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Systematic review

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

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Abstract

Background Task-specific training is an effective form of rehabilitation for improving mobility in neurological conditions. However, it remains unclear if task-specific training is effective in people with progressive disease.

Objective To establish the efficacy of task-specific training on the mobility of individuals with progressive neurological conditions.

Data sources Electronic databases MEDLINE, EMBASE, CINAHL and Cochrane Database of Systematic Reviews.

Study eligibility criteria Randomised controlled trials investigating the effect of task-specific training on mobility and falls rate in individuals with progressive neurological conditions.

Study appraisal/synthesis methods Risk of bias of individual studies was assessed using the Physiotherapy Evidence Database (PEDro) Scale. Mean differences (MD) and 95% confidence intervals were calculated and combined in meta-analysis.

Results Analysis of 16 trials found treadmill training improved comfortable walking velocity (m/second) in people with Parkinson's disease (MD 0.21 m/second, 95%CI 0.15 to 0.27) and multiple sclerosis (MD 0.36 m/second, 95%CI 0.20 to 0.52). Treadmill training improved stride length (m) (MD 0.12 m, 95%CI 0.02 to 0.23) and step length (m) (MD 0.12 m, 95%CI 0.01 to 0.23) in people with Parkinson's disease and walking endurance in people with multiple sclerosis (MD 26.53 m, 95%CI 12.23 to 40.84). Treadmill training had no effect on cadence and did not improve walking endurance in Parkinson's disease. Over-ground walking did not improve mobility in Parkinson's disease or multiple sclerosis.

Limitations Study sample sizes were small and findings must be interpreted with caution.

Conclusion Treadmill training may be effective for improving mobility in people with Parkinson's disease and multiple sclerosis. The effectiveness of over-ground walking is uncertain.

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Keywords: Physical therapy; Progressive neurological conditions; Multiple sclerosis; Parkinson's disease; Treadmill

Introduction

Progressive neurological conditions are a group of complex diseases characterised by the degeneration of neural cells [1]. Over time this progressive degeneration causes significant physical impairment limiting mobility and physical

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activity. These limitations can lead to loss of independence or a traumatic event (e.g. fall) that requires hospitalisation and rehabilitation to regain functional independence. Therefore, effective interventions that enhance or restore functional independence are required to ensure people with progressive neurological conditions can reside safely in the community.

Task-specific training describes therapeutic interventions that involve the repetitive practice of task-orientated motor tasks with the incorporation of feedback [2]. Task-orientated training can be further defined as 'context specific' and 'non-context specific' [2]. Over-ground walking is considered context specific as participants are required to negotiate environmental features specific to daily activity [3]. In contrast, treadmill training may be considered non-context specific as locomotion on a motorised treadmill has different biomechanical requirements [4]. Task-specific training improves mobility and the performance of activities of daily living in people with stroke [5]. In contrast to progressive neurological conditions, stroke is a single event which is followed by a period where the brain is actively creating new neural pathways to compensate for the damage caused during the event [2]. It is during this process when the brain is actively creating new neural pathways that task-specific training is thought to be most effective at enhancing functional ability. Despite differences in aetiology, it is hypothesised that neuroplasticity is possible in people with progressive neurological conditions [6] and task-specific training may provide similar benefits in this population.

The effects of task-specific training for people with progressive neurological disorders are uncertain. Mehrholz *et al.* [7] reported that treadmill training improves gait hypokinesia, walking speed, distance and stride length in people with Parkinson's disease [7]. However, this systematic review [7] included studies that incorporated treadmill training with adjunct interventions and control groups which also received interventions, making it difficult to attribute positive findings to treadmill training alone. Another review [8] stated that exercise should address the underlying impairments that affect mobility in Parkinson's disease and should address several of these impairments simultaneously. However, this review did not specifically investigate the effects of task-specific training. For people with multiple sclerosis, Snook *et al.* [9] found that exercise training significantly improved walking mobility [9]. However, this review did not distinguish task-specific therapy from interventions such as stretching and resistance training. These findings suggest interventions with elements of task-specific training can benefit people with progressive neurological conditions. However, due to the variability of interventions and absence of a clear control group it is difficult to provide succinct clinical recommendations on the benefit of task-specific training. Moreover, it remains unknown whether people with differing progressive neurological conditions can benefit and which types of task-specific training are effective.

Therefore, the aim of this systematic review was to establish the effectiveness of task-specific training in improving mobility and reducing rate of falls in individuals with progressive neurological conditions.

Methods

Search sources and searches

A comprehensive search strategy was applied to online databases MEDLINE, EMBASE, CINAHL and Cochrane Database of Systematic Reviews, from the earliest available time until 20th December 2017. The search strategy used synonyms and MeSH subject headings of the following key terms: progressive neurological conditions and task-specific training, combined with Boolean operators OR within each concept and the operator AND between concepts (Appendix A and B in supplementary material). The search was supplemented by citation tracking using Google Scholar and hand searching reference lists of included studies.

Study selection

Two reviewers independently screened title and abstract of each article using pre determined inclusion/exclusion criteria (Appendix A in supplementary material). Studies were eligible if: (1) participants were adults diagnosed with a progressive neurological condition and primary physical impairments; (2) the intervention was task-specific training; and (3) the control group received no physiotherapy intervention or newly prescribed exercise program. For example, participants in the control group were able to continue their usual physical activity permitting no new exercise was introduced. The decision to have a non-active control group was made to provide clean comparisons on intervention effects [2]. We focussed on motor tasks specifically related to mobility, including spatial-temporal measures of gait, walking endurance, functional tasks such as transfers, and locomotion scales. Locomotion scales were defined as outcome measures assessing gait by measuring a combination of walking velocity, distance, level of independence, analysing the ability to negotiate different terrains and/or perform everyday walking tasks [10].

Studies that included interventions that incorporated repetitive training of functional tasks including transfers, ambulation and stair negotiation were eligible for inclusion. Interventions not based on functional motor tasks were identified as 'non-task-specific' and were excluded, including progressive resistance training, stretching and bicycle riding. Interventions were also required to provide the participant with feedback on their performance for a minimum of one session. Interventions incorporating visual cueing or supervision by a therapist were assumed to have provided feedback unless specified otherwise. Studies were ineligible for review if participants had a progressive neurological condition where the primary deficit was cognitive impairment (e.g. Alzheimer's disease). Task-specific train-

ing combined with non-task-specific training (e.g. resistance or balance training without a task-specific component) was also excluded, unless it was specified as the warm up only and not the primary intervention (Appendix A2 in Supplementary material).

Full texts of potentially eligible studies were retrieved and independently assessed for eligibility by two reviewers (AR, DS), with discussion ensuing to reach a consensus. Agreement between the two reviewers was calculated using the Kappa (κ) statistic [11]. Where consensus could not be met, a third reviewer was consulted (AD).

Data extraction and quality assessment

A pre designed form was used to extract data on participants, interventions, outcome measures and post intervention results. Where there was insufficient data presented contact with the authors was made for clarification.

Quality assessment of the studies that met the inclusion criteria were assessed independently by two reviewers (AR, AD) using the validated Physiotherapy Evidence Database (PEDro) scale [12]. The 11 items on the PEDro Scale are rated "yes" or "no", with a maximum score of 10 achieved for internal validity. Disagreements between reviewers were resolved by discussion until a consensus was reached.

Data synthesis and analysis

Mean differences (MD) and 95% confidence intervals were calculated from immediate post intervention means and standard deviations to calculate intervention effect size. A positive MD indicated the outcome favoured the intervention.

Meta-analyses of clinically homogenous data were conducted using the inverse variance method and random effects model. Data were analysed in sub-groups of intervention and disease type. For the purpose of analysis interventions were classified as context and non-context specific interventions. Where separate outcomes were provided for left and right limbs, the results for the left limb only were analysed for consistency. Sensitivity analysis was completed to assess the influence of outliers. Statistical heterogeneity was described with the I-squared statistic (I^2). Data which were unable to be included in meta-analyses were reported in tables and descriptive format.

The clinical significance of statistically significant effect sizes was interpreted by comparing effect sizes to published minimum detectable change (MDC) and/or minimum clinically important difference (MCID) values found in Table 1 [13–16]. Results were considered clinically significant where the MD between groups exceeded the MCID value. Differences between groups were considered to be beyond measurement error where the MD exceeded the MDC.

Quality of the evidence was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach for each meta-analysis [17]. This approach requires downgrading of evidence from 'high' to 'moderate', 'moderate' to 'low' and 'low' to 'very low'. For the purpose of assessing the quality of evidence a score of six or more on the PEDro scale was considered high methodological quality and a low risk of bias [18]. Evidence is downgraded one place if: (1) the PEDro scores were <6 for the majority of trials included in the meta-analysis; (2) high levels of statistical heterogeneity between trials ($I^2 \geq 25\%$) [19]; (3) large confidence intervals [20]; and (4) evidence of publication bias as demonstrated by asymmetry of a funnel plot if ≥10 trials were included in the meta-analysis [21].

Table 1
MDC/MCID values for statistically significant outcomes.

Measure	MDC	MCID
Comfortable walking velocity (m/s)		
Parkinson's disease	0.18 m/s [16]	0.13 to 0.18 m/s [13]
Multiple sclerosis	0.26 m/s [15]	0.14 m/s [15]
2-minute walk test (m)		
Parkinson's disease	No reported MDC	No reported MCID
Multiple sclerosis	No reported MDC	No reported MCID
6-minute walk test (m)		
Parkinson's disease	82 m [16]	No reported MCID
Timed Up and Go Test (secs)		
Parkinson's disease	3.50 secs [14]	No reported MCID
Step length (m)		
Parkinson's disease	No reported MDC	No reported MCID
Stride length (m)		
Parkinson's disease	No reported MDC	No reported MCID
Tinetti POMA-Gait		
Parkinson's disease	No reported MDC	No reported MCID
Ambulation index		
Parkinson's disease	No reported MDC	No reported MCID
Human activity profile		
Parkinson's disease	No reported MDC	No reported MCID
Northwestern university disability scale		
Parkinson's disease	No reported MDC	No reported MCID

MDC = minimal detectable change, MCID = minimum clinically important difference, m/s = metres/second, m = metres, secs = seconds, POMA = Tinetti Performance Oriented Mobility Assessment.

Results

Study selection

The combined electronic database search yielded 2299 trials with an additional trial identified through citation tracking. Forty trials were retrieved for full text review following screening of title and abstract. Eighteen trials fulfilled the inclusion criteria when applied to full texts. Agreement between reviewers for screening full text articles was very good ($\kappa = 0.90$, 95%CI 0.76 to 1.0). Two articles [22,23] provided data on the same trial. Therefore, these two articles were considered one trial. One further trial was removed to improve the clarity of results [24], which led to a final yield of 16 trials (Fig. 1). Fifteen of the included trials were identified through database searching and one trial was identified from checking reference lists of included studies. No authors (n = 5 trials) responded to our request for additional data.

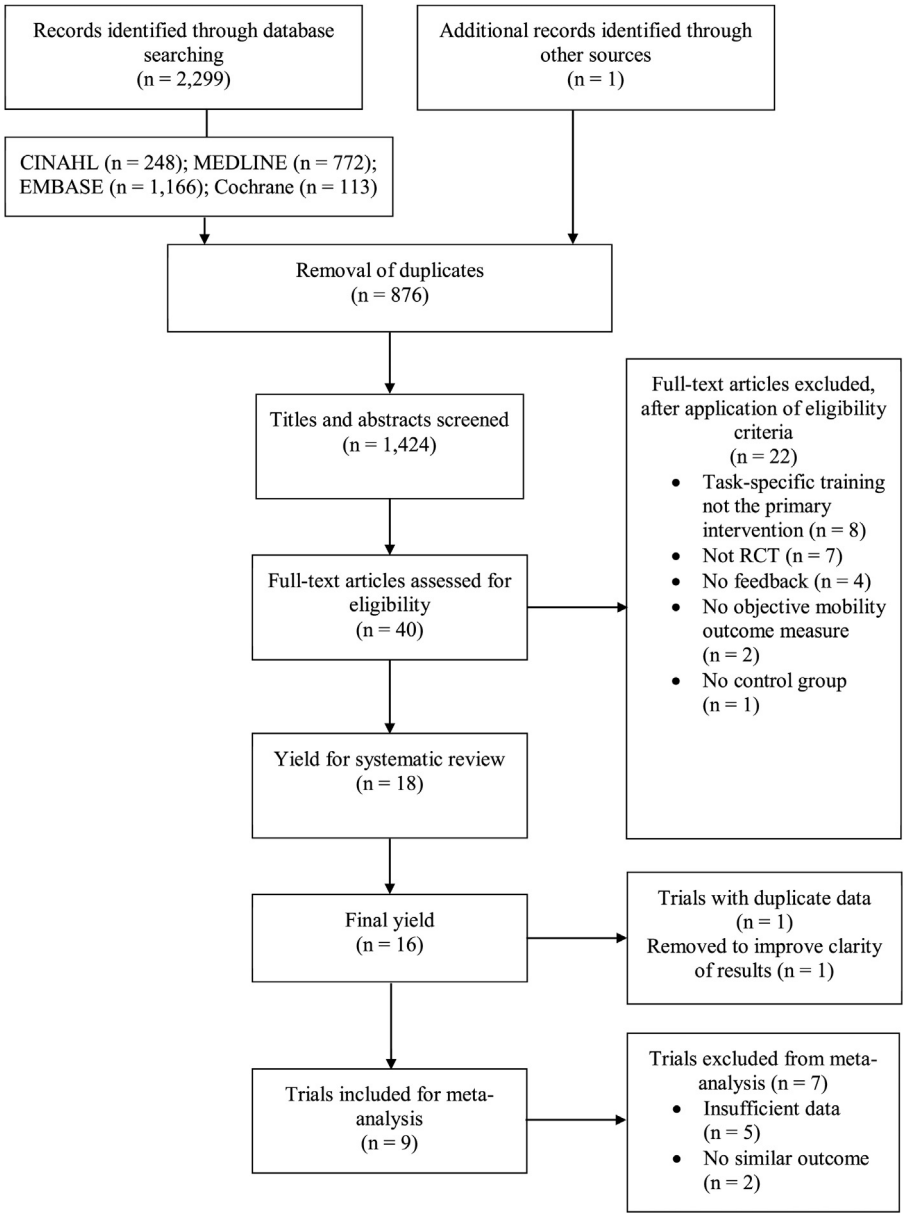

Fig. 1. Flow of studies through the review.

Study characteristics

The results of 563 participants were included. Progressive neurological conditions included Parkinson's disease (PD) (n = 11 trials) and multiple sclerosis (MS) (n = 5 trials). Disease severity for participants with Parkinson's disease was reported using the Hoehn and Yahr Scale (HY). All 11 trials included participants assessed, on average, as mild to moderate in disability (HY score 1 to 3), ranging from unilateral impairments with no altered function to being physically independent with bilateral impairments and impaired balance [25]. Disease subtypes for participants with multiple sclerosis were reported in two trials [26,27], with both trials including a combination of relapse remitting and primary progressive multiple sclerosis and one trial [27] also including secondary progressive multiple sclerosis. The other three trials [28–30] did not disclose disease subtypes. Disease severity was reported for participants with multiple sclerosis in four trials [26–29] using the Expanded Disability Status Scale (EDSS). All four trials scored an average of less than five on the EDSS, indicating participants were fully ambulatory without aid and may have some limitations of full activity [31]. The mean age of participants was 60 years and 40% were female. The average disease duration was 7.6 years (PD 7.3 years, MS 8.5 years) (Table 2).

Interventions

Seven trials [22,23,28–30,32–34] investigated treadmill training interventions, including two trials [22,23,33] util-

Table 2
Summary of included studies.

Study	PEDro Score (/10)	Health Condition	Participants	Intervention	Outcome Measures	MD (95%CI) (TST vs Control) (Positive MD favours intervention)
Ahmadi et al., 2010 [28]	4	MS- N/A, mean DD 5.3 yrs, mean EDSS 2.3	Exp (n = 10) Con (n = 10) Mean age 36.8 yrs, 100% females	Treadmill training *Intensity:* 40-75% age predicted max HR *Warm Up:* 10mins trunk and lower body stretches *Dosage:* 30mins 3days/w, for 8w *Feedback*: supervised by therapist	Spatial-temporal gait measures comfortable walking velocity (10MWT) Walking endurance distance in 2mins	 **0.37m/s (0.15 to 0.59)*†‡** **31.30m (11.90 to 50.70)***
Ahmadi et al., 2013 [29]	4	MS- N/A, mean DD 5.1 yrs, mean EDSS 2.3	Exp (n = 10) Con (n = 10) Mean age 35.2 yrs, 100% females	Treadmill training *Intensity:* 40-75% age predicted max HR *Warm Up:* 10mins trunk and lower body stretches *Dosage:* 30mins 3days/w, for 8w *Feedback*: supervised by therapist	Spatial-temporal gait measures comfortable walking velocity (10MWT) Walking endurance distance in 2mins	 **0.35m/s (0.13 to 0.57)*†‡** 20.85m (-0.33 to 42.03)
Bhatt et al., 2013 [39]	4	PD, mean DD 4.7 yrs, mean HY 2.8	Exp (n = 13) Con (n = 8) Mean age 64.4 yrs, 29% females	Sit-to-stand training Audio-visual cued sit-to-stand training with an Equitest-Balance Master *Dosage:* 20mins 3days/w, for 4w *Feedback*: visual cueing	Sit-to-stand performance[#] COM velocity	 N/A
Bridgewater et al., 1996 [35]	2	PD, mean DD 4 yrs, mean HY 2	Exp (n = 13) Con (n = 13) Mean age 66.9 yrs, 38% females	Walking aerobic group *Intensity:* 65-85% max HR *Warm Up/Cool Down:* 15mins ROM stretches and strengthening exercises *Dosage:* 30mins 2days/w, for 12w *Feedback*: supervised by physiotherapist	Locomotion scale[#] NUDS HAP- MAS HAP- AAS	 N/A N/A N/A
Canning et al., 2012 [32]	8	PD, mean DD 5.7 yrs, HY Stage 1-2	Exp (n = 10) Cont (n = 10) Mean age 61.8 yrs, 45% females	Treadmill training Semi-supervised treadmill training at home *Intensity:* 50, 60, 70% mean speed 6MWT *Warm up/cool down:* 5mins walking, sit-to-stand exercises and stretches *Dosage:* 40mins 4days/w, for 6w *Feedback*: seven sessions supervised by investigators	Spatial-temporal gait measures comfortable walking velocity (analysis technology) Walking endurance 6MWT Dual task dual task velocity	 0.16m/s (-0.09 to 0.41) 5.60m (-105.11 to 116.31) 0.12m/s (-0.17 to 0.41)
Conradsson et al., 2015 [41]	8	PD, mean DD 5.8 yrs, HY Stage 2-3	Exp (n = 51) Con (n = 49) Mean age 73.3 yrs, 41% females	Functional exercise training program Functional balance exercises, including dual task *Dosage:* 60mins 3days/w, for 10w *Feedback*: supervised by physiotherapists	Spatial-temporal gait measures comfortable walking velocity (analysis technology) step length cadence Dual task dual task velocity	 **0.11m/s (0.03 to 0.19)*** 0.05m (-3.65 to 3.75) 2.00steps/min (-0.77 to 4.77) 0.11m/s (0.00 to 0.22)
Cugusi et al., 2015 [36]	6	PD, mean DD 7 yrs, mean HY 2.3	Exp (n = 10) Con (n = 10) Mean age 67.3 yrs, 20% females	Nordic walking program Nordic Walking program *Intensity:* 60-80% maximum HR *Warm up/cool down:* practicing Nordic Walking *Dosage:* 60mins 2days/w, for 12w *Feedback*: three sessions supervised by professionals in the program	Walking endurance 6MWT Timed Up and Go Test	 **66.40m (7.80 to 125.72)*** **2.00secs (0.15 to 3.85)***
Fisher et al., 2008 [33]	6	PD, mean DD 16.2 yrs, mean HY 1.9	Exp (n = 10) Con (n = 10) Mean age 63.6 yrs, 60% females	Treadmill training with BWSTT Treadmill training with 10% BWSTT *Intensity:* 75% maximum HR *Dosage:* 45mins 3days/w, for 8w	Spatial-temporal gait measures comfortable walking velocity (analysis	 0.11m/s (-0.05 to 0.27)

Table 1 (*Continued*)

				Feedback: supervised by one physiotherapist and one aide	technology) step length stride length cadence	 0.06m (-0.02 to 0.14) 0.13m (-0.04 to 0.30) -0.24steps/min (-7.73 to 7.25)
Ganesan et al., 2014 [23]	6	PD, mean DD 5.4 yrs, HY Stage 2-2.5	Exp (A) (n = 20) Exp (B) (n = 20) Com (n = 20) Mean age 58.2 yrs, 23% females	Over-ground walking (A): Conventional walking training over-ground including, turning strategies and walking in parallel bars (B): Treadmill training with 20% BWSTT and visual biofeedback *Intensity:* self-selected fast walking speed *Warm up/cool down:* 5mins walking *Dosage:* 30mins 4days/w, for 4w *Feedback*: supervised by therapist	Locomotion scale Tinetti POMA- Gait (A) Over-ground (B) Treadmill	 **1.90units (1.01 to 2.79)*** **2.90units (2.12 to 3.68)***
Ganesan et al., 2015 [22]	6	PD, mean DD N/A, HY Stage 2-2.5	Exp (A) (n = 20) Exp (B) (n = 20) Com (n = 20) Mean age 58.2 yrs, 23% females	Over-ground walking (A): Conventional walking training over-ground including, turning strategies and walking in parallel bars (B): Treadmill training with 20% BWSTT and visual biofeedback *Intensity:* self-selected fast walking speed *Warm up/cool down:* 5mins walking *Dosage:* 30mins 4days/w, for 4w *Feedback*: supervised by therapist	Spatial-temporal gait measures comfortable walking velocity (analysis technology) (A) Over-ground (B) Treadmill step length (A) Over-ground (B) Treadmill Walking endurance distance in 2mins (A) Over-ground (B) Treadmill Locomotion scale Ambulation Index (A) Over-ground (B) Treadmill	 0.00m/s (-0.06 to 0.06) **0.23m/s (0.17 to 0.29)*†‡** 0.05m (-0.01 to 0.11) **0.17m (0.11 to 0.23)*** 0.05m (-8.33 to 8.43) **28.30m (19.55 to 37.05)*** -2.00units (-9.16 to 5.16) **6.90units (0.56 to 13.24)***
Geddes et al., 2009 [26]	3	MS- RR/ PP, mean DD N/A, mean EDSS 4.7	Exp (n = 8) Con (n = 4) Mean age 45.8 yrs, 60% females	Walking program Home based walking program *Intensity:* unspecified targeted heart rate *Warm up/cool down:* 5-15mins walking *Dosage:* 30mins 3days/w, for 12w *Feedback*: visual cueing from Polar Fitwatch Heart Rate Monitor	Walking endurance 6MWT	 -15.85m (-176.61 to 144.91)
Mak et al., 2008 [40]	6	PD, mean DD 5.9 yrs, mean HY 2.7	Exp (n = 21) Con (n = 18) Mean age 63 yrs	Sit-to-stand training Audio-visual cued sit-to-stand training with an Equitest-Balance Master *Dosage:* 20mins 3days/w, for 4w *Feedback*: visual cueing	Sit-to-stand performance[#] peak horizontal velocity	 0.02m/s (-0.02 to 0.06)
Martin et al., 2015 [38]	5	PD, mean DD 11 yrs, mean HY 2.8	Exp (n = 12) Con (n = 9) Mean age 72 yrs, 38% female	Cued Up! functional home exercise program Functional exercises completed using audio cues *Dosage:* 30-60mins *Feedback*: supervised by physiotherapist	Falls rate[#]	N/A
Protas et al., 2005 [34]	7	PD, mean 7.6 yrs, mean HY 2.8	Exp (n = 9) Con (n = 9) Mean age 72.5 yrs, 0% females	Treadmill training Multi-directional step training on a treadmill with the participants in a harness. The treadmill is turned on and off to improve balance recovery *Intensity:* self-selected walking speed *Dosage:* 60mins 3days/w, for 8w *Feedback*: supervised by	Spatial-temporal gait measures comfortable walking velocity (analysis technology) stride length cadence Falls rate[#]	 0.18m/s (-0.11 to 0.47) 0.12m (-0.01 to 0.25) -4.00steps/min (-15.23 to 7.23) N/A

Table 1 (*Continued*)

				physiotherapist		
Song et al., 2015 [37]	4	PD, mean DD 6.8 yrs, mean HY 2.8	Exp (n = 56) Con (n = 56) Mean age 65.9 yrs, 15% females	Walking program with RAS Home based walking program with RAS *Dosage:* 30mins 5days/w, for 4w *Feedback*: visual cueing from ground markers	Spatial-temporal gait measures[#] comfortable walking velocity (analysis technology) stride length cadence Walking endurance[#] 6MWT	N/A N/A N/A N/A
Straudi et al., 2014 [27]	6	MS- RR/ PP/ SP, mean DD 15.2 yrs, mean EDSS 4.9	Exp (n = 12) Con (n = 12) Mean age 52.6 yrs, 71% females	Task-orientated circuit training Circuit training including functional exercises such as step ups, obstacles and treadmill walking *Dosage:* 120mins 5days/w, for 2w *Feedback*: supervised by physiotherapist	Spatial-temporal gait measures comfortable walking velocity (10MWT) Walking endurance 6MWT Locomotion scale DGI Timed Up and Go Test	0.11m/s (-0.08 to 0.30) 34.95m (-22.83 to 92.73) 2.92units (-0.01 to 5.85) 2.18secs (-0.21 to 4.57)
Van Den Berg et al., 2006 [30]	4	MS- N/A, mean DD N/A, mean EDSS N/A	Exp (n = 10) Con (n = 9)	Treadmill training *Intensity:* 55-85% max HR *Dosage:* 30mins 3days/w, for 4w *Feedback*: supervised by therapist	Spatial-temporal gait measures[#] comfortable walking velocity (10MWT) Walking endurance[#] distance in 2mins	N/A N/A

N/A = not available, MD = mean difference, MS = multiple sclerosis, PD = Parkinson's disease, HR = Huntington's disease, DD = disease duration, EDSS = Expanded Disability Status Scale, HY = Hoehn and Yahr Scale, Exp = experimental, Con = control, yrs = years, w = weeks, 10 MWT = ten metre walk test, mins = minutes, HR = heart rate, COM = centre of mass, ROM = range of motion, NUDS = Northwestern University Disability Scale, HAP-MAS = Human Activity Profile- Maximal Activity Score, HAP-AAS = Human Activity Profile-Adjusted Activity Score, m = metre, 6 MWT = six minute walk test, RR = relapsing remitting, PP = primary progressive, SP = secondary progressive, RAS = rhythmic auditory stimulation, FAP = Functional Ambulation Performance, POMA = Tinetti Performance Oriented Mobility Assessment, BWSTT = body weight support treadmill training, x = times, km/hour = kilometres per hour, DGI = Dynamic Gait Index.

[a]=Unable to report post intervention MD due to insufficient data provided by authors.

[b]>MDC.

[c]>MCID.

[*]Significant difference between groups $p < 0.05$.

ising body weight support. Five trials [22,23,26,35–37] investigated over-ground walking programs, of which one trial [37] incorporated audio cueing and one trial [36] a Nordic walking program. One trial [38] investigated a task-specific home exercise program and two trials [39,40] investigated sit-to-stand training. The remaining two trials investigated a gym based task-specific exercise training program [41] and a circuit-training program [27] (Table 2).

All interventions were completed in the community. The duration of each session varied from 20 to 120 minutes with an average time of 42 minutes. Sessions varied from twice weekly to daily. The average program duration ran for seven weeks (range 2 to 12 weeks). The majority of control groups received no intervention, maintaining their current level of physical activity [22,23,27–30,32,34,36–41]. Two control groups received education on health issues [33,35] and one control group were asked to refrain from regular physical activity [26].

Adverse events and adherence

Nine of the 16 trials reported adverse events. Eight trials reported no adverse events [22,23,26–29,32,33,36]. One trial [41] reported 13 falls during completion of the intervention across 1,380 training sessions, resulting in an incidence rate of 0.9%. However, no group comparisons were made and falls rate was not assessed as apart of the trials outcomes [41]. Seven trials [22,23,26,32,33,35,36,41] reported participant adherence, ranging from 75 to 100% of sessions attended.

Methodological quality within studies

The mean PEDRO score was 5 ($\kappa = 0.77$, 95%CI 0.68 to 0.87), with 8 trials scoring >6. Two trials [32,41] achieved a score of 8 on the PEDro scale, which is the highest possible score due to the nature of the intervention [42].

Synthesis of results

Effect of task-specific training by disease type

Parkinson's disease – treadmill training. Meta-analysis of four studies and 96 participants provided high quality evidence that treadmill training significantly improved comfortable walking velocity (m/second) in people with Parkinson's disease (MD 0.21 m/second, 95%CI 0.15 to 0.27) (Table 3 Fig. 2). The improvement in comfortable walking velocity was greater than the MCID for people with Parkinson's disease (0.18 m/second). All four studies investigated

Table 3
Meta-analyses for task-specific training by disease type.

Outcome	No. of trials	No. of participants	MD (95% CI), I^2	Quality of evidence (GRADE)
Parkinson's disease				
Comfortable walking velocity (m/s)				
Treadmill training	4 [22,32–34]	96	**0.21 m/s [0.15, 0.27], 0%** *,a,b	High
Over-ground training	2 [22,41]	130	0.05 m/s [−0.06, 0.16], 77%	Low a,b
Comfortable step length (m)				
Treadmill training	2 [22,33]	60	**0.12 m [0.01, 0.23], 76%** *	Very Low a,b,c
Over-ground training	2 [22,41]	130	0.05 m [−0.01, 0.11], 0%	High
Comfortable stride length (m)				
Treadmill training	2 [33,34]	38	**0.12 m [0.02, 0.23], 0%** *	High
Comfortable cadence (steps/min)				
Treadmill training	2 [33,34]	38	−1.40 steps/min [−7.63, 4.83], 0%	Moderate b
Multiple sclerosis				
Comfortable walking velocity (m/s)				
Treadmill training	2 [28,29]	40	**0.36 m/s [0.20, 0.52], 0%** *,a,b	Low b,c
Walking endurance (m)				
Treadmill training (m/2 min)	2 [28,29]	40	**26.53 m [12.23, 40.84], 0%** *	Low b,c
Over-ground training (m/6 min)	2 [26,27]	36	29.14 m [−25.23, 83.51], 0%	Low b,c

GRADE = GRADE working group grades of evidence (see reasons for downgrade).
Reason for downgrade: a Statistical heterogeneity ($I^2 \geq 25\%$); b large confidence interval; c majority of trials rated lesser quality (PEDro < 6).
[a] >MDC.
[b] >MCID.
* **p < 0.05**.

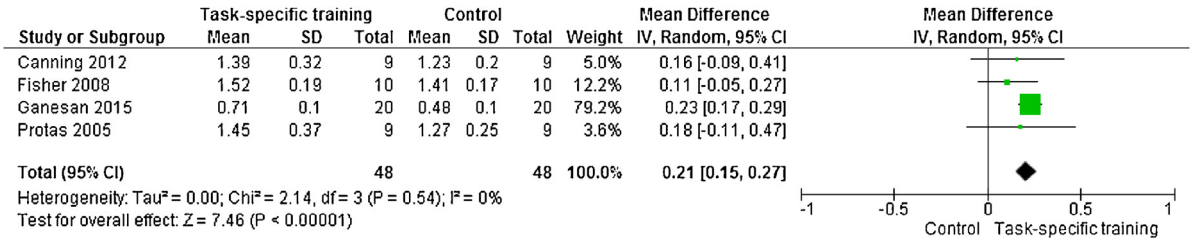

Fig. 2. The effect of non-context specific treadmill training versus control on comfortable walking velocity (m/second) in Parkinson's disease.

treadmill training of 30 to 60 minutes, three to four times per week over a four to eight week time period.

Sub-group analyses showed that body weight support treadmill training (BWSTT) had a significant effect on comfortable walking velocity (MD 0.19m/second, 95%CI 0.08 to 0.30) while treadmill training without body weight support did not have a significant effect (MD 0.17 m/second, 95%CI −0.02 to 0.30).

Meta-analysis of two studies and 38 participants provided high quality evidence that treadmill training significantly improved stride length (m) (MD 0.12m, 95%CI 0.02 to 0.23) but had no effect on cadence (Table 3 Fig. 3). Both treadmill trials were completed for 45 to 60 minutes, three times per week over an eight week time period.

Meta-analyses of two studies and 60 participants provided very low quality evidence that treadmill training significantly improved step length (m) (MD 0.12 m, 95%CI 0.01 to 0.23) in people with Parkinson's disease (Table 3 Fig. 4). These treadmill trials were completed for 30 to 45 minutes, three to four times per week, across a four to eight week time period.

Two studies investigated the effect of treadmill training on walking endurance [22,32]. One trial [22] found that treadmill training significantly improved walking distance on the 2-minute Walk Test (MD 28.3 m, 95%CI 19.55 to 37.05). While the other found that treadmill training had no effect on walking distance during a 6-minute walk test [32]. One trial [22,23] showed significant improvements in locomotion scales (Tinetti POMA-Gait [23] and Ambulation Index [22]) in people with Parkinson's disease after completing treadmill training.

No improvements were found in dual task velocity [32] or falls rate [34] following treadmill training.

Parkinson's disease – over-ground training. Meta-analyses of trials investigating the effects of over-ground walking training interventions in Parkinson's disease did not show improvements in comfortable walking velocity or step length (Table 3). However, two individual trials found improvements in locomotion scale scores following over-ground walking training compared to control. One trial [23] found significant between group improvements in the Tinetti POMA-Gait, while a second trial [35] reported significant between group improvements in the Northwestern University Disability Scale and the Human Activity Profile Maximal Activity Score and Adjusted Activity Score. There was insufficient data to conduct meta-analysis for locomotion scales.

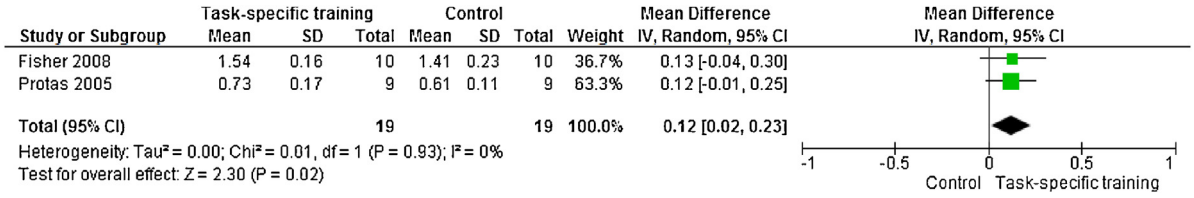

Fig. 3. The effect of non-context specific treadmill training versus control on stride length (m) in Parkinson's disease.

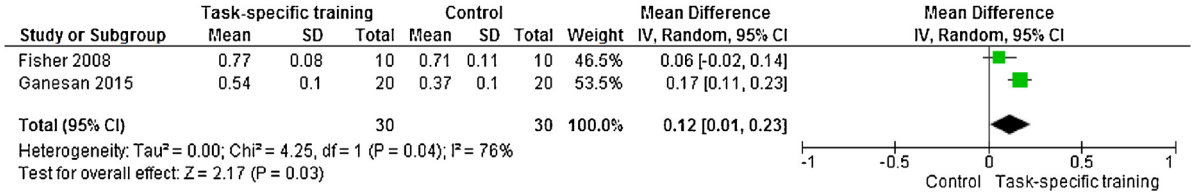

Fig. 4. The effect of non-context specific treadmill training versus control on step length (m) in Parkinson's disease.

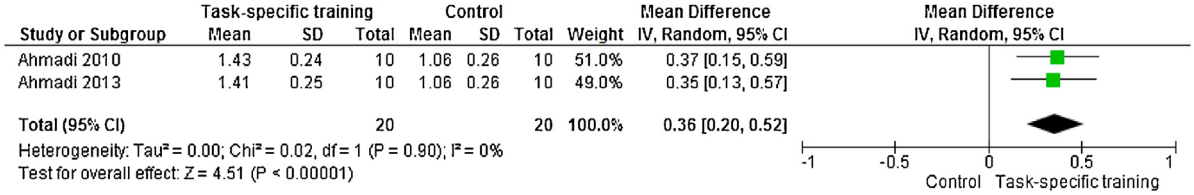

Fig. 5. The effect of non-context specific treadmill training versus control on comfortable walking velocity (m/second) in multiple sclerosis.

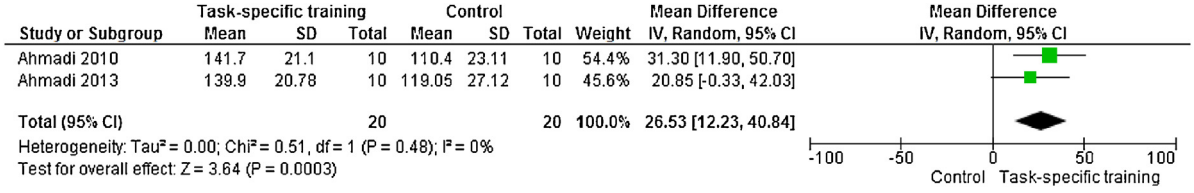

Fig. 6. The effect of non-context specific treadmill training versus control on walking endurance (m/6 minutes) in multiple sclerosis.

Two studies investigated the effect of over-ground training on walking endurance [22,36]. One study found that a Nordic walking program significantly improved walking distance on the 6-minute walk test (MD 66.40 m, 95%CI 7.80 to 125.72) [36]. This result was less than the MCD for the 6-minute walk test (82 m). The other study found no improvement in walking distance on the 2-minute walk test [22]. The study investigating a Nordic walking program also found significant improvements in the time required to complete the Timed Up and Go Test (MD 2.00 seconds, 95%CI 0.15 to 3.85) [36]. This result was less than the MDC for the Timed Up and Go Test (3.50 seconds). No improvements were found in dual task velocity [41] or falls rate [38] following over-ground training.

Parkinson's disease – sit-to-stand training. Two trials [39,40] investigated the effect of task-specific training on sit-to-stand performance. One study [40] did not show any improvements in sit-to-stand velocity while, the second trial [39] noted a significant improvement in centre of mass velocity during sit-to-stand with audio-visual cueing of people with Parkinson's disease.

Multiple sclerosis – treadmill training. Meta-analysis of two studies with 40 participants found low quality evidence that treadmill training significantly improves comfortable walking velocity (m/s) (MD 0.36 m/second, 95%CI 0.20 to 0.52) (Table 3 Fig. 5) and walking endurance (2-minute walk test) (MD 26.53m, 95%CI 12.23 to 40.84) (Table 3 Fig. 6) in people with multiple sclerosis. The improvement in comfortable walking velocity was greater than the MCID for people with multiple sclerosis (0.14 m/second). Both treadmill training trials were completed for 30 minutes, three times per week across an eight week time period.

Multiple sclerosis – over-ground training. Meta-analyses of studies investigating the effects of over-ground walking train-

ing in multiple sclerosis found no difference in walking endurance (Table 3).

No improvements were found in the locomotion scale scores (Dynamic Gait Index) [27] or Timed Up and Go Test [27] following over-ground walking training.

Discussion

This review demonstrates non-context specific task-specific training may be effective in improving mobility in individuals with Parkinson's disease and multiple sclerosis. Treadmill training significantly improved spatial-temporal measures of gait including comfortable walking velocity in participants with Parkinson's disease and multiple sclerosis. Treadmill training also improved walking endurance in people with multiple sclerosis. There was insufficient evidence to support the use of over-ground training in Parkinson's disease and multiple sclerosis.

Task-specific training may improve spatial-temporal measures of gait in people with Parkinson's disease and multiple sclerosis. These findings are consistent with the use of task-specific training for improving mobility in people with other neurological conditions including stroke [5]. It is hypothesised that task-specific training improves mobility through changes in neural circuits within the central nervous system [2]. The cortex responds to the demands of task-specific training by reorganising the injured and uninjured parts of the brain. These neuroplastic changes stimulate neural output, changing overall functional performance [2]. Neuroplastic change may explain our findings that task-specific training can improve mobility in people with Parkinson's disease and multiple sclerosis.

The results of this review show that treadmill training may be an effective form of task-specific training in people with Parkinson's disease and multiple sclerosis for improving gait. Our findings are consistent with previous findings in Parkinson's disease rehabilitation [7]. Walking on a treadmill can provide repetitive external cues which activate neuronal central pattern generators and provide gait rhythm [43]. This is important as gait patterns are often altered in people with Parkinson's disease due to reduced basal nuclei functioning [43]. It can be hypothesised that this is one of the reasons treadmill training is effective in improving spatial-temporal measures in people with Parkinson's disease.

Subgroup meta-analysis suggested BWSTT significantly improved comfortable walking velocity in contrast to treadmill training without body weight support, which was not statistically significant. Despite differences in statistical significance, the effect sizes for both treadmill conditions were similar and results are likely affected by small sample sizes. Therefore, these results must be interpreted with caution. Previous literature [44] suggests that BWSTT and treadmill training without body weight support has similar effects on mobility in people with Parkinson's disease. This may be explained by the fact that gait kinematics are similar when walking on a treadmill with up to 30% body weight support unloading compared to walking without body weight support [45]. All trials that investigated the effect of BWSTT used 10 to 20% body weight unloading. Therefore, the decision to use BWSTT should be based on clinical reasoning, taking into account the patient's functional level and any safety concerns.

In patients with multiple sclerosis, fatigue is a significant issue and treadmill training at a moderate to high intensity has been found to reduce energy expenditure and effort when walking [46]. Treadmill training also involves the prescription of a set walking pace, which enables the therapist to better set an intensity that will challenge the patient's aerobic system and can lead to improvements in cardiovascular function. These factors may explain why treadmill training is effective in improving walking endurance in people with multiple sclerosis.

The effects of treadmill training on the mobility of people with either multiple sclerosis or Parkinson's disease are limited to those who are ambulating independently with only moderate disability. On average, the sample of Parkinson's disease and multiple sclerosis participants were able to walk independently, the latter without aids. There was greater variability in the treatment parameters, making it difficult to determine the ideal prescription of treadmill training. Studies that found an effect provided treadmill training for 30 to 60 minutes treatment duration, three to four times per week, over a four to eight week period. Indicating that sessions of at least 30 minutes and multiple sessions throughout the week (repetitive practice) are important for treadmill training to be effective. Further research is required to determine the effects of treadmill training on people with more severe impairment and the ideal treatment parameters for treadmill training.

Supervision of interventions may have impacted the effectiveness of interventions. Sessions were mostly supervised by qualified therapists in the treadmill training trials, comparative to the over-ground training trials where four [26,37,39,40] were conducted without any supervision. During over-ground training walking speed is variable and difficult to measure. Thus less supervision may result in over-ground training being conducted at a lesser intensity due to more difficulty in monitoring and maintaining walking intensity. Furthermore, step length is typically longer and more stable on a treadmill compared with over-ground walking, resulting in a faster walking velocity and greater distance covered during treadmill training [43]. These factors may explain the effectiveness of treadmill training and why over-ground training did not demonstrate positive effects.

It is also possible that spatial-temporal outcome measures used in our meta-analyses were unresponsive to effects of over-ground walking training. Over-ground walking involves negotiating environmental obstacles and varied surfaces. Compared with spatial-temporal gait measures, locomotion scales analyse multi faceted physical requirements and envi-

ronmental demands of walking, and therefore, may be more appropriate when quantifying the effects of over-ground walking [10]. The locomotion scales used by studies in this review (e.g. Human Activity Profile and Tinetti POMA-Gait) each include a combination of mobility tasks, including: walking indoors; walking up inclines; walking outdoors; gait initiation; and the ability to deviate path with obstacles [23,35]. This demonstrates that locomotion scales assess individual's walking performance in a functional context, as they measure dynamic balance and require negation of environments that are confronted in every day walking. Hence, these measures reflect the context specific nature of over-ground training and future studies investigating the effectiveness of over-ground walking training should utilise these measures.

This was the first review to our knowledge that evaluated the effects of task-specific training in people with progressive neurological conditions. Compared to previous reviews we investigated the effect of a variety of forms of task-specific training (i.e. treadmill, over-ground, sit-to-stand) compared to control groups that did not receive an exercise/mobility intervention [7,9]. We also excluded studies that investigated the effects of task-specific training as an adjunct to a non-task-specific intervention (e.g. strengthening). This review included only randomised controlled trials-and the majority of these trials had low risk of bias. However, the methodological quality of studies included were limited due to inability to blind participants and therapists, introducing a risk of performance and detection bias [42]. Multiple studies also failed to complete intention to treat analysis, which further limits confidence in the findings of this review. Furthermore, due to small sample sizes of included studies care must be taken when interpreting the results of this review and further research is required before recommendations for practice can be made.

The literature search incorporated four databases and hand-searching of relevant trials however, we did not source grey literature, creating a risk of publication bias [47]. Reporting bias may have also influenced the findings of this review as data were missing without explanation from five studies included in this review and authors did not respond to data requests. Our review also comprised meta-analyses containing small numbers of studies, thus reducing the power and increasing the risk of a type two error. However, analyses with this number of studies is supported and further high quality studies are recommended to confirm these results [48]. Another limitation is the absence of established MDC and MCID values for outcome measures in people with Parkinson's disease and multiple sclerosis. The clinical significance of improvements in step length, stride length, 2-minute Walk Test, Timed Up and Go Test and the locomotion scales could not be determined due to the absence of established values. It must also be acknowledged that there was a deviation to the protocol for this systematic review. One article that investigated the effects of task-specific training on mobility of people with Huntington's disease was excluded from this study to improve the clarity of the results [24].

There is a need for further research on the effects of task-specific training on the mobility of people with progressive neurological disorders. In particular, further research is required on the less prevalent progressive neurological conditions. The predominance of findings in Parkinson's disease and multiple sclerosis limit the generalisability of our findings. Furthermore, our review encompassed studies with participants of mild to moderate disease severity, limiting our findings to this population. Further research should be directed towards establishing the effectiveness of task-specific training in the more severe stages of progressive neurological conditions. Last, this review consisted of studies that investigated the effects of community-based task-specific training on spatial-temporal walking measures. Very few studies included in this review investigated other functional tasks, such as sit-to-stand, stair climbing and outdoor walking. Further research should focus on other functional tasks and the effects of task-specific training on hospitalised persons with progressive neurological disorders.

Conclusion

Treadmill training may be an effective form of task-specific training for improving mobility in people with Parkinson's disease and multiple sclerosis. Treadmill training significantly improved spatial-temporal gait measures, including comfortable walking velocity. It is uncertain if context specific over-ground training is effective at improving walking in people with Parkinson's disease or multiple sclerosis. Further research with larger sample sizes is required before recommendations for practice can be made

Key messages

- Treadmill training may be an effective form of task-specific training for improving mobility in people with Parkinson's disease and multiple sclerosis.
- The effects of over-ground training on mobility in people with Parkinson's disease and multiple sclerosis are uncertain.
- Further research with larger sample sizes is required before recommendations for practice can be made.

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Conflicts of interest: None declared.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.physio.2018.11.007.

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