

# An Overview of the Rehabilitation Strategies for Improving Balance in Multiple Sclerosis

Alqasem Sultan Ahmed Althagafi<sup>1</sup>, Ali Ibrahim Alfaqeh<sup>1</sup>, Muhannad Alawi Alqhtani<sup>1</sup>, Riyadh Abdullah Almobarki<sup>2</sup>, Shamsia Obaid Aljaddani<sup>3</sup>, Faten Mohammed Ismail<sup>4</sup>, Samar Mohammad Hassan Ghonaim<sup>5</sup>, Salwa Mohammad Hassan Ghonaim<sup>5</sup>, Nesreen Fahad Abdulaziz Janbi<sup>5</sup>

1. Physiotherapist At Khulais General Hospital
2. Physiotherapy Technician At Khulais General Hospital
3. Physical Therapy Technician At Eradah & Mental Health Complex
4. Physio Therapist At King Fahad General Hospital
5. Physiotherapy Technician At King Fahad General Hospital

## ABSTRACT

Individuals with multiple sclerosis (MS) frequently encounter balance difficulties during physical activity. Multiple sclerosis is a gradually progressive condition; immunosuppressants and other medications may postpone its advancement, yet most patients will experience varying degrees of neurological deficits, including muscle weakness, muscle spasms, ataxia, sensory impairments, dysphagia, cognitive dysfunction, and psychological disorders. The aim of this review was to address the variable rehabilitation strategies for improving balance in multiple sclerosis. Professional rehabilitation treatment can mitigate functional impairments in multiple sclerosis patients from the initial phase of the disease through its course, enhance neurological function, and alleviate familial and societal obligations. The advancement of diverse rehabilitation technologies, including transcranial magnetic stimulation, virtual reality, robot-assisted gait, telerehabilitation, and transcranial direct current stimulation, has further solidified the benefits of rehabilitation therapy in multiple sclerosis treatment, offering additional therapeutic options for patients.

**KEYWORDS:** multiple sclerosis, immunosuppressants, rehabilitation strategies.

## 1. Introduction

Multiple sclerosis (MS) is an autoimmune inflammatory demyelinating disorder, recognized as a primary contributor to chronic neurological impairment. Statistics indicate that over 2.5 million individuals globally are afflicted with multiple sclerosis, the majority of them are aged between 18 and 50 years. The prevalence of female patients exceeds that of male patients. The predominant form in the clinical categorization of multiple sclerosis is relapsing-remitting. Some patients may transition to secondary progressive multiple sclerosis, while 15% exhibit continuous progressive impairment from onset, indicative of primary progressive multiple

sclerosis [2]. Classic multiple sclerosis is prevalent in European and American populations, whereas the majority in China exhibit relapsing optic neuromyelitis. Multiple sclerosis is marked by recurrent episodes that lead to the progressive accumulation of neurological deficits, resulting in persistent nerve dysfunctions such as muscle weakness, spasms, tremors, ataxia, fatigue, sensory impairments, bowel dysfunction, sexual dysfunction, pain, dysarthria, dysphagia, cognitive deficits, and psychological disorders, ultimately culminating in a gradual decline in daily living capabilities. It has significantly impacted the health and social engagements of patients [3,4]. Rehabilitation constitutes a component of multiple sclerosis treatment and has demonstrated advantageous results in many studies. Although conventional rehabilitation methods continue to be prominent, innovative technologies are enhancing the management of disabling symptoms. Balance rehabilitation proved to be an effective method for decreasing fall incidence and enhancing balance abilities in individuals with multiple sclerosis. Exercises in various sensory settings may enhance dynamic balance [5].

Equilibrium disorders and falls Emphasized the significance of balance rehabilitation, the establishment of intervention parameters, disability, and treatment type, which can influence the outcomes of balance rehabilitation; however, treatment methodologies and intervention dosage are two critical aspects. In recent decades, numerous rehabilitation strategies have been devised to enhance balance in multiple sclerosis (MS) [6]. Despite the efficacy of various rehabilitation methods, it is crucial to comprehend the extent of mobility and balance enhancement achieved by an increased therapeutic dosage. Determining the appropriate dosage of a specific therapeutic intervention is essential for the use of evidence-based treatment and for enhancing the efficacy of interventions. The difficulty in determining the optimal dosage for rehabilitation arises from the ambiguity around the active components, their targets, and methods of action, which hinders the formulation of theoretical models for rehabilitation [7].

## **2. Review:**

Disease modification therapy, disease recurrence control, and symptomatic treatment are among the treatment methods for multiple sclerosis [8]. Research has demonstrated that cannabinoid drugs can alleviate muscle spasms, tremors, pain, and other symptoms associated with multiple sclerosis (MS). Additionally, they play a neuroprotective function by inhibiting neurotoxicity and regulating the immune system. Currently, there is no effective medication treatment that can completely halt the progression and cure the disease in MS patients, despite the fact that immunosuppressants can delay the progression and deterioration of the disease [9]. The most recent research has demonstrated that rehabilitation treatment can enhance the functional status of patients and decrease their disability level, making it a critical treatment method for enhancing the ability to perform daily activities. In recent years, rehabilitation therapy has emerged as a prominent area of international medical research and has garnered increasing attention from developing countries as a critical treatment for multiple sclerosis. The rehabilitation treatment for MS patients has become increasingly modern and diversified as a result of the rapid

development of technologies such as transcranial magnetic stimulation (TMS), virtual reality (VR), robot-assisted gait training (RAGT), telerehabilitation (TR), and transcranial direct current stimulation (tDCS). This has further established the status and benefits of rehabilitation medicine in MS treatment, and has significantly improved the treatment effect of MS patients [10].

Axons are relatively preserved, while focal demyelination, inflammatory reaction, and gliosis are the fundamental pathological characteristics of MS. Presently, the precise pathogenesis remains unclear. In their opinion, Paintlia et al. believed that certain factors activated the peripheral immune system, which was mediated by T cells and B cells. This process resulted in the release of a significant number of inflammatory factors, which then attacked the blood-brain barrier (BBB) and infiltrated the central nervous system (CNS) [11]. Yeung et al. postulated that the proliferation of glial cells and the secretion of inflammatory factors to attack foreign bodies were the result of changes in the inflammatory microenvironment of the central nervous system (CNS). The oligodendrocyte (OL) was damaged by the excessive secretion of inflammatory factors, which led to necrosis and apoptosis, which was subsequently followed by myelin shedding [12]. Kasper et al. hypothesized that the immune system is a significant factor in the pathogenesis of MS, which is characterized by the involvement of white and gray matter in the spinal cord and central nervous system. The primary pathological changes include the activation of T cells and B cells, the secretion of a variety of inflammatory factors, migration to the central nervous system (CNS), which leads to inflammatory infiltration of tissues, apoptosis and necrosis of OL, and hyperplasia of MG and AST. Consequently, demyelination occurs, which ultimately results in neurodegeneration and the subsequent loss of neuronal function [13]. In addition, Nishino et al. proposed that inflammatory factors and myelin fragments induced MG polarization to M1 type, which in turn stimulated AST activation and the secretion of inflammatory cytokines and chemokines. The inflammatory factors secreted by MG and AST can exacerbate demyelination and further exacerbate the severity of MS [14]. Sparaco et al. hypothesized that the presence of high levels of estrogen may provide protection to women with multiple sclerosis. This was based on their discovery that the severity of the disease was considerably diminished in women with multiple sclerosis at the conclusion of pregnancy [15].

Recent research has demonstrated that the pathogenesis of MS is complex and may be influenced by a variety of factors, including the interaction between glial cells, immune factors, and environmental and nutritional factors [14,15]. They are of the opinion that the primary mechanism may be that certain predisposing factors act on patients with genetic susceptibility in a specific environment, resulting in an abnormal autoimmune response and the development of MS. The pathogenesis of MS is fundamentally linked by the immune mechanism, which encompasses cellular immunity, humoral immunity, and other components.

Ultimately, rehabilitation therapy delays the progression of the disease, protects the central nervous system, slows neurodegeneration, induces neuroplasticity, and reduces inflammatory cytokines in the peripheral immune system [15]. White et al. conducted a study that demonstrated a decrease in the levels of inflammatory mediators, including interleukin-4, interleukin-10, and C-reactive protein, in patients

following rehabilitation training. This reduction in inflammatory mediators may mitigate the inflammatory response of multiple sclerosis [16]. Patients in the rehabilitation training group exhibited substantially higher levels of neurotrophic factors and growth factors than those in the control group, as determined by Hotting et al. [17]. Furthermore, rehabilitation training can alleviate symptoms such as fatigue and paralysis in MS patients by altering their pathophysiological processes. Rehabilitation treatment is predicated on rehabilitation evaluation. Rehabilitation assessment enables us to gain a comprehensive understanding of the dysfunction of MS patients, which can serve as a foundation for the development and modification of rehabilitation treatment plans [17].

The complexity of the rehabilitation evaluation content is determined by the multi-system disease characteristics of MS, which result in a variety of functional disorders in patients, including limb movement disorders, sensory disorders, cognitive function changes, speech and swallowing disorders, bowel and stool dysfunction, ataxia, walking instability, and other symptoms. Consequently, the focus of the evaluation is the dysfunction of function and living ability. The Disability Status Scale (DSS) was initially devised by Kurtzke in 1955 on a 10-point scale, with 0 representing regular and 10 representing death. However, the scale is unable to differentiate between minor changes in disease severity [18]. Kurtzke devised the Extended Disability Status Scale (EDSS) in the 1980s and 1990s, which was based on the DSS and was used to evaluate MS dysfunction in detail [19].

The living ability was typically evaluated using the Activities of Daily Living (ADL), Operational Activities of Daily Living (IADL), and Multiple Sclerosis Quality of Life (MSQOL). In addition to the 36-item Short Form Health Survey (SF-36), the MSQOL is a modular and specific assessment scale that includes nine specific clinical symptom assessments: fatigue, pain, bladder function, gastrointestinal function, mood, perception and cognitive function, visual function, sexual satisfaction, and social relationships. The 6-minute walk test (6MWT) is frequently employed to assess motor function, while the fatigue severity Score (FSS) is frequently employed to assess fatigue. The Fatigue Scale-14 (FS-14) is a tool that assesses the severity of fatigue symptoms in MS and evaluates clinical efficacy. It comprises 14 items, each of which is a fatigue-related issue [19].

The social disability of MS can be assessed using the Environmental Status Scale (ESS) and the Socioeconomic Status Scale (SES). A comprehensive cognitive function screening scale and memory function assessment can be used to evaluate cognitive impairment. The MS Screening Examination for Cognitive Impairment (SEFCI) and the Mini-mental State Examination (MMSE) were among the comprehensive cognitive function screening instruments. Memory function was evaluated using the Wechsler Memory Scale (WMS-R) and the Rey Auditory Verbal Learning Test (AVLT). The evaluation of motor functions, including muscle strength, muscle tone, range of motion, limb coordination, balance, and walking ability, is also possible. Additionally, the patient's sensory, speech, and digestive functions must be assessed [19].

Complex and varied dysfunction is a hallmark of multiple sclerosis. The objective of its rehabilitation treatment is to enhance the quality of life and preserve and enhance

its functionality. Rehabilitation treatment principles should be tailored to the individual and should differ from one to another. Sports training, sensory training, psychological rehabilitation, cystorectal (second bowel) function training, speech and swallowing training, cognitive function, rehabilitation education, and more comprise the content of rehabilitation treatment. Exercise therapy, occupational therapy, muscle strength exercise, application of assistive devices, physical factor therapy, percutaneous nerve stimulation, vibration therapy, acupuncture, and psychological intervention are among the specific measures that may be implemented [17,19].

In order to achieve the objective of targeted treatment, transcranial magnetic stimulation (TMS) induces axon depolarization, which increases the excitability of the corticospinal system, stimulates the plasticity of neurons, improves the responsiveness of the nervous system, and enhances the ability of synaptic transmission. rTMS exhibits excellent tolerance, high temporal and spatial resolution, and virtually no side effects.

The impact of TMS or intermittent Theta explosive magnetic stimulation (iTBS) on patients with secondary spasms of multiple sclerosis was assessed by Korzhova et al. The modified Ashworth scale (MAS) scores of patients in both the TMS and iTBS groups were substantially enhanced at the conclusion of the treatment. However, the sham stimulation control group did not experience any significant improvement [20]. Gaede et al. recruited 33 MS patients who were randomly assigned to receive high-frequency stimulation of the prefrontal cortex (PFC), the primary motor cortex (M1), or false stimulation. A follow-up evaluation of the fatigue severity scale (FSS) was conducted six weeks later. The fatigue relief rate of the PFC group and M1 group was greater than that of the false stimulation group, and no apparent adverse reaction was observed [21]. Hulst conducted a study on the impact of TMS on the cognitive function of MS patients. He discovered that the frontal lobe was activated in the MS patients who were treated with TMS, and the accuracy of task-oriented training was also enhanced, resulting in a partial improvement in the cognitive function of MS patients [22]. Centonze et al. administered TMS to 10 MS patients. Of these patients, 6 exhibited decreased detrusor activity, 3 exhibited excessive detrusor activity, and 9 exhibited improved urination symptoms. However, there was no improvement in urinary storage function [23].

In terms of non-invasive brain stimulation technologies, TMS is among the most advanced. It has advantages that other treatment methods do not possess, including the ability to directly regulate the central nervous system. Nevertheless, additional multicenter and large-sample studies are required to ascertain the most effective treatment strategy for TMS stimulation parameters, such as frequency, intensity, stimulation mode, location, and treatment frequency [23].

Virtual reality (VR) technology stimulates the brain through high-intensity, multi-sensory, repetitive, task-oriented strong feedback, and intervenes in motor, cognitive, and sensory functions. This allows patients to fully immerse themselves in the virtual environment and achieve the optimal effect of rehabilitation training. The activation of the mirror neuron system in MS patients can be facilitated by rehabilitation training using VR technology, which can lead to cortical and subcortical alterations

in the brain. Additionally, it can stimulate the reorganization and remyelination of the brain's motor regions. The balance, movement, and cognitive function of MS patients are enhanced by rehabilitation training conducted in VR technology, which has been shown to stimulate synaptic reorganization and remyelination in brain motor regions [24].

Multiple sclerosis can result in significant impairment. VR technology is employed to conduct rehabilitation training in order to enhance the cognitive function, movement, and equilibrium of patients with multiple sclerosis. Munari et al. divided MS patients into two groups: the VR combined with robot training group and the robot training group. The BBS score of the VR combined with robot training group was substantially higher than that of the robot training group ( $P < 0.05$ ) after 6 weeks of rehabilitation training [25]. Nevertheless, Casuso-Holgado et al. conducted a review of the VR balance function rehabilitation training of MS patients and incorporated five studies that utilized BBS as a measuring instrument. The results indicated that the balance function enhancement effect did not differ statistically significantly between the VR group and the conventional training group ( $P > 0.05$ ) [26].

Transcranial direct current stimulation (tDCS) is a non-invasive nerve regulation technique. To accomplish the objective of neural regulation, this technology transmits a weak direct current to the surface of the cerebral cortex through a minimum of two electrodes. In comparison to other neural control methods, tDCS possesses a certain level of portability, safety, and user-friendliness [25,26].

tDCS has been extensively employed in recent years as a means of regulating cognitive function, enhancing mental disorders, and treating neurological disorders. Nevertheless, the mechanism of tDCS on MS is currently unclear, and it is primarily employed to alleviate the symptoms of MS.

In a randomized, double-blind experiment, Mori et al. divided MS patients into two groups. False stimulation was administered to one group, while the other group received anode-tDCS for five consecutive days. The research findings indicated that the quality of life and pain of patients subjected to anode-stimulation were considerably enhanced, and no instances of anxiety or depression were identified. This demonstrates that anode tDCS can alleviate the chronic central pain of MS patients, and the action time can attain an optimal effect. While the mechanism of anode tDCS in the treatment of MS disease remains obscure, it is probable that it is closely associated with the remodeling of brain nerve function [27]. Workman et al. assessed the impact of transcranial direct current stimulation (tDCS) on melancholy, fatigue, and pain in patients with multiple sclerosis. In this randomized, double-blind, pseudo-control study, women with multiple sclerosis who were moderately disabled were enrolled. The patients were randomly assigned to either pseudo-tDCS stimulation or tDCS stimulation. The knee extensor fatigue, fatigue, and discomfort of patients in the tDCS group decreased after five days of treatment; however, the depression score did not undergo a substantial change [28].

### 3. Conclusion:

MS patients are susceptible to relapse and exhibit numerous clinical manifestations and associated complications. There are numerous clinical and rehabilitation issues that necessitate additional research, including bladder rectal dysfunction, pain, and autonomic dysfunction. Rehabilitation therapy has become an essential treatment method for MS as a result of the development of a variety of novel rehabilitation technologies, including TMS, VR, RAGT, TR, and tDCS. Nevertheless, in certain developing countries, it is imperative to employ advanced rehabilitation treatment technologies to the treatment of MS patients and to learn from the experience of developed countries. The treatment of MS will be enhanced by the application of more sophisticated rehabilitation treatment methods in the future, as relevant research continues to be deepened. Evidence regarding the efficacy of balance interventions in enhancing mobility. Furthermore, based on the principles of neurological rehabilitation, interventions that are task-specific and of high intensity are associated with superior treatment outcomes.

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