

# Therapeutic Role of Exercise in Multiple Sclerosis: A Narrative Review on Fatigue, Strength, and Quality of Life

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## ABSTRACT

**Background:** Multiple sclerosis (MS) is a chronic autoimmune disease of the central nervous system that leads to a great deterioration in the quality of life. Exercise studies including only fatigued persons with multiple sclerosis (PwMS) with fatigue as primary endpoint are lacking. Studies like High-intensity resistance training, powerball® system on muscle fatigue, Transcranial Direct Current Stimulation and Exercise on Fatigue, agility-based exercise training may help address these challenges.

**Objective:** To review and synthesize evidence from 2021–2025 on physiotherapy-based interventions for managing fatigue in individuals with multiple sclerosis (MS), with a focus on the effectiveness, safety, feasibility, functional outcomes, and adherence to various exercise and rehabilitation approaches.

**Methods:** A narrative review was conducted following systematic search principles across PubMed, PEDro, Web of Science, and Scopus for studies published from 2021 to 2025. Studies were included if they investigated physiotherapy-based interventions targeting fatigue management in individuals with multiple sclerosis (MS), including randomized controlled trials (RCTs), feasibility studies, and pilot studies. Eligible interventions included physiotherapist-supervised exercise programs such as endurance training, resistance training, and other rehabilitation approaches aimed at reducing fatigue. Methodological quality of the included studies was assessed using an appropriate critical appraisal tool. A total of relevant studies meeting the inclusion criteria were reviewed and synthesized for analysis.

**Results:** All studies reported significant improvements following exercise-based interventions in individuals with multiple sclerosis. Blood flow restriction and combined training improved muscle strength, fatigue, physical activity, and quality of life. Multimodal agility training showed physical and psychological benefits without increased fatigue. tDCS combined with exercise enhanced quality of life and reduced fatigue in over half of participants. Powerball® training improved upper limb coordination and dexterity. High-intensity resistance training significantly reduced fatigue and improved psychological outcomes compared to controls.

**Conclusion:** Exercise interventions are effective in improving strength, reducing fatigue, and enhancing quality of life in people with multiple sclerosis. Combined and high-intensity training, as well as adjunct therapies like tDCS, show beneficial effects and can be considered safe and effective rehabilitation strategies.

**Keywords:** Multiple Sclerosis ; Physiotherapy ; Fatigue ; High-Intensity

## INTRODUCTION

Multiple sclerosis (MS) is a leading contributor to neurological impairment and reduced ability to work among individuals in early and mid-adulthood. While people living with MS experience a broad range of symptoms that vary in type and intensity, fatigue is consistently identified as one of the most common and debilitating challenges. [1] In numerous countries, multiple sclerosis (MS) is the primary cause of non-trauma-related neurological conditions in young adults.[2] Fatigue may be described as a personal feeling of diminished energy and overwhelming tiredness.[3] In contrast, fatigability describes observable and measurable declines in performance, such as reduced ability during activities like walking.[4][5]

The clinical features of MS are thoroughly established and encompass impairments affecting the sensory, motor, cerebellar, and visual systems. These symptoms differ among individuals, depending on the size, location, and progression of lesions, as well as periods of disease relapse.[6] Fatigue can be characterized as a personal sense of depleted physical and/or mental energy that interferes with everyday activities. It affects roughly two-thirds of individuals living with MS.[7] Individuals with MS who had an Expanded Disability Status Scale (EDSS) score below 6 demonstrated reduced maximum grip strength and greater fatigue during sustained contractions compared to healthy individuals.[8]

Resistance training has also been shown to help decrease muscle weakness.[9] The body of research supporting physical exercise as a treatment for inflammatory diseases is increasing, both in terms of its positive clinical outcomes and its underlying mechanisms of action.[9] Another supportive treatment for MS symptoms is transcranial direct current stimulation (tDCS). Applying anodal tDCS can enhance cortical excitability and also influence neurotransmission in glial cells, along with altering cerebral microvascular activity and inflammatory responses.[10] Reduced muscle strength and impaired hand dexterity in the upper limbs are directly linked to difficulties in activities of daily living (ADLs), which strongly influence independence and quality of life in individuals with MS.[11] The Fatigue Severity Scale (FSS) is a self-reported questionnaire used to evaluate how strongly fatigue affects a patient's daily activities and it includes 9 items scored from 1 to 7 giving a total score range from 9 to 63 where higher scores reflect a greater impact of fatigue on the individual's life.[12] The kind of exercise has been identified as one of the key factors that encourage adherence and participation, and it needs to be aligned with an individual's abilities and personal preferences.[13]

Blood flow restriction (BFR) training has recently gained attention as a promising alternative approach, in which external pressure is applied to the limbs to limit venous return while performing low-load resistance exercises at about 20–30% of one-repetition maximum (1RM).[14] It promotes increases in muscle size and strength comparable to those achieved with high-load training, while placing lower mechanical and cardiovascular demands on the body.[15] BFR training has demonstrated positive effects in enhancing muscle strength and functional ability in healthy adults, older populations, and individuals with neurological

conditions.[16][17] Endurance training is also a suitable non-pharmacological approach for individuals with MS, and growing evidence shows that it can lead to improvements in aerobic fitness.[18]

## METHODOLOGY

A systematic search was conducted across PubMed, PEDro, Web of Science, and Scopus for studies published between January 2017 and June 2025. The search terms and Boolean operators included combinations of “multiple sclerosis,” “MS,” “fatigue,” “physiotherapy,” “exercise therapy,” “endurance training,” “resistance training,” “rehabilitation,” and “physical activity.” Filters were applied to include peer-reviewed articles published in English involving human participants.

**Inclusion and Exclusion Criteria** Inclusion criteria comprised randomized controlled trials (RCTs), feasibility studies, and pilot studies investigating physiotherapy-led or supervised interventions for fatigue management in individuals with multiple sclerosis. Studies were required to include a minimum intervention duration of 2 weeks, report fatigue-related outcomes using validated assessment tools, and provide information on functional, physical, or quality-of-life measures along with safety or adverse event reporting.

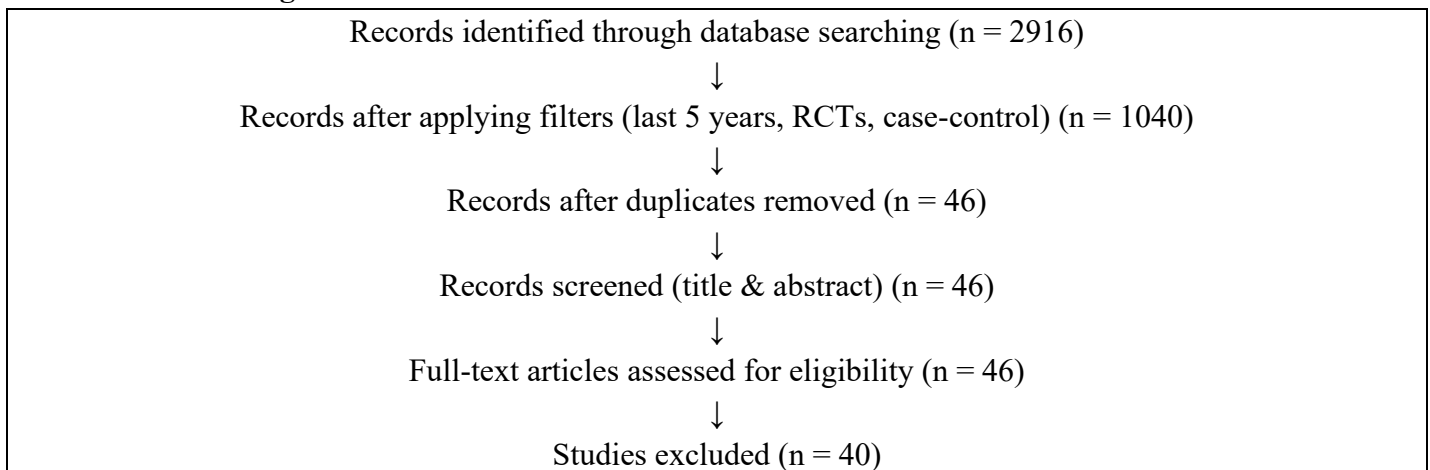
Exclusion criteria included studies without physiotherapy or exercise-based interventions, pharmacological or surgical treatments, review articles, case reports, conference abstracts without full text availability, and non-English publications.

### Study Selection and Screening

The initial search identified 2916 records related to multiple sclerosis and fatigue management. After applying preliminary filters focusing on fatigue-specific physiotherapy interventions, study designs such as randomized controlled trials (RCTs) and case-control studies were prioritized. Further refinement limited the selection to studies published within the last 5 years, resulting in 1040 articles.

Following removal of duplicates, a total of 46 unique articles were retained for screening. Titles and abstracts were reviewed for relevance to physiotherapy-based fatigue management in MS. From these, full-text assessment was conducted, and studies not meeting inclusion criteria such as lack of physiotherapy intervention, irrelevant outcomes, or inappropriate study design were excluded. Finally, 6 studies met all eligibility criteria and were included in the review for detailed analysis and synthesis.

### PRISMA Flow Diagram



- Not physiotherapy-based intervention
  - Irrelevant outcomes
  - Inappropriate study design



Studies included in qualitative synthesis (n = 6)

**MAIN FINDINGS :**

Article	Design	Participants	Intervention	Outcome Measures	Key Results
Blood flow restriction training improves strength, fatigue, and function in middle-aged adults with multiple sclerosis: A randomized controlled trial	Randomized Controlled Trial	65 adults (40–65 yrs) with MS (EDSS <7)	Low-load Blood Flow Restriction (BFR) training, 2x/week for 12 weeks	MSIS-29, 1RM, handgrip, STS-30, FSS, IPAQ, NHPT	Significant improvements in strength, fatigue, physical activity, dexterity; no adverse events
Effects of Combined Endurance and Resistance Training in Women With Multiple Sclerosis: A Randomized Controlled Study	Randomized Controlled Study	27 women with MS	Combined endurance + resistance training (12 weeks) + 12-week detraining	MVIC, 1RM, fatigue, depression, QoL	Improved strength, fatigue, depression, QoL; benefits sustained after detraining
Experiences of fatigued persons with multiple sclerosis with multimodal	Qualitative study within feasibility RCT	22 participants; 12 interviewed	Multimodal agility training vs standard exercise during rehab (4–6 weeks)	Interview themes (facilitators, barriers, benefits)	Improved balance, psychological benefits; barriers included pressure

agility- based exercise training and the ReFEx study protocol: a qualitative extension of a feasibility study					& fatigue perception
Influence of Transcranial Direct Current Stimulation and Exercise on Fatigue and Quality of Life in Multiple Sclerosis	Experimental study	12 MS patients	tDCS + exercise over 4 weeks	QoL, fatigue (MFIS)	Significant QoL improvements; >50% showed reduced fatigue
Effects of the powerball® system on muscle strength, coordination, fatigue, functionality and quality of life in people with multiple sclerosis. A randomized clinical trial	Double-blind RCT	25 participants	Powerball® upper limb training + conventional therapy	Grip strength, BBT, NHPT, FSS, MSIS-29	Improved coordination and dexterity; high satisfaction scores
High-intensity resistance training in people with multiple sclerosis experiencing fatigue: A	Randomized Controlled Trial	71 PwMS + 69 controls	High-intensity resistance training (1x or 2x/week for 12 weeks)	FSMC, HADS, MSIS-29	Reduced fatigue significantly; greater psychological benefits with 2x/week training

randomised controlled trial					
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## Results

Across the six studies, various exercise-based and adjunct interventions demonstrated significant positive outcomes in individuals with multiple sclerosis (MS), particularly in relation to fatigue, muscle strength, functional ability, and quality of life.

Blood flow restriction (BFR) training showed statistically significant improvements in muscle strength, fatigue reduction, physical activity levels, and manual dexterity compared to usual care, with moderate to large effect sizes and no reported adverse events.

Similarly, combined endurance and resistance training resulted in significant enhancements in muscular strength (MVIC and 1RM), fatigue, depression, and both physical and mental components of quality of life. Notably, these improvements were sustained even after a 12-week detraining period, indicating lasting benefits.

Findings from the qualitative study on multimodal agility-based training (MAT) revealed both physical and psychological benefits, particularly improved balance and engagement. Participants highlighted facilitators such as variety and group interaction, while barriers included perceived exertion and group pressure. Importantly, no accumulation of fatigue was reported during the intervention.

Interventions involving transcranial direct current stimulation (tDCS) combined with exercise demonstrated significant improvements in quality of life domains, including activities of daily living and psychological well-being. Additionally, more than half of the participants experienced reduced fatigue scores following combined therapy.

Upper limb training using the Powerball® system resulted in significant improvements in coordination and manual dexterity, particularly in the more affected limb. High participant satisfaction further supported the feasibility and acceptability of this intervention.

High-intensity resistance training (HIRT) significantly reduced fatigue levels compared to non-intervention controls, with associated improvements in psychological outcomes such as anxiety and MS-related impact. Training frequency (once vs. twice weekly) showed comparable results overall, although slightly greater psychological benefits were observed with higher frequency training.

## Conclusion

Collectively, the evidence indicates that structured exercise interventions—including resistance training, combined aerobic programs, BFR training, and task-specific upper limb exercises—are effective in improving physical and psychological outcomes in individuals with multiple sclerosis.

These interventions consistently demonstrated reductions in fatigue, improvements in muscle strength and functional performance, and enhanced quality of life. Importantly, some benefits were sustained over time, even after cessation of training, highlighting the long-term value of exercise in MS management.

Adjunct therapies such as transcranial direct current stimulation may further enhance outcomes when combined with exercise. Additionally, patient-centered approaches that incorporate variety, engagement, and individualized intensity appear to improve adherence and perceived benefits.

Overall, exercise-based rehabilitation can be considered a safe, feasible, and effective non-pharmacological strategy for managing symptoms and improving overall well-being in people with multiple sclerosis.

## Discussion

The present review highlights the effectiveness of various exercise-based interventions in improving physical and psychological outcomes in individuals with multiple sclerosis (MS). Across all included studies, consistent improvements were observed in fatigue, muscle strength, functional performance, and quality of life, reinforcing the growing evidence supporting exercise as a key component in MS rehabilitation.

Blood flow restriction (BFR) training demonstrated significant improvements in strength, fatigue, and functional outcomes, even with low-load resistance, suggesting it as a viable alternative for individuals with limited exercise tolerance [19]. Similarly, combined endurance and resistance training showed sustained benefits in strength, fatigue, depression, and quality of life, even after a detraining period, indicating long-term physiological and psychological adaptations [20].

The qualitative findings from multimodal agility training (MAT) provided valuable insight into patient experiences, highlighting that variety, engagement, and group-based settings enhance motivation and adherence, although perceived exertion and group pressure may act as barriers [21]. These findings emphasize the importance of patient-centered program design in rehabilitation.

Adjunct interventions such as transcranial direct current stimulation (tDCS), when combined with exercise, further improved quality of life and reduced fatigue, suggesting a synergistic effect between neuromodulation and physical activity [22]. In addition, task-specific upper limb training using the Powerball® system significantly improved coordination and manual dexterity, supporting the role of targeted functional training in MS [23].

High-intensity resistance training (HIRT) was also found to significantly reduce fatigue and improve psychological outcomes compared to non-intervention controls, with similar benefits observed across different training frequencies [24]. This supports the feasibility and safety of higher-intensity protocols in individuals experiencing fatigue.

From a physiological perspective, these improvements may be attributed to enhanced neuromuscular efficiency, increased muscle fiber recruitment, and improved cardiovascular capacity. Exercise may also promote neuroplasticity, reduce inflammation, and enhance central nervous system functioning, all of which are particularly relevant in a neurodegenerative condition such as MS. Additionally, reductions in fatigue may be linked to improved energy metabolism and psychological well-being.

Another important aspect highlighted by the included studies is the role of exercise in addressing both physical and psychological domains simultaneously. Improvements in depression, anxiety, and overall quality of life suggest that exercise interventions extend beyond physical rehabilitation and contribute significantly to mental health. This is particularly important in MS, where fatigue and psychological distress are closely interrelated.

Despite the positive findings, certain limitations must be considered. The sample sizes in some studies were relatively small, which may limit generalizability. Variability in intervention protocols, duration, and outcome measures also makes direct comparison between studies challenging. Additionally, long-term follow-up data

are limited, and more research is needed to determine the sustainability of these benefits over extended periods.

Future research should focus on larger randomized controlled trials with standardized protocols to strengthen the evidence base. There is also a need to explore individualized exercise prescriptions based on disease severity, fatigue levels, and patient preferences. Furthermore, combining exercise with emerging therapies such as neuromodulation may provide more comprehensive and effective rehabilitation strategies.

Overall, these findings align with existing literature suggesting that structured and individualized exercise programs are effective, safe, and beneficial in managing MS-related symptoms. The inclusion of both physical and psychosocial outcomes across studies strengthens the evidence for a holistic rehabilitation approach.

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