients	Not reported	Not specified	Gait training without VR	VR-enhanced gait training improves gait outcomes across CNS disorders; strongest evidence for post- stroke population; limited data for PD, MS, TBI

Seuthe et al. 2019 (Seuthe, D'Cruz et al. 2019)	Systematic review	7 studies	118 patients with PD (44 with FOG)	Narrative synthesis (no pooled meta-analysis)	Split-belt treadmill walking	Mild to moderately severe PD; age not specified; H&Y not reported	Gait adaptation, gait variability, bilateral coordination, gait asymmetry	Gait variability and bilateral coordination on adapted similarly to healthy controls; gait asymmetry adaptation results inconsistent; FOG subgroup showed slower adaptation	Perception of belt speed differences (FOG subgroup impaired)	Various SBT paradigms; details varied across studies	Healthy controls or within-subject comparison across belt conditions	SBT may modulate gait asymmetry for some PD patients; standardization of protocols recommended; less effective for FOG subgroup
Stuckenschneider et al. 2019 (Stuckenschneider, Askew et al. 2019)	Systematic review of RCTs	11 RCTs	508 PD patients	Narrative synthesis (no pooled meta-analysis)	Aerobic exercise, resistance training, coordination exercise, combined interventions	Mean age 68 ± 4 years; H&Y 1–4	Cognitive function (global and domain-specific: memory, executive function), UPDRS	UPDRS as secondary outcome	Memory, executive function, global cognition	Not fully standardized across studies; varied by study	Non-exercising controls or alternative exercises	All exercise modes improved cognitive function; aerobic exercise tended to improve memory most; coordination exercise improved executive function; study quality modest (PEDro 3–8/10)
Dincher et al. 2019 (Dincher, Schwarz et al. 2019)	Systematic review and	17 studies (7 high/moderate)	People with Parkinson's	Meta-analysis	Whole-body vibration (harmonic vs randomized)	Not specified in abstract	Motor symptoms, balance, gait, mobility	Motor symptoms, balance, gait, mobility	None reported	Variable; trials per session, vibration frequency/am	Respective control conditions	Effects inconsistent; only few studies showed significant group differences; overall evidence

	meta-analysis	quality quantitatively analyzed)	disease			(PD patients)					plitude, trial/rest duration (high heterogeneity)	unclear; further high-quality studies needed
Raffegau et al. 2019 (Raffegau, Krehbiel et al. 2019)	Meta-analysis	19 studies	People with Parkinson's disease	Meta-analysis	Dual-task walking	Not specified in abstract	Gait performance under dual-task conditions	Walking speed	None reported	Not applicable (observational synthesis)	Single-task walking as control	Strong negative effect of dual tasks on gait; effect consistent across gait speed and type of dual task
Ni et al. 2018 (Ni, Hazzard et al. 2018)	Systematic review and meta-analysis	40 RCTs	1656 patients with Parkinson's disease	Meta-analysis	Gait-specific exercise	Not specified in abstract	Walking function, gait parameters	Timed up-and-go, walking speed (comfortable/fast), stride/step length, cadence, DLST, DGI, 6-minute walk, FOG-Q Berg Balance Scale, Timed Up and Go, spatiotemporal gait parameters, 6-	None specified	Variable; cuing and exercise duration considered as moderators	Non-exercise control and other exercise controls	Exercise improved most gait parameters; cuing improved stride length; gait-specific training recommended over general exercise; exercise duration negatively influenced comfortable walking speed
Patterson et al. 2018 (Patterson, Wong et al. 2018)	Systematic review	9 studies (4 pre-post, 3 case reports, 2 controlled)	Adults with neurological conditions other than Parkinson	Narrative synthesis	Dance interventions	Not specified	Balance, gait, functional mobility	Balance, gait, functional mobility	None reported	Variable; frequency, type, duration varied; intensity reported in 1 study	Some controlled studies, others pre-post or case reports	Emerging evidence supports feasibility of dance; high adherence; further high-quality RCTs needed

		ed studies)	son's diseases (stroke, MS, SCI, Huntington's diseases)					minute walk test					
Cano Porras et al. 2018 (Cano Porras, Siemonsma et al. 2018)	Systematic review	97 studies	Adults with neurological conditions (PD, MS, stroke, TBI, cerebral palsy)	Narrative synthesis	Virtual reality-based rehabilitation	Not specified	Balance, gait	Balance, gait performance	None specified	Variable; details often lacking	Some studies combined VR with conventional rehab; others not specified	VR improves balance and gait, especially combined with conventional rehab; methodological quality often poor; more robust RCTs recommended	
Hirsch et al. 2018 (Hirsch, van Wegen et al. 2018)	Systematic review and meta-analysis	6 studies (2 RCTs, 4 pre-experimental)	100 ambulatory PD patients	Meta-analysis	Exercise interventions	Hoehn & Yahr ≤3; age not specified	BDNF blood levels, motor function	UPDRS-III motor scores	BDNF levels as biochemical marker	Variable; not detailed	RCT control groups (not specified in abstract)	Exercise increased BDNF levels and improved motor scores; studies small and moderate/low quality; preliminary evidence only; further research needed	
da Silva et al. 2018 (Da Silva et al. 2018)	Systematic review	9 RCTs	PD patients,	Narrative	Physical exercise programs	Mild to moderate PD;	Cognitive function (global cognition,	Some interventions	Cognitive function	Treadmill training: 3x/week, 60 min	Control groups in RCTs	Exercise improves cognitive function; treadmill training	

Silva, Iop et al. 2018)			mild to moderate stage, 6-year mean disease duration	synthesis	(adapted tango, cognitive+motor training, treadmill training)	age not specified	processing speed, sustained attention, mental flexibility)	included motor components		min, 24 weeks; other programs variable		showed largest improvements; methodological quality generally good; heterogeneity in cognitive tests and exercise programs
Morales-Gomez et al. 2018 (Morales-Gomez, Elizagaray-Garcia et al. 2018)	Systematic review	4 RCTs	PD patients	Narrative synthesis	Virtual reality-based rehabilitation	Not specified	Balance, motor function, quality of life, cognition	Balance (variable results)	QoL, cognition	Not specified	Conventional physiotherapy	VR not consistently more effective than conventional physiotherapy; contradictory results for balance; no superior effect on non-motor outcomes
Gordt et al. 2018 (Gordt, Gerhardy et al. 2018)	Systematic review and meta-analysis	8 RCTs	Healthy adults and patient populations (PD n=3, stroke n=2, peripheral neuropathy)	Meta-analysis	Wearable sensor-based balance and gait training	PD: not specified (Hoehn & Yahr not reported)	Balance, gait, functional performance	Static balance (medial & anterior-posterior sway), selected gait variables (single support time, fast gait speed), proactive	None specified	Variable; heterogeneous training paradigms (static, dynamic, proactive balance); small sample sizes; short durations	Usual care or conventional balance training	WS training improves static balance; limited evidence for gait and proactive balance; small sample sizes and heterogeneity limit generalizability; larger studies needed

			n=2, frail/h ealthy older adults n=2) 465 partici pants (vario us neurol ogical disabil						balance (Alternate Step Test)				
Mura et al. 2018 (Mura, Carta et al. 2018)	Systema tic review and meta- analysis	13 studies	ities: MS, post- stroke hemip aresis, PD, demen tia, dyslex ia, Down syndr ome) People with neurol ogical disord ers (PD,	Meta- analysis	Active exergames	Adults with neurolo gical disabiliti es; age not specified	Cognitive function	Motor function indirectly addressed via exergames	Executive function, visuo-spatial perception, attention, global cognition	Variable; intervention types, duration, and frequency differed among studies	Alternative intervention or no intervention	Exergames improved executive functions and visuo-spatial perception; no effect on attention or global cognition; flexible tool for neurorehabilitation; further high-quality trials needed	
Mackay et al. 2017 (Mackay, Kuys et al. 2017)	Systema tic review and meta- analysis	11 studies		Meta- analysis	Aerobic exercise	Not specified	BDNF levels	Not specified	BDNF as biochemical marker	Programs of aerobic exercise (variable); single bout studies mixed	Usual care / no therapy	Aerobic exercise programs increased BDNF levels; single bouts had mixed effects; study quality low (PEDro 4.3/10)	

Flach et al. 2017 (Flach, Jaegers et al. 2017)	Meta-analysis	7 RCTs	MS, stroke) Individuals with Parkinson's disease	Meta-analysis	Endurance exercise	Not specified	UPDRS total and motor scores	UPDRS III (motor)	None reported	Variable; defined as endurance exercise per ACSM	Non-exercising control	Endurance exercise improves UPDRS scores; effect size d = -0.32; supports integration of endurance exercise in PD treatment Aquatic physiotherapy may improve motor function, balance, and
Terrens et al. 2018 (Terrens, Soh et al. 2018)	Systematic review	10 studies	People with Parkinson's disease	Narrative synthesis	Aquatic physiotherapy	Not specified	Motor function, balance, quality of life	Motor symptoms, balance	Quality of life	Variable; details not consistently reported	Not specified	QoL; safety and feasibility underreported; standardised outcome measures recommended for future studies Physical activity, especially aerobic exercise, improves motor function, depression, and QoL; balance training and Qigong also beneficial; study quality moderate-high
Wu et al. 2017 (Wu, Lee et al. 2017)	Systematic review	11 studies	342 patients with PD, mean age ≥60	Narrative synthesis	Physical activity programs (aerobic, Qigong, Tai Chi, balance training)	PD patients, mean age ≥60; H&Y not specified	Motor function, depressive symptoms, quality of life	UPDRS-III, postural stability	Depression (Beck Depression Inventory), quality of life	Variable; 17 types of programs; aerobic training showed best results	Not specified	Physical activity, especially aerobic exercise, improves motor function, depression, and QoL; balance training and Qigong also beneficial; study quality moderate-high
Zhang et al. 2017 (Zhang, Liu et al. 2017)	Systematic review and meta-analysis	8 studies (11 analyses)	241 patients with Parkinson's disease	Meta-analysis	Music-based movement therapy	Not specified	Motor function, cognitive function, quality of life	Berg Balance Scale, Timed Up and Go, UPDRS-	Cognitive function, quality of life	Variable; not consistently reported	No-music control	Music-based movement therapy improves motor function; neutral evidence for cognition and quality of life; all

								III, PDQ-39					studies had acceptable PEDro scores
Stanmore et al. 2017 (Stanmore, Stubbs et al. 2017)	Systematic review and meta-analysis	17 RCTs	926 participants	Meta-analysis	Active video games (exergames)	Clinical and non-clinical populations; not specific to PD	Global cognition, executive function, attentional processing, visuospatial skills	Not reported	Cognitive function	Variable; intervention details differed across studies	Waitlist, alternative physical activity, or no intervention	Exergames improve global cognition and specific cognitive domains; benefits seen in both healthy and clinical populations; first meta-analytic evidence for exergames on cognition	
Ramazzina et al. 2017 (Ramazzina, Bernazzoli et al. 2017)	Systematic review	13 RCTs	Patients with Parkinson's disease	Narrative synthesis (no quantitative meta-analysis)	Strength training (against external resistance)	Not specified	Motor function, muscle strength, quality of life	Physical parameters, muscle strength (limited assessment)	Quality of life	Variable; different protocols across studies	Usual care or alternative interventions	Strength training appears safe and beneficial; limited assessment of muscle strength; heterogeneity in study design and outcomes; further studies needed	
Bombieri et al. 2017 (Bombieri, Schena et al. 2017)	Systematic review with meta-analysis	9 studies (4 RCTs)	127 PD patients	Meta-analysis on 4 RCTs	Nordic Walking	Not specified; PD patients	UPDRS-3, motor and non-motor variables	UPDRS-3 (statistically significant reduction, <1 point)	Non-motor outcomes variably reported	Variable protocols; high-intensity activity using poles	Standard medical care or other physical exercise	Generally beneficial effects, but limited clinical significance; benefits persistence unclear; small sample sizes; more large, well-designed RCTs needed	
Dockx et al. 2016 (Dockx, Bekkers et al. 2016)	Systematic review with meta-analysis (Cochrane)	8 trials	263 PD patients	Meta-analysis	Virtual Reality (VR) exercise	Not specified; PD patients	Gait, balance, step/stride length, quality of life	Step/stride length (SMD 0.69; moderate improvement), gait (SMD 0.20; similar to physiother	Quality of life (mean difference 3.73; similar to physiotherapy)	4–12 weeks; commercially available devices; frequency not specified	Physiotherapy or passive control	Low-quality evidence; no adverse events reported; exercise adherence similar; more large, high-quality trials needed	

								apy), balance (SMD 0.34; similar to physiother apy) Upper limb function (fine motricity, hand/arm capacity, finger/han d tapping), mobility (gait parameter s), gait velocity and cadence					
Moumdjian et al. 2017 (Moumdjian, Sarkamo et al. 2017)	Systema tic review	19 studies (13 RCTs, 4 controll ed trials, 2 cohort studies)	649 total (exper imenta l N=327 , contro l N=322)	Narrativ e synthesi s (no meta- analysis)	Music-based interventions: instrument- based, listening- based, rhythm-based, multicompone nt	Stroke, Parkinso n's disease, multiple sclerosis	Motor function, cognition		Cognition: verbal memory, focused attention	≥3 weeks; frequency not specified	Conventiona l rehabilitatio n or no intervention	Evidence strongest for motor improvements in stroke; rhythm- based interventions improve gait in stroke, PD, and MS; listening- based interventions improve cognition; more studies needed on combined motor- cognition outcomes	
Bonnechère et al. 2016 (Bonnechere, Jansen et al. 2016)	Systema tic review	126 studies (RCTs, cohort, observa tional)	Varied ; includ ed stroke, cerebr al palsy, Parkin son's diseas e,	Narrativ e synthesi s (no meta- analysis)	Commercial video games (e.g., PlayStation, Nintendo Wii, Xbox Kinect)	Stroke, cerebral palsy, Parkinso n's disease, aging; age not consiste ntly reported	Motor function, balance, psychomotor outcomes	Motor function, balance	Psychomotor outcomes, motivation	Variable across studies; protocols differed in number of sessions, intervention duration, outcome measures	Conventiona l rehabilitatio n or no intervention	Video games generally produced similar results as conventional therapy; may serve as adjunct treatment or home-based rehabilitation; high variability in protocols and populations	

Sherrington et al. 2017 (Sherrington, Michaleff et al. 2017)	Systematic review & meta-analysis	88 trials (99 comparisons)	balance training, aging populations 19,478 older adults; included community-dwelling, Parkinson's disease, cognitive impairment	Random-effects meta-analysis, meta-regression	Exercise (balance-challenging and general programs)	Older adults (community-dwelling); Parkinson's disease and cognitive impairment subgroups	Fall rates	Fall prevention, balance	Cognitive function	Variable; >3 hours/week more effective	Control group (usual care or no exercise)	Exercise reduces falls by 21% overall; higher dose and balance-challenging programs more effective; fall prevention effect also observed in Parkinson's disease and cognitive impairment subgroups; no significant effect in residential care or stroke patients
Cusso et al. 2016 (Cusso, Donald et al. 2016)	Systematic review	20 controlled, randomized intervention studies	≥10 participants per study; idiopathic PD	Narrative synthesis (no quantitative meta-analysis)	Physical activity (including physiotherapy, occupational therapy, dance, martial arts)	PD patients; age and H&Y variable across studies	Non-motor symptoms (NMS) including depression, cognition, fatigue, apathy, anxiety, sleep	Some studies assessed motor outcomes, but focus on NMS	Depression, cognition, fatigue, apathy, anxiety, sleep	Variable across studies	Control groups varied (usual care or no intervention)	Physical activity positively impacts global NMS burden; methodological heterogeneity and demographic variability limited comparability; further well-powered studies recommended to assess NMS in PD

Methajaruno n et al. 2016 (Methajarun on, Eitivipart et al. 2016)	Systema tic review	8 RCTs or quasi- experim ental trials	Patien ts with multip le scleros is, Parkin son's diseas e, or hemip legia	Narrativ e synthesi s (no quantita tive meta- analysis)	Aquatic exercise	MS, PD, hemiple gia; age variable; PD sample very small	Balance, gait	Improvem ents in static and dynamic balance in MS and hemiplegi a; gait improved in MS only	Not assessed	Variable across studies	Control groups varied (usual care, land exercise, or no intervention)	Aquatic exercise appears effective for balance in MS and hemiplegia; insufficient evidence for PD; methodological quality fair to good; further research needed in PD
Yitayeh and Teshome 2016 (Yitayeh and Teshome 2016)	Systema tic review with meta- analysis	8 RCTs (5 include d in meta- analysis)	483 partici pants with idiopa thic Parkin son's diseas e	Quantita tive meta- analysis	Conventional physiotherapy (balance training, muscle strengthening, range of motion, walking exercises, treadmill training)	Idiopath ic PD; age variable; H&Y stage not specified	Balance dysfunction, postural instability, falls	Significant improvem ents in Berg Balance Scale (SMD 0.23), largest effects for balance- specific interventio ns (SMD 5.98); decreased incidence of falls (non- significant trend)	Not reported	Variable across studies; included high- challenge balance and speed- dependent treadmill	Control: no exercise or sham treatment	Physiotherapy interventions combining balance, strength, ROM, and walking training are effective; more effective than balance exercises alone; evidence supports inclusion of challenging balance and treadmill training in PD rehabilitation

Mehrholz et al. 2016 (Mehrholz, Kugler et al. 2016)	Systematic review	18 RCTs	Patients with Parkinson's disease (age variable, H&Y not consistently reported)	Quantitative meta-analysis	Treadmill training	PD patients, aged, mixed H&Y stages	Gait speed, stride length, walking distance, cadence, adherence, adverse events	Improved gait speed (MD=0.09 m/s), stride length (MD=0.05 m), no significant improvement in walking distance or cadence	Not reported	Variable across studies; treadmill protocols differed	Control: no treadmill training	Treadmill training improves gait speed and stride length in PD; results for other gait parameters less clear; heterogeneous interventions; long-term effects unknown
Cascaes da Silva et al. 2016 (Cascaes da Silva, Iop Rda et al. 2016)	Systematic review of RCTs	14 RCTs	Patients with Parkinson's disease (mild to moderate stage, disease duration ~6 years)	Narrative synthesis (no pooled meta-analysis)	Physical-exercise-based rehabilitation programs	PD patients, mild to moderate	Quality of Life	Not specifically reported	QoL improved	2–4 times/week, 60 min/session, 6–12 weeks, 3-month follow-up	Control: usual care or no exercise	Exercise-based rehabilitation programs positively impact quality of life in PD; programs were short-to medium-term; interventions were heterogeneous
Saltychev et al. 2016 (Saltychev, Barlund et al. 2016)	Systematic review and	12 RCTs (6 included in meta-)	Adults with idiopathic Parkinson	Random-effects meta-analysis	Progressive resistance training	Adults with PD, all H&Y stages	Walking speed, 6-min walk test, TUG, VO ₂ max	Walking speed, TUG, 6-min walk	Not specifically reported	Small number of reps until fatigue, sufficient rest between	Control: no treatment, placebo, or other treatment	Pooled effects were below minimal clinical significance; no evidence of superiority over other training;

	meta-analysis	analysis)	son's disease (any severity)							exercises, progressive load; follow-up 0–1 month		small sample sizes and short follow-up
Klamroth et al. 2016 (Klamroth, Steib et al. 2016)	Meta-analysis	22 RCTs	1072 participants with Parkinson's disease	Random-effects meta-analysis	Exercise therapy	Adults with PD, all H&Y stages	Postural stability: Berg Balance Scale, postural sway, Timed Up and Go, Functional Reach	Postural stability, balance, TUG	Not assessed	Varies by study; includes targeted balance interventions vs. non-specific exercises	Control: no exercise or sham treatment	Targeted balance interventions showed largest efficacy (SMD 0.43); home-based or non-targeted interventions had little effect; moderate effect size for targeted balance training
Lötzke et al. 2015 (Lötzke, Ostermann et al. 2015)	Systematic review & meta-analysis	13 (9 RCTs, 1 non-RCT, 2 case studies, 1 uncontrolled pre-post)	Small samples, max 75 per study	Quantitative meta-analysis + qualitative syntheses	Dance therapy (Argentine Tango)	PD patients, mixed stages (age not specified, H&Y not detailed)	UPDRS-III, Mini-BESTest, Berg Balance Scale, TUG, 6MWT, Freezing of Gait, fatigue, participation, QoL	Significant improvements in UPDRS-III (motor severity), balance (Mini-BESTest, BBS), gait (TUG). No effect on 6MWT, FoG	Tendencies toward improvements in fatigue, activity participation, PD-related QoL	Variable across studies; not standardized, tango sessions (details not pooled)	Mostly active controls (conventional exercise or no intervention)	Small samples, many studies from same groups, few independent replications; need larger/long-term studies
Kalron and Zeilig 2015 (Kalron and Zeilig 2015)	Systematic review & meta-analysis	12 controlled clinical trials (3 PD, 1	Neurological patients with MS, stroke, PD	Meta-analysis (cognition outcome, executive	Aerobic exercise (8), VR-based active exercise (1), Yoga (3), Sport climbing (1)	PD (3 studies), Stroke (1), MS (8). Age not specified	Cognitive performance (executive functions, general cognition)	Not assessed	Cognitive performance: 9/12 studies significant improvements, but pooled effect size not significant (ES	Intervention duration/frequency varied; not standardized, heterogeneous	Active or usual care controls, depending on study	Lack of consistency in cognitive measures, training protocols and durations; inconclusive overall effect; heterogeneity limits conclusions

		stroke, 8 MS)		e function s)		; PD stages not detailed			= 0.18, 95% CI -4.1 to 3.8)				
Harris et al. 2015 (Harris, Rantalainen et al. 2015)	Systematic review & meta-analysis	11 studies (9 older adults, 2 IPD)	325 older adults, 56 IPD	Quantitative meta-analysis	Exergaming / VR-based exercise	Older adults + people with idiopathic PD (age not specified ; PD stage not specified in abstract)	Static balance, postural control, dynamic balance	Improvements in static balance, postural control, dynamic balance (significant for older adults; mixed for PD, but postural control strong effect) Significant improvements in muscular strength (knee extension, flexion, leg press) with RT compared to controls; combined	Not reported	Duration/frequency varied, heterogeneous across studies (not standardized)	Conventional therapy or no intervention (varied by study)	Stronger evidence in older adults than PD; only 2 PD studies included → need more large-scale trials for PD	
Roeder et al. 2015 (Roeder, Costello et al. 2015)	Systematic review & meta-analysis	9 controlled trials (parallel-group design)	People with PD	Quantitative meta-analysis	Resistance training (alone or combined with aerobic/balance/stretching)	PD patients (age not specified , H&Y not specified)	Muscular strength (knee extension, knee flexion, leg press strength)		Not assessed	Variable across studies; RT interventions of different duration/frequency/intensity	Controls: no intervention, stretching, treadmill, balance, or other active comparators	Moderate-high risk of bias; RT beneficial but not always superior to other exercises; combined RT + other forms of exercise may be most effective	

Alves Da Rocha et al. 2015 (Alves Da Rocha, McClelland et al. 2015)	Systematic review & meta-analysis	35 studies (20 RCTs, 2 non-RCTs, 13 case series)	1210 PD patients	Meta-analysis + narrative synthesis	Complementary physical therapies (dance, water exercises, robotic gait training, VR, mental practice, aerobic training, boxing, Nordic walking)	Idiopathic PD, outpatients, H&Y I-IV, adults, both sexes	Motor performance, quality of life, falls	RT + other exercise sometimes most effective Improvements with dance, hydrotherapy, robotic gait training; some evidence for VR, boxing, Nordic walking, aerobic training	Quality of life ↑, enjoyment, social participation; impact on falls reported	Heterogeneous across interventions; variable duration/frequency	Controls varied (medical management, conventional therapy, or none)	Evidence moderately strong; dancing, water exercise, robotic gait training most promising; heterogeneity in protocols; considered good adjunct to medical management
Fritz et al. 2015 (Fritz, Cheek et al. 2015)	Systematic review	14 studies	Adults with neurological disorders: PD, AD, brain injury (n not specified in	Narrative synthesis (no pooled quantitative meta-analysis)	Motor-cognitive dual-task training (cued walking, cognitive tasks paired with gait, balance/strength training, VR/gaming)	PD, AD, brain injury; adults (age not specified); PD stage not specified)	Gait velocity, stride length, balance, cognition	Improved single- and dual-task gait velocity and stride length in PD, AD, brain injury; possible balance improvements	Possible improvements in cognition in PD and AD	Heterogeneous protocols; varied frequency/duration (not standardized)	Usual care / standard therapy	Evidence suggests DTT effective in improving dual-task ability, but protocols and outcomes vary; diagnostic groups limited; promising for gait, balance, cognition

Uhrbrand et al. 2015 (Uhrbrand, Stenager et al. 2015)	Systematic review & meta-analysis of RCTs	15 RCTs	abstract)	Meta-analysis (for RT on muscle strength); narrative synthesis for other outcomes	Resistance Training (RT), Endurance Training (ET), Other Intensive Training Modalities (OITM)	Idiopathic PD; age not specified; H&Y not detailed in abstract	Muscle strength, cardiorespiratory fitness, balance, walking performance, UPDRS-III, quality of life	RT significantly ↑ muscle strength (g'=0.54, 95% CI 0.22–0.86); RT/ET/OITM may improve balance, walking, UPDRS-III	QoL improvements reported but inconsistent	Intensive training protocols; varied duration/frequency across trials (not standardized)	Active or non-active controls, depending on RCT	Strong evidence for RT on strength; moderate evidence for ET on cardio-fitness; other benefits possible but inconsistent; all modalities feasible and safe, no negative outcomes reported
								Leg strength: significant improvement (SMD 1.42, 95% CI 0.464–2.376); gait speed: not significant (SMD 0.418, 95% CI -0.219–1.055); balance: no significant effect				
Tillman et al. 2015 (Tillman, Muthalib et al. 2015)	Systematic review & meta-analysis	7 studies	172 PD participants (experimental n=84, control n=88)	Quantitative meta-analysis	Progressive resistance training (PRT)	PD patients, adults (age not specified, H&Y not detailed)	Leg strength, gait speed, balance		Not assessed	Duration/frequency/intensity varied	Active or passive controls (varied by study)	PRT improves leg strength but not gait or balance; may need to combine with balance or functional training for greater effect; limited number of studies

Yang et al. 2015 (Yang, Qiu et al. 2015)	Systematic review & meta-analysis	15 trials	PD patients (n not specified)	Quantitative meta-analysis	Tai Chi and Qigong, combined with medication	Mild-to-moderate PD; adults (age not specified; H&Y not specified)	Motor function, balance, gait, functional reach, TUG, quality of life	Tai Chi + medication improved motor function (SMD - 0.57 to - 0.78), BBS (SMD - 0.99 to - 1.22), TUG (SMD - 1.06); gait not significantly improved	QoL: no significant improvements	Intervention duration/frequency not detailed in abstract	Comparators: other therapy + medication	Tai Chi + medication shows positive effects on motor function and balance; Qigong + medication shows potential gains but insufficient evidence; more high-quality studies needed
Cruickshank et al. 2015 (Cruickshank, Reyes et al. 2015)	Systematic review & meta-analysis	20 articles (14 RCTs, 6 non-RCTs; 6 RCTs and 2 non-RCTs pooled)	PD and MS patients (n not specified)	Quantitative meta-analysis (pooled for some trials)	Strength training (traditional: free weights/machines; nontraditional: eccentric cycling)	PD and MS adults (age not specified; PD stage not specified)	Muscle strength, mobility, disease progression, fatigue, functional capacity, QoL, power, EMG activity	mobility ↑ 15%-83.2%, disease progression ↑ 11.4%, functional capacity ↑ 21.5%, QoL ↑ 8.3%, EMG activity ↑ 24.4% MS: muscle strength ↑ 4.5%-36%, power ↑ 17.6%	MS: fatigue ↓ 8.2%, functional capacity ↑ 21.5%, QoL ↑ 8.3%, EMG activity ↑ 24.4%	Duration/frequency/intensity varied; heterogeneous across studies	Controls varied (active, passive, or usual care)	Heterogeneity of interventions and outcomes limits conclusions; strength training beneficial for PD (stronger) and MS (moderate)

Adamson et al. 2015 (Adamson, Ensari et al. 2015)	Systematic review & meta-analysis	26 RCTs (data from 23 trials pooled)	1324 adults with neurologic disorders: AD (4), migraine (1), MS (13), PD (2), SCI (1), stroke (2), TBI (3)	Quantitative meta-analysis	Exercise interventions (varied: aerobic, resistance, mixed)	Adults with neurologic disorders (age not specified; PD stage not specified)	Depression	Not assessed	Depression significantly reduced; overall ES = 0.28 (SE=0.07; 95% CI 0.15–0.41); higher effect (ES = 0.38) when interventions met physical activity guidelines	Intervention duration/frequency varied; interventions meeting PA guidelines more effective	Active or passive controls	Exercise reduces depressive symptoms across neurologic disorders; more effective when meeting physical activity guidelines; only 2 trials included PD patients
Sharp and Hewitt 2014 (Sharp and Hewitt 2014)	Systematic review & meta-analysis	5 RCTs	People with PD (n not specified)	Quantitative meta-analysis	Dance therapy	Adults with PD (age not specified; H&Y not detailed)	UPDRS-III, Berg Balance Scale, gait speed, PDQ-39 QoL	UPDRS motor score improved (-10.73, CI -15.05 to -6.16); Berg Balance improved (0.72, CI 0.31–1.44); gait speed improved (0.14 m/s, CI 0.02–0.26)	QoL improved (PDQ-39) when compared to other exercise (-4.00, CI -7.13 to -0.87)	Duration/frequency/intensity varied; details not standardized in abstract	Controls: no intervention or other exercise	Dance shows short-term clinically meaningful benefits; future RCTs needed to define optimal dose/type and long-term effects

Shanahan et al. 2015 (Shanahan, Morris et al. 2015)	Systematic review	13 studies	People with PD (n not specified)	Narrative synthesis	Dance therapy	Adults with PD (age not specified ; H&Y not detailed)	Endurance, motor impairment, balance	Beneficial effects reported on endurance, motor impairment, and balance. Motor function improved (SMD -0.57; 95% CI -1.11 to -0.04), balance improved (SMD 1.22; 95% CI 0.80–1.65), functional mobility improved (SMD 1.06; 95% CI 0.68–1.44); gait velocity, step length, gait endurance not significant	Not explicitly assessed	Typically 2 × 1-hour dance classes per week for 10–13 weeks	Not standardized across studies	Dance appears helpful; methodological limitations and study quality varied; higher-quality studies needed to define optimal dose and type of dance
Yang et al. 2014 (Yang, Li et al. 2014)	Systematic review & meta-analysis	7 RCTs + 1 non-RCT	People with PD (n not specified)	Quantitative meta-analysis (random-effects model)	Tai Chi	Adults with PD (age not specified ; H&Y not detailed)	Motor function, balance, gait	gait velocity, step length, gait endurance not significant	Not assessed	Intervention details not specified in abstract	Comparator: other active therapies or usual care	Tai Chi effective for motor function and balance; more long-term studies needed; compared with other therapies, significant improvement only in balance

Shu et al. 2014 (Shu, Yang et al. 2014)	Systematic review & meta-analysis	18 RCTs	901 patients with PD	Quantitative meta-analysis (random-effects model)	Aerobic exercise	Adults with PD (age not specified; H&Y not detailed)	Motor actions, balance, gait, quality of life	ly improved Motor actions improved (SMD -0.57; 95% CI -0.94 to -0.19), balance improved (SMD 2.02; 95% CI 0.45–3.59), gait improved (SMD 0.33; 95% CI 0.17–0.49) UPDRS III improved (MD -4.34, 95% CI -6.67 to -2.01);	Quality of life not significantly improved (SMD 0.11; 95% CI -0.23–0.46)	Duration/frequency/intensity varied; not standardized in abstract	Comparator: usual care or no intervention	Aerobic exercise shows immediate benefits; no evidence on long-term follow-up; large-scale RCTs with follow-up needed
Ni et al. 2014 (Ni, Liu et al. 2014)	Systematic review & meta-analysis of RCTs	10 trials (9 included in meta-analysis)	409 PD patients	Quantitative meta-analysis	Tai Chi (with or without medication)	PD patients with mild-to-moderate severity	UPDRS III, Berg Balance Scale, Timed Up and Go, stride length, falls, health-related quality of life	balance improved (BBS MD 4.25, FRT MD 3.89); TUG improved (MD -0.75); stride	Health-related quality of life improved (SMD -1.10)	Duration/frequency/intensity not specified in abstract	Comparator: usual care, medication only, or no intervention	Tai Chi plus medication showed the greatest benefits; safe and well-tolerated; high risk of bias in blinding; more high-quality RCTs needed

Barry et al. 2014 (Barry, Galna et al. 2014)	Systematic review	7 studies (1 RCT)	PD patients, sample sizes not specified	Narrative synthesis (no quantitative meta-analysis)	Exergaming (mostly Nintendo Wii Fit)	PD patients (severity not specified)	UPDRS II, standing balance, cognition, clinical balance measures	length improved (SMD 0.56); reduction of falls Improvement in UPDRS II, standing balance, clinical balance measures; motor symptoms reduced	Cognition improved (in RCT)	Duration/frequency/intensity varied; not consistently reported	Comparator: traditional balance training (in RCT) or usual care	Feasible and enjoyable; safety not formally assessed; commercial games may be too complex for some; more high-quality RCTs needed
Tambosco et al. 2014 (Tambosco, Percebois-Macadre et al. 2014)	Systematic review	5 literature reviews + 31 RCTs	PD patients	Narrative synthesis (no quantitative meta-analysis)	Aerobic training, strength training (physical rehabilitation programs)	PD patients (age and H&Y not consistently reported)	Gait, balance, muscle strength, aerobic capacity	Improvement in walking, posture, balance, and muscle strength	Cognition mentioned but not primary; general physical capacities improved	Programs lasting several weeks; include aerobic training (bike/treadmill) + muscle strengthening; repeated cycles recommended; intensity and ON/OFF timing debated	Comparator: usual care or no intervention	Evidence supports aerobic + strength training; programs should be individualized based on patient abilities; questions remain on intensity and timing relative to medication phases

Murray et al. 2014 (Murray, Sacheli et al. 2014)	Systematic review	14 original reports (6 pre-clinical animal, 8 human clinical)	Animal models of PD and humans with PD	Qualitative synthesis (no quantitative meta-analysis)	Aerobic exercise, resistance training, dance	Human studies: PD patients (age and H&Y not consistently reported)	Cognitive function (global cognition, executive function)	Not primary focus; some studies report indirect motor improvements	Improvement in cognition; executive function improvements rated higher by GRADE	Varied by study; details not consistent; types included aerobic, resistance, dance; duration varied	Comparator: usual care or no intervention	Animal studies support neuroprotection, neurogenesis, neuronal proliferation; clinical studies show exercise can improve cognition, though optimal type, dose, and duration are unclear; quality of human evidence low to moderate, recommendations weak to strong
Tomlinson et al. 2013 (Tomlinson, Patel et al. 2013)	Systematic review, meta-analysis	39 RCTs	1827 participants	Quantitative meta-analysis	General physiotherapy, exercise, treadmill training, cueing, dance, martial arts	PD patients (age not consistently reported; mixed H&Y stages)	Gait, balance, functional mobility, clinician-rated UPDRS, falls, quality of life	Speed, 2- or 6-min walk test, Freezing of Gait, Timed Up & Go, Functional Reach Test, Berg Balance Scale, UPDRS motor	ADL (UPDRS-ADL), patient-rated QoL (PDQ-39), falls	Varied by study; short term (<3 months); frequency/intensity varied	Placebo or no intervention	Benefits seen in gait, balance, functional mobility, and clinician-rated UPDRS; no difference in falls or patient-rated QoL; quality of trials generally low; no evidence that type of physiotherapy alters effect; effects mostly short-term; small but sometimes clinically meaningful differences.
Vásquez-Morales et al. 2013 (Vasquez-Morales, Sanz-Valero et al. 2013)	Systematic review	10 RCTs	People over 65 (healthy or with cardiovascular)	Qualitative synthesis	Eccentric exercise (cycloergometer, knee dynamometer, treadmill,	Age >65, mixed health status	Muscle strength, mobility, fall risk, quality of life	Improved mobility, reduced fall risk	Quality of life	Varied by study; low metabolic cost, low oxygen consumption	Not always specified	Eccentric training is safe and feasible in older adults, including frail and cardiovascular populations; may prevent sarcopenia; upper body

			ar, muscu loskele tal, PD, hemip aresis)		machine exercises)							interventions less studied; more large- scale studies needed.
Briennesse and Emerson 2013 (Briennesse and Emerson 2013)	Systema tic review	5 controll ed trials (3 RCTs, 2 non- RCTs)	People with Parkin son's diseas e	Qualitati ve synthesi s	Resistance training	Adults with PD, mixed H&Y stages	Muscle strength, functional performance, mobility	Increased muscle strength, endurance , fat-free mass, improved mobility and functional tasks Improved gait speed (0.04 m/s), Berg Balance Scale (+3.71 points), UPDRS total (-6.15 points), UPDRS motor (- 5.01), UPDRS ADL (- 1.36)	Not specifically assessed	Varied by study; interventions included standard resistance exercises	Control groups varied (usual care or no intervention)	Resistance training shows positive effects on strength and functional mobility; studies moderately robust; more RCTs needed to define optimal prescription.
Tomlinson et al. 2012 (Tomlinson, Patel et al. 2012)	Systema tic review and meta- analysis	39 RCTs (29 trials for meta- analysis)	1827 partici pants with PD	Quantita tive synthesi s	Physiotherapy	Adults with PD, mixed H&Y stages	Gait, functional mobility, balance, falls, clinician-rated impairment/disa bility, patient- rated QoL	Patient-rated QoL (no significant change), falls (no significant change)	Varied across studies; included general physiotherap y, exercise, treadmill, cueing, dance, martial arts	Control: no physiothera py	Short-term benefits noted; no strong evidence of differences between physiotherapy techniques; need for large, well-designed RCTs for long-term efficacy and cost- effectiveness.	

Allen et al. 2011 (Allen, Sherrington et al. 2011)	Systematic review and meta-analysis	16 RCTs and quasi-RCTs	People with PD	Quantitative syntheses	Exercise and motor training	Adults with PD, mixed H&Y stages	Balance-related activity performance, falls	Balance-related activities improved (Hedges' g = 0.33)	No significant effect on falls (RR = 1.02)	Varied across studies; programs with highly challenging balance training tended to show greater improvement	Control: no intervention or placebo	Exercise improves balance performance; insufficient evidence that falls are prevented; further research needed.
Lau et al. 2011 (Lau, Teo et al. 2011)	Systematic review	6 RCTs and non-RCTs	People with PD	Narrative syntheses	Whole-body vibration (WBV)	Adults with PD, mixed H&Y stages	Sensorimotor performance, UPDRS	Some reduction in tremor and rigidity; other UPDRS scores conflicting	Not reported	3-5 weeks in longer-term studies; protocols varied	No intervention or conventional exercise	Evidence insufficient to confirm efficacy (grade D); more high-quality studies needed; small, heterogeneous samples; conflicting results.
Goodwin et al. 2008 (Goodwin, Richards et al. 2008)	Systematic review and meta-analysis	14 RCTs	People with PD	Random-effects meta-analysis, narrative, vote counting	Exercise interventions (various types: aerobic, resistance, balance, mixed)	Adults with PD, mixed H&Y stages	Physical functioning, balance, gait speed, strength, quality of life, falls, depression	Improvements in strength, balance, gait speed, physical functioning	Improvements in health-related quality of life; insufficient evidence for depression	Protocols varied across studies; frequency, intensity, and duration not standardized	No intervention or usual care	Exercise beneficial for motor and some non-motor outcomes; insufficient evidence for falls and depression; optimal dosing, components, and stage-specific prescriptions remain unclear.
Gage and Storey 2004 (H and L 2004)	Systematic review	44 studies (reported in 51 papers)	Community-living adults with PD	N/A	Physiotherapy, occupational therapy, speech and language therapy,	PD adults, setting: Home or outpatient clinics	Mobility, functional status, speech, swallowing, psychological well-being	Improvements reported in mobility and functional	Improvements reported in speech, swallowing, psychological well-being in most studies	Varied across studies; not standardized	Usually usual care or no intervention	Most studies showed improvement in ≥1 outcome; methodological quality varied; difficult to interpret clinical

Deane et al. 2001 (Deane, Jones et al. 2001)	Systematic review	11 RCTs	280 PD patients	N/A	Physiotherapy (various techniques)	psychological counseling, education, multidisciplinary (Age/H &Y not specified)	PD adults (Age/H &Y not specified) Walking velocity, stride length, other motor and functional outcomes	Walking velocity improved significantly in 2/4 trials; stride length improved in 2 trials; other motor outcomes mixed	status in most studies	Not specifically reported	Varied across studies; generally short-term	Placebo or no intervention	importance; publication bias likely; need for robust RCTs with meaningful follow-up and cost- effectiveness data. Methodological quality varied; small sample sizes; potential bias; overall evidence insufficient to support or refute efficacy; wide range of physiotherapy approaches used; need for consensus on best- practice, larger RCTs, standardized outcomes, and longer follow-up.

Legend: **6MWT**, 6-Minute Walk Test; **6-OHDA**, 6-Hydroxydopamine; **10MWT**, 10-Meter Walk Test; **ABC Scale**, Activities-specific Balance Confidence Scale; **ACSM**, American College of Sports Medicine; **AD**, Alzheimer's Disease; **ADL**, Activities of Daily Living; **AE**, Adverse Event; **AEP**, Aquatic Exercise Program; **ALE**, Activation Likelihood Estimation; **AMPA**, α -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid; **AR**, Augmented Reality; **AT**, Argentine Tango; **BBS**, Berg Balance Scale; **BDI**, Beck Depression Inventory; **BDNF**, Brain-Derived Neurotrophic Factor; **BFRE**, Blood Flow Restriction Exercise; **BGT**, Balance and Gait Training; **BMLSS**, Brief Multidimensional Life Satisfaction Scale; **BWS**, Body Weight Support; **BWSTT**, Body Weight Support Treadmill Training; **CBT**, Cognitive Behavioral Therapy; **CD**, Creative Dance; **CE**, Conventional Exercise; **CI**, Confidence Interval; **CMI**, Cognitive Motor Intervention; **CNS**, Central Nervous System; **COP**, Center of Pressure; **CP**, Cerebral Palsy; **CT**, Conventional Therapy; **DAT**, Dopamine Active Transporter; **DE**, Dance Exercise; **DGI**, Dynamic Gait Index; **DMT**, Dance Movement Therapy; **DT / DTT**, Dual-Task / Dual-Task Training; **EMST**, Expiratory Muscle Strength Training; **EMT**, Expiratory Muscle Training; **ES**, Effect Size; **FAE**, Functional Aerobic Exercise; **FAB**, Frontal Assessment Battery; **FES**, Functional Electrical Stimulation; **FITT-VP**, Frequency, Intensity, Time, Type, Volume, Progression; **FOG**, Freezing of Gait; **FOG-Q**, Freezing of Gait Questionnaire; **FR**, Functional Reach; **FRT**, Functional Reach Test; **FSS**, Fatigue Severity Scale; **FWS**, Fast Walking Speed; **g**, Hedges' g; **GAITRite**, [Brand Name for Gait Analysis System]; **GDS**, Geriatric Depression Scale; **GDNF**, Glial Cell Line-Derived Neurotrophic Factor; **GE**, Group Exercise; **GLT-1**, Glutamate Transporter 1; **Gln**, Glutamine; **GRADE**, Grading of Recommendations, Assessment, Development and Evaluations; **GS**, Glutamine Synthetase; **H&Y**, Hoehn and Yahr Scale; **HADS**, Hospital Anxiety and Depression Scale; **HAMA**, Hamilton Anxiety Rating Scale; **HAMD**, Hamilton Depression Rating Scale; **HBEMO**, Home-Based Exercise with Minimal Oversight; **HBE**, Home-Based Exercise; **HIIT**, High-Intensity Interval Training; **HR**, Heart Rate; **HRmax**, Maximum Heart Rate; **HRQoL**, Health-Related Quality of Life; **HYB**, Hybrid; **ICF**, International Classification of Functioning, Disability and Health; **IE**, Individual Exercise; **IGF-1**, Insulin-like Growth Factor 1; **I²**, I-squared statistic; **IMT**, Inspiratory Muscle Training; **LED**, Levodopa Equivalent Dose; **LSVT BIG**, Lee Silverman Voice Treatment BIG; **MCI**, Mild Cognitive Impairment; **MDS-UPDRS**, Movement Disorder Society-Sponsored Revision of the UPDRS; **MD**, Mean Difference; **MET**, Metabolic Equivalent of Task; **MFI**, Multidimensional Fatigue Inventory; **mGluR**, Metabotropic Glutamate Receptor; **MIRT**, Modified Intensive Rehabilitation Training; **MiniBESTest**, Mini-Balance Evaluation Systems Test; **MMSE**, Mini-Mental State Examination; **MoCA**, Montreal Cognitive Assessment; **MPTP**, 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine; **MR**, Multidisciplinary Rehabilitation; **MRI**, Magnetic Resonance Imaging; **MS**, Multiple Sclerosis; **NIVR**, Non-Immersive Virtual Reality; **NMA**, Network Meta-Analysis; **NMDA**, N-methyl-D-aspartate; **NMS**, Non-Motor Symptoms; **NMSQ**, Non-Motor Symptoms Questionnaire; **NR**, Not Reported; **NS**, Not Significant; **NS-LBP**, Non-

Specific Low Back Pain; **NW**, Nordic Walking; **OA**, Osteoarthritis; **OE**, Oriental Exercises; **OR**, Odds Ratio; **OT**, Occupational Therapy; **PASE**, Physical Activity Scale for the Elderly; **PA**, Physical Activity; **PD**, Parkinson's Disease; **PD-MCI**, Parkinson's Disease with Mild Cognitive Impairment; **PDQ-39/-8**, Parkinson's Disease Questionnaire (39 or 8 items); **PEDro**, Physiotherapy Evidence Database; **PE**, Physical Exercise; **PFS**, Parkinson's Fatigue Scale; **POMA**, Performance-Oriented Mobility Assessment; **PRISMA**, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; **PRT**, Progressive Resistance Training; **PSD-95**, Postsynaptic Density Protein 95; **PSP**, Progressive Supranuclear Palsy; **PT**, Physiotherapy; **PwPD**, People with Parkinson's Disease; **Qigong**, [Chinese Mind-Body Practice]; **QoL**, Quality of Life; **RAGT**, Robot-Assisted Gait Training; **RaR**, Rate Ratio; **RAT**, Robot-Assisted Therapy; **RCT**, Randomized Controlled Trial; **RE**, Resistance Exercise; **REML**, Restricted Maximum Likelihood; **rTMS**, Repetitive Transcranial Magnetic Stimulation; **SCI**, Spinal Cord Injury; **SCWT**, Stroop Color and Word Test; **SD**, Standard Deviation; **SDPA**, Self-Directed Physical Activity; **SES**, Standardized Effect Size; **SF-36**, 36-Item Short Form Survey; **SMD**, Standardized Mean Difference; **SR**, Systematic Review; **SUCRA**, Surface Under the Cumulative Ranking Curve; **T2DM**, Type 2 Diabetes Mellitus; **TBI**, Traumatic Brain Injury; **TCE**, Traditional Chinese Exercise; **TCQ**, Tai Chi Quan; **TE**, Traditional Exercise; **TH**, Tyrosine Hydroxylase; **TUG**, Timed Up and Go Test; **tDCS**, Transcranial Direct Current Stimulation; **TMS**, Transcranial Magnetic Stimulation; **TR**, Telerehabilitation; **UPDRS**, Unified Parkinson's Disease Rating Scale; **VASt**, Video-Assisted Swallowing Therapy; **VGULT1**, Vesicular Glutamate Transporter 1; **VO₂max**, Maximal Oxygen Consumption; **VR**, Virtual Reality; **WBV**, Whole-Body Vibration; **WE**, Water-Based Exercise; **WHODAS**, World Health Organization Disability Assessment Schedule.

Extended Acknowledgements: A Threshold

These lines are not meant to be an exhaustive list of names or achievements, but an attempt to convey the human essence of a scientific journey that has been inextricably intertwined with people, places, and life choices.

Whoever reads this text, in which I will express my thanks, should know that, at the moment I am beginning to write, I am not in Italy. I am in Norway, in the land of the Vikings (as Prof. Venturelli would say), specifically at Molde University College - Science College in Logistics, in Molde, in the county of Møre og Romsdal (as Wikipedia suggests), with the notes of the royalty-free music track by Egzod & Maestro Chives as the engine of my thoughts in the background.

It is a period that is stressful at times but certainly better than what I experienced in Italy because, for the first time, I am dedicating myself to myself; perhaps it is also Norwegian culture transmitting this to you. Then the silence and tranquility make this set of sensations even more evocative (to the notes of the soundtrack ODESZA – A Moment Apart, as the beating heart of this Scandinavian adventure).

As Prof. Masala would say, "I believe the best victory is the one yet to come." Indeed, nothing precludes the future, nothing can hinder, I add, what you are destined to achieve—something inevitable, especially when you have a strong motivation behind you that you have been carrying forward for about eight years or perhaps more, if I think back to my high school years. The memory of my paternal grandfather, Andrea, has been the flame that fueled itself relentlessly, always in a crescendo. It was precisely when my mother and father reminded me that my grandfather had Parkinson's disease that our mission had just begun.

A PhD, by definition, is the highest degree of education and the highest academic qualification, and its main purpose is to train for high-level research and university teaching (Wikipedia). Well, in my opinion, the path I am completing was and is, first and foremost, the highest degree of personal formation and growth, and only then the research part, because you are in contact with many people and you must know how to react and communicate with maturity about all the events that revolve around you. All the values you were taught and instilled with as a child and that you must not forget (perhaps it is also the emotional aspect that is strongly influencing me).

If I think back to how it all began, at least to remind those who don't know, it took time to get here; the value of waiting is very precious, and this perhaps rewarded all the obstacles encountered and overcome. If it hadn't been for the contact with Prof. Castellani in my second year of the bachelor's degree in Motor and Sports Sciences (L-22), none of this would have started. I was first intrigued by Prof. Misiti's biochemistry lectures and, subsequently, by Prof. Castellani's human physiology lectures, and then I deepened these disciplines in relation to neurodegenerative diseases and exercise. The focal point was that I was interested in two in particular: Parkinson's and Alzheimer's. For what reason? The first was for my grandfather (when I found out from my parents, from which I started researching), the second for a girl I had become very attached to (a strong infatuation,

perhaps in love, albeit in vain) in memory of her father who died during Covid. Prof. Castellani told me to choose between the two, to bring a scientific article as my final thesis, since the two diseases, although closely related, are different. But before continuing, she suggested two names to give me a clear idea: Prof. De Pandis from the San Raffaele Hospital in Cassino and Prof. Langiano, a professor at the University of Cassino and Southern Lazio, whom I contacted and who were very willing to be my supervisors. However, the latter also suggested Prof. De Pandis to me; in the end, I chose Parkinson's. A path with San Raffaele began, with the possibility of doing an experimental thesis for the master's degree, entrusting me to Prof. Federico as my internal supervisor. However, due to tight deadlines, I then conducted a literature review, expanded with a research protocol to be carried forward in the PhD... scenarios were already opening up in this perspective and enthusiasm was not lacking. The collaboration between the University and San Raffaele thus began, with a broad program to be realized (reviews, experiments, observational studies, etc.) on high- and low-intensity exercise in Parkinson's disease, specifically evaluating serum levels of BDNF and oxidative stress biomarkers, which are correlated with each other as a function of the intensity of the activity.

No one can foresee what happens, when the first misunderstandings begin, different reasoning, mentalities, and ways of working. If you don't find a meeting point from your "inferior" position, everything changes, even the suggestion of changing the topic... I would never have allowed something you cared about to be changed, and I repeat: you must believe in it and want it all the way if you want to start a path, whether it's a PhD, a job, or something else—a sort of vocation that comes from your "gut," almost obsessively, where you don't sleep at night because you think about the future, planning your own future while still blind... it's your vision that few will understand.

The unexpected happened, in the middle of the year (June 21, 2022), for an event on Parkinson's and exercise at the University of Verona. I left and lived that experience; I had the chance to meet and begin to expand contacts I never thought I would make. I understood that I had to insert myself into that context to shake up a situation that was almost at a standstill at that moment... I decided to join several scientific societies to deepen my knowledge and consolidate my academic network. I became a member of the Italian Society of Motor and Sports Sciences (SISMES), which allows me to stay updated on the latest research on exercise and its applications to health. I joined the LIMPE Foundation for Parkinson's Onlus and the Italian Society for Parkinson's Disease and Movement Disorders (LIMPE-DISMOV), coming into contact with experts in the field and participating in initiatives aimed at research and improving the quality of life of people with Parkinson's. Furthermore, I joined the Italian Association of Exercise Specialists (AISE), which promotes integration between movement science and rehabilitation practices. Thanks to these new connections, what initially seemed a solitary battle transformed into a journey of growth, made of challenges, unexpected encounters, and opportunities that shaped the path I was undertaking.

My ongoing research and international collaborations, including work at the University of Verona, Molde University College, and Rey Juan Carlos University, will further enrich my knowledge and skills in the field of Parkinson's disease research. During my PhD, I developed and maintained valuable academic collaborations in the United States with Prof. Merrill Landers (University of

Nevada, Las Vegas), whose work on exercise-based rehabilitation in neurodegenerative diseases closely aligns with my research focus, as well as with Prof. Daniel Montie Corcos (Northwestern University, Chicago).

Another significant attempted collaboration was with Prof. Erika Franzén (Karolinska Institute), who has contributed significantly to the development of balance and mobility interventions for Parkinson's patients, opening perspectives for joint studies on exercise-based neurorehabilitation.

A further attempt in my network was with Prof. Bas Bloem (Radboud University, Netherlands), a world-renowned expert in movement disorders and Parkinson's disease. This collaboration was facilitated by Dr. Nicola Modugno (IRCCS Neuromed, Pozzilli, Italy), one of my PhD supervisors, currently involved in developing new research projects on sports interventions, both aquatic and terrestrial, for Parkinson's rehabilitation, both in Italy and abroad (Spain). This line of research represents a promising direction I could explore in the future.

Furthermore, Prof. Leonardo Alexandre Peyré-Tartaruga (University of Pavia & UFRGS, Brazil) showed interest in Parkinson's disease through the study of integrative mechanisms of minimizing human locomotion, focusing in particular on Nordic Walking, dance-based interventions, and other adapted physical activities. These strategies, currently the subject of ongoing research projects in Porto Alegre (Brazil), could offer new perspectives on how different exercise modalities contribute to neuroplasticity and functional recovery in Parkinson's patients.

Finally, I established an interesting collaboration with Dr. Anna Ferrusola-Pastrana, a postdoctoral researcher specialized in Neurodegenerative Diseases, Exercise, and Biomarkers of Neuroplasticity. After an experience at Kent University (UK), she currently works at the University of Girona (Spain). Her experience adds further value to the network of collaborations and potential research directions I can explore throughout my academic and professional journey.

So much so that at a conference in Turin, I met a neurologist who will most likely change my life... I am not exaggerating, but the chain of events will accumulate more and more, reaching unthinkable networks. His name is Nicola Modugno, from IRCCS Neuromed in Pozzilli, with whom a program began that was not entirely concrete but which, in my view, lays the foundations for the future. Imagine finding yourself on the phone on December 31st, talking with him before leaving for the new year for Verona (another chapter), discussing and listening to ideas to realize in the world of Parkinson's and exercise, sport as a factor capable of modifying the course of the disease (sport as a disease-modifying factor), studying and implementing therapeutic strategies aimed at improving the lives of these people (and not "subjects" nor "patients") to try to slow down, unfortunately, the progression of these neurodegenerations, sometimes devastating. I promised myself to spread, from that moment on, this concept he was trying to convey to me in the new year to whomever I would meet—which research groups, professors, institutions, etc.—to create an ever-widening network. It also means, in these cases, putting oneself on the line with experts in the field, where, on the other side, there is a guy who only wants to dream big.

During my time at the University of Verona, I was actively involved in a research project examining the effects of maximal strength training in individuals with Parkinson's disease. Under the

supervision of Prof. Massimo Venturelli, I contributed to investigating how targeted high-intensity strength training affects motor function, muscle strength, and overall physical performance in Parkinson's patients. A key aspect of this study is the use of Intermittent Theta Burst Stimulation (iTBS) to explore neurophysiological adaptations to strength training, particularly its impact on motor control and neuroplasticity.

Parallel to this research activity, I was completing a second-level Master's degree in "Exercise Therapy: Design and Implementation of Exercise in Exercise-Sensitive Conditions," which includes a specific focus on Parkinson's disease. This path allowed me to further deepen exercise-based intervention strategies and integrate scientific skills with a more practical and applied approach.

Furthermore, I was involved in several hospital internships, which I used productively by working closely with neurologists and physiatrists. These experiences allowed me to broaden my scientific training on various pathologies, including cancer and multiple sclerosis, offering me a broader view on the application of exercise as a therapeutic tool in different clinical contexts. Through these multidisciplinary experiences, I consolidated my understanding of the role of physical activity in neurodegenerative and oncological diseases, enriching my research path with a more comprehensive and integrated approach.

Alongside the encounter with people with Parkinson's, another element profoundly marked this journey: the people I worked with. Even before roles, titles, and skills, I encountered human beings. Researchers, clinicians, colleagues who, in the different contexts I traversed, showed that the quality of scientific work also depends—and perhaps above all—on the quality of relationships.

In these environments, I learned that humanity is not a limit to research, but its condition. Listening, respecting others' times, the ability to recognize the other person before the project were silent but decisive lessons. It is in this space that I understood that there is no true innovation without care, nor rigor without responsibility.

Places also played an active role. The nature encountered in different countries was not a simple backdrop but a constant presence. The Nordic silence, the open landscapes, the slow rhythm imposed by the climate and light changed my way of thinking and inhabiting time. In Norway, I learned to slow down; in Spain, I rediscovered the value of sharing; in Edinburgh, I experienced solitude as a space for clarification.

Time, in this journey, ceased to be just an organizational variable. It became living matter. There were periods of acceleration and others of apparent stasis, moments of enthusiasm and phases of sedimentation. I learned that not everything slow is unproductive, and that some understandings arrive only when you stop forcing them.

It is in this intertwining of people, places, and times that my idea of research was formed: not as an accumulation of results, but as a situated, responsible human practice, capable of holding together scientific competence and deep respect for those met along the way.

In that phase, a new feeling began to emerge, difficult to define but impossible to ignore: a growing adrenaline, born not from the absence of fear, but from the decision not to stand still. It was the

moment to show the best of oneself, not in terms of already achieved results, but as an inner push to expose oneself, to try, to fail.

From Verona, I began contacting research groups all over Europe, and beyond. France, with an interview from Paris; Portugal, Finland, Denmark, the Czech Republic, Poland, Greece, Germany, England. Every email sent was a minimal act of faith, every reply received—even partial, even uncertain—became a concrete possibility.

That movement did not stop at European borders. I sought contacts also in Africa and Asia, driven more by the desire to try than by a real expectation of success. I remember in particular contacts with the International Parkinson and Movement Disorder Society, in Nigeria and South Africa, and some attempts in Asian contexts. Not everything led to an outcome, but each step contributed to building a new awareness: I was doing everything within my power, perhaps even more.

In that period, adrenaline grew along with confidence. Not a naive confidence, but the kind born when small external signals—an interview, a reply, an interest shown—confirm that the attempt makes sense. It was in this space, between uncertainty and possibility, that the path began to take a real direction.

When great scenarios open up, you wish for nothing more than to think positively and have optimistic people, as well as professional ones. There comes a moment when you must make decisions for yourself and for those around you. Everything is happening while I am in Norway telling you, month after month, about all the various upheavals. But first, I ask you readers: would you choose professional people who do not convey a zest for life, or people open to doing great things, by osmosis? In the end, true strength lies in the osmosis between people: it is through the interaction and contagion of positive energies that great things are born. It is not enough to be professional; one must also transmit passion and a desire to grow together. Choosing people who bring optimism and are willing to work as a team to achieve ambitious goals creates an environment where growth is natural and collective. In a constantly evolving world, it is precisely this ability to 'absorb' motivation and transform it into action that allows us to face every challenge with courage and determination. And that is what is about to happen when you decide to choose people you met in Pavia who gave you more hope in the things I am doing—Luca Correale and Leonardo himself (yes, him, who contacted me at the beginning of my PhD like a signal from heaven that I will never thank enough). There are people who hope in others and not only for themselves, who do not fight for their own survival, for their own selfishness, but there is a common basis: that of doing something important for Parkinson's.

This path is born from encounters, more than from places. Some were chosen, others imposed themselves like sudden waves, capable of setting in motion what seemed to have stopped. The choice of Modugno falls exactly in this space: not as a random landing, but as the outcome of a bond built over time. In this sense, the role of Prof. Federico and Prof. Raimondo was decisive. Through a shared interest in Tai Chi, cultivated already during my bachelor's degree, a scientific dialogue opened that connected different worlds: the University of Cassino, the Istituto Superiore di Sanità, research groups in Rome, and the historic collaboration with Neuromed.

At a time when some paths seemed closed or difficult to travel, these contacts represented a concrete form of continuity and trust. From there, the meeting with Modugno, the discussion in Turin, and the experience in Verona with Prof. Tinazzi and his group gave meaning to a trajectory that was not linear but coherent. Norway, Spain, and Edinburgh were not just geographical stops, but existential passages, each with its own load of enthusiasm and effort.

In Edinburgh, in particular, I rediscovered something I thought I had lost: a form of vital energy. The visit of my cousin Miranda and her partner Will, even for just a few days, had the effect of a sudden wave. Reflecting on Massimo Recalcati's words, the impact of the wave is not what overwhelms, but what reconnects the subject with their own desire. In this open sea, made of uncertainties, displacements, and obstacles, that wave represented a silent but decisive push to proceed.

To this path, often narrated as solitary, I must however make a necessary clarification. While it is true that many steps are taken alone, it is equally true that no journey takes shape without presences that, in different ways, keep the breath open.

My family was the first form of continuity. Even at a distance, even in silence, it remained the place to return to mentally when the weight became excessive. The memory of my grandfather Andrea was not only the origin of this scientific trajectory but a constant, discreet presence that gave meaning even to the most difficult moments.

Some friendships have crossed this path as intermittent but necessary points of light. Deborah, in particular, was, as already written years ago, a candle always lit: not to indicate a direction, but to remind that a possibility of warmth existed even in the coldest periods.

The experience in Norway, marked by formative and at times harsh solitude, found a human counterweight in the subsequent experience in Madrid, Spain. There, the company of Renato and Nicolas, with their story, their origins, and their way of inhabiting life, restored lightness to a period that risked becoming rigid. Finally, the Edinburgh experience had a particular value. Sharing the last stretch of this journey with Melony, thanks to her positivity and zest for life, made a phase that could have been exclusively about closure and tension more livable. It is also thanks to these presences that the final stretch was not just resistance but a transformation.

To all those who have been close, even just for a stretch, in joy or difficulty, goes my most authentic thanks. Roads then separate, each follows their own time, makes mistakes, changes shape. But each encounter left something. And it is also from these traces that what I have become was born.

There are moments in life when I stop asking myself what to do and begin to ask what is happening. It is not a crisis, although it is often mistaken for one. It is rather a threshold. I know I am there, on a thin line, difficult to explain to those who have never crossed it. If there is one thing this journey has taught me, it is that not everything that is possible is also right, and not everything that is ambitious is worthy of being pursued. Having reached this point, I feel the responsibility to choose not only what to do, but how to do it. I do not want to become a researcher who loses people along the way, nor a professional who confuses recognition with meaning.

The promise I feel I must keep—even before towards science—is towards the people I have met: those who believed in me, those who suffered, those who shared a stretch of the path. If this work will have value, it will not only be for the results it will produce, but for the way it will manage to remain human. This is the threshold I am now crossing: not that of the title, but that of responsibility. When I speak of opportunity, luck, destiny, I realize that I am actually speaking of something deeper: the relationship between desire and reality. Because the point is not whether things arrive by chance or by merit. The point is that, at a certain level of involvement, reality begins to respond to desire. Not because it is magical, but because authentic desire organizes one's gaze, choices, time. It makes things recognizable. I have not simply "had" opportunities; I have become someone to whom they can happen. And from here arises the doubt: do I deserve it? This question does not come from greed, but from awareness. It arises when one realizes they are receiving more than they had dared to imagine at the beginning. It is a question that weighs, not exalts. It arrives only to those who do not want to live beyond their ethical possibilities.

I have learned that there is a profound misunderstanding around the word "sacrifice." We are taught that the more one sacrifices, the more "valid" the things obtained will be. But blind sacrifice guarantees nothing. Oriented sacrifice, on the other hand, slowly builds a trajectory. And when a trajectory is coherent, at a certain point it begins to seem like destiny. But it is not: it is fidelity protracted over time.

What I sometimes call "obsession" is not pathological. It is what happens when something becomes bigger than my ego. I am not trying to prove I am good. I am trying to be worthy of a promise I have never uttered aloud, but that I have felt upon me for years. Parkinson's, the memory of my grandfather, the people encountered, the places traversed are not separate causes: they are the same question changing language. It happens then that some doors open. And when it happens, instead of exulting, I stop and ask myself: why me? But the right question is not: "Why me?" It is: what am I doing with this? Because true responsibility is not obtaining possibilities, but not betraying them.

The loneliness I experience today is not an accident of the journey. It is a consequence. Living in constant displacement, not only geographical but also of identity, inevitably leads to territories devoid of emotional maps. Edinburgh, Norway, Spain are not just places: they are spaces where I am learning to be with myself without the immediate reflection of others. It is tiring, but clarifying. It forces one to ask who one is when no one is watching, when no one confirms.

This is where the wave arrives. Not as a poetic image, but as a structure of experience. It does not promise success: it is a dynamic. It originates far away, accumulates energy, advances, encounters resistance, changes shape. I cannot stop it, but I can lose it if I stop listening to it. And I can get hurt if I try to dominate it. I am not riding the wave to arrive before others; I am riding it not to fall back relative to myself.

And that is why I feel confusion: because this is a moment when life does not ask to push, but to integrate. To hold together the researcher and the man, ambition and fragility, movement and the need for home. This passage is silent and, because of this, is often mistaken for being lost. But I do not feel lost: I find myself in a phase of sedimentation.

There will be a moment when the wave will break. Not as an end, but as good waves do: leaving something on the shore. A trace, a change, a possibility that was not there before. And then, perhaps, stillness. Or perhaps another wave, different, more mature. The final question is not whether I deserve it. It is whether I am willing to remain faithful even when the wave ceases to be euphoric and becomes responsibility. The answer is not yet a sentence. It is a life that, step by step, is already responding.

If this work will be read as a doctoral thesis, I hope it can also be recognized as an honest attempt to hold together science and responsibility, research and humanity.

In the last days before concluding this experience abroad, a phrase from my mother gave all of this an unexpected resonance. As a child, I needed speech therapy; I struggled to express myself as I wished. A teacher told my mother that I was a "child with great potential": not immediate, but capable, with time, of finding my own voice. Today, on the threshold of the final defense, I recognize in those words a metaphor faithful to this journey. This thesis, and these acknowledgements, are also the attempt to give form to that voice, matured slowly, thanks to the encounters, the waves, and the people who believed in me.

With gratitude,
Andrea

The present thesis concludes with an extended acknowledgements section, conceived as a reflective closure to the doctoral journey.