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Review Paper – Derleme Makalesi

COGNITIVE FUNCTIONS, POSTURAL CONTROL AND GAIT IN MULTIPLE SCLEROSIS: REVIEW

MULTİPL SKLEROZ'DA BİLİŞSEL FONKSİYONLAR, POSTÜRAL KONTROL VE YÜRÜYÜŞ: DERLEME

Hatice AYAN[1]

Özet

Multipl Skleroz (MS)'de bilişsel bozukluk, postüral kontrol güçlükleri ve yürüme bozuklukları yaşam kalitesini ve günlük işlevselliği derinden etkileyen yaygın belirtilerdir. Postüral kontrolün sağlanması için duyusal, motor ve bilişsel sistemlerin entegrasyonu gereklidir. Artan kanıtlar, postüral kontrolün dikkat kaynaklarını tükettiğini göstermektedir. Merkezi motor, duyusal ve bilişsel bozukluklar, postüral kontrolün planlanmasını ve sürdürülmesini etkileyebilir ve yürüme sırasında problem çözme yeteneklerini azaltabilir. Bu durum, postüral kontrol bozukluğu nedeniyle daha yavaş yürüme hızı, kısalmış tek destek süresi ve gecikmiş salınım fazı ile sonuçlanabilir. Ancak, MS'de bilişsel yükün postüral kontrol ve yürüyüş üzerindeki etkileri hakkında çok az bilgi bulunmaktadır. Bu çalışma, biliş ve postüral kontrol arasındaki ilişkiyi anlamayı ve bunların MS'in etkili yönetimindeki önemini açıklamayı amaçlamaktadır. MS'de biliş ve denge üzerine gelecekte yapılacak araştırmalar, longitudinal çalışmalara öncelik vermeli, hedefe yönelik müdahaleler geliştirmeli ve ileri nörogörüntüleme tekniklerini kullanmalıdır. Bu yaklaşımlar, hastalığın ilerleyişinin daha iyi anlaşılmasına, daha etkili tedavilerin geliştirilmesine ve rehabilitasyon sonuçlarının izlenmesinin iyileştirilmesine katkı sağlayacaktır.

Anahtar Kelimeler: Multipl Skleroz, Biliş, Postüral Kontrol, Yürüyüş, Bilgi İşlemleme Hızı

Abstract

Cognitive impairment, postural control difficulties, and gait disturbances are common manifestations of Multiple Sclerosis (MS) that profoundly affect the quality of life and daily functioning. The integration of sensory, motor, and cognitive systems is necessary to ensure postural control. Increasing evidence suggests that postural control consumes attention. Central motor, sensory, and cognitive disorders can affect the planning and preservation of postural control and reduce problem-solving abilities during walking. This can result in a slower gait, shortened single support time, and delayed swing phase because of postural control impairment. However, little is known about the effects of cognitive burden on postural control and gait in MS. This study aimed to understand the relationship between cognition and postural control and to explain their importance in the effective management of MS. Future research on cognition and balance in MS should prioritize longitudinal studies, develop targeted interventions, and utilize advanced neuroimaging techniques. These approaches will contribute to a better understanding of disease progression, the development of more effective treatments, and improved monitoring of rehabilitation outcomes in patients with MS.

Keywords: Multiple Sclerosis, Cognition, Postural Control, Gait, Information Processing Speed.

Geliş Tarihi (Received Date): 21.08.2025, Kabul Tarihi (Accepted Date): 31.12.2025, Basım Tarihi (Published Date): 31.12.2025. [1] Izmir Katip Çelebi University, Vocational School of Health Services', Physiotherapy Programme, Izmir, Türkiye. **E-mail:** hatice_010188@hotmail.com **ORCID ID's:** H.A.; https:/orcid.org/0000-0002-6641-3540.

1. INTRODUCTION

Multiple sclerosis (MS) is an autoimmune disease of the central nervous system (CNS) that is characterized by demyelination, and neurodegeneration. It results from complex interactions between genetic predisposition and environmental factors, leading to a range of physical, mental, and psychiatric symptoms (1).

Neuropsychological studies have shown that the rate of cognitive impairment in people with multiple sclerosis (pwMS) is between 43-63% (2). PwMS generally have problems with attention, visual-spatial perception, information processing speed, and working memory. Language, speech, and intellectual abilities are often protected (3). Magnetic resonance imaging studies have shown that cognitive impairment is more correlated with cortical atrophy than with lesion loadc The main loss in the cognitive area in MS is related to high-level functions, such as the ability to perform multiple tasks. To accomplish these complex functions, excessive mental energy consumes resources, leaving little energy for other daily activities. Therefore, cognitive impairment can disturb various aspects of daily living. Increasing evidence suggests that postural control consumes attention (5).

Evidence suggests that cognitive disfunction is related to poor postural control and mobility impairments in MS. Abnormal postural control increases the risk of falling and negatively affects the quality of life in patients with MS (6). However, the association between specific cognitive domains and postural control in pwMS remains controversial. For instance, a previous study reported a significant relationship between cognition and postural control in pwMS with minimal disability (7), whereas another investigation could not find such a relationship in pwMS with very mild disability (8).

The inconsistent findings regarding the relationship between cognition and postural control in pwMS may be attributed to several methodological and conceptual differences between studies. Variations in disability level, disease duration, and sample characteristics can influence the extent to which cognitive deficits affect balance. Furthermore, variations in the types of cognitive evaluations, assessments of postural control (whether involving static or dynamic tasks), and use of dual-task paradigms might explain the differing outcomes. Additionally, smaller sample sizes and variations in statistical power may further obscure genuine correlations (5). Clinically, these inconsistencies underscore the importance of personalized assessments and the inclusion of cognitive screening, especially focusing on attention and executive function, when assessing balance performance in pwMS.

1.1. Neuroimaging

One of the key neuroimaging findings is the presence of focal T2 hyperintense lesions and diffuse white matter damage on MRI scans. These markers are associated with cognitive impairment, although they do not completely explain cognitive dysfunction in patients with MS (9). In addition to white matter damage, atrophy of the corpus callosum and cortical and deep gray matter has been noted. Specifically, severe atrophy of the corpus callosum has been suggested as a morphological marker of severe cognitive impairment (10).

A critical aspect of the neuroimaging findings in MS is damage to the deep gray and diffuse white matter. Significant predictors of cognitive impairment, particularly in chronic MS cases, include deep gray matter shrinkage and widespread white matter deterioration (11). Beyond structural damage, fMRI is increasingly used to study the brain's functional connectivity changes in MS, which have significant implications for understanding cognitive dysfunction. These neuroimaging techniques have been used to understand the balance between damage accrual and the brain's capacity for functional reorganization to mitigate cognitive deficits(12).

Notably, neuroimaging findings highlight the variability in cognitive impairment among patients with MS, suggesting that some individuals display cognitive resilience despite significant radiographic evidence of brain damage. Factors such as brain and cognitive reserves are thought to play protective roles, although these require further investigation (9).

1.2. Cognitive Impairment and Functional Relevance in MS

Cognitive impairment in patients with MS significantly influences treatment decisions and patient management strategies, necessitating a comprehensive approach to care. Cognitive impairment affects up to 65% of patients with MS in all disease phases, impacting their daily functioning and quality of life (13).

People with MS frequently experience difficulties in several cognitive domains, particularly in learning and memory, attention, processing speed, executive abilities, and visuospatial performance. Among these, information processing speed is considered the most widely affected and often the first cognitive deficit to appear in pwMS (14).

Interestingly, cognitive impairment in patients with MS does not necessarily correlate with physical disability, disease duration, or course of the disease (15). This lack of a direct relationship makes it challenging to predict cognitive deficits based on other MS symptoms or disease progression. Moreover, standard assessments of neurological disability frequently lack the sensitivity required to identify cognitive impairment during regular check-ups (16).

The diversity in cognitive profiles observed among individuals with MS may result from multiple influences, such as genetic factors, sex differences, intellectual capacity, coexisting medical conditions, and health-related behaviors (17). Recent research suggests that cortical pathology, including inflammatory focal lesions and atrophy, plays a primary role in determining cognitive disability in patients with MS (18). Early detection and assessment of cognitive impairment are crucial for managing MS and improving the patients' quality of life. Given its prevalence and impact, cognitive assessment should be a routine part of clinical evaluations, with tools such as the Symbol Digit Modalities Test recommended for regular screening (19).

Cognitive impairment in MS is closely associated with a decline in activities of daily living, often leading to difficulties in performing routine tasks and increasing the need for assistance, thereby reducing independence. This decline affects not only basic activities but also more complex tasks such as medication management, financial responsibilities, and meal preparation (20). Cognitive deficits also contribute to employability challenges, as many workplace tasks demand attention, memory, and executive functioning, domains commonly affected in MS, which can result in work disability or necessitate job modifications (17). Moreover, cognitive dysfunction may impair driving ability, posing serious safety concerns due to reduced reaction times and compromised judgment (20). Beyond these functional

consequences, cognitive impairment has a profound impact on quality of life, influencing social interactions, communication, and emotional well-being. The psychological burden of cognitive decline often contributes to mental health problems such as depression and anxiety, further diminishing overall quality of life (21).

The concept of cognitive reserve, defined as the brain's resilience to pathological damage, is particularly relevant in MS; individuals with higher cognitive reserve tend to better withstand the cognitive effects of the disease and maintain daily functionality despite a substantial disease burden. In this context, cognitive rehabilitation emerges as a valuable approach to mitigating the effects of cognitive decline and promoting adaptive functioning in everyday life (22).

Interestingly, although disease-modifying therapies (DMTs) have shown efficacy in reducing MS relapse rates, they have limited effectiveness in treating cognitive dysfunction. This contradiction highlights the need for alternative treatment approaches that specifically target cognitive impairment. Cognitive rehabilitation and exercise training have emerged as promising interventions; however, their integration into clinical practice requires further research (23).

1.3. Postural Control, Motor Planning and Gait in Multiple Sclerosis

Postural control is crucial for maintaining balance and preventing falls in patients with MS. Patients with MS often experience postural control deficits, predisposing them to accidental falls and fall-related injuries, which significantly impact their quality of life and healthcare systems. These impairments are marked by an increase in postural sway when standing still, a reduction in walking speed, and a higher frequency of falls compared to healthy individuals (24).

Motor planning and postural control in MS are often significantly impaired due to complex interactions between cognitive and motor dysfunction. MS affects both upper and lower extremity motor functions, which are strongly influenced by cognitive capacities, particularly processing speed and executive function (17). Patients with MS often demonstrate deficits in the coordination of movement, potentially leading to disruptions in motor planning tasks that require the simultaneous processing of multiple inputs (25). Rehabilitation programs, especially those incorporating virtual reality and telerehabilitation, have shown promise in improving postural control in patients with MS by enhancing sensory integration and motor planning strategies. These programs aim to optimize sensory information processing and improve the anticipatory postural control mechanisms necessary for maintaining balance (26).

Several factors influence postural control in patients with MS. Neuroanatomical correlates suggest a multifactorial etiology, with balance problems associated with the cerebellum, spinal cord, and processing network. Slowed somatosensory conduction and impaired central integration are the primary mechanisms underlying the observed changes in balance and gait (25). Additionally, trunk muscle performance plays a role in postural control, with patients with MS showing worse isometric trunk endurance than healthy controls (24). Objective assessment methods, such as force platforms and computerized dynamic posturography, can detect balance abnormalities even in patients with minimal impairment (27). Understanding these factors is crucial for developing effective rehabilitation strategies and fall prevention programs for patients with MS. Rehabilitation remains the most important approach to improving balance in patients with MS, although some pharmacological interventions may also be beneficial (28).

Walking performance is another critical aspect of functional mobility in patients with MS. Various studies have examined different measures and factors associated with walking performance in patients with MS. Interestingly, walking performance in patients with MS is associated with various physiological and psychological factors. Studies have found associations between walking performance and force steadiness of the lower leg muscles, motor unit discharge characteristics, and muscle strength (29). Additionally, self-efficacy, particularly in MS functioning, has been correlated with objective walking performance measures (30).

Individuals with MS often demonstrate a decrease in walking speed and stride length, an increase in the time spent with both feet on the ground, variations in the timing of ankle muscle activity, and modifications in ankle movement patterns while walking. These gait abnormalities can occur even in the early stages of MS, with recently diagnosed and minimally impaired patients showing significant differences compared to healthy controls (31).

Gait impairments in patients with MS can be observed even in the absence of clinical signs of pyramidal dysfunction or changes in the Expanded Disability Status Scale (EDSS) scores (32). This suggests that subtle gait abnormalities may precede the more obvious clinical manifestations of the disease.

2. ASSOCIATIONS BETWEEN COGNITIVE FUNCTIONS, POSTURAL CONTROL, AND GAIT

Cognitive impairments, postural control deficits, and gait abnormalities are common in patients with MS, with studies showing significant associations between these domains. Structural and functional neuroimaging techniques have revealed the underlying pathophysiology related to impaired social cognition and other cognitive deficits in MS (33). Specifically, decreased gray matter volume in the frontotemporal and limbic regions has been associated with disabilities in cognition, theory of mind, and empathy in patients with MS (33). Interestingly, a study found that aerobic capacity, postural sway, and knee extensor asymmetry were associated with cognitive processing speed in patients with MS and accounted for differences between the MS and control groups (34). This suggests a link between the physical measures of balance and strength and cognitive performance in MS.

Moreover, neuroimaging studies have linked cognitive dysfunction in MS to focal T2 hyperintense lesions, widespread white matter abnormalities, and atrophy in both cortical and deep gray matter regions (9). Studies have revealed correlations between balance impairment and damage to the cerebellum, spinal cord, and higher-order processing networks (28). The heterogeneity in cognitive and postural control deficits among patients with MS reflects the influence of various factors, including genetics, sex, intelligence, disease course, and comorbidities (17).

Evidence suggests that assessments of processing speed and executive functioning serve as strong predictors of both upper and lower motor performance in individuals with MS, independent of disease duration and physical disability levels (35). This relationship suggests that neural damage in patients with MS may impair both cognitive processing speed and gait control. Interestingly, innovative rehabilitation approaches that combine robot-assisted gait training with virtual reality have shown promise in improving both cognitive and motor

functions in patients with MS. A study comparing standard robot-assisted gait training to robot-assisted gait training combined with virtual reality found significant improvements in walking endurance and executive functions in the virtual reality group, with gains maintained at a one-month follow-up (36). This suggests that virtual reality-based training may provide enhanced opportunities for stimulating cognitive abilities through repetitive practice, feedback information, and motivation for endurance practice.

2.1. Dual-Task Paradigms and Cognitive-Motor Interference (CMI)

Cognitive-motor interference (CMI) is a significant challenge for individuals with MS, affecting their ability to perform motor and cognitive tasks simultaneously. The dual-task Cost (DTC) was calculated as the percentage change in performance between the single- and dual-task conditions. An increase in negative outcomes (e.g., sway) is considered a positive DTC, reflecting interference. Studies have consistently demonstrated that people with MS experience greater DTC when performing concurrent motor and cognitive tasks than healthy controls. This interference is particularly evident in walking tasks, where gait speed typically decreases in dual-task conditions (37).

In MS research, dual-task paradigms often involve postural control or walking tasks combined with cognitive tasks, such as the Stroop Color-Word Test, Word List Generation, or Backward Counting. These paradigms have revealed that patients with MS frequently exhibit performance decrements during more demanding dual-task conditions, indicating impairment in the central executive system of working memory (38).

The model presented in Figure 1 outlines the complex, non-linear interactions among cognitive function, motor control, and postural stability, which are highly relevant in the context of MS pathology (39). The central component is the cognitive domains in MS, which encapsulate common deficits across core areas, such as attention, processing speed, and executive function (40). These cognitive limitations directly affect motor control, gait, and postural control. A critical element of this interaction is the Dual-Task Paradigm (DTP). When faced with a dual task, the necessity to simultaneously process both tasks creates a competition for finite attentional resources, leading to Dual-Task Interference (DTI), a mechanism widely studied in neurological populations (41).

This DTI was operationalized as a measurable DTC, which is the percentage deterioration in performance from single-task to dual-task conditions. Specifically, in patients with MS, this interference often manifests as a decline in mobility performance, increasing gait variability, and directly impairing stability, resulting in postural instability (28). The cumulative effect of increased gait variability and reduced postural stability is a significant predictor of increased fall risk in the MS population. Thus, the conceptual diagram (Figure 1) provides a comprehensive framework illustrating how impairments in cognitive domains can influence postural control and gait parameters through DTI, ultimately leading to reduced functional mobility and increased fall risk in pwMS (42).

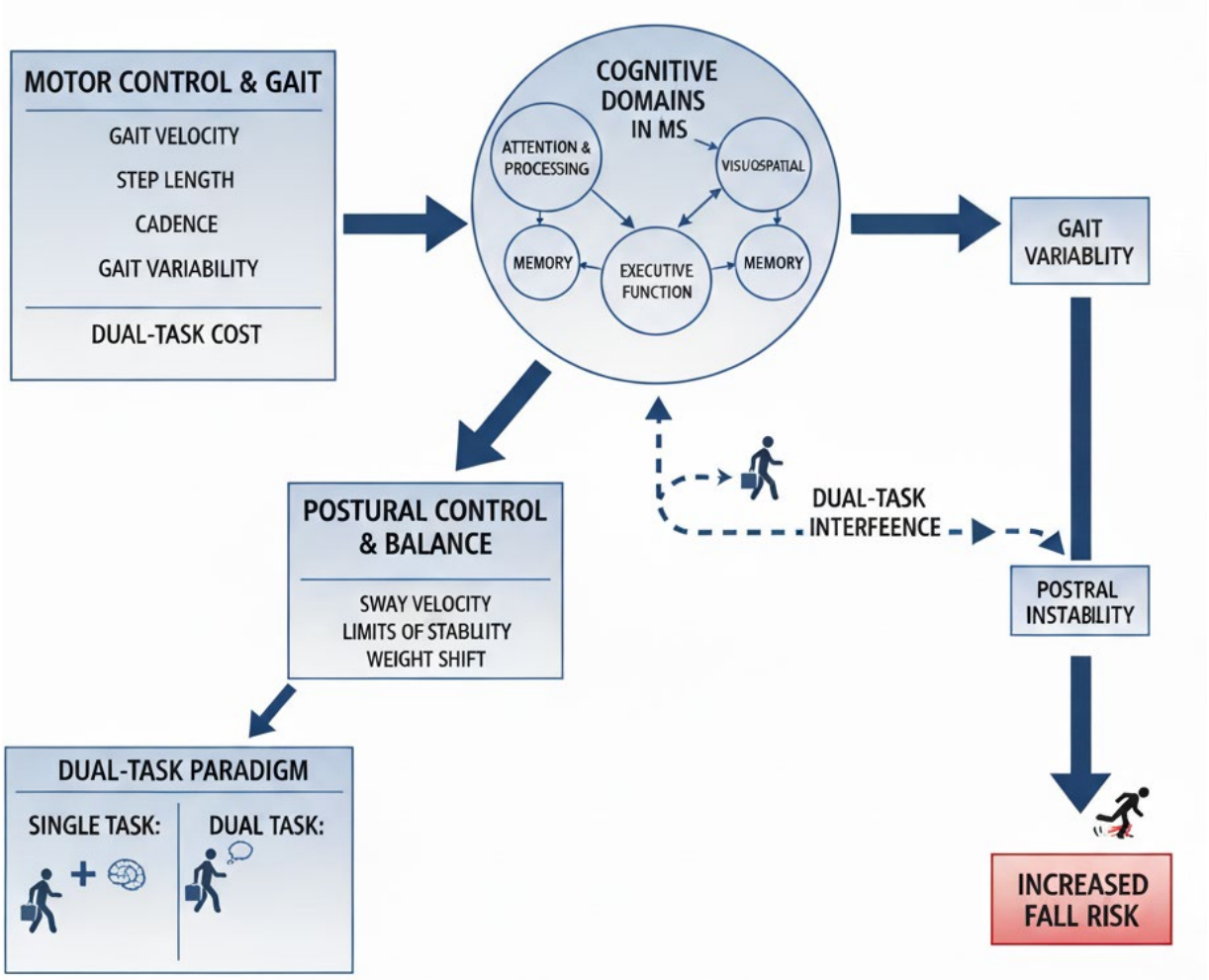

Figure 1: Cognitive-Motor-Postural Interactions and Dual Task

As summarized in Table 1, the literature consistently demonstrates that the simultaneous execution of a cognitive task with gait or balance tasks results in a measurable DTC in individuals with MS, reflecting significant cognitive-motor interference (39). This interaction often results in a "motor-priority" strategy in patients with MS, where attention is diverted from walking, leading to detrimental effects on rhythmic parameters such as gait velocity and stride length when combined with demanding cognitive tasks such as verbal fluency or serial subtraction (42). Conversely, static balance tasks are particularly sensitive to interference from cognitive loads that involve working memory. This attention reallocation significantly increases postural sway velocity and reduces limits of stability (LOS), thereby amplifying the risk of falls. Ultimately, the deterioration of both gait and postural control under dual-task conditions, as indexed by the DTC, is a key clinical marker that links cognitive processing deficits directly to a heightened fall risk in the MS population (43).

Table 1. Cognitive-Motor Dual-Task Interactions in MS Patients

Dual-Task Paradigm	**Cognitive Task Example**	**Affected Gait Parameter**	**Affected Postural Parameter**	**Dual-Task Cost**
Walking + Verbal Fluency	Number of words generated per minute	Stride Length, Gait Velocity	None (Primarily Gait Focused)	Decrease in Gait Speed, Reduction in Word Generation Rate
Walking + Serial Subtraction	Number of Errors, Accuracy	Double Support Time, Step Variability	None (Primarily Gait Focused)	Decrease in Gait Speed, Increase in Gait Variability
Standing + Auditory Attention Task	Reaction Time (RT) to target tone	Not Applicable	Postural Sway Velocity, Sway Area	Increase in Sway Velocity, Prolongation of Reaction Time
Standing + Working Memory	Percentage of Correct Responses	Not Applicable	Limits of Stability (LOS)	Reduction in LOS, Increase in Fall Risk
Standing + Visuospatial Task	Object Recognition Accuracy	Not Applicable	Center of Pressure (COP) Variability	Increase in COP Variability, Decrease in Task Accuracy

This table is a conceptual synthesis based on dual-task research in individuals with Multiple Sclerosis (39).

3. METHODOLOGICAL GAPS AND CLINICAL IMPLICATIONS

Cognitive deficits, like other MS symptoms, are also variable. Cognitive decline may increase over time, affecting many cognitive domains. Longitudinal studies have shown that cognitive performance can be either stable or deteriorating. It is often impossible to diagnose cognitive deficits despite their frequent negative effects on MS functionality. In particular, in patients with mild cognitive impairment, symptoms may be unobservable during routine neurological examinations. Studies have also shown that self-assessment reports are not sufficiently reliable and may point to psychological problems when cognitive performance is the real issue (44).

A comprehensive cognitive assessment is crucial in MS because of the high prevalence and significant impact of cognitive impairment on patients' quality of life. Interestingly, although comprehensive neuropsychological examinations are considered the gold standard for assessing cognitive impairment in MS, they are often time-consuming and resource-intensive. This has led to the development of brief cognitive assessment tools and computerized neuropsychological assessment devices to improve the accessibility and efficiency of cognitive screening in patients with MS. Regular cognitive screening is recommended as part of routine clinical assessment of MS (19).

Existing studies on the association between cognition and postural control have generally failed to adopt well-established measures for pwMS, especially for the assessment of cognitive impairment. Additionally, since the majority of the studies have included pwMS with overt disability, there is a lack of data on the association between cognition, postural control, and fall risk in the early stages of MS (45).

The integration of the sensory, motor, and cognitive systems is necessary to ensure postural control. Increasing amounts of evidence suggest that postural control consumes attention sources. However, little is known about the effects of cognitive burden on postural control, specifically in patients with minimally disabled MS (46).

A previous study reported that the cognitive domains related to static postural control differed according to disability levels (8); however, no study has focused on the relationship between dynamic balance, fall risk, and cognition in the early stages of MS. In addition, no healthy control group was used in any of the limited number of studies (7,8) investigating the relationship between posturography measurements and cognition in pwMS. A previous study found no significant relationship between verbal function and static postural control at low disability levels, but reported that verbal function affects the static balance in MS at higher levels of disability (EDSS 4.0-5.5) (8).

Central motor, central sensory and cognitive disorders can affect the planning and preservation of postural control, and reduce the problem-solving abilities during walking. This can result in slower gait, shortened single support time, and delayed swing phase because of postural control impairment (47). A previous study (48) with MS subjects with higher disability levels (EDSS 3.0, SD=1.8, range 1.5-6) reported that pwMS with a fall history had lower verbal function scores than non-fallers. A prospective multicenter study showed that patients receiving combined cognitive and motor rehabilitation significantly improved in terms of spatial memory, attention, cognitive flexibility, depression, balance, and gait(49). Similarly, semi-immersive virtual reality training has been shown to positively impact both cognitive and motor performance in pwMS (50).

The CMI is closely linked to reduced community ambulation and increased fall risk in patients with MS. Therefore, addressing CMI in clinical practice is crucial. The degree of CMI appears to be influenced by task complexity and the cognitive domain. However, some inconsistencies exist in the literature, with certain studies suggesting that MS patients and healthy controls may respond similarly across varying task complexities (37). Future research should prioritize the development of standardized dual-task assessment protocols and targeted interventions to mitigate the effects of CMI in MS.

4. CONCLUSION AND RECOMMENDATIONS

Practical recommendations for clinical assessments and rehabilitation interventions targeting cognitive functions, postural control, and gait in MS should emphasize a multidisciplinary and individualized approach. Clinicians are advised to incorporate comprehensive neuropsychological evaluations alongside standardized balance and gait assessments to capture the multifaceted impairments common in MS. Rehabilitation programs should integrate cognitive training with physical therapies, such as balance exercises and gait retraining, to address the interaction between cognitive deficits and motor dysfunction.

Utilizing dual-task paradigms during assessment and intervention can help simulate real-life challenges and improve functional outcomes. Regular monitoring and adaptation of interventions based on patient progress and symptom fluctuations are essential, given the variable nature of MS. Additionally, incorporating assistive technologies and patient education can enhance adherence and safety. This integrated strategy supports optimizing functional independence and quality of life in individuals with MS.

Rehabilitation strategies addressing cognitive-motor interactions in MS have shown promising results in improving both cognitive and motor function. The evidence supports the use of integrated rehabilitation approaches that address both cognitive and motor functions in patients with MS. These strategies appear to enhance brain plasticity and improve overall functional outcomes in stroke patients. Future research should extend the follow-up duration and include larger sample sizes to better understand the long-term trajectory of cognitive impairment in patients with MS. The development of targeted interventions is another critical area for future research in this field. Collaborative initiatives are required to develop interventions grounded in cognitive neuroscience principles, potentially informed by neuroimaging findings, and integrating traditional neuropsychological approaches with cognitive-behavioral therapy, physical activity, and therapeutic gaming.

4.1. Contribution to the Field

The findings underscore the potential of motor and cognitive rehabilitation interventions to promote both functional and structural brain plasticity in individuals with MS. This review highlights the importance of addressing cognitive deficits, even in patients with minimal disability, as a key component of rehabilitation strategies aimed at improving postural control, gait and reducing fall risk. Accordingly, comprehensive assessments of cognitive function and postural control should be integrated into clinical evaluation and treatment planning for patients with MS.

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