REVIEW ARTICLE

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

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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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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
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 also included in the search strategy, methods, such as physical therapy modalities, were also 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 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
effects, and approximately 0.2 was considered a small effect, approximately 0.5 the RCT was not taken into account in the meta-analyses. An ES of authors to supply this information. If two requests were not answered, (standard deviation, SD)) were not reported, a request was sent to the baseline values were used. If adequate pre-post treatment values (mean differences (effect size; ES), follow-up values adjusted for combinations of single effects of RCTs. To calculate standardized evidence (poor-quality RCT or no RCTs). The overall effect was tested among the comparisons to ensure that we counted the control partici-
Pants only once in the meta-analysis. The overall effect was tested its width the degree of heterogeneity. In multiple comparisons with
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<tr>
<th>Study/year</th>
<th>Methodological qualitya</th>
<th>Randomization method</th>
<th>Population</th>
<th>Intervention</th>
<th>Setting, follow-up, frequency and/or intensity</th>
<th>Balance-related functional outcome measures</th>
<th>Main findings based on paper</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specific balance exercises (sensory and motor strategy training)</td>
<td>Quality: moderate</td>
<td>Randomization method: computer-generated random numbers</td>
<td>Sample: n = 50</td>
<td>(E1) Balance rehabilitation to improve motor and sensory strategies (n = 20)</td>
<td>Inpatient; 10–12 sessions spread over 3 weeks, 45 min/session</td>
<td>BBS (0–56), DGI (0–24), mDHI (0–100), ABC Scale (0–100)</td>
<td>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)</td>
</tr>
<tr>
<td>Cattaneo et al., 2007 (28)</td>
<td></td>
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<td>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</td>
<td>Drop-outs: 6</td>
<td>(E2) Balance rehabilitation to improve motor strategy (n = 11)</td>
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<tr>
<td>Brockmans et al., 2010b</td>
<td>Quality: poor</td>
<td>Randomization method: NR</td>
<td>Sample: n = 36</td>
<td>(E1) ACSM-based resistance training periods in combination with simultaneous electro-stimulation (n = 11)</td>
<td>Outpatient; 20-week ACSM-based standardized resistance training programme</td>
<td>TUG (s), FR (cm)</td>
<td>Significant effect of E2 on FR compared with C (p &lt; 0.05) No significant effect on TUG</td>
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<td>MS course: RR, SP, PP Disability: EDSS 2.0–6.5 (mean ± SD 4.3 ± 0.2)</td>
<td>Drop-outs: 3</td>
<td>(E2) ACSM-based resistance training periods without simultaneous electro-stimulation (n = 10)</td>
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<td></td>
<td></td>
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<td>(C) No physiotherapy (n = 12)</td>
<td></td>
<td>(C) No physiotherapy</td>
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<tr>
<td>Cakt et al., 2010 (30)</td>
<td>Quality: moderate</td>
<td>Randomization method: computer-generated random numbers</td>
<td>Sample: n = 43</td>
<td>(E1) Cycling progressive resistance training (n = 14)</td>
<td>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) (n = 10) (C) Control group (n = 9)</td>
<td>TUG (s), FR (cm), DGI (0–24), FES (1–10)</td>
<td>Significant improvement in TUG, (p &lt; 0.01), FR (p &lt; 0.05), DGI (p &lt; 0.01) and FES (p &lt; 0.01) in E1 group Significant improvement in FES (p &lt; 0.05) in E2 group No significant improvement in any of the outcomes in control group Significant effect of E1 on TUG (p &lt; 0.01), FR (p &lt; 0.05), DGI (p &lt; 0.001) and FES (p &lt; 0.01) compared with E2 Significant effect of E1 on TUG (p &lt; 0.05), FR (p &lt; 0.05), DGI (p &lt; 0.01) and FES (p &lt; 0.01) compared with C No significant effect of E2 on any of the outcomes compared with C</td>
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<td>MS course: NR Disability: EDSS ≤ 6.0</td>
<td>Drop-outs: 12</td>
<td>(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)</td>
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Table II. contd.

<table>
<thead>
<tr>
<th>Study</th>
<th>Quality</th>
<th>Randomization method</th>
<th>Sample</th>
<th>MS course</th>
<th>Disability</th>
<th>Drop-outs</th>
<th>Exercise programme</th>
<th>Time and setting</th>
<th>Outcomes</th>
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<tbody>
<tr>
<td>Harvey et al., 1999 (31)</td>
<td>Moderate</td>
<td>Sealed envelopes</td>
<td>n = 19</td>
<td>RR</td>
<td>EDSS NR, Ambulant with or without the use of walking aid</td>
<td>2</td>
<td>(E1) Exercise programmes specifically to strengthen the quadriceps (n = 4)</td>
<td>Outpatient; 8 weeks</td>
<td>Significant improvement in Timed transfer (p &lt; 0.05) in E1 group</td>
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<tr>
<td>Plow et al., 2009 (32)</td>
<td>Poor</td>
<td>NR</td>
<td>n = 50</td>
<td>NR</td>
<td>EDSS NR, ability to walk with or without an assistive device</td>
<td>12</td>
<td>(E1) Home exercise plus individualized physical rehabilitation (n = 22)</td>
<td>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</td>
<td>No significant improvement in any of the outcomes</td>
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<tr>
<td>Whole-body vibration</td>
<td>Poor</td>
<td>NR</td>
<td>n = 25</td>
<td>RR, SP, PP</td>
<td>EDSS 1.5–6.5, (mean ± SE: 4.3 ± 0.2)</td>
<td>2</td>
<td>(E) A leg muscle training programme consisting of static and dynamic leg squats and lunges on a vibration platform (n = 11)</td>
<td>Outpatient; 20 weeks; 5 training sessions per 2-week cycle for a 50 min/session</td>
<td>No significant effects of E on BBS and TUG compared with C</td>
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<tr>
<td>Schyns et al., 2009 (34)</td>
<td>Moderate</td>
<td>Sealed envelopes</td>
<td>n = 16</td>
<td>NR</td>
<td>EDSS NR, Hauser ambulation index 1–6</td>
<td>4</td>
<td>(C) No physiotherapy (n = 12)</td>
<td>Cross-over</td>
<td>No significant effect of E1 on TUG compared with E2 (p = 0.720)</td>
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<tr>
<td>Group therapy</td>
<td>Poor</td>
<td>NR</td>
<td>n = 12</td>
<td>RR, PP, CP</td>
<td>EDSS 3.5–6.0</td>
<td>NR</td>
<td>(E1) Awareness Through Movement (Feldenkrais) focusing on body awareness and motor learning programme (n = 6)</td>
<td>Outpatient; 10 weeks</td>
<td>Significant effect of E1 on mCTSIB (p = 0.046) and ABC scale (p = 0.044) compared with E2</td>
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<tr>
<td>Stephens et al., 2001 (35)</td>
<td>Poor</td>
<td>NR</td>
<td>n = 12</td>
<td>RR, PP, CP</td>
<td>EDSS 3.5–6.0</td>
<td>NR</td>
<td>(E2) Control group involved in social/educational classes (n = 6)</td>
<td>No significant effect of E1 on Equiscale, COP sway Velocity Composite and LOS compared with E2</td>
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### Neurotherapeutic approaches

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<tr>
<th>Authors, Year</th>
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<th>Randomization method:</th>
<th>Sample:</th>
<th>MS course:</th>
<th>Sample size:</th>
<th>Drop-outs:</th>
<th>Conditions:</th>
<th>Treatment:</th>
<th>Outcomes:</th>
<th>Comments:</th>
</tr>
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<tbody>
<tr>
<td>Lord et al., 1998 (37)</td>
<td>Moderate</td>
<td>Sealed envelopes and block randomization</td>
<td>n=23</td>
<td>CP, RR</td>
<td>3</td>
<td>No</td>
<td>(E1) A facilitation (improvement-based) approach (e.g., passive and active techniques)</td>
<td>BBS (0–56)</td>
<td>Significant improvements on BBS (p&lt;0.01) of both groups</td>
<td>No significant effect of E1 on BBS compared with E2</td>
</tr>
<tr>
<td>Wiles et al., 2001 (38)</td>
<td>Moderate</td>
<td>Sealed envelopes</td>
<td>n=42</td>
<td>NR</td>
<td>2</td>
<td>No</td>
<td>(E1) Hospital outpatient physiotherapy focused on facilitation techniques; (E2) Home exercises focused on functional activities</td>
<td>Timed 1-leg stance (s); Timed anterior balance (cm); Timed equilibrium coordination tests: walking-on-2-lines (steps) and tandem walking (steps)</td>
<td>Significant effect (p&lt;0.05) of E1 on Timed 1-leg stance and Walking-on-2-lines compared with E2</td>
<td></td>
</tr>
</tbody>
</table>

*The methodological quality of the RCTs was rated with criteria and decision rules modified from van Tulder et al. (2003) (25).*

- 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 Canadian Thoracic Society for Injured Back; mDHI: Modified Dizziness Handicap Inventory; N: Not Reported; PNF: Proprioceptive Neuromuscular Facilitation; PP: Primary Progressive; PT: Physiotherapy; RR: Relapsing Remitting; SE: Standard error; SP: Secondary Progressive; TUG: Timed Up and Go test.

- Components of the intervention:
  - A randomized controlled trial.
  - The type of PT intervention.
  - The study design.
  - The number of participants.
  - The duration of the intervention.
  - The number of treatment sessions.
  - The number of outcome assessors.
  - The methodological quality of the selected studies.

- Components of the outcome assessment:
  - The type of outcome measure.
  - The number of outcome assessors.
  - The methodological quality of the selected studies.

- The EDSS score was used to describe disease severity. The EDSS score was used to describe disease severity.

- The methodological quality of the selected studies was assessed using the ABC Scale and the mDHI.

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Effects of PT on balance in MS

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.
<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental</th>
<th>Control</th>
<th>Std. Mean Difference IV, Random, 95% CI</th>
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<tr>
<td></td>
<td>Mean SD</td>
<td>Total</td>
<td>Mean SD</td>
</tr>
<tr>
<td><strong>3.1.1 Timed Up&amp;Go test (s)</strong></td>
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</tr>
<tr>
<td>Broekmans et al. 2010a (29) E1</td>
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<td>0.4 1.7</td>
</tr>
<tr>
<td>Broekmans et al. 2010a (29) E2</td>
<td>1.4 0.4</td>
<td>15 6</td>
<td>0.4 1.7</td>
</tr>
<tr>
<td>Cakt et al. 2010 (30) E1</td>
<td>1.4 0.4</td>
<td>14 6</td>
<td>0.2 1.7</td>
</tr>
<tr>
<td>Cakt et al. 2010 (30) E2</td>
<td>0.8 0.5</td>
<td>11 5</td>
<td>0.2 1.7</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>1.46 0.5</td>
<td>15 6</td>
<td>1.0 1.7</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
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<tr>
<td></td>
<td>1.46 0.5</td>
<td>15 6</td>
<td>1.0 1.7</td>
</tr>
</tbody>
</table>

Test for overall effect: Z = 1.25 (P = 0.21); I² = 55.6%

Test for subgroup differences: Chi² = 4.63, df = 3 (P = 0.11); P = 0.80

Heterogeneity: Not applicable

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
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<tr>
<td></td>
<td>Mean SD</td>
<td>Total</td>
<td>Mean SD</td>
</tr>
<tr>
<td><strong>3.1.2 Functional Reach (cm)</strong></td>
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<td></td>
</tr>
<tr>
<td>Broekmans et al. 2010a (29) E1</td>
<td>1.4 0.4</td>
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<td>Broekmans et al. 2010a (29) E2</td>
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Heterogeneity: Not applicable

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<tbody>
<tr>
<td></td>
<td>Mean SD</td>
<td>Total</td>
<td>Mean SD</td>
</tr>
<tr>
<td><strong>3.1.3 Dynamic Gait Index (0-24)</strong></td>
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<tr>
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</tr>
<tr>
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<td>11 5</td>
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<td>1.51 0.5</td>
<td>15 6</td>
<td>0.9 1.7</td>
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<tr>
<td></td>
<td>Mean SD</td>
<td>Total</td>
<td>Mean SD</td>
</tr>
<tr>
<td><strong>3.1.4 Falls Efficiency scale (1-10)</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Cakt et al. 2010 (30) E1</td>
<td>2.1 1.4</td>
<td>14 6</td>
<td>0.2 1.7</td>
</tr>
<tr>
<td>Cakt et al. 2010 (30) E2</td>
<td>0.1 1.4</td>
<td>11 5</td>
<td>0.2 1.7</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>1.13 0.5</td>
<td>15 6</td>
<td>0.5 1.7</td>
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<tr>
<td><strong>Total (95% CI)</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>1.13 0.5</td>
<td>15 6</td>
<td>0.5 1.7</td>
</tr>
</tbody>
</table>

Test for overall effect: Z = 1.25 (P = 0.21); I² = 55.6%

Test for subgroup differences: Chi² = 4.63, df = 3 (P = 0.11); P = 0.80

Heterogeneity: Not applicable

**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.
Effects of PT on balance in MS

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.

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. However, a significant effect on FR (ES 0.56; 95% CI, 0.02–1.11) was found.

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. 3B).

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.

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. 3B).

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) Armuth 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.

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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) classes 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 is 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.
The evidence assembled here suggests that there is a need for relevant methodological aspects, e.g. inclusion and exclusion criteria, 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.

**ACKNOWLEDGEMENTS**

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