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REVIEW ARTICLE

EFFECTS OF PHYSIOTHERAPY INTERVENTIONS ON BALANCE IN MULTIPLE SCLEROSIS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

Jaana Paltamaa, PhD, PT[1,2,3], Tuulikki Sjögren, PhD, PT[3], Sinikka H. Peurala, PhD, PT[3,4] and Ari Heinonen, PhD, PT[3]

From the [1]JAMK University of Applied Sciences, School of Health and Social Studies, Jyväskylä, [2]Peurunka Medical Rehabilitation Center, Laukaa, [3]Department of Health Sciences, University of Jyväskylä, Jyväskylä and [4]Lahti Rehabilitation Centre, Lahti, Finland

Objective: **To determine the effects of physiotherapy interventions on balance in people with multiple sclerosis.**
Data sources: **A systematic literature search was conducted in Medline, Cinahl, Embase, PEDro, both electronically and by manual search up to March 2011.**
Study selection: **Randomized controlled trials of physiotherapy interventions in people with multiple sclerosis, with an outcome measure linked to the International Classification of Functioning, Disability and Health (ICF) category of "Changing and maintaining body position", were included.**
Data extraction: **The quality of studies was determined by the van Tulder criteria. Meta-analyses were performed in subgroups according to the intervention.**
Data synthesis: **After screening 233 full-text papers, 11 studies were included in a qualitative analysis and 7 in a meta-analysis. The methodological quality of the studies ranged from poor to moderate. Low evidence was found for the efficacy of specific balance exercises, physical therapy based on an individualized problem-solving approach, and resistance and aerobic exercises on improving balance among ambulatory people with multiple sclerosis.**
Conclusion: **These findings indicate small, but significant, effects of physiotherapy on balance in people with multiple sclerosis who have a mild to moderate level of disability. However, evidence for severely disabled people is lacking, and further research is needed.**

Key words: multiple sclerosis; systematic review; balance; physiotherapy; exercise training.

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Correspondence address: Jaana Paltamaa, JAMK University of Applied Sciences, School of Health and Social Studies, PL 207, FI-40101 Jyväskylä, Finland. E-mail: jaana.paltamaa@jamk.fi

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INTRODUCTION

Multiple sclerosis (MS) is a chronic progressive disease of the central nervous system (CNS) that affects a wide range of neurological functions, including cognition, vision, muscle strength and tone, coordination and sensation (1). The many symptoms associated with MS cause mobility limitations (2), e.g. gait and balance disorders in later stages of the disease (1), and sometimes even early stages of the disease in recently diagnosed people with MS who present with no clinical disability (3, 4).

The maintenance of upright stance or balance requires the interaction of multiple sensorimotor processes (visual, vestibular, proprioception) to generate coordinated movements that maintain the centre of mass within the limits of stability (5, 6). Balance is an integrated component of physical function, and a product of the task undertaken and the environment in which it is performed (7). Therefore, the components of balance training include multisensory and motor strategy training, resistance and aerobic training and several neurotherapeutic approaches in individual tailored or group therapy (6, 7). According to the World Health Organization's (WHO) International Classification of Functioning, Disability and Health (ICF), balance is operationalized as "Changing and maintaining body position" in the Mobility domain of the Activities and Participation component (2).

Abnormalities in balance and the underlying physical functions are common findings in people with MS (8–13). A recent review of postural control in MS demonstrated that people with MS have balance impairments characterized by increased sway in quiet stance, delayed responses to postural perturbations, and reduced ability to move towards their limits of stability (14). Many people with MS fall frequently (14–16), fear falling (17), and risk of fall-related injuries is increased (18, 19). Increased risk of fall has also been found in connection with various gait assessments (14) and with the use of a walking aid (20).

Many studies have examined the effects of exercise training on walking mobility in people with MS. The cumulative evidence of reviews (21, 22) and a meta-analysis (23) indicate that exercise training is associated with a small improvement in walking among individuals with MS. Although evidence-based rehabilitation techniques are of interest in the care of people with MS, there is a lack of information on the correlation of physiotherapy (PT) with balance disorders.

The aim of this systematic review was to determine the effectiveness of PT interventions on balance in people with MS. Specifically, the evidence is based on sub-meta-analyses

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according to the intervention, content of the control group therapy and quality of the randomized controlled trials (RCTs) selected for review. The ICF classification was used as a framework for classifying the interventions and their outcomes in the RCTs.

METHODS

Eligibility criteria

Studies that investigated the effect of a comprehensive combination of PT intervention were included in the review. Further eligibility criteria for inclusion in the review according to the PICOS (population, intervention, comparison, outcomes) were as follows:

- (P) subjects with MS;
- (I) a method of PT as a single discipline;
- (C) experimental vs control (placebo or no treatment) condition or 2 experimental; and
- (O) an outcome measure of balance linked to the ICF category of "Changing and maintaining body position" including both capacity and performance qualifiers.

Only RCTs published in English, Finnish, Swedish or German were included in the study.

Non-randomized and non-controlled pre-experimental studies, studies with a single session, abstracts and protocols were excluded. Studies including multiple diagnoses without separate analysis of MS and multidisciplinary rehabilitation studies without separate analysis of a single PT method were also excluded.

Search strategy

The following databases were searched from the beginning of each database to December 2008: OVID Medline, Cumulative Index to Nursing & Allied Health Literature (CINAHL) and Embase. An update search was conducted in OVID Medline and CINAHL databases for the period January 2009 to March 2011. Fig. 1 shows the combined flow chart for these searches.

Two information specialists performed the searches in the selected electronic databases in conjunction with the researchers. The search strategy was designed to include a broad range of research on PT interventions in people with MS. In addition, a supplementary manual search was conducted and, where appropriate, the authors of the relevant publications were contacted for further information.

The following key words were used: type of disease, i.e. multiple sclerosis, MS or demyelinating autoimmune diseases, CNS AND type of physiotherapy intervention AND type of study, i.e. randomized controlled trial or clinical trial. A comprehensive combination of keywords describing the PT intervention, e.g. exercise therapy, ambulation, balance, musculoskeletal equilibrium or postural stability, were used. Additional treatment methods, such as physical therapy modalities, were allowed. Search terms were entered into each database using either MeSH or keyword headings specific to the requirements of the database.

The full search strategies for each database are available on request from the corresponding author; the original Ovid Medline search strategy (Appendix S1 (available from http://www.medicaljournals.se/jrm/content/?doi=10.2340/16501977-1047)) is also available (24) on the following web link: https://helda.helsinki.fi/bitstream/handle/10138/24581/VAKE_liiteS32.pdf?sequence=35.

Review process

In accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for systematic reviews, two reviewers (JP and SHP/TS/EA) independently screened all the titles and abstracts of the articles. After these steps, potentially relevant articles were retrieved for full-text assessment. Two members of the research team (JP and SHP/TS/EA) independently evaluated all the potential full-text articles in order to identify potentially eligible studies. They also grouped the included studies according to the PT

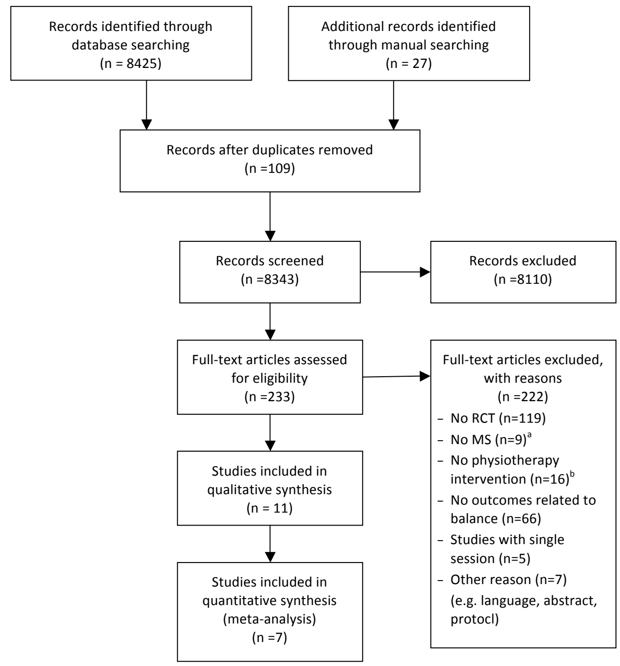

Fig. 1. Study selection. [a]No multiple sclerosis (MS) and multiple diagnoses included into study without separate analysis of MS results. [b]No physiotherapy intervention and multidisciplinary rehabilitation studies without separate analysis of a single physiotherapy method.

intervention. In the event of disagreement, a third reviewer (AH) evaluated the article to achieve a joint consensus.

Rating of study quality

The methodological quality of RCTs was rated using van Tulder scale (25). This scale rates RCTs based on random concealed allocation of participants, the similarities of participants at baseline, blinding the patient, care provider and outcome assessor, co-interventions, compliance, the dropout rate, similar timing of outcome assessment and the use of intention-to treat analysis (Table I). All 11 items were scored positive ("yes") if the criterion was fulfilled, negative ("no") if it was not fulfilled, or unclear ("don't know"). If the article did not contain information on the methodological criteria, the authors were contacted for additional information. If the authors could not be contacted, or if the information was no longer available, the criteria were scored as "unclear". The methodological quality and content analysis were evaluated by two blinded and independent reviewers (JP with undergraduate or doctoral students). Any disagreements were resolved by seeking a consensus between the reviewers, while a third reviewer (TS or SHP) was brought in to help resolve any remaining disagreements. A total score was computed by counting the number of positive scores. The maximum score was 11. The RCTs were considered to be of high, moderate or poor level depending on the number of yes-rated items and the number of subjects (26) (Table I).

Data extraction

Seven out of 11 studies included in the qualitative analysis were accepted for the meta-analysis. All of these studies presented PT as a single discipline. The meta-analyses were performed in the following subgroups according to the intervention: specific balance exercises, resistance and aerobic training, whole-body vibration, group therapy and neurotherapeutic approaches.

Standardized outcome measures excluding quality of life questionnaires were linked to the ICF category of "Changing and maintaining body position". Measures were linked to the ICF domains according to the international guidelines (27). Both capacity (which refers to the

Table I. *Quality analysis randomized controlled trials (RCTs) (n=11) concerning physiotherapy (PT) interventions on balance in people with multiple sclerosis (MS)*[a]

Intervention group Study/year	A: randomization method acceptable	B: treatment allocation concealed	C: group similarity	D: blinding of patient	E: blinding of care provider	F: blinding of outcome assessor	G: determination of co-interventions	H: compliance	I: drop-outs and reasons	J: timing of outcomes assessment similar	K: intention-to-treat analysis	Number of "yes" scores (max 11)[a]	Methodological quality level[b]
Specific balance exercises													
Cattaneo et al., 2007 (28)	Yes	?	Yes	Yes	?	No	Yes	?	Yes	Yes	No	6	Moderate
Resistance and aerobic training													
Broekmans et al., 2010[a] (29)	No	Yes	Yes	?	?	No	Yes	Yes	No	?	No	4	Poor
Cakt et al., 2010 (30)	Yes	?	Yes	?	?	Yes	Yes	Yes	No	Yes	No	6	Moderate
Harvey et al., 1999 (31)	Yes	?	No	?	?	?	Yes	?	Yes	Yes	No	4	Moderate
Plow et al., 2009 (32)	?	?	No	?	?	Yes	?	Yes	?	Yes	No	3	Poor
Physical therapy modalities													
Broekmans et al., 2010[b] (33)	?	?	Yes	?	?	No	Yes	Yes	Yes	Yes	No	5	Poor
Schyns et al., 2009 (34)	Yes	No	?	?	?	Yes	Yes	?	No	Yes	No	4	Moderate
Group therapy													
Stephens et al., 2001 (35)	?	No	Yes	No	No	No	?	?	?	Yes	?	2	Poor
Overall PT intervention													
Armutlu et al., 2001 (36)	?	No	Yes	No	No	Yes	?	?	Yes	Yes	No	4	Poor
Lord et al., 1998 (37)	Yes	No	Yes	No	No	?	?	Yes	Yes	Yes	?	5	Moderate
Wiles et al., 2001 (38)	Yes	No	?	No	No	Yes	?	Yes	Yes	Yes	No	5	Moderate

[a]The methodological quality of the RCTs was rated with criteria and decision rules modified from van Tulder et al. (2003) (25). These include 11 items (A–K) rated as positive ("yes"), negative ("no") or "don't know" (?).

[b]Quality level is based on the following criteria (26): High: overall ≥6 "yes" scores, "yes" score for items (A), (B), (C) and (I), and ≥30 subjects in a study. Moderate: overall ≥4 "yes" scores and method of randomization adequate ("yes" score for item (A)). Poor: overall ≥4 "yes" scores and method of randomization not adequate ("no" or "don't know" score for item (A)); or 0–3 "yes" scores; or number of subjects ≤5 in intervention or control group.

ability to execute a task or action if the environment were uniform or standard) and performance (which relates to what a person does in the area in question, in the environmental context in which they actually live) qualifiers were used.

In the meta-analyses, Cochrane Collaboration's Review Manager 5.1.3 program was used to calculate pooled effect estimates for the combinations of single effects of RCTs. To calculate standardized mean differences (effect size; ES), follow-up values adjusted for baseline values were used. If adequate pre-post treatment values (mean (standard deviation, SD)) were not reported, a request was sent to the authors to supply this information. If two requests were not answered, the RCT was not taken into account in the meta-analyses. An ES of approximately 0.2 was considered a small effect, approximately 0.5 a medium effect, and ≥0.8 a large effect.

For all the analyses, the inverse variance weighted random effects method was used. This incorporates heterogeneity into the model. The centre of this distribution describes the average of the effects and its width the degree of heterogeneity. In multiple comparisons with two or more intervention groups, the number of controls was divided among the comparisons to ensure that we counted the control participants only once in the meta-analysis. The overall effect was tested with the *z*-test, where the null hypothesis is that there is no difference between the intervention group and the control group. Results were considered to be significant at an alpha level of <0.05. In the results section of this systematic review and meta-analysis, the findings from the meta-analysis are presented using forest plots of the standardized mean differences for each subgroup.

The findings are summarized in the discussion section. Evidence was categorized into 4 levels depending on the quality and number of RCTs, as follows: high (at least two high-quality RCTs with parallel results), moderate (one high-quality RCT or several high-quality RCTs with some contradictions in the results or several acceptable-quality RCTs with parallel results), low (high-quality RCTs with notable contradictions in the results or at least one acceptable study) and no evidence (poor-quality RCT or no RCTs).

RESULTS

Study selection and characteristics of participants with MS

The initial search yielded 8,376 publications and the update search 76 publications. Screening of 233 full-text papers revealed 81 potentially eligible publications. A total of 11 studies (28–38) published during the years 1998–2011 fulfilled the inclusion criteria and were deemed relevant for this review. Fig. 1 presents a flow chart of the structured review.

Collectively, the selected papers included a total of 340 persons with MS who completed the interventions (Table II). The mean age of the participants across the studies was 46 years. Approximately 68% of the participants were women. Five studies out of 11 included both relapsing-remitting and progressive

Table II. *Summary of randomized controlled trials (RCTs) that include outcomes related to balance according to the physiotherapy (PT) intervention groups*

Study/year	Methodological quality[a] Randomization method	Population	Intervention (subjects included into analysis)	Setting, follow-up, frequency and/or intensity	Balance-related functional outcome measures	Main findings based on paper
Specific balance exercises (sensory and motor strategy training)						
Cattaneo et al., 2007 (28)	Quality: moderate Randomization method: computer-generated random numbers	Sample: $n=50$ MS course: RR, SP, PP Disability: EDSS NR, Ability to stand independently for more than 3 seconds, BBS max 53 points and ability to walk 6 minutes Drop-outs: 6	(E1) Balance rehabilitation to improve motor and sensory strategies ($n=20$) (E2) Balance rehabilitation to improve motor strategy ($n=11$) (C) Control group (conventional therapy not specifically aimed at improving balance) ($n=13$)	Inpatient; 10–12 sessions spread over 3 weeks, 45 min/session	BBS (0–56) DGI (0–24) mDHI (0–100) ABC Scale (0–100)	Significant effect of E1 on BBS compared with C ($p=0.01$) Significant effect of E2 on BBS compared with C ($p=0.03$) Significant effect of E1 on DGI compared with C ($p=0.04$) BBS and DGI showed an overall improvement in E1 and E2 groups No significant effect on self-reported tests; Dizziness Handicap Inventory ($p=0.43$) and ABC scale ($p=0.79$)
Resistance and aerobic training						
Broekmans et al., 2010[a] (29)	Quality: poor Randomization method: NR	Sample: $n=36$ MS course: RR, SP, PP Disability: EDSS 2.0–6.5 (mean ± SD 4.3 ± 0.2) Drop-outs: 3	(E1) ACSM-based resistance training periods in combination with simultaneous electro-stimulation ($n=11$) (E2) ACSM-based resistance training periods without simultaneous electro-stimulation ($n=10$) (C) No physiotherapy ($n=12$)	Outpatient; 20-week ACSM-based standardized resistance training programme	Timed Get Up and Go Test TUG (s) FR (cm)	Significant effect of E2 on FR compared with C ($p<0.05$) No significant effect on TUG
Cakt et al., 2010 (30)	Quality: moderate Randomization method: computer-generated random numbers	Sample: $n=43$ MS course: NR Disability: EDSS ≤6.0 Drop-outs: 12	Cross-over (E1) Cycling progressive resistance training ($n=14$) (E2) A home-based exercise programme to improve lower-limb muscle strength and balance (the same exercise programme with group E1 patients excluding the cycling) ($n=10$) (C) Control group ($n=9$)	Outpatient and home-based; twice a week during the 8 week period (E1) bicycle ergometer (2 min of high resistance pedalling, 40 % of the tolerated maximum workload, 15 sets of repetitions each session) plus 30–35 min training (warm-up walking, balance exercises and stretching) (E2) 30–35 min training (warm-up walking, balance exercises and stretching)	TUG (s) FR (cm) DGI (0–24) FES (1–10)	Significant improvement in TUG, ($p<0.01$), FR ($p<0.05$). DGI ($p<0.01$) and FES ($p<0.01$) in E1 group Significant improvement in FES ($p<0.05$) in E2 group No significant improvement in any of the outcomes in control group Significant effect of E1 on TUG ($p<0.01$), FR ($p<0.05$), DGI ($p<0.001$) and FES ($p<0.01$) compared with E2 Significant effect of E1 on TUG ($p<0.05$), FR ($p<0.05$), DGI ($p<0.01$) and FES ($p<0.01$) compared with C No significant effect of E2 on any of the outcomes compared with C

Table II. *contd.*

Harvey et. al., 1999 (31)	Quality: moderate Randomization method: Sealed envelopes	Sample: $n=19$ MS course: RR Disability: EDSS NR, Ambulant with or without the use of walking aid Drop-outs: 2	(E1) Exercise programmes specifically to strengthen the quadriceps ($n=4$) (E2) General mobility exercises (stretching, general balance and mobility exercises and swimming) ($n=6$) (C) Control group (supportive phone calls but no exercise) ($n=5$)	Outpatient; 8 weeks (E1) 10 leg extensions on both legs twice a day (E2) intensity not reported	Timed transfer (s) (a modified version of the TUG)	Significant improvement in Timed transfer ($p<0.05$) in E1 group
Plow et al., 2009 (32)	Quality: poor Randomization method: NR	Sample: $n=50$ MS course: NR Disability: EDSS NR, ability to walk with or without an assistive device Drop-outs: 12	(E1) Home exercise plus individualized physical rehabilitation ($n=22$) (E2) Home exercise plus a group wellness intervention ($n=20$)	Outpatient; 8 weeks; home exercise programme (minicycle and elastic bands); 45 min 5 days per week plus (E1) 4 physical therapy sessions once every other week plus telephone call between the session (E2) 7 educational sessions; 2 h each week	Time (s) maintained on pivot board (horizontal and sagittal plane)	No significant improvement in any of the outcomes
Whole-body vibration						
Broekmans et al. 2010[b] (33)	Quality: poor Randomization method: NR	Sample: $n=25$ MS course: RR, SP,PP Disability: EDSS 1.5–6.5, (mean±SE: 4.3±0.2) Drop-outs: 2	(E) A leg muscle training programme consisting of static and dynamic leg squats and lunges on a vibration platform ($n=11$) (C) No physiotherapy ($n=12$)	Outpatient; 20 weeks; 5 training sessions per 2-week cycle for a 50 min/session	BBS (0–56) TUG (s)	No significant effects of E on BBS and TUG compared with C
Schyns et al., 2009 (34)	Quality: moderate Randomization method: Sealed envelopes	Sample: $n=16$ MS course: NR Disability: EDSS NR, Hauser ambulation index 1–6 Drop-outs: 4	Cross-over (E1) Whole-body vibration training combined with exercises ($n=8$) (E2) Exercise alone (without whole-body vibration) ($n=8$)	4 weeks; 3 times per week	TUG (s)	No significant effect of E1 on TUG compared with E2 ($p=0.720$)
Group therapy						
Stephens et al., 2001 (35)	Quality: poor Randomization method: NR	Sample: $n=12$ MS course: RR, PP, CP Disability: EDSS 3.5–6.0 Drop-outs: NR	(E1) Awareness Through Movement (Feldenkrais) focusing on body awareness and motor learning programme ($n=6$) (E2) Control group involved in social/educational classes ($n=6$)	Outpatient; 10 weeks (E1) 8 classes, 2–4 h each for a total of 20 h (E2) 4 sessions, 90 min each	Equiscale (score 0–16) Computerized balance assessment on balance mCTSIB, COP sway and LOS ABC Scale	Significant effect of E1 on mCTSIB ($p=0.046$) and ABC scale ($p=0.044$) compared with E2 No significant effect of E1 on Equiscale, COP sway Velocity Composite and LOS compared with E2

Table II. *contd.*

Neurotherapeutic approaches						
Armutlu et al., 2001 (36)	Quality: poor Randomization method: NR	Sample: $n=26$ MS course: PP, SP Disability: EDSS 3.5–5.5 Drop-outs: No	(E1) Neuromuscular rehabilitation with Johnstone Pressure Splints in addition ($n=13$) (E2) Neuromuscular rehabilitation alone ($n=13$)	Outpatient; 4 weeks; neuromuscular rehabilitation (PNF, Frenkel Coordination Exercise, postural stability and balance training and walking exercise) (E1) The splint was applied for 20 min to both lower extremities before exercise sessions and were used during exercise	Timed 1-leg stance (s) Timed anterior balance (cm) Timed equilibrium coordination tests: walking-on-2-lines (steps) and tandem walking (steps)	Significant improvement ($p<0.05$) on Timed 1-leg stance and walking-on-2-lines of both groups No significant effect on Timed anterior balance and Tandem gait of both groups Significant effect ($p<0.05$) of E1 on Timed 1-leg stance and Walking-on-2-lines compared with E2.
Lord et al., 1998 (37)	Quality: moderate Randomization method: sealed envelopes and block randomization	Sample: $n=23$ MS course: CP, RR Disability: EDSS NR, ambulatory Drop-outs: 3	(E1) A facilitation (impairment-based) approach (e.g. passive and active techniques) ($n=10$) (E2) A task-oriented (disability-focused) approach (e.g. functional exercises) ($n=10$)	Outpatient; for a minimum of 15 treatments over a 5–7-week period (15–19 times)	BBS (0–56)	Significant improvements on BBS ($p<0.01$) of both groups No significant effect of E1 on BBS compared with E2
Wiles et al., 2001 (38)	Quality: moderate Randomization method: sealed envelopes	Sample: $n=42$ MS course: NR Disability: EDSS 4.0–6.5 Drop-outs: 2	Cross-over (E1) Hospital outpatient physiotherapy focused on facilitation techniques (E2) Home exercises focused on functional activities (C) No physiotherapy	Outpatient and home; based on an individualized problem-solving approach; 2 session of 45 min each week for 8 weeks	Timed 1-leg stance (s)	Significant effect of E1 on 1-leg stance compared with C ($p=0.004$) Significant effect of E2 on 1-leg stance compared with C ($p=0.001$) No significant effect of E1 on 1-leg stance compared with E2 ($p=0.69$)

[a]The methodological quality of the RCTs was rated with criteria and decision ruled modified from van Tulder et al. (2003) (25), [b]Quality level is based on the following criteria (26) see on Table I. ABC Scale: Activities-specific Balance Confidence Scale; ACSM: American College of Sports Medicine; BBS: Berg Balance Scale; C: Control group; COP: center of pressure; CP: Chronic Progressive; DGI: Dynamic Gait Index; EDSS: Expanded Disability Status Scale; E: Experimental group; FES: Falls Efficacy scale; FR: Functional Reach; LOS: Limits of Stability; mCTSIB: modified Clinical Test of Sensory Interaction in Balance; mDHI: Modified Dizziness Handicap Inventory; NR: Not Reported; PNF: Proprioceptive Neuromuscular Facilitation; PP: Primary Progressive; PT: Physiotherapy; RR: Relapsing Remitting; SD: Standard deviation; SE: Standard error; SP: Secondary Progressive; TUG: Timed Up and Go test.

forms of MS (28, 29, 33, 35, 37), one RCT only progressive forms (36), and one RCT only relapsing-remitting MS (31). Overall, 4 papers did not report the course of the MS (30, 32, 34, 38). In all the studies, the persons with MS were ambulatory. Six studies used the Expanded Disability Status Scale (EDSS) (39) to describe disease severity. The EDSS scores was ≤6.5, i.e. all these studies included participants with a minimal to moderate level of disability (29, 30, 33, 35, 36, 38). The other 5 studies (28, 31, 32, 34, 37) included participants who were able to walk with or without an assistive device or whose Hauser ambulation index ranged from 1 to 6 (40).

Methodological quality of the selected studies

Van Tulder score ranged from 2 to 6 out of 11 points (mode 4). Overall, the methodological quality was poor, with none of the studies scored as high quality (Table I). Five RCTs were classified as poor and 6 as moderate quality. The most common methodological flaw was selection bias. While half of the studies used an adequate randomization method (item A: 55%), only one of the studies used concealed treatment allocation (item B: 9%). Most of the studies used similar timing of outcome assessment (item J: 91%), but only 45% of the studies conducted blinding of outcome assessor (item F). In addition, none of the studies conducted intention-to-treat analysis (item K), and many studies also had a small sample size.

Components of the interventions

Five groups (a–e) were identified according to the type of PT intervention: (a) specific balance exercises, i.e. multisensory and motor strategy training ($n=1$) (28), (b) resistance and aerobic training ($n=4$) (29–32), (c) whole-body vibration ($n=2$) (33, 34), (d) group therapy ($n=1$) (35), and (e) neurotherapeutic approaches ($n=3$) (36–38). Sample sizes were small in most studies, varying from 12 (35) to 50 (28, 32) participants. The mean duration of the interventions was 9.0 weeks, ranging from 3 to 20 weeks. Table II presents a summary of the interventions in detail.

One RCT reported a single PT intervention group (E) compared with placebo or no treatment (C) (33), 5 RCTs had two intervention groups (E1, E2) compared with placebo or no treatment (C) (28–31, 38), and 5 RCTs compared two PT interventions (E1 vs. E2) (32, 34–37).

A total of 11 different outcome measures were identified from the selected 11 studies (column 6 of Table II presents the measures used in each study). There were a mean of two measures per study (range 1–4) in the aforementioned ICF category. The most common measures were the Timed Up and Go test (TUG) (41), Berg Balance Scale (BBS) (42), timed one-leg stance (43), Functional Reach test (FR) (44) and Dynamic Gait Index (DGI) (45). In addition, 3 self-report questionnaires were used. Two studies used the Activities-specific Balance Confidence (ABC) scale (46), one the Falls Efficacy Scale (FES) (47) and 1 the Modified Dizziness Handicap Inventory (mDHI) (48, 28). A higher score on the BBS, FR, ABC scale and mDHI and longer one-leg stance time denote better function. A lower TUG time and lower FES score denote better function.

Effects of the PT interventions

Of the 11 analysed RCTs, the data needed for the estimations of ES were reported in 5 articles, and in 2 others the authors provided these data on request. Thus the meta-analyses were conducted for 7 RCTs (28–30, 35–38) with 230 participants (Figs 2–5). The findings from the 4 remaining RCTs (31–34) could not be entered into the model. However, the results were quantitatively analysed (Table II), and the findings are discussed below.

Specific balance exercises

With regard to the effects of specific balance exercise, one RCT of moderate methodological quality was conducted (28). Our meta-analysis of this study evaluating inpatient training of specific motor and sensory strategies compared with placebo treatment indicates that there was a small but significant effect on balance (ES 0.34; 95% confidence interval (CI), 0.01–0.67)

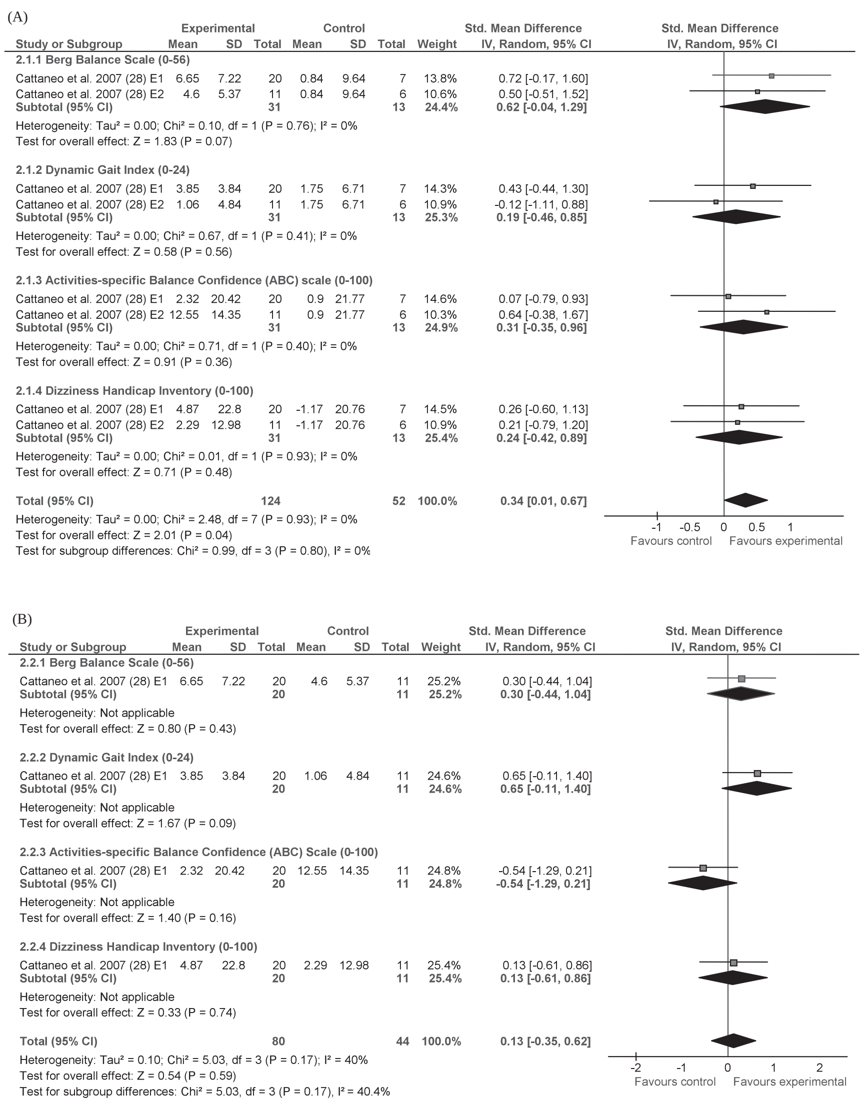

Fig. 2. Specific balance exercises. The squares and diamonds represent the test values for individual studies and the overall effect, respectively; standard mean difference, 95% confidence interval (CI). (A) Effects of specific motor strategies training (E1) and sensory strategies training (E2) vs no treatment (Control). (B) Effects of motor strategies training (Experimental) vs sensory strategies training (Control). SD: standard deviation; df: degrees of freedom.

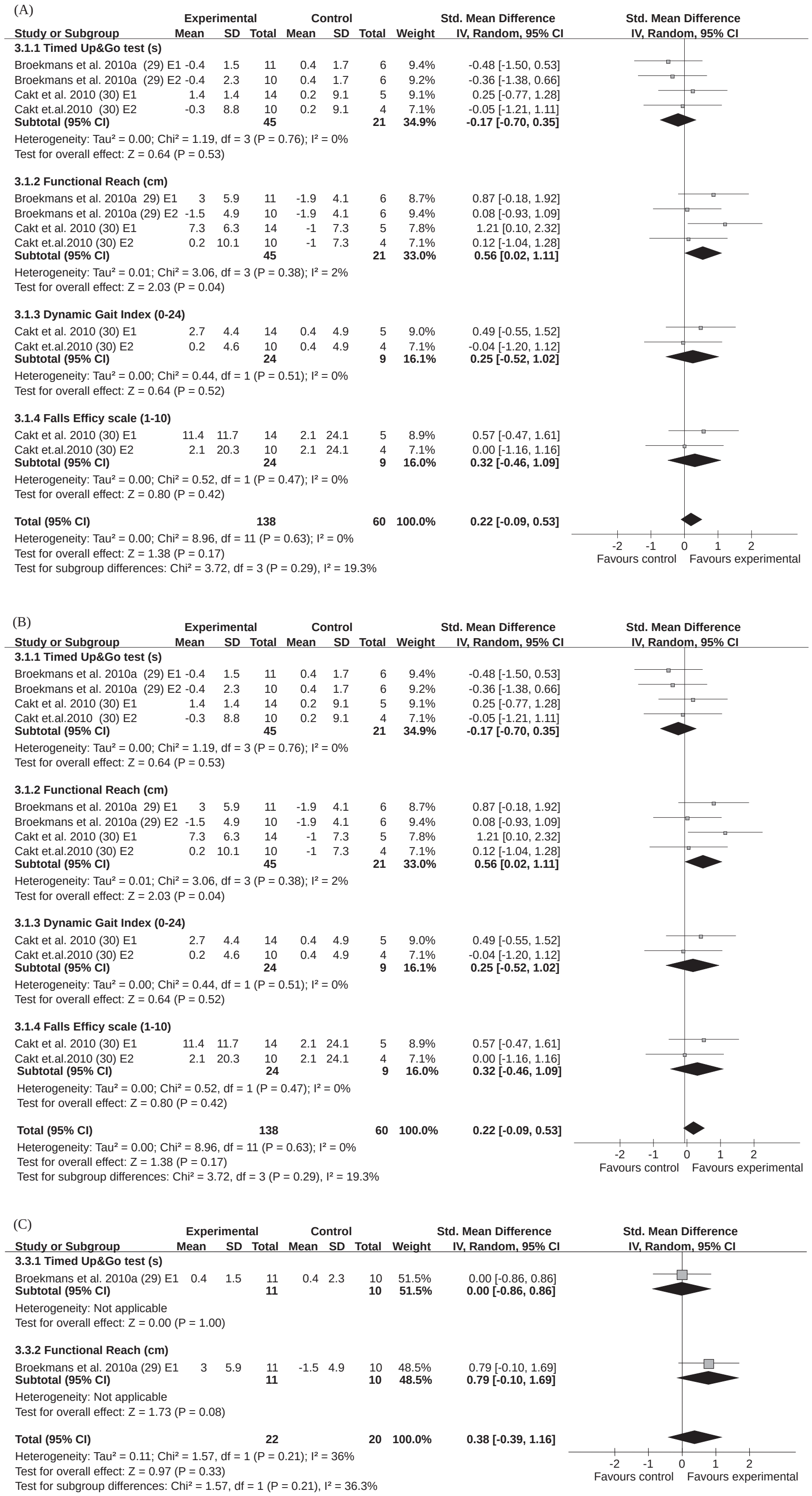

Fig. 3. Resistance and aerobic training. The squares and diamonds represent the test values for individual studies and the overall effect, respectively; standard mean difference, 95% confidence interval (CI). (A) Effects of resistance and aerobic training vs no treatment (Control). (B) Effects of cycling progressive resistance training (Experimental) vs a home-based exercise programme (Control). (C) Effects of American College of Sports Medicine (ACSM)-based resistance training periods in combination with simultaneous electro-stimulation (Experimental) vs ACSM-based resistance training without simultaneous electro-stimulation (Control). SD: standard deviation; df: degrees of freedom.

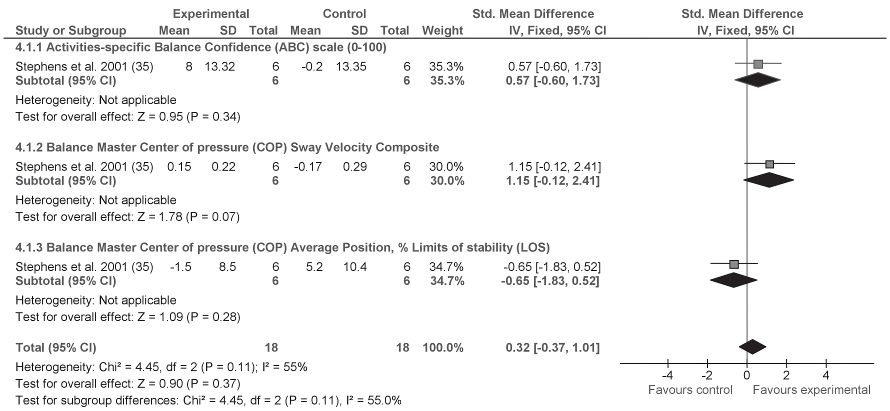

Fig. 4. Awareness Through Movement (Feldenkrais) therapy (Experimental) vs educational sessions (Control). The squares and diamonds represent the test values for individual studies and the overall effect, respectively; standard mean difference, 95% confidence interval (CI). SD: standard deviation; df: degrees of freedom.

(Fig. 2A). The strongest effect was found on the BBS, but no significant effect was observed on the DGI and the two self-report tests, i.e. the mDHI and the ABC scale. No effect was found when training of motor strategies was compared with training of sensory strategies (Fig. 2B).

Resistance and aerobic training

A small, but non-significant, overall effect on balance was found when outpatient and home-based resistance and aerobic training were compared with no treatment (Fig. 3A). However, a significant effect on FR (ES 0.56; 95% CI, 0.02–1.11) was found (Fig.

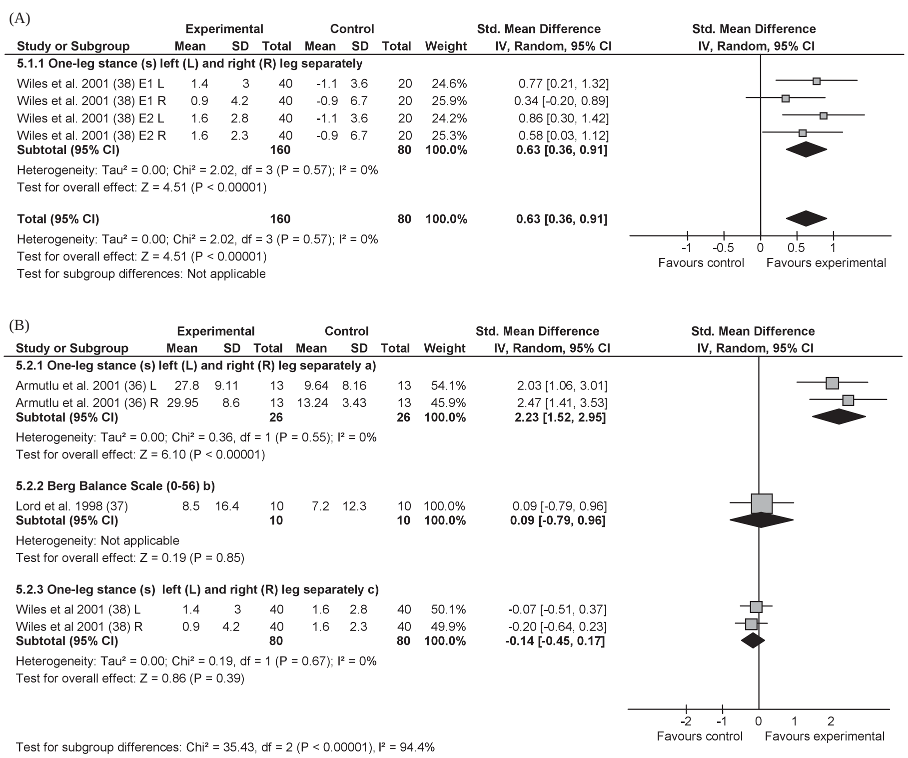

Fig. 5. Neurotherapeutic approaches. The squares and diamonds represent the test values for individual studies and the overall effect, respectively; standard mean difference, 95% CI. (A) Effects of an individualized problem-solving approach in outpatient (E1) and in home exercises (E2) vs no treatment (Control). (B) Effects of neurotherapeutic approach (Experimental) vs other treatment (Control).

a) Armutlu et al., 2001 (36): Neuromuscular rehabilitation with Johnstone Pressure Splints (Experimental) vs neuromuscular rehabilitation alone (Control).

b) Lord et al., 1998 (37): A facilitation (impairment-based) approach (Experimental) vs a task-oriented (disability-focused) approach (Control).

c) Wiles et al., 2001 (38): Hospital outpatient physiotherapy focused on facilitation techniques (Experimental) vs home exercises focused on functional activities (Control). SD: standard deviation; df: degrees of freedom.

3A). Furthermore, a significant overall effect on balance (ES 0.55; 95% CI, 0.14–0.97) was found when outpatient cycling progressive resistance training was compared with a home-based exercise programme (Fig. 3B). Our analysis revealed that simultaneous electro-stimulation during an American College of Sports Medicine (ACSM)-based resistance training programme did not enhance training efficiency, as no significant overall effect on functional balance was reported (Fig. 3C). The results of Harvey et al. (31) and Plow et al. (32) were excluded from our meta-analysis because adequate pre-post treatment values were not obtained. The authors' (31, 32) analysis showed no significant differences between interventions (Table II).

Whole-body vibration

Both the studies of physical therapy modalities (33, 34) were acceptable quality RCTs and used whole-body vibration (WBV) training combined with exercises in outpatient setting. They were excluded from our meta-analysis because adequate pre-post treatment values were not obtained. They both reported statistically unchanged TUG performance following additional WBV training performance compared with no PT (33) or exercise alone (34) (Table II).

Group therapy

One RCT, of poor methodological quality, was conducted on the effects of group therapy (35). Our meta-analysis indicated a small, but non-significant, overall effect on balance when Awareness Through Movement (Feldenkrais) classes were compared with educational sessions (Fig. 4).

Neurotherapeutic approaches

All 3 studies of the overall PT intervention group focused on outpatient rehabilitation for 4–8 weeks periods, using different neurotherapeutic approaches. Our analysis revealed a significant effect on the timed one-leg stance test (ES 0.63; 95% CI, 0.36–0.91) when outpatient PT and home exercises based on an individualized problem-solving approach were compared with no treatment (Fig. 5A), but no significant effect when hospital outpatient PT was compared with home exercises (Fig. 5B). Furthermore, both Lord et al. (37) and Wiles et al. (38) compared a facilitation approach with functional exercises using different outcome measures. In line with our meta-analysis (Fig. 5B), they both reported statistically unchanged performance on the BBS and timed one-leg stance test following the facilitation approach when compared with functional exercises (Table II). Following neuromuscular rehabilitation (proprioceptive neuromuscular facilitation, Frenkel Coordination Exercise, postural stability and balance training, walking exercise) with Johnstone Pressure Splints, a significant effect was found on the timed one-leg stance test compared with neuromuscular rehabilitation alone (ES 2.23; 95% CI, 1.52–2.95) (Fig. 5B).

DISCUSSION

The primary goal of this meta-analysis was to evaluate of the effects of PT interventions on balance in people with MS. Studies evaluating the effects of PT intervention on balance in people with MS showed heterogeneous results. The studies included in this systematic review and meta-analysis had various aims and a range of different outcome measures. This makes direct comparison between the studies, and hence meta-analyses, difficult, and consequently the overall evidence from a single study is weak. However, some general conclusions can be drawn.

Our meta-analysis of 7 RCTs found low evidence for positive effects on various balance outcomes of specific balance exercises (28), PT based on an individualized problem-solving approach (38), and of resistance and aerobic exercises (29, 30) in ambulatory people with MS. There was also low evidence that resistance and aerobic training appears to be more effective than home-based exercise (30). One RCT including progressive forms of MS found that neuromuscular rehabilitation accompanied with Johnstone Pressure Splints (36) is more effective than neuromuscular rehabilitation alone. Furthermore, inspection of the results based on the authors' analyses, as reported in the original articles, indicated a significant effect of Awareness Through Movement (Feldenkrais) groups on the modified Clinical Test of Sensory Interaction in Balance (mCTSIB) and ABC scale compared with educational sessions (35), but no effect of whole-body vibration training on balance (33, 34). Also, there was insufficient evidence that whole-body vibration (33, 34), or electro-stimulation (29) improved functional balance outcomes for people with MS. The results of the analyses conducted with studies rated as yielding low evidence should be viewed critically, as new high-quality studies may change the magnitude and/or direction of this evidence.

Overall, the methodological quality of the studies was poor and sample sizes were small. The sample sizes of the RCTs in this review ranged from 4 to 40 per group, with most studies lacking sufficient statistical power. It has been stated that studies need to be adequately powered, or designed to fit into a meta-analysis, in which case the inclusion and exclusion criteria, outcomes, and time-points for assessment need to be established *a priori* (49). Obviously, it is very difficult, and perhaps impossible, to blind patients and care providers in studies of exercise therapy. Thus, a comprehensive criterion was adopted in order to determine high-quality methodological study (see Table I). Information on several methodological quality items was missing from most of the articles, thus decreasing the level of quality of the original paper. This should be taken into account when planning new studies and reporting results. In addition, we found that randomization procedures and concealed treatment allocation were poorly reported, as was the exact content of the interventions. Consequently, for the reasons given above, along with the methodological differences between the studies, such as the use of different outcome measures and types of intervention, meaningful comparison between the RCTs is severely limited.

Half of the studies included in this review did not report the course of the MS of the participants and half of the studies had a mixed group of MS types. Thus, most of the results could be generalized to all forms of MS, i.e. both relapsing-remitting and progressive forms. When the determinants of balance (6, 7) and the previous results on balance problems in people with MS (8–13) are considered, the form of MS does not seem to be a crucial factor in balance. However, we would encourage future researchers to study the effect of balance interventions separately for relapsing-remitting and progressive MS. More importantly, the level of disability of the participants must be considered when evaluating the results. The analysed studies all comprised only ambulatory people with MS, with the result that the EDSS scores varied widely (EDSS 1–6.5) within and between the studies. In other words, people with no disability (EDSS score 1) and people who used constant bilateral support (EDSS score 6.5) both received the same intervention. As studies have not taken mobility levels into account, the optimal type of intervention and its frequency and duration is unknown.

In general, PT interventions for the improvement of balance have adopted various theoretic approaches, e.g. motor and sensory strategies (28), Feldenkrais (35) and neuromuscular facilitation (37, 38). Some significant effects on balance compared with no/placebo treatment (28, 38) were found. When two treatments were compared (E1 vs E2), no significant effects were found (28, 35, 37, 38). Thus, the optimal type of intervention for people with MS remains unclear. In this situation, the PT should choose the most appropriate method, or combination of methods, on the basis of a careful assessment.

It is known that there is a need for specificity of training, e.g. specific balance exercises to improve balance among older adults (50). Adequate balance relies on inputs from the visual, somatosensory and vestibular systems (6), which are frequently impaired in people with MS (21). Surprisingly, only one study (28) was based on this theoretical framework. Muscle weakness and spasticity have been found to further compromise the ability to balance, as they affect the sequencing and force of muscle contraction (21). Four RCTs included in this review studied the effects of resistance and aerobic training on balance (29–32).

The strongest evidence for positive outcomes in the present analyses are associated with interventions based on the theoretical background of balance (i.e. specific balance exercises) and interventions using a well-defined progressive exercise training programme. Future studies could provide a better estimate of the effects of PT interventions on balance if the interventions were planned and described in more detail (e.g. type of exercise, duration of intervention, weekly frequency of exercise, amount of exercise per session).

Therapeutic exercise is a method of general, non-specific, active, functional therapy. In another part of this larger study, 3 occupational therapy (OT) studies were identified after screening of 35 full-text papers (24). All of these studies dealt with an energy conservation course in persons with MS, and none of them used an outcome measure linked to the ICF category of "Changing and maintaining body position". In addition, multidisciplinary rehabilitation is an important component of symptomatic and supportive treatment for MS. Overall, 13 multidisciplinary treatment interventions were taken into consideration in our review, but none of them fulfilled inclusion criteria. That is, no separate analysis of a single method was conducted and no outcome measures linked to the ICF category of "Changing and maintaining body position" were found. The Cochrane Review on multidisciplinary rehabilitation for adults with MS (51) expressed no outcome measures linked to the ICF category of "Changing and maintaining body position". Overall, further studies focusing on balance and different therapies in people with MS are needed.

Balance control is an integral component of all daily activities, but its complex and flexible nature makes it difficult to assess adequately (7). Understanding the biomechanical and information processing demands imposed by the task and by the environmental context allows us to evaluate their probable impact on motor performance and balance. Drawing on this model (7), most of the functional measures (e.g. BBS, FR, DGI, timed standing) used in the studies included here have a closed task condition and simple and stable environmental conditions; however, they differ in terms of the base of support (stationary or moving) and balance mechanism (predictive or proactive) used. Only one study (35) used the mCTSIB, which features more constraints from the environmental context. The Cochrane Review recommended that the WHO's ICF classification (2) should be used as a basis for outcome measurement (52). Most of these measures represent the ICF "Changing and maintaining body position" category and capacity qualifiers. In addition, 3 self-report questionnaires that were used to assess the participants' performance in their current environment were included in the meta-analysis. The studies analysed here also, to a varying extent, included outcome measures of the ICF components of body functions, such as muscle strength or spasticity, but they were not included in the analysis. The ICF is closely related to the concept of well-being and it contains the content of items of instruments to address Health-Related Quality of life (53). However, there are non-health aspects which are part of the universe of well-being not covered in the ICF. Therefore quality of Life (QoL) measures were not included in our review. A further review of the effects of balance exercises on QoL is needed. In agreement with a previous review (54), our review also highlights the need for the use of more consistent measures across studies, allowing comparison of results.

Despite the fact that many people with MS fall frequently, fear falling and are at increased risk of fall-related injuries (14–20), falls were not a primary focus of any of the studies. The results of our review reveal that, while motor and sensory strategies training (28) had no significant effect on the self-reported tests, they reduced the fall rate. In addition, both cycling progressive resistance training and a home-exercise programme (30) reduced FES and Feldenkrais-based group therapy (35) yielded significant improvements in balance confidence (ABC-scale). Consequently, we recommend further interventions focusing on fall prevention in people with MS.

Previously, several meta-analyses have been conducted to evaluate the overall effects of exercise on walking mobility (23) and quality of life (55) in MS. Some reviews have focused on mobility (21, 22) and one on hippotherapy (56). Bronson et al.

(56) found that hippotherapy had a positive effect on balance in people with MS, but this finding was based on only 3 non-RCT studies. To our knowledge, our study was the first meta-analysis to explore the effect of PT interventions on balance.

The search strategy was designed to include a broad range of research regarding PT interventions in people with MS. Inclusion criteria were set to ensure rigorous searching and to enable this review to be replicated by others. Although our results are mostly positive, the limitations of this meta-analysis should be taken into account. Table I shows that the studies included in this review have a moderate or high risk of bias, e.g. selection, performance, attrition and detection bias. However, it should be noted that all the PT treatments studied were well tolerated by the participants and had no negative effects. Therefore, further high-quality studies are needed in order to develop treatment recommendations for clinicians treating people with MS.

Implications for future studies

Recommendations for future research, based on this review, are similar to those of the Cochrane Review on exercise therapy (52) and from mobility reviews (21–23). Methodological weaknesses, such as small sample sizes, lack of adequate randomization and blinding, and inadequate reporting of intervention protocols, continue to be as evident now as they were in 2004 (52). This review reiterates the need for better quality studies that address these weaknesses.

The present results indicate clearly that it is of the utmost importance to conduct studies that stratify people with MS according to their mobility level. It is also important that future studies carefully consider the sample size required to detect any potential between-group differences. Only then will it be possible to determine the most effective intervention for treating people with MS who have different mobility problems. To allow for data pooling, future studies need to standardize the relevant methodological aspects, e.g. inclusion and exclusion criteria for subjects, outcome measures and follow-up time.

Conclusion

The evidence assembled here suggests that there is a need for specificity of training, e.g. specific balance exercises to improve balance. In addition, there is some evidence that progressive resistance and aerobic training have positive effects on balance in people with MS whose level of disability is mild or moderate. Evidence for severely disabled people is lacking. The review emphasizes the need for high-quality RCTs with larger numbers of participants and a longer follow-up period. There is a need for more rigorous, scientifically sound research that is based on the theoretical background of balance. The use of standardized assessment instruments would ultimately improve the quality of MS research and would enable comparisons across studies.

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