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Review Article

Motor Band Sign in Motor Neuron Diseases Using Magnetic Resonance Imaging: A Systematic Review

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Motor neuron diseases (MNDs) like amyotrophic lateral sclerosis (ALS) are progressive neurodegenerative disorders affecting upper and lower motor neurons (UMN and LMN). Magnetic resonance imaging (MRI) often reveals a "motor band sign" (MBS) of hypointensity along the precentral gyri in ALS, considered a radiologic hallmark. This review comprehensively summarizes the literature on MBS in ALS and related MNDs using multiple MRI techniques. A systematic search was conducted in the PubMed and Scopus databases to identify relevant studies on MBS in MNDs published until August 2023. Twelve studies were included. Most patients had UMN involvement at the onset. MBS was correlated with UMN impairment severity. Susceptibility-weighted imaging (SWI) detected MBS in the majority of MND patients. The use of SWI could be particularly useful in detecting MBS, and it should be considered as part of the routine clinical MRI protocols. Recent studies suggest that hypointensity and atrophy of the primary motor cortex (M1) and nearby regions can be used as MRI markers of UMN impairment in MNDs. Other MRI techniques like T2-weighted (T2-w), T2*-w, and fluid-attenuated inversion recovery (FLAIR) also showed characteristic changes. Furthermore, quantitative susceptibility mapping (QSM) is an advanced MRI technique that allows sensitive quantification of iron deposition and has shown promise for accurately detecting MBS in MNDs. The findings suggest that MR neuroimaging techniques can provide valuable insights into the pathophysiology of MND and can be used to detect biomarkers such as MBS. The review demonstrates that advanced MRI techniques can detect cortical and white matter changes reflecting upper motor neuron degeneration in MNDs like ALS. To find out how sensitive and suggestive the MBS is in MNDs and neurodegenerative movement disorders and how well it works as a prognostic indicator, we will need to do more research that combines comprehensive prospective and longitudinal research.

1. Introduction

Amyotrophic lateral sclerosis (ALS) is a type of motor neuron disease (MND) [1]. MND is a group of neurological disorders that affect the nerve cells, called motor neurons, that control muscle movement in the body through the central nervous system (CNS) [2–4]. In ALS magnetic resonance imaging (MRI), corticospinal tract (CST) hyperintensities have been proposed as a marker of UMN neurodegeneration, while a band-like (motor band sign (MBS)) hypointensity along the precentral gyri is best described as a radiological sign in ALS [5].

The MBS or "black ribbon sign," a motor cortex hypointensity, is a sensitive and suggestive marker in ALS patients [5–11]. Most people with MBS have problems in the precentral gyrus, where the primary motor cortex (M1) is located, as well as in the nearby supplementary motor area (SMA) and the premotor cortex (PMC) [12]. These regions are responsible for planning and executing voluntary movement, and damage to these regions can result in weakness, spasticity, and other motor deficits. In addition to the motor cortex, MBS can also affect the white matter (WM) tracts that connect the cortex to the spinal cord and brainstem [6, 13]. In particular, MBS often affects the CSTs [2], which

start in the motor cortex and go down through the brainstem and spinal cord. When these tracts are damaged, it can cause a number of motor symptoms, such as weakness, spasticity, and hyperreflexia.

MBS is produced due to the presence of multivalent cations (e.g., iron) within the microglia of the motor cortex [14]. In MRI, a low signal pattern, or a curvilinear "band," is observed almost entirely along the M1 in patients with MND and has been linked to upper motor neuron (UMN) degeneration in neurological disorders, making it a potential clinical marker. Both unilateral and bilateral reports of this pattern have been received, and it is believed to be caused by iron overload, fibrillary gliosis, and macrophage infiltration [12, 15].

Multiple MRI techniques have been used to identify MBS in patients with ALS. Susceptibility-weighted imaging (SWI), gradient-echo T2-weighted (T2-w) and T2*-weighted (T2*-w), fluid-attenuated inversion recovery (FLAIR), and diffusion-weighted imaging (DWI) are the most sensitive MRI techniques that can find iron deposits, which are linked to MBS in MND, especially patients with ALS [16–20]. In addition, an advanced MRI method called quantitative susceptibility mapping (QSM) has been used to look at iron deposition and accumulation in the motor and extramotor cortices. The QSM data can be merged and fused in machine learning approaches [21, 22]. Furthermore, based on the literature, MBS is much more likely to be seen with SWI than with these other MRI techniques.

MRI findings such as cortical atrophy and T2/FLAIR hyperintensities in the CSTs are somewhat specific for ALS, but their utility in distinguishing clinical ALS phenotypes has been questioned. However, the hypointensity of the motor cortex detected by SWI has been observed as a potential tool for distinguishing clinical ALS phenotypes. Additionally, diffusion tensor imaging (DTI) [23, 24] has been used to assess changes in microstructural integrity using DTI biomarkers. Functional MRI (fMRI) and magnetization transfer imaging (MTI) have been used to assess the extent of neuronal loss and brain activity in response to motor tasks in the motor cortex, respectively [2].

Recently, it is essential to note that MBS is not specific to MNDs and can also be seen in other diseases such as Huntington's disease (HD), phenocopy-spinocerebellar ataxia type 17 (SCA17) [8], Alzheimer's disease (AD), and Parkinson's disease (PD) [25–28]. Therefore, a comprehensive MRI and clinical evaluation is necessary to accurately diagnose the underlying pathology causing MBS. However, the presence of MBS in conjunction with clinical features consistent with ALS and other related MND types can aid in diagnosing and managing the disease. The aim of this work is to comprehensively overview all the available literature on MBS and signal hypointensity in the diagnosis and management of ALS and related MNDs. The review will summarize the various MRI techniques that have been utilized to identify MBS and evaluate their comparative sensitivity in detecting this imaging biomarker.

2. Neuroanatomy, Pathophysiology, and Imaging of MNDs for MBS

2.1. Motor Cortex. The major purpose of the motor cortex is to create signals that guide bodily movement. It is located anterior to the central sulcus and is a component of the frontal lobe [9]. The motor cortex is a complex brain region composed of several subregions that work together to control movement [29]. The M1 is responsible for executing voluntary movements, while the SMA coordinates complex movements, and the PMC plans and prepares motor actions. The frontal eye field (FEF) controls eye movements, while the cingulate motor areas (CMA) are involved in motor control and pain processing. Lastly, the parietal motor areas (PMA) integrate sensory information and plan reaching movements. The motor cortex, as a whole, is responsible for planning, executing, and controlling movement, including both fine and gross motor skills [30].

The precentral gyrus is a part of the motor cortex, which is the region of the brain responsible for controlling voluntary movement. More specifically, the precentral gyrus is located on the anterior portion of the paracentral lobule, and M1 is embedded within the precentral gyrus and is in charge of voluntary motor movement control [28]. The subfields of the precentral gyrus include the hand knob, which is responsible for the fine motor control of the fingers; the face area, which is responsible for the voluntary control of facial muscles; and the arm and leg areas, which are responsible for the voluntary control of the limbs [26]. MBS is most commonly observed in the precentral gyrus. Also, the neurodegeneration of the CST in the precentral gyrus leads to the loss of UMNs, which are responsible for initiating voluntary movement. The severity and distribution of MBS can vary among patients, with some exhibiting symptoms limited to one limb while others may have more widespread involvement. MBS is most commonly observed in the precentral gyrus. Also, the neurodegeneration of the CST in the precentral gyrus leads to the loss of UMNs, which are responsible for initiating voluntary movement. The severity and distribution of MBS can vary among patients, with some exhibiting symptoms limited to one limb while others may have more widespread involvement [5, 26].

2.2. The Fundamental Pathophysiology of ALS and MBS. ALS is a progressive and fatal neurodegenerative disease. The pathophysiology of ALS involves a complex interplay between multiple mechanisms, including oxidative stress, mitochondrial dysfunction, protein misfolding and aggregation, neuroinflammation, and glutamate excitotoxicity [3, 4]. The exact underlying mechanism of ALS remains unclear, but it is thought to involve a combination of genetic, environmental, and cellular factors that lead to the accumulation of abnormal proteins and oxidative stress, ultimately resulting in motor neuron degeneration. The loss of motor neurons in the cortex and spinal cord disrupts the connection between the brain and muscles, leading to muscle atrophy, spasticity, and fasciculations. This eventually leads to respiratory failure and death, typically within 3-5 years of symptom onset [4, 22].

The presence of MBS in ALS patients has been associated with a poorer prognosis and faster disease progression [6, 31]. The reason for this correlation is not fully understood, but it is believed that the involvement of the motor cortex in ALS pathophysiology may play a role. The motor

cortex is responsible for the initiation and control of voluntary movements, and damage to this area can lead to weakness and spasticity. MBS can be a predictor of the spread of the disease to other regions of the brain and spinal cord. This spread, also known as "neurodegeneration," is a hallmark of ALS and is thought to be responsible for the progressive loss of motor function [31, 32]. MBS has been linked to the involvement of the UMNs, suggesting that it may be an indicator of widespread neurodegeneration [7].

The pathophysiology of MBS and the cause of iron accumulation and observations in the motor cortex are complex and involve multiple cellular and molecular mechanisms. The degeneration of corticospinal neurons and their axons is thought to be caused by a combination of genetic and sporadic factors, including oxidative stress, protein misfolding, and excitotoxicity. Iron accumulation in the motor cortex in MBS is a complex phenomenon, and its underlying mechanism is not fully understood [2, 4]. However, it is thought to involve a combination of oxidative stress, neuroinflammation, abnormal iron metabolism, and genetic factors. Increased iron deposition in the motor cortex may result from the imbalance between the production of reactive oxygen species (ROS) and the body's antioxidant defenses, as well as the inflammatory response to injury or infection [4, 7, 9]. Dysregulation of iron metabolism, such as altered iron transport or storage, is another potential mechanism. Genetic variations in genes involved in iron metabolism, oxidative stress, and neuroinflammation may also contribute to iron accumulation in the motor cortex [33].

Microglia are a type of glial cell in the CNS that play a key role in the immune response and inflammatory processes. In ALS patients with MBS, microglial activation has been observed in the motor cortex, indicating that neuroinflammation may contribute to the pathogenesis of MBS [5, 7, 13]. Microglial activation is associated with the release of proinflammatory cytokines and ROS, which can cause damage to neurons and other cells in the motor cortex. It is thought that microglial activation in response to injury or disease is a normal part of the inflammatory response, but excessive or prolonged activation can lead to neuroinflammation and neuronal damage. This activation is triggered by several factors, including the accumulation of misfolded proteins, mitochondrial dysfunction, and oxidative stress. Additionally, as earlier noted, genetic factors may also contribute to microglial activation and neuroinflammation in MBS [4, 34].

Understanding the pathophysiology of MBS is crucial for the development of effective diagnostic and therapeutic strategies for ALS and related MNDs. MRI is a valuable tool for detecting MBS and monitoring disease progression, but its accuracy depends on a thorough understanding of the underlying pathophysiology [2, 5, 35, 36].

2.3. Magnetic Susceptibility Imaging. Magnetic susceptibility imaging techniques are a type of MRI method that can detect subtle changes in the magnetic susceptibility of tissues. Magnetic susceptibility imaging can provide information about the distribution and concentration of paramagnetic substances such as iron, which is particularly useful in neurodegenerative diseases like ALS, where iron accumulation is a common feature. There are several different techniques used for magnetic susceptibility imaging, including T2*-w, SWI, and QSM [12, 32, 37, 38].

T2*-w imaging is a fast technique that can detect magnetic susceptibility differences, but it has a relative low spatial resolution and is susceptible to artifacts from motion and other sources of magnetic field inhomogeneity. SWI is a more advanced technique that combines T2*-w imaging (magnitude) with phase information to enhance the contrast between tissues with different susceptibilities, allowing for better visualization of small structures and iron deposition, like the accumulation of iron in microglial cells [32]. QSM is a newer technique that can quantitatively map the magnetic susceptibility of tissues, providing more precise information about the concentration and distribution of paramagnetic substances [39, 40]. Magnetic susceptibility imaging techniques have shown promise in detecting the MBS in ALS, which is a characteristic pattern of iron deposition.

3. Methods

3.1. Search Strategy. We implemented a comprehensive search strategy, adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [41] and synthesis without meta-analysis (SWiM) guidelines [42], to identify all relevant literature (Figure 1). This systematic review was not registered in PROSPERO or any other prospective register of systematic reviews. Searches were conducted across multiple databases, including PubMed and Scopus, from their inception up until August 2023. The search query was designed to be inclusive and comprehensive, utilizing a combination of MeSH terms and keywords related to MBS and MRI in the context of ALS and other MNDs. The search terms were as follows: ("motor band sign" OR "MBS" OR "ribbon sign") AND ("magnetic resonance imaging" OR "MRI") AND ("motor neuron disease" OR "MND" OR "amyotrophic lateral sclerosis" OR "ALS" OR "primary lateral sclerosis" OR "PLS" OR "progressive muscular atrophy" OR "PMA" OR "progressive bulbar palsy" OR "PBP" OR "spinal muscular atrophy" OR "SMA") (supplementary Table 1).

3.2. Study Selection. The study selection process involved several stages. Firstly, titles and abstracts were screened for relevance. Full texts of potentially relevant articles were then obtained and assessed against our inclusion and exclusion criteria. Inclusion criteria were as follows: (1) studies providing information on the use of MRI for the detection of MBSs in the diagnosis and management of ALS or other MNDs, (2) studies must have employed a human sample, (3) articles must have been published in English, and (4) studies must have provided information on the MRI techniques used. Exclusion criteria were as follows: (1) articles not relevant to MBS, MRI, and MNDs, (2) animal or in vitro studies, and (3) articles not providing sufficient information on diagnosis or management of MNDs with MBS and MRI. We also conducted a manual search of the reference lists of all

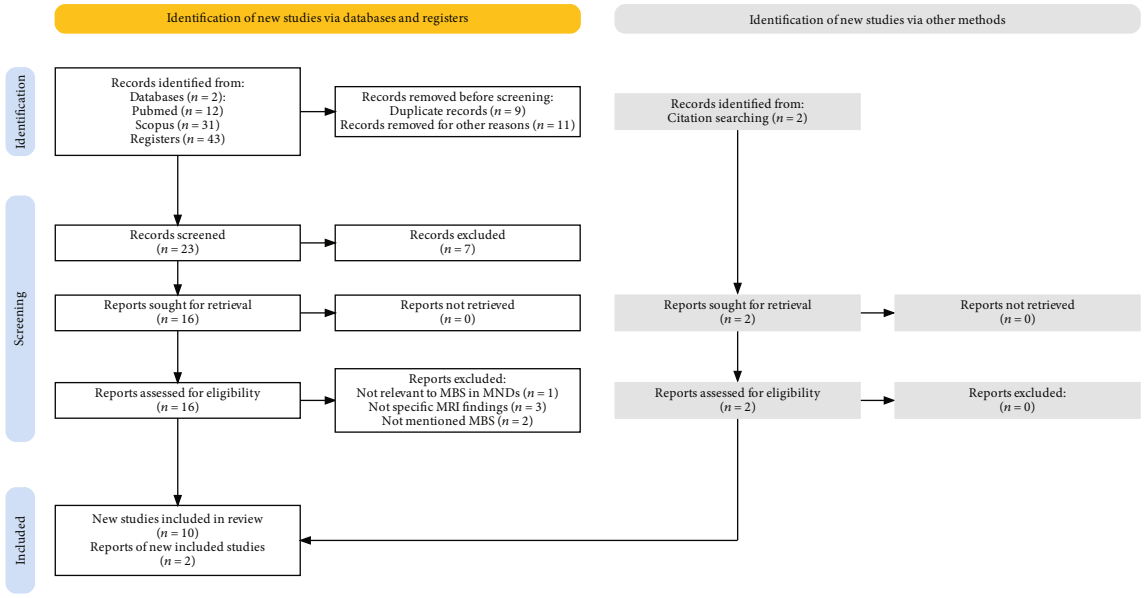

Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram showing the study selection process.

included articles to identify additional relevant studies that may have been missed in the initial search.

3.3. Data Extraction and Quality Assessment. Data extraction was conducted by two independent reviewers using a standardized form. The extracted data included study characteristics (e.g., study design, sample size, demographics), MRI techniques, and findings related to MBSs in the diagnosis and management of ALS or other MNDs. Any discrepancies were resolved through discussion and consensus. Quality assessment of the included studies was performed using the appropriate tools depending on the study design. The Newcastle-Ottawa scale [43] and the Cochrane risk of bias tool were used [44]. Any potential source of bias was discussed and agreed upon by all authors.

The studies were found to be of fair (4-6 stars) to good (7-9 stars) quality, while the randomized trials were at low risk of bias (Table 1). Some common sources of potential bias were the lack of blinding and the lack of control groups in case reports. Any potential source of bias was discussed by the reviewers and agreed upon by all authors. Given the small number of studies included, statistical tests for publication bias were not performed. However, the comprehensive search strategy is aimed at identifying all relevant studies to minimize the potential for publication bias. In the PRISMA flow diagram, we precisely detailed the number of articles identified from each source, the number of articles screened, the number for full-text review, and the reasons for exclusion at each stage. This transparency ensures a rigorous and reproducible methodology.

4. Results

4.1. Overview of Results. We included a total of 12 articles in this review. These articles included original research studies, case reports, and case series. The information from these articles was synthesized and summarized in the results section. Eventually, our literature screening and search strategies were designed to identify all relevant studies on the use of MRI for the detection of MBS in ALS and other MNDs. We used a combination of electronic and manual searches and included all types of articles that met the inclusion criteria.

Multiple studies have reported the presence of MBS in patients with MND. Twelve articles were selected to summarize the findings related to study design, sample size, onset and/or involvement, and MRI techniques and findings in the context of MBS in MNDs and other subtypes. The studies included patients with different disease subtypes, including ALS, frontotemporal dementia-MND (FTD-MND), primary lateral sclerosis (PLS), and FTD-ALS [9, 16, 45].

The studies had various designs, including original studies, case reports, and retrospective analyses. The sample sizes varied widely, ranging from single cases to over 100 patients. The studies included patients with different onsets, including UMN, LMN, and spinal and cervicobrachial onsets. In seven studies, patients had UMN involvement at onset, while in three studies, patients had both UMN and LMN involvement. In other studies, patients had onsets of symptoms that included UMN, cervicobrachial, bulbar, lower limb, and spinal involvement. The variation in onset across studies highlights the heterogeneity of neurodegenerative diseases and the need for comprehensive imaging techniques that can detect changes in various regions of the brain [9, 31].

The MRI techniques used in the studies included T1-w (T1-weighted), T2-w, T2*-w, FLAIR, DWI, SWI, and QSM. The most commonly used technique was SWI, which was used in 9 out of 12 studies. T2*-w imaging was used in 5 studies, T2-w and FLAIR were used in 6 studies each, and T1-w and DWI were each used in 3 studies. R2* maps and QSM were each used in one study. It is worth noting that

Table 1: Risk of bias assessment for studies included in the systematic review.

Study	Newcastle-Ottawa scale	Cochrane risk of bias
Kwan et al. [13]	Good quality—8/9 stars	Low risk of bias
Chakraborty et al. [2]	Fair quality—5/9 stars	Moderate risk of bias due to no blinding
Boll et al. [10]	Good quality—7/9 stars	Low risk of bias
Boll et al. [45]	Good quality—8/9 stars	Low risk of bias
Roeben et al. [9]	Good quality—7/9 stars	Low risk of bias
Prabhu and Sajja [5]	Fair quality—4/9 stars	High risk of bias due to no blinding, no control group
Budhu et al. [17]	Fair quality—5/9 stars	Moderate risk of bias due to no blinding
Makkawi et al. [24]	Fair quality—6/9 stars	Moderate risk of bias due to no blinding
Pai et al. [15]	Fair quality—5/9 stars	Moderate risk of bias due to no blinding
Chung et al. [7]	Good quality—8/9 stars	Low risk of bias
Zanovello et al. [16]	Good quality—7/9 stars	Low risk of bias
Valaparla et al. [46]	Fair quality—6/9 stars	Moderate risk of bias due to no blinding

Chung et al. used the most MRI techniques, including all of the above techniques except for R2* maps [7].

4.2. FLAIR and T2-w Imaging Findings. Kwan et al. found that motor cortex hypointensity on FLAIR images showed a higher frequency in patients with ALS and correlated with UMN impairment severity [13]. Similarly, Chakraborty et al. identified subtle bilateral hyperintensity along the CSTs using FLAIR and T2-w imaging [2]. Roeben et al. observed a hypointense signal of the cortical band along the precentral gyrus on both T2-w and SWI [9]. Zanovello et al. found mild to moderate CST hyperintensities in 8% of patients with FTD-MND and 40% of ALS patients using T2-w FLAIR imaging [16].

4.3. SWI Findings. Chakraborty et al. found that SWI images revealed linear hypointensity along the cortical margin of the precentral gyrus. This was distinctly limited to its posterior border and detected T2 hypointensity in the motor cortex in two ALS patients, likely correlated with UMN involvement [2]. Boll et al. reported that paramagnetic effects were seen in 88% of ALS patients [10], while Boll et al. found that most ALS patients (91.66%) exhibited a "black ribbon sign," or MBS [45]. Roeben et al. also reported that MBS was present in 78% of patients where SWI was available [9]. Prabhu and Sajja found bilateral motor cortex involvement in MBS in SWI, with higher hypointensity on the right motor cortex compared to the left [5]. Budhu et al. and Makkawi et al. reported MBS in SWI images [17, 24]. Pai et al. found symmetric gyriform susceptibility exclusively along the posterior cortex of the precentral gyrus in SWI [15]. Chung et al. reported that MBS was present in 9/13 and 4/5 of ALS and PLS patients, respectively [7]. Zanovello et al. found that SWI in ALS patients revealed a variable degree of MBS in 64% of patients [16]. Lastly, Valaparla et al. identified sulcal hypointensities in T2-w and SWI images in the precentral regions on both sides [46].

4.4. Other Findings. Chakraborty et al. reported a variable degree of atrophy involving the M1 with prominence of the adjacent central sulcus [2]. Boll et al. observed significant changes in the MBS related to the rapid progression of the disease in follow-up studies [45]. Makkawi et al. noted high signal intensity involving the ventral gray matter (GM) of the cervical cord extending from the C3-C6 spines and a mild volume loss in the cord [24]. Pai et al. found symmetric hyperintensity in the centra semiovale, corona radiata, and the posterior limbs of the internal capsules, along the expected course of the CSTs, in T1-w and T2-w images. The coronal T2-w revealed the entire extent of the signal abnormality [15]. Chung et al. found that susceptibility measurements in the left motor cortices had a significantly positive correlation with contralateral UMN signs in ALS MBS [7].

The findings suggest that MR neuroimaging techniques can provide valuable insights into the pathophysiology of MND and can be used to detect biomarkers such as MBS. The use of SWI could be particularly useful in detecting MBS, and it should be considered as part of the clinical routine MRI protocol in the diagnostic work-up of MND patients. In total, Table 2 provides a summary of MBS findings in MNDs.

5. Discussion

5.1. General Discussion. Our systematic review provides compelling evidence for the presence of MBS in patients diagnosed with MNDs, particularly ALS. Across the studies, MBS was detected using various conventional and advanced MRI techniques. The studies consistently reported the presence of MBS in patients with MNDs, and the detection of MBS often correlated with the severity of UMN impairment. The MBS is usually bilateral and symmetric, but it can also be unilateral or asymmetric, depending on the clinical severity and progression of the disease (Figure 2). The MBS can be present in isolation or in combination with other MRI signs of UMN degeneration, such as CST hyperintensity on T2-w or FLAIR, or cervical cord atrophy or hyperintensity. The MBS can be more suggestive than CST hyperintensity for UMN involvement, as it can be seen in patients without CST hyperintensity, but not vice versa.

Table 2: Motor band sign findings in motor neuron diseases.

Article	Study design	Sample size	Onset and/or involvement	MRI	MRI findings	Significance
Kwan et al. [13]	Original and postmortem	19 ALS, 19 controls, and 1 postmortem	UMN	FLAIR, T2*-w, and R2* maps	(i) Motor cortex hypointensity on FLAIR images is more frequent in ALS patients and correlates with UMN impairment severity (ii) 7 T T2*-weighted imaging localized signal alteration to deeper motor cortex layers (iii) Increased iron accumulation was found in microglial cells in areas corresponding to signal changes	(i) Motor cortex hypointensity in ALS is due to increased iron accumulation by microglia (ii) High-field 7 T MRI is better than 3 T localized signal alteration
Chakraborty et al. [2]	Case report	Case 1: 1 female and case 2: 1 male	UMN	T2-w, FLAIR, and SWI	(i) FLAIR and, to a lesser extent, T2-w showed subtle bilateral hyperintensity along the expected course of the CSTs (subcortical frontal WM, posterior limb of the internal capsule, and cerebral peduncles and pons) in both patients (ii) Variable degree of atrophy involving the M1 with a prominence of the adjacent central sulcus (iii) SWI images revealed linear hypointensity along the cortical margin of the precentral gyrus, distinctly limited to its posterior border. This was clearly present bilaterally in case 1 but affected mostly the left precentral gyrus in case 2 (however, hypointensity is limited to the posterior border of the precentral gyrus in both cases) (iv) SWI detects T2 hypointensity in the motor cortex in two ALS patients, likely correlated with UMN involvement (v) T2 hypointensity in the motor cortex of ALS patients has been described before, but the increased resolution of SWI makes it visible within the motor cortex in a band-like fashion within the GM	(i) SWI can detect motor cortex changes in ALS
Boll et al. [10]	Original	25 ALS and 15 controls	UMN and cervicobrachial	T2*-w	(i) Paramagnetic effects were seen in 88% of ALS patients, absent in all controls and other cases with spinal amyotrophy or diabetic neuropathy	(i) T2*-w may be a useful technique to identify MBS
Boll et al. [45]	Original	36 ALS and 15 controls	Cervicobrachial, bulbar, and lower limb	T2*-w	(i) Most of the patients with ALS (91.66%) exhibited a "black ribbon sign," or MBS (ii) Follow-up exhibited significant changes in the MBS related to the rapid progression of disease	(i) This MBS, or black ribbon sign, represents a valuable tool for the selection of candidates and their follow-up in clinical trials

Table 2: Continued.

Article	Study design	Sample size	Onset and/or involvement	MRI	MRI findings	Significance
	Case report	1 female (index case)		T2-w and SWI	(i) Hypointense signal of the cortical band along the precentral gyrus on both T2-w and SWI	
Roeben et al. [9]	Retrospective analysis	157 ALS	UMN	T2-w, T2*-w, FLAIR, DWI, and SWI	(i) MBS was present in 5% of patients in the total series, but in 78% of patients where SWI was available (ii) MBS is a recurrent finding in ALS, which can be identified even on clinical routine 3 T and as part of more complex motor neuron syndromes, such as FTD-ALS (iii) SWI sequences should be considered as part of the clinical routine MRI protocol in the diagnostic work-up of ALS patients	(i) The significance of SWI sequences in detecting MBS in ALS patients
Prabhu and Sajja [5]	Case report (letter to the editor)	1 male	UMN	SWI	(i) Bilateral motor cortex involvement is seen in MBS in SWI, with higher hypointensity on the right motor cortex compared to the left, corresponding with clinical severity	(i) SWI can detect motor cortex changes in ALS
Budhu et al. [17]	Case report (teaching)	1 female	UMN and LMN	SWI	(i) SWI showed MBS consistent with superficial siderosis along the central sulcus. Intracellular iron may be from microglial phagocytosis of degenerated neurons in the motor strip	(i) SWI can detect motor cortex changes in ALS
Makkawi et al. [24]	Case report	1 male	UMN and LMN	SWI, T2-w, FLAIR, and SWI	(i) Abnormal linear areas of blooming/iron deposition along the cortices of the precentral gyri, indicating an MBS (ii) High signal intensity involving the ventral GM of the cervical cord extending from the C3-C6 spines. A mild volume loss was also noted in the cord (iii) SWI showed MBS involving bilateral M1 in a band-like fashion. This finding is not seen on the corresponding T2-w (iv) FLAIR shows subtle signal changes in the subcortical WM, more on the left side, indicating the degeneration of the CST	(i) SWI and T2-w can detect motor cortex changes in ALS

Table 2: Continued.

Article	Study design	Sample size	Onset and/or involvement	MRI	MRI findings	Significance
Pai et al. [15]	Case report	1 male	UMN and LMN	T1-w, T2-w, and SWI	(i) Symmetric gyriform susceptibility exclusively along the posterior cortex of the precentral gyrus in keeping with the MBS in SWI (ii) Symmetric hyperintensity in the centra semiovale, corona radiata, and the posterior limbs of the internal capsules, along the expected course of the CSTs, in T1-w and T2-w images. The coronal T2-w reveals the entire extent of the signal abnormality (iii) Without cord swelling or atrophy, T1-w images of the cervical spine demonstrate symmetric T1 hyperintensity along the anterolateral columns of the cervical cord	(i) The MBS and symmetric hyperintensity in specific areas of the brain and cervical spine can help diagnose MNDs with UMN and LMN involvement
Chung et al. [7]	Original	13 ALS, 5 PLS, and 10 controls	UMN	T1-w FLAIR, T2-w, T2-w FLAIR, DWI, T2*-w. SWI, and QSM	(i) MBS were present in 9/13 and 4/5 of ALS and PLS, respectively, and none in controls (ii) 2/13 ALS and 3/5 PLS had MBS in the absence of corticospinal T2/FLAIR hyperintensity sign (iii) Susceptibility measurements in the left motor cortices had a significantly positive correlation with contralateral UMN signs in ALS MBS, and susceptibility quantification measurements in the motor cortices may serve as surrogate markers of UMN involvement in MND	(i) The MBS and susceptibility measurements in motor cortices may be useful markers for diagnosing UMN involvement in MNDs
Zanovello et al. [16]	Original	16 ALS, 12 ALS-FTD, and 13 controls	UMN, bulbar, and spinal	T1-w, T2-w FLAIR, DWI, and SWI	(i) T2-w FLAIR found mild to moderate CST hyperintensities in 8% of FTD-MND and 40% of ALS patients (ii) SWI in ALS patients revealed a variable degree of MBS (cortical ferromagnetic deposition in M1) in 64% of patients	(i) CST hyperintensities and the MBS can be useful in differentiating ALS from other MNDs
Valaparla et al. [46]	Case report	1 female (PLS)	UMN	T2-w and SWI	(i) T2-w and SWI images in the precentral regions on both sides (the bilateral motor strip area) showed sulcal hypointensities	(i) The MBS and susceptibility measurements in motor cortices may be useful markers for diagnosing UMN involvement in MNDs

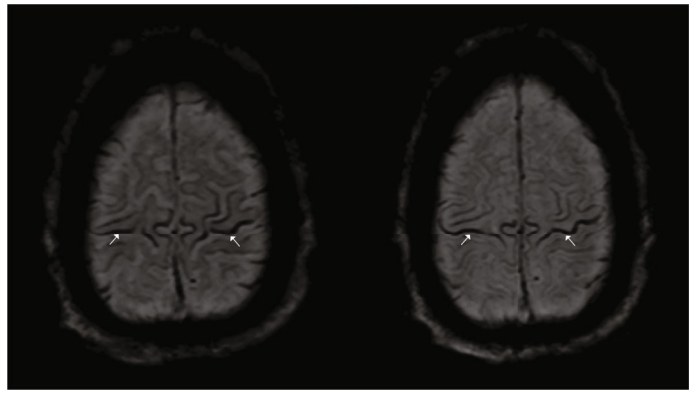

Figure 2: Susceptibility-weighted imaging (SWI) on 1.5 Tesla MRI demonstrating bilateral symmetric motor band sign (white arrows) along the central sulcus, layering the precentral gyrus. This figure has been adapted from Budhu et al., with minor modifications [17].

The studies reviewed demonstrate that advanced MRI techniques, particularly SWI, can detect characteristic changes in the motor cortex and CSTs in MND patients. Multiple studies found an MBS on SWI, indicating paramagnetic effects and iron deposition in the motor cortex, in a high proportion of MND patients [5, 9]. This finding was not seen in healthy controls or patients with other neurological conditions, suggesting it is specific to MND. The MBS on SWI likely reflects underlying cortical pathology and UMN degeneration in ALS. Furthermore, the relationship between iron accumulation and MBS in the motor cortex is significant in ALS patients and can be detected using SWI MRI.

Some studies correlated the presence and severity of MBS with UMN signs and disease progression [5, 13]. Quantification of cortical susceptibility on SWI could potentially serve as an imaging biomarker to monitor upper motor neuron involvement over time in ALS patients. Other advanced MRI techniques, like 7 T T2*-w imaging, localized the cortical signal changes to deeper motor cortex layers [13]. Boll et al. [10, 45] introduced the term "black ribbon sign," another term for MBS, and identified its presence in a significant percentage of ALS patients. They also observed changes in MBS related to the disease's rapid progression.

In addition to findings in the motor cortex, several studies also identified hyperintense signals along the CSTs on T2-w and FLAIR images, indicative of CST degeneration [2, 15, 16, 24]. However, T2/FLAIR changes along the CSTs were less sensitive than SWI for detecting pathology in ALS. Some patients with MBS on SWI had normal-appearing CSTs on T2/FLAIR, suggesting SWI can identify UMN involvement earlier [7].

5.2. Interpretations. Early MND diagnosis provides a diagnostic challenge since indications and symptoms are not always obvious. As a result, the diagnosis of MNDs is typically delayed until the onset of symptoms [28, 47]. MBS is an MR neuroimaging biomarker observed especially in patients with MND, specifically those with UMN involvement. The MBS is characterized by a linear hypointensity or blooming artifact on SWI or T2*-w, which indicates ferromagnetic deposits within the motor cortex. The accumulation of iron in degenerated neurons or microglia phagocytosis of degenerated neurons in the motor cortex may cause this. Multiple studies have reported the presence of MBS in patients with different subtypes of MND, including ALS, FTD-MND, PLS, and FTD-ALS [7, 15, 16, 24].

SWI has also been shown to be more sensitive than other conventional MRI sequences, such as T2*-w and T2/FLAIR, in detecting the MBS. SWI and QSM were particularly effective in detecting MBS in the motor cortex of patients with ALS. The presence of MBS in the motor cortex was also found to be correlated with UMN signs in patients with ALS, suggesting that MBS may serve as a surrogate marker of UMN involvement in MND.

A few reports of MBS in other neurodegenerative disorders such as SCA17, AD, and PD indicate that a neurodegenerative disease process likely causes these microstructural alterations. Several MRI studies investigating iron accumulation in ALS have found elevated iron levels in the motor cortex of ALS patients utilizing a variety of iron-sensitive MRI sequences and MRI analysis methods [8, 9, 13, 28]. Decreased signal intensity on SWI was found in conjunction with high antiferritin staining of macrophages and microglia in the precentral gyrus of ALS patients, providing additional evidence for iron accumulation in the motor cortex in ALS [6, 9, 13, 16, 17, 24, 26, 48].

Ferritin is paramagnetic and produces strong susceptibility effects on T2*-w images. SWI-filtered-phase images allow a better distinction, and QSM data are particularly suitable for showing increased iron content in the brain. Abnormally elevated iron levels are evident in many neurodegenerative disorders, including PD, AD, HD, and ALS. The ability to measure the amount of ferritin in the brain can be used for a better understanding of the progression of the disease and is also helpful in predicting the treatment outcome [8, 38, 49, 50].

As earlier noted, SWI is the most sensitive sequence to detect this low signal intensity of precentral cortices in ALS patients [6, 17, 31, 48]. In one recent study, adding SWI to the conventional MRI sequences (T2/FLAIR) improved the accuracy of MRI to diagnose ALS with a sensitivity of 70%, a specificity of 81%, a positive predictive value (PPV) of 90%, a negative predictive value (NPV) of 51%, and an accuracy of 73% [32, 51]. In another study, the MBS reported was observed in 78% of ALS patients in SWI [2, 9, 23, 34].

In one new study, the case of a 68-year-old woman who presented with Huntington's phenocopy and generalized chorea was later shown to have SCA17. There have been reports of T2 hypointensity cortical signals in other neurodegenerative disorders, including AD and PD, but no evidence of MBS in SCA17. The presence of MBS has been shown not just in neurodegenerative conditions but also in healthy people and people with acquired disorders, including stroke and progressive multifocal leukoencephalopathy [2, 5, 6, 8, 17, 52]. MBS was suspected when an MRI showed hypointensity in both the left and right precentral gyri. This first example of SCA17 with MBS illustrates the expanding range of radiological manifestations of SCA17. MBS, however, may also be seen in a patient with SCA17 and is likely an indication of the continuous neurodegenerative process that is characteristic of this progressive disease [8].

Iron deposition in normal aging is mainly observed in the deep GM structures, such as the basal ganglia and the thalamus, but can also affect some cortical regions, such as the prefrontal and temporal cortex. Moreover, iron accumulation in MNDs may have different cellular and subcellular patterns than in normal aging. For example, iron deposits in motor neuron diseases are mainly found in microglia, whereas in normal aging, they are more distributed among astrocytes and remain stable in oligodendroglia [53–55].

In T2-w MRI, hyperintensity in the CSTs, initially seen in the internal capsule, is usually the first manifestation of ALS. Over time, the entire tract from the motor strip to the spinal cord demonstrates a T2 signal increase and progressive volume loss. In the CSTs, the specificity and sensitivity of the T2 hyperintensity are above 70%, while the sensitivity is below 40% [23].

At 7 T, the increased magnetic field strength leads to a higher signal-to-noise ratio (SNR) and better spatial resolution, which allows for better visualization and detection of small, subtle changes in the motor cortex. This increased sensitivity enables researchers to detect the MBS more reliably, which in turn leads to more accurate and precise mapping of the motor cortex. However, ultra-high-field imaging at 7 T comes with some challenges and limitations, such as increased susceptibility artifacts and decreased homogeneity of the magnetic field. These challenges need to be carefully considered and addressed when designing and interpreting studies using ultra-high-field imaging. Eventually, ultra-high-field imaging at 7 T will have a higher sensitivity to capture the MBS compared to imaging at 3 T [13, 56].

According to most studies, neuroimaging is not considered mandatory for the diagnosis of ALS; its primary role is to rule out differential diagnoses. Several MRI strategies have been proposed to detect radiologic markers of neurodegeneration in ALS. For example, the band-like hypointensity of the precentral gyri (MBS) and hyperintensities in the CSTs have been suggested as markers of especially UMN degeneration [7, 15, 16].

5.3. Consideration Points. The MBS, which is a suggestive pattern of motor cortex involvement, might be a clue to UMN involvement in ALS. These changes are not invariably seen in every ALS patient, and they may be expressed differently depending on the disease course and the degree of clinical UMN involvement. In the following, some points to consider regarding signal hypointensity in the motor cortex and adjacent regions are listed. These studies make no direct mention of MBS, although they do discuss hypointensity in the motor cortex.

Cervo et al. found reduced T2 signal intensity and N-acetylaspartate (NAA) levels in the M1 correlated with UMN impairment in ALS patients [57]. Celso et al. showed M1 hypointensity on SWI correlated with UMN scores in patients with ALS and PLS [58].

Endo et al. also demonstrated reduced M1 signal intensity on SWI correlated with UMN clinical scores in ALS. Importantly, the extent of susceptibility changes in the bilateral precentral gyri was significantly correlated with UMN scores [59]. Donatelli et al. evaluated M1 signal hypointensity in ALS patients using high-resolution T2*-weighted MRI at 3 T and 7 T field strengths. The hypointensity-to-thickness ratio was greater in ALS patients versus controls and correlated with UMN impairment. Targeting the orofacial M1 region, they found M1 hypointensity detected bulbar dysfunction with high sensitivity and specificity [56, 60].

In 2020, Conte et al. showed higher M1 hypointensity on SWI in ALS, especially UMN-predominant ALS, compared to mimics and controls [21]. Rizzo et al. found that combining corticospinal tract hyperintensity and M1 hypointensity on SWI had high diagnostic accuracy for ALS and predicted shorter survival [51]. To differentiate hereditary spastic paraplegia (HSP), PLS, and ALS, since the microglial iron accumulation was reported in the M1 of ALS cases, Cosottini et al. evaluated the radiological appearance of the M1 in a group of HSP patients using iron-sensitive MR imaging. M1 findings were compared between HSP, PLS, and ALS patients [61]. Recently, Yasui et al. found M1 low signal intensity on SWI correlated with disease progression rate and UMN score in ALS patients [22]. To sum up, changes in signal intensity are suggestive of ALS patients and clinical UMN involvement. Recent studies have suggested that thinning and hypointensity of the M1 can be MRI markers of UMN impairment in MNDs. The hypointensity of M1 has also been found to be higher in UMN-ALS. MRI features such as CST hyperintensity and motor cortex SWI hypointensity may be useful for diagnosing and prognosing ALS.

One of the most important points in MRI is artifacts. Motion artifacts can occur due to involuntary patient movements during the MRI scan, resulting in blurring or distortion of the images. This can make it difficult to accurately identify the MBS in the motor cortex. Similarly, entry slice phenomenon artifacts can occur at the edges of the brain slice, resulting in signal loss or distortion that can affect the identification of the MBS. Both of these artifacts were observed in the studies conducted by Pai et al. and Makkawi et al., respectively [15, 24]. Magnetic susceptibility artifacts occur when there is a disturbance in the magnetic field, resulting in signal loss or distortion in the images. This can also affect the identification of the MBS in the motor cortex. However, techniques such as SWI and QSM can be used to minimize the impact of these artifacts. In sum, while T2*-weighted, SWI, and QSM techniques can be useful in

identifying the MBS in ALS patients, the accuracy of these techniques may be limited by motion artifacts, entry slice phenomenon artifacts, and magnetic susceptibility artifacts. Further research is needed to develop methods to minimize the impact of these artifacts and improve the accuracy of MBS diagnosis in ALS patients [39, 40, 50].

5.4. Limitations and Recommendations. Although the reviewed studies consistently reported the presence of MBS in patients with MNDs, there are some limitations to consider. The exact pathophysiological mechanism leading to MBS is not fully understood, and the role of iron accumulation in disease progression remains unclear. Furthermore, the sensitivity and specificity of MBS in diagnosing MNDs and distinguishing them from other neurological conditions are yet to be comprehensively evaluated.

There are several limitations to the current literature on the use of MRI for detecting MBS in MNDs. These limitations include the small sample sizes and heterogeneity of patient populations, as well as the lack of multicenter studies. The observed variability in the detection and interpretation of MBS across the studies also suggests that the use of standardized imaging protocols and analysis methods could enhance the utility of this neuroimaging biomarker.

Additionally, there may be variability in MRI findings depending on the stage and severity of the disease. To address these limitations, future studies should aim to use larger and more homogeneous patient populations, with standardized imaging protocols and outcome measures. Longitudinal studies may also be useful for assessing changes in MRI findings over time and their correlation with clinical outcomes. Furthermore, the use of advanced MRI techniques, such as DTI and MRS, may provide additional information about WM integrity and metabolic changes in the CNS.

There are also technical limitations to consider when using MRI to detect MBS in MNDs. These include artifacts from patient motion, the need for specialized imaging coils and software, and the potential for false positives and negatives. Therefore, future studies should strive to optimize imaging techniques and protocols to minimize these technical limitations and improve the accuracy and reproducibility of MRI findings.

Based on the findings of Chung et al., which demonstrated the utility of QSM in detecting MBSs in patients with ALS and PLS, QSM could be recommended for future studies investigating MBSs in MNDs [7]. Based on literature, QSM may provide more accurate and sensitive detection of MBSs compared to other MRI techniques, particularly in patients with mild or early disease as well as those with motion artifacts or calcifications.

To improve the clinical utility of QSM, it can be beneficial to develop automated or semiautomated algorithms for QSM analysis, which could facilitate the detection and quantification of MBSs and other MRI biomarkers of MND. Furthermore, the integration of QSM with other MRI techniques, such as DTI, fMRI, and magnetic resonance fingerprinting (MRF), may provide a more comprehensive understanding of the neurodegenerative process in motor neuron disease.

6. Conclusion

Early diagnosis of MND is difficult because the signs and symptoms are not always clear. Several MRI strategies have been proposed to detect radiologic markers of neurodegeneration in ALS. Magnetic susceptibility imaging is a type of MRI technique that can detect subtle changes in the magnetic susceptibility of tissues. There are several different techniques used for magnetic susceptibility imaging, including T2*-w, SWI, and QSM. For example, the band-like hypointensity of the precentral gyri (MBS) and hyperintensities in the CSTs have been suggested as markers of, especially, UMN degeneration. SWI is the most sensitive sequence to detect this low signal intensity in precentral cortices in ALS patients. To sum up, MBS is suggestive for ALS patients and a few other diseases, such as SCA17. Recent studies suggest that hypointensity and atrophy of the M1 and nearby regions can be used as MRI markers of UMN impairment in MNDs. To find out how often, how sensitive, and how suggestive the MBS is in MNDs and neurodegenerative movement disorders and how well it works as a prognostic indicator, we will need to do more research that combines comprehensive prospective and longitudinal research.

Abbreviations

ALSFRS-r: ALS functional rating scale-revised
AD: Alzheimer's disease
ALS: Amyotrophic lateral sclerosis
CMA: Cingulate motor areas
CST: Corticospinal tract
DTI: Diffusion tensor imaging
FLAIR: Fluid-attenuated inversion recovery
FEF: Frontal eye field
FTD: Frontotemporal dementia
fMRI: Functional MRI
GM: Gray matter
HSP: Hereditary spastic paraplegia
HD: Huntington's disease
LMN: Lower MN
MRF: Magnetic resonance fingerprinting
MRI: Magnetic resonance imaging
MTI: Magnetization transfer imaging
MESH: Medical subject headings
MBS: Motor band sign
MND: Motor neuron disease
NAA: N-acetyl aspartate
NPV: Negative predictive value
PMA: Parietal motor areas
PD: Parkinson's disease
PPV: Positive predictive value
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PMC: Premotor cortex
PLS: Primary lateral sclerosis
M1: Primary motor cortex
QSM: Quantitative Susceptibility mapping
ROS: Reactive oxygen species
SCA17: Spinocerebellar ataxia type 17

SMA: Supplementary motor area
SWI: Susceptibility-weighted imaging
SWiM: Synthesis without meta-analysis
T2*-w: T2*-weighted
T2-w: T2-weighted
UMN: Upper MN
WM: White matter.

Data Availability

This article contains all of the data produced or analysed during this investigation. Any further inquiries should be forwarded to the corresponding author.

Conflicts of Interest

No conflict of interest was identified by the authors.

Authors' Contributions

S. Mohammadi and S. Ghaderi contributed equally to this manuscript and were involved in all aspects of the study, including study design, data collection and analysis, and manuscript preparation. Both authors reviewed and approved the final version of the manuscript for publication.

Supplementary Materials

Supplementary Table 1 provides the full list of search terms used in the systematic literature review. Supplementary Table 1: search results for motor band sign and associated terms in MNDs on PubMed and Scopus databases. *(Supplementary Materials)*

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