REVIEW

Efficacy of Dual-Task Training in Patients with Parkinson's Disease: A Systematic Review with Meta-Analysis

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ABSTRACT: Background: Dual-task training (DTT) involves simultaneously motor and cognitive exercises.
Objectives: To determine the effectiveness of DTT, in comparison to other interventions [single-task training (STT) and usual care (UC)], on gait and balance parameters, motor impairments, activities of daily living (ADLs) and quality of life (QoL) in patients with Parkinson's disease (PD) immediately post-intervention and at 3, 6, and 12 months after therapy.
Methods: A meta-analysis was performed following PRISMA Guidelines through searching in PubMed, SCOPUS, WOS, CINAHL, SciELO and PEDro up to September 2022. We included randomized controlled trials (RCTs) that compare the effect of DTT versus STT and UC on gait (speed, step and stride length, cadence and steps per day), balance (functional and dynamic balance), motor impairments, ADLs and QoL. Methodological quality was assessed using the PEDro scale. The pooled effect was calculated through Cohen's Standardized Mean Difference (SMD) and its 95% confidence interval (95%CI).
Results: Seventeen RCTs with 826 participants and a mean PEDro score of 6.59 ± 1 points were included. In comparison to STT and UC, DTT is effective in improving walking speed (SMD 0.42, 95%CI 0.23–0.6), stride length (SMD 0.69, 95%CI 0.23–1.15), cadence (SMD 0.41, 95%CI 0.19–0.63), functional balance (SMD 1.15, 95%CI 0.92–1.4), dynamic balance (SMD −0.5, 95%CI −0.81 to −0.18) and motor impairments (SMD −0.86, 95%CI −1.25 to −0.47). No adverse effects related to DTT were reported.
Conclusions: DTT is an effective and safe therapy for improving gait, balance and motor impairments in patients with PD.

Parkinson's disease (PD) is the second most common neurodegenerative disorder after Alzheimer's disease,[1] and it is expected to affect 9.1 million patients by 2030.[2] PD is a multifactorial neurodegenerative disorder characterized by a loss of dopaminergic neurons in the basal ganglia[3] and an increase of Lewy bodies[4] in these neurons in midbrain locomotor areas[5] and in the motor cortex.[6] The alterations in these neuroanatomical areas, responsible for controlling and coordinating movements,[7] produce the cardinal signs of PD, such as bradykinesia, tremor, rigidity, and impaired balance.[8]

Gait and balance disorders are disabling consequences of PD[9] that reduce the functional independence required to perform activities of daily living (ADLs).[10,11] Parkinsonian gait (or freezing of gait[12]) is characterized by decreased propulsive force resulting in small, slow steps, stooped posture, low toe-off, and impaired coordination between limbs.[13] In addition, gait speed and cadence are reduced. The stooped posture and difficulties to integrate somatosensory information decreases the postural and anticipatory reflexes needed to maintain balance while standing or during locomotion.[14,15] These postural disorders

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increase the risk of falling,[16] and are the leading cause of minor musculoskeletal injuries.[17] Gait and balance disorders are exacerbated during ADLs that require dual-task conditions (carrying out cognitive and motor tasks simultaneously). For example, speaking or paying attention to different environments and people while walking.[13,18]

Currently, dopaminergic drug therapy (such as Levodopa) is the most widely used treatment to minimize bradykinesia or tremor.[19] However, previous studies have shown that after 2 years using Levodopa, around 46% of patients experience motor fluctuations and 26% experience dyskinesias,[20,21] thus increasing balance and gait disorders and reducing the possibility of performing two tasks at the same time.[22] Dual task-training (DTT) is defined as the combination of two motor tasks with different objectives, or the combination of a motor task with a cognitive task.[10] DTT allows the patients to undergo cognitive and physical rehabilitation at the same time.[23] The effectiveness of DTT depends on the patient's ability to perform motor tasks automatically and the cognitive (executive) ability to combine different types of tasks.[24] DTT can be used to implement the classical approaches of rehabilitation,[25] using virtual reality or robotic devices that require the patient's full attention to complete the motor activity.[26,27] DTT has been shown to improve gait and balance disorders in stroke[28] or multiple sclerosis[29] patients, albeit with inconclusive evidence.

The effect of DTT on gait, balance and motor impairments in PD patients has been analyzed in three previous reviews, published in 2020, with data from 3,[25] 7,[30] and 11 studies,[31] respectively. The low number of studies included per variables in these reviews and the language restrictions could decrease the quality of the evidence of the findings.[25,30,31] In addition to the aforementioned limitations, the sample size for providing data was small in each review and few analyzed variables such as dynamic balance, quality of life (QoL), ADLs and whether the effect of DTT is maintained over time. Considering these limitations and the latest studies published, there is a need for a new review to analyze the effect of DTT. We performed a systematic literature search with the aim of compiling all scientific evidence available to date to assess the effectiveness of DTT in comparison to single-task approaches or usual care (UC) on gait and balance disorders, motor impairments, ADLs and QoL. More specifically, data permitting, we will analyze the effect of DTT over time (immediately post-intervention and at 3, 6, and 12 months after therapy).

Methods

Design

A systematic review and meta-analysis was carried out in adherence with the 2020 updated version of the *Preferred Reporting Items for Systematic Reviews and Meta-analyses* (PRISMA),[32] and *A Measurement Tool to Assess Systematic Reviews* (AMSTAR version 2).[33] This review was registered in PROSPERO database (CRD42022348336).

Search Strategy

Two authors independently performed a systematic literature search (without language or publication date restrictions) in PubMed Medline, Scopus, Web of Science, CINAHL Complete, PEDro, and SciELO up to September 15, 2022. In addition, the authors revised the reference lists of previously published relevant papers and gray literature. Our search was carried out following the PICOS tool developed by the Cochrane Library.[34,35] The following Medical Subjects Headings (MeSH) were used as keywords and entry terms in our search: "Parkinson disease," "dual-task," "gait," "gait disorders," "postural balance," "balance disorders," "motor impairments," "activities of daily living" and "quality of life". All of these keywords and entry terms were combined using the Boolean operators AND/OR and its appropriate tags, following the guidelines of each database. A third expert author supervised the search. The search strategy employed in each database can be found in Table S1 in Supporting File 1.

Inclusion and Exclusion Criteria

The study selection process was carried out by two authors, who independently revised all retrieved references by title and abstract. When a reference was selected as a potential study to be included by one author, it was examined in detail by both authors. A third author resolved the discrepancies.

In order to be included in the meta-analysis, the studies had to meet all of the following inclusion criteria: (1) Randomized controlled trials (RCT); (2) that assesses the effect of DTT; (3) in comparison to other single task activities or UC; (4) on gait and balance disorders, motor impairments, QoL and ADLs; (5) in patients with PD; and (6) studies that reported statistical data that can be included in a meta-analysis. The exclusion criteria were: (1) RCT that comprises patients with different neurological diseases, not only PD; (2) studies that did not provide outcomes assessed with tests that enable them to be grouped in the meta-analysis; and (3) RCT in which both groups performed activities under dual task conditions.

Data Extraction

Two authors independently extracted the data of the studies included in a Microsoft Excel standardized data-collection form and a third author resolved the discrepancies. We extracted the following data from each included study: (1) Overall characteristics of the study: authorship, publication date, country, setting, funding, sample size and number of groups. (2) Characteristics of intervention and comparison groups: sample size, age, gender, years since diagnosis and level of disability and ON/OFF dopaminergic medication. (3) Characteristics of the DTT in the intervention group: type of DTT and intervention protocol. (4) Data of the outcomes: variable, test and quantitative data (mean and

standard deviation) and follow-up period (immediately post-intervention and follow-up at 3, 6 and 12 months). When studies reported error, range, interquartile range and median, we used standardized procedures.[35,36]

Variables

The main outcomes were gait (gait speed, step and stride length, cadence and the number of steps per day), and balance impairments (functional and dynamic balance). A second objective was to assess the effect of DTT on motor impairments, ADLs and QoL.

Methodological Quality and Quality of Evidence

The methodological quality and the risk of bias of the studies included were assessed by two authors. First, methodological quality was assessed using the PEDro Scale,[37,38] a checklist of 11 items than can be answered as "yes" if the criterion is met and "no" if not. The total score (sum of items 2–11) can range between 0 (very low methodological quality) and 10 (high). The methodological quality of the studies can be excellent (10–9 points), good (8–6 points), fair (5–4 points) and low (3 or fewer points). With regard to risk of bias, items 2 and 3 are related to selection bias, items 5 and 6 to performance bias and item 7 to detection bias. A recent study of Berardi et al[39] has reported that the PEDro checklist presents excellent construct validity, good accuracy and test–retest reliability.

The quality of the evidence was assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE)[40] and the GRADE checklist of Meader et al[41] Taking into account the risk of bias, inconsistency, indirectness, imprecision and risk of publication bias of each included study, the quality of evidence can be: high, if findings are robust; moderate, if new studies can change our findings; low, if the confidence level of the pooled effect is small; and very low, if the effect estimate is uncertain.

Statistical Analysis

Two authors used version 3.0 of the Comprehensive Meta-Analysis (Biostat, Inc.) to perform the meta-analysis.[42] The meta-analysis was only conducted if more than one study assessed the outcome of interest. The pooled effect was calculated using the Cohen's Standardized Mean Difference (SMD) and its 95% Confidence Interval (95% CI)[43] in a random-effects model by DerSimonian and Laird.[44] We used a random-effects model because heterogeneity was over 50% in fixed-effects model calculations. The effect size can be null (SMD = 0), low (SMD = 0.2–0.4), medium (SMD = 0.4–0.7) and large (SMD ≥ 0.8).[45] In variables assessed with the same tests, we calculated the Mean Difference (MD) between groups, with the aim of comparing this result to the Minimal Clinically Important Difference (MCID) for this test, and to assess if our findings present clinic impact. Risk of publication bias was assessed taking into account the funnel plot's symmetry,[46] P-value for Egger test ($P < 0.1$ indicates publication bias),[47] and the trim-and-fill

estimation (more than 10% of variation with the original SMD indicates risk of publication bias and downgrades the level of evidence one level even though the funnel plot was symmetric).[48,49] Finally, heterogeneity level was assessed through the Q-test and its P-value ($P < 0.1$ indicates heterogeneity) and the degree of inconsistency (I^2). Heterogeneity can be low ($I^2 < 25\%$), moderate (I^2 25–50%) and large ($I^2 > 50\%$).[50,51]

Additional Analyses

The leave-one-out method was used to perform the sensitivity analysis with the aim of understanding the contribution of each study to the pooled effect. Subgroup analyses were performed on the time of assessment (immediately post-intervention, and at 3, 6 and 12 months). A meta-regression was performed to assess the differences in the effect between DTT and STT, and between DTT and UC. We performed a qualitative synthesis of the adverse effects reported by the studies included.

Results

Study Selection

Figure 1 (PRISMA flow diagram) shows the study selection process. A total of 1853 references were retrieved in initial searches; 814 were deleted for not having a relevant title or abstract and 132 for not meeting the inclusion criteria. Finally, 17 studies[52–68] were included in the systematic review and meta-analysis.

Characteristics of the Studies Included

The studies included in our meta-analysis were carried out in Spain,[54,67] Saudi Arabia,[56] Brazil,[60,63] China,[58] Taiwan,[59] United States,[57,64,68] Belgium and Netherlands,[55,66] Portugal,[65] Canada,[52,62] and Sweden[53,61] between 2000 and 2022, reporting data from 826 participants with PD (62.2% males) with a mean age of 66.8 ± 3.72 years and a mean duration of disease of 5.91 ± 1.98 years. Among the patients included, the range of Hoehn-Yahr varied between I and IV, with status II and III being the most common. The experimental intervention group comprised 418 participants (62.44% males) with a mean age of 67.22 ± 0.03 years; the patients underwent a DTT intervention (combining motor and cognitive tasks, balance exercises and cognitive tasks, music therapy and cognitive tasks, cycling and cognitive tasks or walking and cognitive tasks, among others). The control group comprised 408 participants (63% males) with a mean age of 66.38 ± 3.52 years; the patients performed isolated cognitive or motor exercises or continued with their daily activities. In 14 studies[52,53,64–66,68,54,55,57–62] patients received dopaminergic medication and in three studies[56,63,67] this information was not reported. The interventions and assessments were evaluated in ON medication state in 13 studies[52,53,65,66,68,54,55,58–62,64] and were only assessed in OFF medication state in one study.[57]
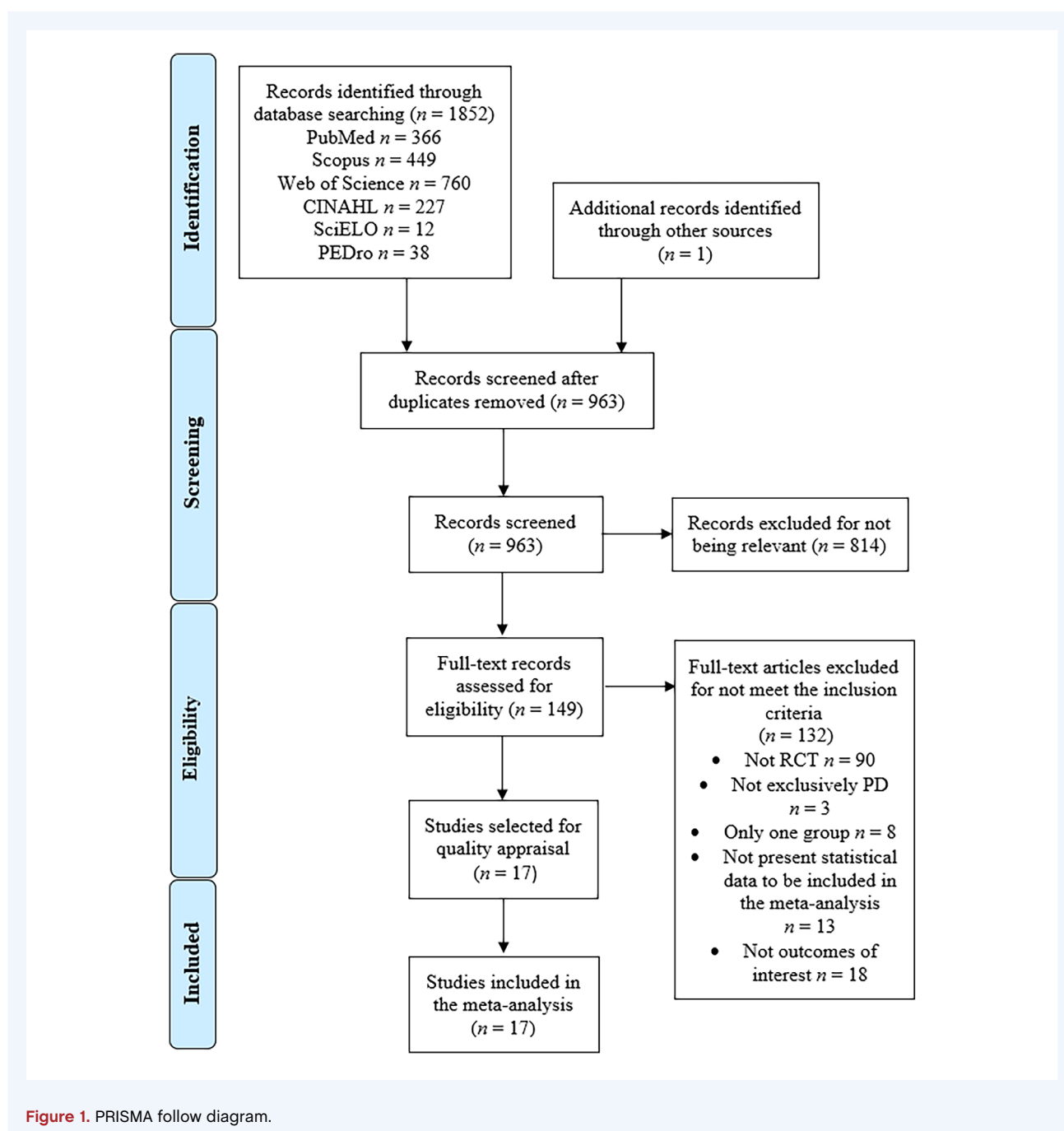
Figure 1. PRISMA follow diagram.

The duration of the intervention ranged between 4 and 48 weeks with between one and three sessions per week and a treatment time for each session that ranged between 20 and 60 min. Thirteen studies received external funding to carry out the research,[52,53,65,66,68,55,57–62,64] one did not receive[67] any and three did not provide this information.[54,56,63] Table 1 shows the characteristics of all the studies included in this meta-analysis in more detail.

Methodological Quality Assessment

Table S2 in Supporting File 1 shows the PEDro scores for each RCT included. The mean PEDro score was $6.59 + 1$ points, showing good methodological quality. Fourteen studies[53,54,65–68,55,56,58–61,63,64] (82%) show good methodological quality and three studies[52,57,62] (18%) were fair.

TABLE 1 *Characteristics of the studies included in the review*

Study	N	DTT intervention		Control intervention	
		DTT group	**DTT protocol and frequency**	**Control group**	**Control intervention**
Beck, EN et al[52] Setting: Movement Disorders Research and Rehabilitation Center, Waterloo (Canada) Funding: Canada Foundation for Innovation to Quincy J. Almeida	31	n: 20 Age (years): 73.1 ± 7.9 Gender: 4F:16M Years since diagnosis: 6.7 ± 4.2 Hoehn-Yahr: NR	Protocol: Walking, balance, stretching and coordination exercises while counting numbers announced by an audio-track. Frequency: 11 weeks, 3 times per week and 1 h per session.	n: 11 Age (years): 71.3 ± 6.6 Gender: 1F:10M Years since diagnosis: 8.4 ± 5.9 Hoehn-Yahr: NR	Usual care (continue with daily routine)
Benka–Wallén, M et al[53] Setting: Karolinska University Hospital, Stockholm (Sweden) Funding: Swedish research council, the Swedish Research Council for Health, Working Life and Welfare, "Vardalstiftelsen," and the Swedish Parkinson Foundation.	100	n: 51 Age (years): 73.1 ± 5.8 Gender: 19F:32M Years since diagnosis: 5.9 ± 5.1 Hoehn-Yahr: II–III	Protocol: Balance, cognitive task, motor task and gait exercises. Frequency: 10 weeks, 3 times per week, 60 min per session	n: 49 Age (years): 73 ± 5.5 Gender: 24F:25M Years since diagnosis: 5.6 ± 4.8 Hoehn-Yahr: II–III	Usual care
Conradsson et al[61] Setting: Karolinska University Hospital and neurological clinic, Stockholm (Sweden) Funding: Swedish Research Council, the Swedish Parkinson Foundation, the Karolinska Institutet, among others.		n: 47 Age (years): 72.9 ± 6 Gender: 19F:28M Years since diagnosis: 6 ± 5.1 Hoehn-Yahr: II–III	Protocol: Balance exercises combined with cognitive and/ or motor tasks Frequency: 10 weeks, 3 times per week, and 1 h per session	n: 44 Age (years): 73.6 ± 5.3 Gender: 22F:23 M Years since diagnosis: 5.6 ± 5 Hoehn-Yahr: II–III	Usual care
de Bruin et al[62] Setting: University of Lethbridge and Dalhousie University (Canada) Funding: The Canadian Institutes of Health Research.	22	n: 11 Age (years): 64.1 ± 4.2 Gender: 5F:6M Years since diagnosis: 6.4 ± 4.2 Hoehn-Yahr: II–III	Protocol: Music and cognitive task while walking Frequency: 13 weeks, 3 times per week, and 30 min per session	n: 11 Age (years): 67 ± 8.1 Gender: 6F:5M Years since diagnosis: 4.5 ± 3.3 Hoehn-Yahr: II–III	Usual care
Do Nascimento-Silva, R et al[63] Setting: Universidade Federal do Triangulo Mineiro (Brazil) Funding: NR	10	n: 5 Age (years): 64 ± 11.9 Gender: NR Years since diagnosis: 4.8 ± 1.9 Hoehn-Yahr: II–III	Protocol: Walk counting numbers, stepping on geometric shapes and paying attention to different verbal actions Frequency: 8 weeks, 2 times per week, and 1 h per session	n: 5 Age (years): 63 ± 12.7 Gender: NR Years since diagnosis: 3.4 ± 2.9 Hoehn-Yahr: II–III	Stretching and mobilization

(Continues)

TABLE 1 Continued

Study	N	DTT intervention		Control intervention	
		DTT group	DTT protocol and frequency	Control group	Control intervention
Duncan and Earhart[64] Setting: Washington University Movement Disorders Center, St Louis (United States) Funding: Parkinson's Disease Foundation, the Greater St Louis Chapter of the APDA and the APDA Center for Advanced PD Research at Washington University.	52	n: 26 Age (years): 69.3 ± 1.9 Gender: 11F:15M Years since diagnosis: 5.8 ± 1.1 Hoehn–Yahr: I–V	Protocol: Community-based tango programme involved walking while naming words Frequency: 48 weeks, 2 times per week, 1 h per session	n: 26 Age (years): 69 ± 1.5 Gender: NR Years since diagnosis: 7 ± 1 Hoehn–Yahr: I–V	Usual care
Fernandes et al[65] Setting: The Portuguese Association of Parkinson's Patients, Porto (Portugal) Funding: Instituto Politecnico do Porto and Escola Superior de Tecnologia daSaúde (Portugal)	15	n: 7 Age (years): 63.4 ± 9.5 Gender: 2F:5M Years since diagnosis: 8.8 ± 4.3 Hoehn–Yahr: III	Protocol: Motor task and cognitive task Frequency: 6 weeks, 2 times per week, 1 h per session	n: 8 Age (years): 62.3 ±12.9 Gender: 2F:6M Years since diagnosis: 7.7 ± 7.5 Hoehn–Yahr: III	Motor training program
Geroin et al[66] Setting: The University Hospitals Leuven (Belgium) and the Radboud University Medical Center Nijmegen (Netherlands) Funding: The Jacques and Gloria Gossweiler Foundation and the Malou Malou funds of the King Baudouin Foundation	121	n: 56 Age (years): 65.8 ±9.2 Gender: 17F:39M Years since diagnosis: 8.41 ± 5.29 Hoehn–Yahr: II–III	Protocol: Performed the same cognitive tasks and gait exercises simultaneously Frequency: 6 weeks, 2 times per week, 40 min per session	n: 65 Age (years): 66.1 ± 9.3 Gender: 16F:49M Years since diagnosis: 8.9 ± 6.3 Hoehn–Yahr: II–III	Exercises and cognitive tasks independently
Pereira-Pedro et al[67] Setting: Laboratory of HealthyFit, University of Vigo (Spain) Funding: No	14	n: 8 Age (years): 70.5 ±9.3 Gender: 2F:6M Years since diagnosis: NR Hoehn–Yahr: II–III	Protocol: Cycling with a cognitive task Frequency: 7 weeks, 2 times per week, 20 min per session	n: 6 Age (years): 65.4 ± 5.2 Gender: 1F:6M Years since diagnosis: NR Hoehn–Yahr: II–III	Only cycling exercise

(Continues)

TABLE 1 *Continued*

Study	N	DTT intervention		Control intervention	
		DTT group	DTT protocol and frequency	Control group	Control intervention
Rosenfeldt et al[68] Setting: Center for Neurological Restoration at the Cleveland Clinic (United States) Funding: The Davis Phinney Foundation and the Edward and Barbara Bell Endowed Chair	20	n: 10 Age (years): 59 ± 9 Gender: 59 ± 9M Years since diagnosis: 8 ± 4.1 Hoehn–Yahr: II–IV	Protocol: Simultaneous gait and cognitive task Frequency: 8 weeks, 3 times per week, 45 min per session	n: 10 Age (years): 65 ± 8 Gender: 1F:9M Years since diagnosis: 4 ± 3.6 Hoehn–Yahr: II–IV	Only motor training
San Martín-Valenzuela et al[54] Setting: Neurology Service of a Public Hospital and Medicine Department of University of Valencia (Spain) Funding: NR	40	n: 23 Age (years): 66.4 ± 7.1 Gender: 12F:11M Years since diagnosis: 6.3 ± 6 Hoehn–Yahr: I–III	Protocol: Walking while do cognitive and motor tasks Frequency: 10 weeks, 2 times per week, 1 h per session	n: 17 Age (years): 64.8 ± 8.7 Gender: 5F:12M Years since diagnosis: 5.3 ± 3.8 Hoehn–Yahr: I–III	Only gait training
Strouwen et al[55] Setting: The University Hospitals Leuven (Belgium) and the Radboud University Medical Center Nijmegen (Netherlands) Funding: The Jacques and Gloria Gossweiler Foundation and the Malou Malou funds of the King Baudouin Foundation	121	n: 56 Age (years): 65.8 ± 9.2 Gender: 17F:39M Years since diagnosis: 8.4 ± 5.3 Hoehn–Yahr: II–III	Protocol: Gait and cognitive tasks were trained simultaneously Frequency: 6 weeks, 2 times per week, 40 min per session	n: 65 Age (years): 66.1 ± 9.3 Gender: 16F:49M Years since diagnosis: 8.9 ± 6.3 Hoehn–Yahr: II–III	Gait and cognitive tasks were trained separately
Tedla et al[56] Setting: Physical Therapy clinic (Saudi Arabia) Funding: NR	30	n: 15 Age (years): 67.7 Gender: 4F:11M Years since diagnosis: NR Hoehn–Yahr: II	Protocol: Walked concurrent with holding a tray in hand Frequency: 4 weeks, 3 times per week, 1 h per session	n: 15 Age (years): 66.7 Gender: 4F:11M Years since diagnosis: NR Hoehn–Yahr: II	Cognitive training

(Continues)

TABLE 1 *Continued*

Study	N	DTT intervention			Control intervention	
		DTT group	DTT protocol and frequency		Control group	Control intervention
Vergara-Díaz et al[57] Setting: Boston medical center, neurology area, Massachusetts (United States) Funding: Osher Center for Integrative Medicine, the Davis Phinney Foundation for Parkinson's, NCCIH-funded K24, Alfonso Martín Escudero Foundation, among others	32	n: 16 Age (years): 65.7 ±3.9 Gender: 7F:9M Years since diagnosis: 2.9 ± 2.4 Hoehn–Yahr: I–II	Protocol: Combined motor with multiple cognitive components (mindfulnes, focused attention, DT and mindful breathing) Frequency: 24 weeks, 2 times per week, 60 min per session		n: 16 Age (years): 62 ± 7.8 Gender: 9F:7M Years since diagnosis: 2.9 ± 2.2 Hoehn–Yahr: I–II	Usual care
Wong–Yu et al[58] Setting: Hong Kong PD Association and a three public hospitals (China) Funding: Hong Kong Parkinson's Disease Foundation	84	n: 41 Age (years): 59.4 ± 9 Gender: 16F:25M Years since diagnosis: 7.1 ± 4.3 Hoehn–Yahr: I–V	Protocol: Performed daily task while walking Frequency: 8 weeks, 1 session per week, 60 min per session		n: 43 Age (years): 62.6 ± 8.9 Gender: 18F:21M Years since diagnosis: 5.6 ± 3.8 Hoehn–Yahr: I–V	Upper limb exercises
Yang et al[59] Setting: Medical centers in Taipei (Taiwan) Funding: Ministry of Science and Technology	18	n: 6 (EG₁), 6 (EG₂) Age (years): 65 ± 18.3 (EG₁), 69.5 ± 16.2 (EG₂) Gender: 2F:4M (EG₁), 2F:4M (EG₂) Years since diagnosis: 5.5 ± 11.9 (EG₁), 5 ± 16.7 (EG₂) Hoehn–Yahr: I–III	Protocol: EG₁: Cognitive dual tasks EG₂: Motor dual tasks Frequency: 12 weeks, 3 times per week, 30 min per session		n: 6 Age (years): 66.5 ±28.3 Gender: 2F:4M Years since diagnosis: 3 ± 13.1 Hoehn–Yahr: I–III	Usual care
Silva et al[60] Setting: Association of Parkinson's Disease Patients in the state of Paraná (Brazil) Funding: The Brazilian Coordination for the Improvement of Higher Education Personnel	25	n: 14 Age (years): 63.1 ± 13.6 Gender: 8F:6M Years since diagnosis: NR Hoehn–Yahr: I–IV	Protocol: Motor dual-task aquatic exercises Frequency: 10 weeks, 2 times per week, 60 min per session		n: 11 Age (years): 64.2 ± 13.5 Gender: 6F:5M Years since diagnosis: NR Hoehn–Yahr: I–IV	Usual care

Abbreviations: DTT, Dual task therapy; EG, Experimental group; F, Female; M, Male; N, Total sample size; Nc, Patients in control Intervention; Ne, Patients in experimental Intervention; NR, Not reported.

Walking Speed

Twelve studies[52,53,64,68,54–59,61,62] assess the effect of DTT on walking speed (outcome measured in m/s or cm/s) using devices such as *GAITRite*, *ProtoKinectis*, among others at the time of intervention,[52,53,64,68,54–59,61,62] and at 3,[54,55,68] 6,[53,58] and 12 months post-intervention.[53,58] Our findings reported statistically significant differences in favor of DTT in the post-intervention assessment (n = 12; SMD 0.42; 95% CI 0.23–0.6) and at the 3 month follow-up (n = 3; SMD 0.44; 95% CI 0.09–0.79), but not at 6 months (n = 2; SMD 0.28; 95% CI −0.1–0.6) nor 12 months (n = 2; SMD 0.14; 95% CI −0.24–0.52) (Table 2, Fig. 2). DTT increased walking speed by 0.1 m/s in the post-intervention period (n = 12; 95% CI 0.06–0.13) and by 0.09 m/s at 3 months (n = 3; 95% CI 0.02–0.15). The meta-regression showed that DTT is more effective than STT (n = 6; SMD 0.44; 95% CI 0.2–0.74)[54–58,68] and UC (n = 6; SMD 0.4; 95% CI 0.1–0.67).[52,53,59,61,62,64] The risk of publication bias was identified in the post-intervention assessment (Egger *p* 0.21 and 24% of variation after Trim-and-fill estimation). Heterogeneity was not present in statistically significant findings. The sensitivity analysis did not find statistical changes in the pooled effect that would require excluding studies.

Step Length

Four studies[52,53,61,68] reported data that assessed the post-intervention effect of DTT on step length (outcome measured in cm). Our findings did not report statistically significant differences between DTT and control interventions (n = 4; SMD 0.2; 95% CI −0.07–0.46) (Table 2, Fig. 2) without risk of publication bias and heterogeneity. The meta-regression did not show that DTT was better than UC (n = 3; SMD 0.18; 95% CI −0.1–0.45).[52,53,61] The sensitivity analysis did not report substantial variations in effect direction when studies were excluded.

Stride Length

Five studies[54,56,59,62,66] provided data that assessed the effect of DTT on stride length (outcome measured in cm) at post-intervention[54,56,59,62,66] and at the 3 month follow-up.[54,66] Our findings reported a medium-large effect of DTT (n = 5; SMD 0.69; 95% CI 0.23–1.15), on increasing stride length by 0.12 cm (n = 5; 95% CI 0.05–0.16), but this was not the case at the 3 month follow-up (n = 2; SMD 0.26; 95% CI −0.37–0.87) (Table 2, Fig. 2). The meta-regression reported that DTT is better than STT (n = 3; SMD 0.42; 95% CI 0.12–0.71)[54,56,66] and UC (n = 2; SMD 0.79; 95% CI 0.1–1.4).[59,62] Risk of publication bias was present (Egger *p* 0.07) and there was a 27% change after Trim-and-fill estimation (adjusted SMD 0.5; 95% CI 0.02–0.96). Heterogeneity was not present. The sensitivity analysis detected that when Tedla, JS (2017) was excluded, the pooled effect was lower (SMD 0.52; 95% CI 0.04–1).

Cadence

Seven studies[54,56,59,61,62,66,68] provided data that assessed the effect of DTT on cadence (outcome quantified with the number of steps per min) during the post-intervention period[54,56,59,61,62,66,68] and at the 3 month follow-up.[54,66,68] DTT was effective in the post-intervention assessment (n = 7; SMD 0.41; 95% CI 0.19–0.63), increasing cadence by three steps/min (n = 7; 95% CI 1.8–3.7), but not at the 3 month follow-up (n = 3; SMD 0.03; 95% CI −0.27–0.32) (Table 2, Fig. 3). The meta-regression specifically showed that DTT is better than UC (n = 4; SMD 0.5; 95% CI 0.2–0.69),[59,61,62] but not better than STT (n = 3; SMD 0.14; 95% CI −0.13–0.42).[54,56,66,68] Risk of publication bias was present in both assessments (details in Table 2). Heterogeneity level was moderate in post-intervention assessment (I^2 34%). The sensitivity analysis did not reveal substantial variations in any assessment.

Steps per Day

Two studies[53,61] assessed the post-intervention effect of DTT in increasing the number of steps per day, and did not find differences between DTT and UC (n = 2; SMD 0.17; 95% CI −0.14–0.48) (Table 2, Fig. 3). The number of steps per day is indicative of physical activity level, and our findings do not show that DTT can increase the level of physical activity. Heterogeneity was not present and sensitivity analysis did not show variations in the pooled effect.

Functional Balance

Five studies[53,58,60,61,64] using the Berg Balance Scale and MiniBesTest provided data to assess the effect of DTT in the post-intervention period[53,58,60,61,64] and at 6-,[53,58] and 12-month follow-ups.[53,58] Our findings reported a large effect (n = 5; SMD 1.15; 95% CI 0.92–1.4), supporting DTT in the post-intervention period and at 6- (n = 2; SMD 0.56; 95% CI 0.23–0.88) and 12 month follow-ups (n = 2; SMD 0.43; 95% CI 0.09–0.76) (Table 2, Fig. 3). The meta-regression confirmed that the effect of DTT is greater than UC (n = 4; SMD 1.16; 95% CI 0.9–1.43).[53,60,61,64] Risk of publication (Egger *p* 0.03 and 21% of variation after Trim-and-fill estimation) and heterogeneity (I^2 38%) were present in post-intervention assessments. The sensitivity analysis did not report variations.

Dynamic Balance

The effect of DTT on dynamic balance at the time of intervention was assessed with data from six studies that used the Timed Up and Go (TUG) test.[57–60,65,67] Our findings reported a medium effect in favor of the DTT group (n = 6; SMD −0.5; 95% CI −0.81 to −0.18) (Table 2, Fig. 3). DTT reduces the time it takes to complete the TUG by 1.5 s (n = 6; 95% CI −2.27 to −0.73), thus improving dynamic
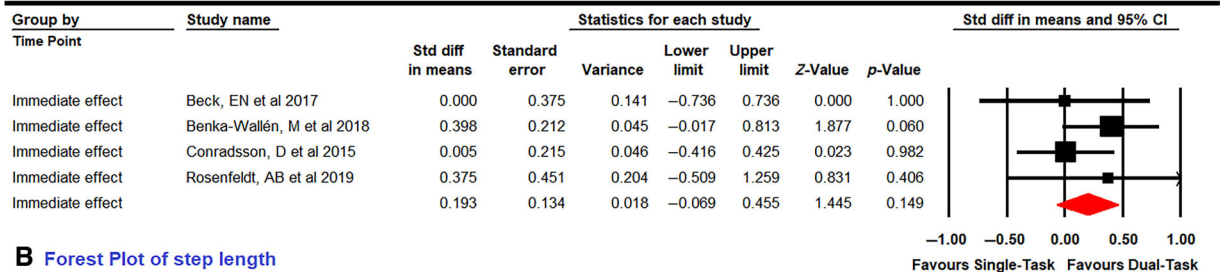
TABLE 2 *Main findings in meta-analyses*

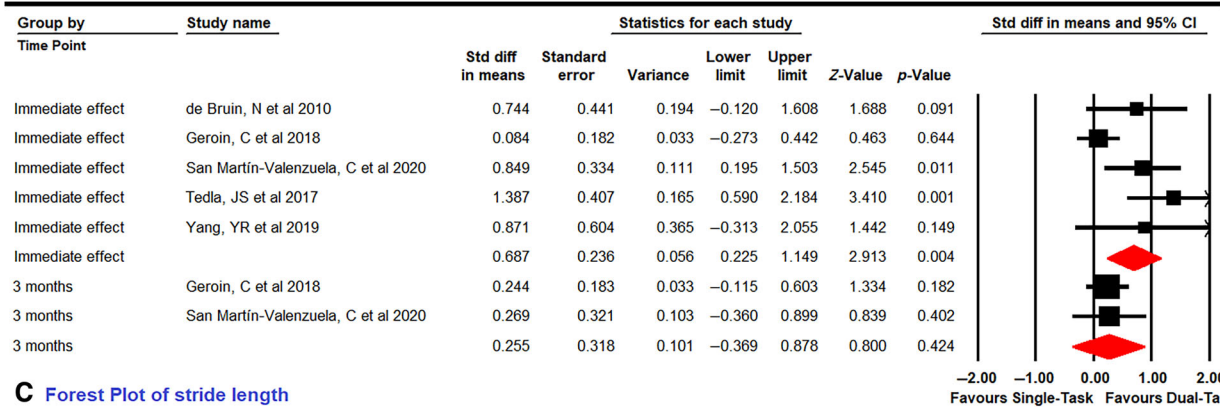| Outcomes and time-point assessment		K	N	N_s	Effect size SMD	Effect size 95% CI	P	Heterogeneity Q (df)	Heterogeneity I^2 (p)	Publication bias Funnel plot (Egger p)	Publication bias Trim and fill Adj SMD	Publication bias Trim and fill % var	Evidence (grade)
Walking speed	IE	12	660	55	0.42	0.23–0.6	<0.001	11.3 (11)	2.5% (0.42)	Asym. (0.21)	0.32	24%	Medium
	3M	3	181	60.3	0.44	0.09–0.79	0.014	0.83 (2)	0% (0.66)	Sym. (0.6)	0.44	0%	Low
	6M	2	184	92	0.28	−0.1–0.6	0.14	3.22 (1)	54.3% (0.07)	NP	NP	NP	Very low
	12M	2	184	92	0.14	−0.24–0.52	0.48	0.53 (1)	0% (0.47)	NP	NP	NP	Very low
Step length	IE	4	276	69	0.2	−0.07–0.46	0.15	2.13 (3)	0% (0.54)	Sym. (0.97)	0.2	0%	Low
Stride length	IE	5	231	46.2	0.69	0.23–1.15	0.004	3.89 (4)	0% (0.42)	Asym. (0.07)	0.5	27%	Low
	3M	2	62	33	0.26	−0.37–0.87	0.424	0.002 (1)	0% (0.96)	NP	NP	NP	Very low
Cadence	IE	7	351	50.1	0.41	0.19–0.63	<0.001	12.4 (6)	34% (0.06)	Asym. (0.3)	0.49	19%	Low
	3M	3	181	60.3	0.03	−0.27–0.32	0.85	0.31 (2)	0% (0.86)	Asym. (0.25)	0.01	77%	Very low
Step per day	IE	2	200	100	0.17	−0.14–0.48	0.281	0.45 (1)	0% (0.5)	NP	NP	NP	Very low
Functional balance	IE	5	371	74.2	1.15	0.92–1.4	<0.001	7.7 (4)	37.7% (0.1)	Asym. (0.03)	0.91	21%	Low
	6M	2	184	92	0.56	0.23–0.88	0.001	2.67 (1)	44% (0.1)	NP	NP	NP	Very low
	12M	2	184	92	0.43	0.09–0.76	0.012	1.79 (1)	44% (0.18)	NP	NP	NP	Very low
Dynamic balance	IE	7	211	30.1	−0.5	−0.81 to −0.18	0.002	6.14 (6)	2.32% (0.41)	Sym. (0.36)	−0.5	0%	Medium
Motor disorders	IE	6	170	28.3	−0.86	−1.25 to −0.47	<0.001	7.9 (5)	36% (0.16)	Asym. (0.08)	−1.39	41%	Low
Limitations in ADL	IE	3	210	70	−0.15	−0.43–0.14	0.31	0.13 (2)	0% (0.93)	Asym (0.21)	−0.16	9%	Very low
Quality of life	IE	3	86	28.6	−0.33	−0.78–0.13	0.157	1.75 (2)	0% (0.42)	Asym. (0.09)	−0.61	100%	Very low

Abbreviations: Adj, Adjusted; Asyn, Asymmetric; df, Degree of freedom; I^2, Degree of inconsistency; IE, Immediate effect; Incons, Inconsistency; Indirect, Indirectness; Imprec, Imprecision; K, Number of comparisons; N, Sample size; NP, Not possible to calculate; Ns, Number of participants per meta-analysis; P, P-value; Pub. Bias; Publication bias; Q, Q-test; SMD, Standardized Mean Difference; Sym, Symmetric; % var, Percentage of variation; 95% CI, 95% confidence interval; 3M, 3 months; 6M, 6 months; 12M, 12 months.
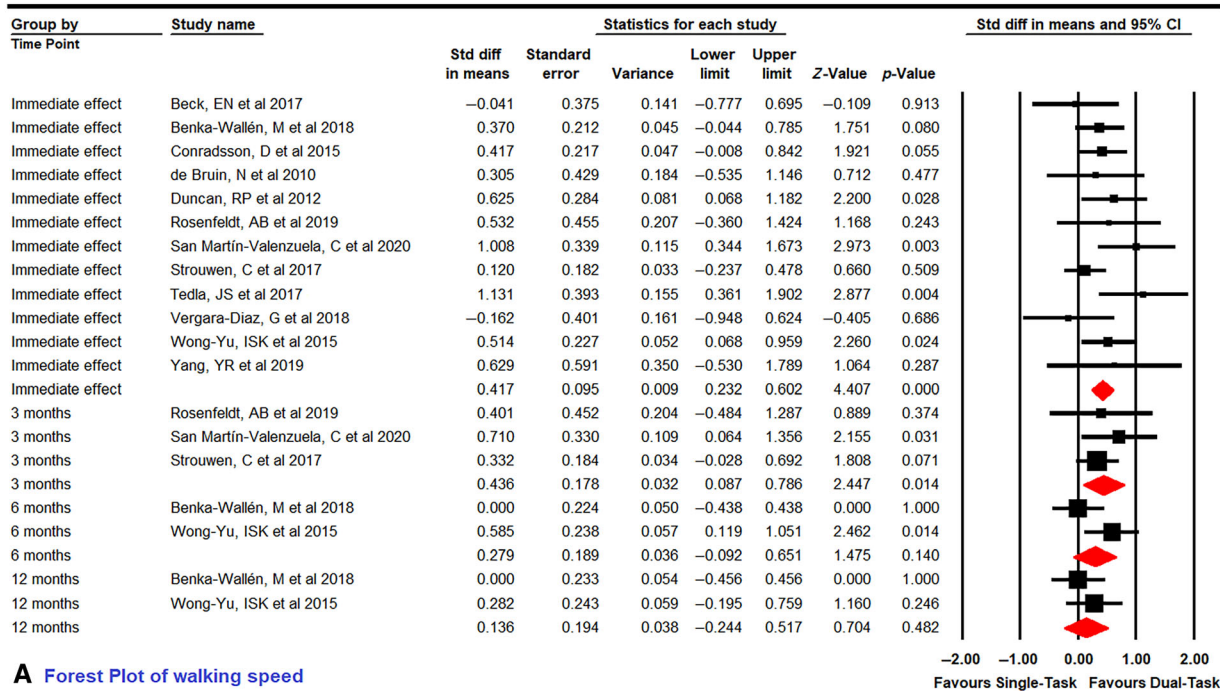
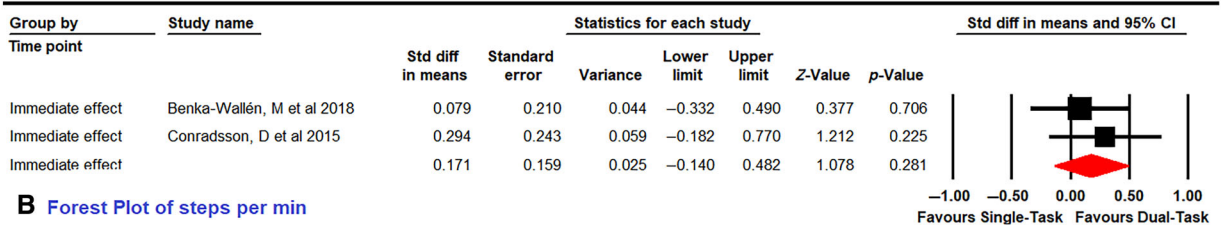**Figure 2.** Forest plot of walking speed (A), step length (B) and stride length (C).

balance. The meta-regression confirmed that DTT is better than STT (n = 4; SMD −0.52; 95% CI −0.86 to −0.15)[57,58,65,67] and UC (n = 2; SMD −0.51; 95% CI −1.1 to −0.04).[59,60] Our findings do not present risk of publication bias and heterogeneity. The pooled effect did not exceed 11% after a sensitivity analysis.
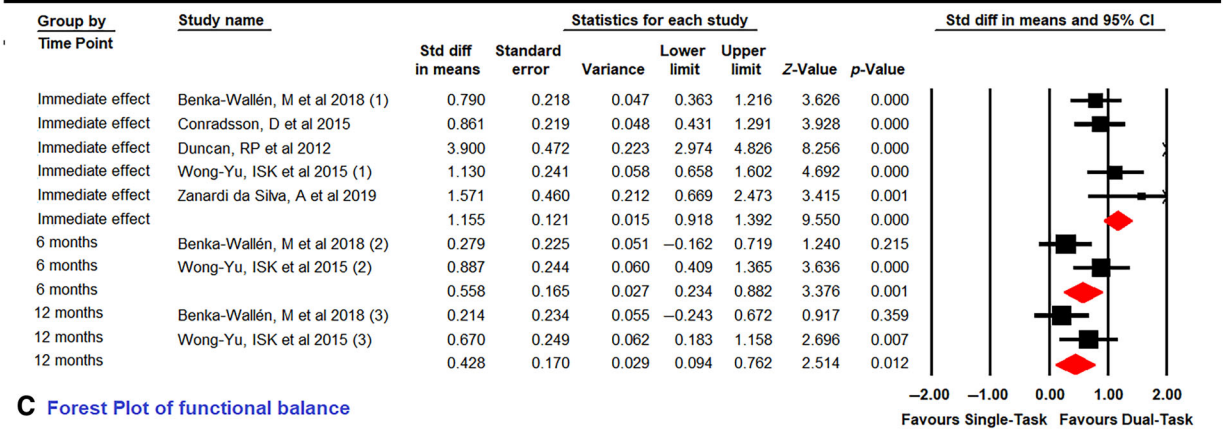
Motor Impairments

Six studies[57,62,64,65,67,68] assessed the immediate effect of DTT on motor impairments using the Unified Parkinson's Disease Rating Scale [UPDRS–motor score (part III)]. Our findings revealed a large effect of DTT (n = 6; SMD −0.86; 95% CI −1.25
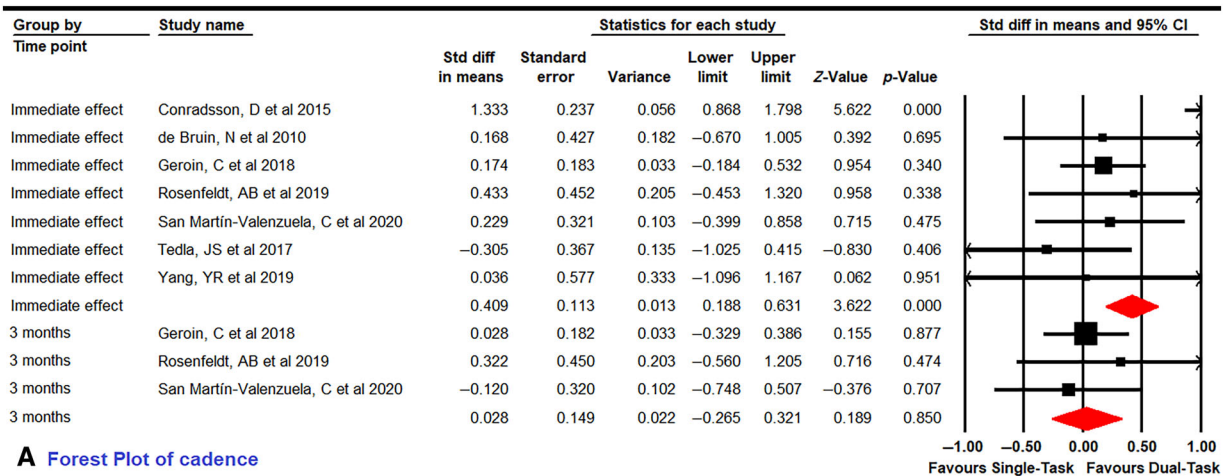
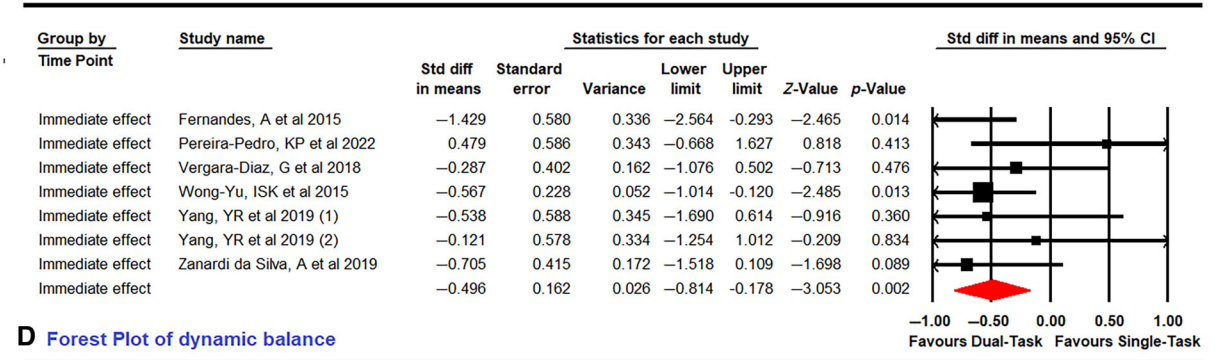**Figure 3.** Forest plot of cadence (A), steps per min (B), functional balance (C) and dynamic balance (D).

to −0.47) (Table 2, Fig. S1), as the UPDRS motor score was reduced by 11 points (n = 6; MD −11.1; 95% CI −12.21 to −10.1). In this meta-analysis, the meta-regression showed that DTT is better than UC (n = 2; SMD −1.9; 95% CI −2.62 to −1.21),[62,64] but not better than STT (n = 4; SMD −0.39; 95% CI −0.86–0.09).[57,65,67,68] Risk of publication bias must be taken into account given that there was a 41% change after Trim-and-fill estimation (adjusted SMD −1.39; 95% CI −1.72 to −1.05). Heterogeneity was low (I^2 36%), and the sensitivity analysis identified change in the pooled effect when Duncan (2012) was excluded.

Activities of Daily Living

Three studies[53,61,63] provided data using the Kat'z Index and UPDRS-ADL dimension score to assess the immediate effect of DTT on limitations in ADL, reporting no statistically significant differences between groups (n = 3; SMD −0.15; 95% CI −0.43–0.14) (Table 2, Fig. S1). The meta-regression confirmed that there were no differences between specific comparisons. Risk of publication bias and heterogeneity bias were not present. The sensitivity analysis did not reveal substantial variations in the effect size.

Quality of Life

Three studies[54,57,67] with three independent comparisons provided data using the PD questionnaire (PDQ-39) related to QoL to analyze the immediate effect of DTT on QoL in comparison to STT. It did not reveal any statistically significant differences (n = 3; SMD −0.33; 95% CI −0.78–0.13) (Table 2, Fig. S1). Risk of publication bias was present (Egger p 0.09). Trim-and-fill estimation determined that without risk of publication bias (2 studies imputed), our findings would change 100%; it showed statistically significant differences between DTT and STT in favor of DTT (SMD −0.61; 95% CI −1.09 to −0.12). Heterogeneity was not present and the sensitivity analysis did not report substantial variations.

Adverse Effects Related DTT

None of the studies included in the meta-analysis reported adverse effects related to DTT (Table S3 in Supporting File 1). The only adverse effects described were linked to the common symptoms of PD; the most frequent was suffering a fall,[55,57,61,68] hence the importance of seeking effective and safe therapies to reduce its prevalence.

ADLs require the simultaneous use of motor and cognitive skills, while maintaining appropriate gait and balance.[69] DTT is a therapy that combines motor and cognitive activities as required in real life situations. It has reported greater improvements in motor and cognitive tasks than if they are performed separately.[70] Therefore, the objective of our meta-analysis was to assess the effect of DTT on gait, balance, motor skills, functional independence and impaired QoL. We have also analyzed whether the effect of DTT on each variable is maintained over time or only

has immediate repercussions. In addition, we have examined whether DTT is better than STT or UC. Thus, we carried out an exhaustive analysis of the scientific literature, obtaining a total of 17 RCTs that provided data on a total of 826 patients with PD. The main findings of our meta-analysis show that DTT is effective in improving the patient's gait, balance and motor impairments immediately after finishing therapy. In addition, the effect of DTT on some variables is maintained at 3, 6 and 12 months post-intervention. However, when observing the results obtained immediately after finishing therapy, it is clear that the effect of DTT decreases over time. Moreover, the impact of DTT seems to be greater than that of STT and UC. Finally, it can be concluded that DTT is a safe therapy, given that the studies included in the review did not report adverse effects in the patients.

With regard to gait, our meta-analysis showed that DTT is effective in improving walking speed, stride length and cadence in the post-intervention period. Our study concurs with Li et al[31] that DTT improves walking speed and cadence. However, the pooled effect on walking speed (SMD 0.42, 95% CI 0.23–0.6) and cadence (SMD 0.41, 95%CI 0.19–0.63) was higher in our meta-analysis. These findings are not in line with Radder et al's[25] results that demonstrate little evidence, given that only two studies or fewer per variable were included. Compared to other reviews, the level of evidence and robustness of our findings is high, as our meta-analyses included a greater number of studies and patients. In contrast to the reviews of Li et al[31] and Radder et al,[25] our results suggest that DTT is more effective than simple task interventions in improving stride length in these patients; an increase of 12 cm in stride length and of three steps/minute in cadence allowed patients to increase their walking speed by 0.1 m/s, thus completing the same distance in less time. One strength of our study is that DTT improves walking speed (0.1 m/s) beyond what is considered the MCID for this outcome (0.06 m/s reported by Hass et al),[71] thus increasing the clinical impact of our findings. Finally, our findings revealed that the improvements of walking speed are maintained at 3 months post-intervention, but not at 6 or 12 months. However, these findings must be considered carefully given that there were few studies that provided data for this assessment.

Our meta-analysis showed that in post-intervention assessments, DTT is more effective than STT in improving functional and dynamic balance. The effect of DTT on functional balance shown in our meta-analysis was twice the size of (SMD 1.15, 95%CI 0.92–1.4) the effect found by Li et al.[31] Therefore, our findings could be considered more robust, taking into account that two more studies were included. It should also be noted that our study demonstrates that the effect of DTT on functional balance is maintained at 6 and 12 months post-intervention, although the effect decreases with time (SMD 0.56, 95% CI 0.23–0.88; and SMD 0.43, 95% CI 0.09–0.76; respectively). Furthermore, DTT may be considered a more effective clinical therapy than others in improving functional balance over time. Dynamic balance has not been assessed in previous reviews with more than one study,[25] so our study is the first meta-analysis that provides results that support DTT, drawing on data from six

studies. In addition, patients with PD who undergo DTT complete the TUG 1.5 s quicker than those receiving STT or UC. However, we cannot compare this finding with the MCID for TUG in PD because this measure is unknown to date. In addition, the effect of DTT overtime could not be assessed due to studies included did not provide data to perform it.

Our findings showed a large effect (SMD −0.86, 95% CI −1.25 to −0.47) in terms of the positive impact of DTT in reducing motor impairments in PD patients. These results are in line with Li et al.[31] By including more studies in our assessment, we have increased the level of evidence, generalization and precision of our findings. However, our meta-analysis did not show differences between DTT and STT or UC on ADLs and QoL, concurring with the findings of Radder et al.[25] With regard to ADLs, the qualitative synthesis of the three studies included questions the effect of DTT, given that two studies showed that DTT was more effective,[53,61] yet the other study showed the opposite.[63] In terms of QoL, a similar example was reported in the qualitative synthesis, as two studies reported that STT was better,[54,67] and one study showed the opposite.[57] Only, occupational therapy has showed to be effective in improving QoL in PD patients,[72] so it would therefore be interesting to assess the effect of occupational therapy under DTT conditions on improvements in the QoL and ADLs of these patients. Therefore, more studies that assess QoL and ADLs should be carried out by physiotherapists to be included in future meta-analyses.

For correct locomotion, movement is designed and executed in the motor cortical regions and refined by the action of the basal ganglia.[73] Patients suffer from a dopaminergic loss in the basal ganglia that produces motor alterations affecting locomotion and balance.[74] A previous study has shown that DTT in PD patients with gait and postural difficulties improves postural instability and the development of dual-task activities due to a better use of brain motor and cognitive networks, which is confirmed with functional magnetic resonance.[75] For this reason, it is essential that these patients undergo therapies that require simultaneous motor and cognitive activities, as this leads to greater activation of brain areas related to movement compared to other simple or passive therapies that focus more on the peripheral anatomical structure where the symptoms are perceived. The results derived from this review highlight DTT as the physiotherapy method of choice for PD patients in order to rehabilitate balance, gait and motor function. In addition, when possible, it would be convenient to complement or combine pharmacological treatments with this type of therapy, thus avoiding the adverse effects of these drugs on gait and balance.

In terms of clinical practice, we suggest that DTT is an effective and safe therapy for PD patients. One of the main strengths of DTT is that it allows patients to train gait while performing other cognitive tasks; this is highly transferrable to real life situations as we usually carry out a complementary motor or cognitive task while walking and needing to maintain balance. However, some limitations should be taken into account. First, it is important to note that the majority of the studies included patients in ON medication state, so the effect of DTT could be overestimated. Only Vergara-Diaz reported that DTT would be effective in improving dynamic balance, QoL, motor impairments and gait speed without interference of dopaminergic therapy. Second, very few of the studies focused on variables such as step and stride length, steps per day, ADLs or QoL, thus reducing the robustness of these findings; however, this could change with new research. When only one comparison provided data for perform a meta-analysis, such as for example DTT versus UC for QoL, meta-analysis could not be performed, and this limitation is important to take into account. Third, the risk of performance and detection bias could underestimate or overestimate our findings. Nevertheless, it is not possible to blind participants and therapists. Furthermore, it was not possible to study the effect of all variables over time due to the lack of studies that have analyzed and reported data. Moreover, it is important to consider the risk of publication bias present in some meta-analyses. In addition, there was a great disparity in terms of dual task protocols in the included studies (task type and application time). Nonetheless, there was hardly any statistical heterogeneity. Lastly, it is important to remark the low level of evidence in some variables given that few studies to date have assessed these outcomes.

Conclusion

Overall, our findings show that DTT is an effective and safe therapy for improving gait, balance and motor impairments in patients with PD. DTT is more effective than STT or UC models in improving walking speed, stride length, cadence, functional balance, dynamic balance and motor impairments immediately after intervention. At 3 months post-intervention, DTT is effective in maintaining the improvements in walking speed, but not in stride length and cadence. Patients with PD who have undergone DTT continue to improve functional balance at 6 months and 1 year post-intervention. However, DTT was not better than STT in improving ADLs and QoL. No adverse effects were reported related to DTT. There is a need to carry out future studies to assess the effect of DTT on outcomes for which follow-up assessments have not been reported. The findings presented in this meta-analysis show that DTT is highly suitable for the recovery of gait, balance and motor disabilities in PD patients, since it allows motor and cognitive tasks to be combined in the same exercise, reflecting the reality of the vast majority of daily activities that require two or more tasks to be carried out simultaneously. We suggest that future studies assess the effect of DTT during OFF dopaminergic medication state.

Author Roles

(1) Research Project: A. Conception, B. Organization, C. Execution; (2) Statistical Analysis: A. Design, B. Execution, C. Review and Critique; (3) Manuscript Preparation: A. Writing of the First Draft, B. Review and Critique.

H.G.L.: 1A, 1B, 1C, 3A
M.d.A.C.P.: 1C, 2C, 3B
A.M.C.S.: 1C, 2B, 3B
I.C.L.P.: 1C, 2B, 3B
E.O.G.: 1A, 1C, 2A, 2B, 3A
I.C.P.: 1A, 1B, 1C, 2A, 2B, 2C, 3A, 3B

Disclosures

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Supporting Information

Supporting information may be found in the online version of this article.

Data S1. Supporting File 1. Supplementary Tables.

Table S1. Search strategy in databases.

Table S2. PEDro scores for each study included.

Table S3. Adverse effects related DTT reported by the studies included.

Data S2. Supporting File 2. Supplementary Figures.

Figure S1. Forest plot of motor disability (A), activities of daily living (B) and quality of life (C).

Figure S2. Funnel plot walking speed immediate.

Figure S3. Funnel plot walking speed 3 months.

Figure S4. Funnel plot step length immediate

Figure S5. Funnel plot stride length immediate.

Figure S6. Funnel plot cadence immediate.

Figure S7. Funnel plot cadence 3 months.

Figure S8. Funnel plot functional balance immediate.

Figure S9. Funnel plot dynamic balance immediate.

Figure S10. Funnel plot motor disorders immediate.

Figure S11. Funnel plot activities of daily living immediate.

Figure S12. Funnel plot quality of life immediate.