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REVIEW

Visual Impairment in Multiple Sclerosis: A Comprehensive Review of Clinical Impact and Pathogenesis

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Abstract

Multiple sclerosis (MS), a chronic immune-mediated disease of the central nervous system with frequent visual involvement and frequently causes visual dysfunction through demyelination, neurodegeneration, and vascular impairment. Among the earliest and most disabling manifestations are optic neuritis, ocular motor dysfunction, and reduced contrast sensitivity, and for optometrists early recognition and consistent monitoring of these deficits are essential for timely referral, rehabilitation, and quality-of-life support. This review discusses the implications for optometric practice by synthesizing recent evidence on visual pathway alterations in MS. A narrative review of literature published between 2018 and 2025 was conducted using PubMed, Scopus, and Web of Science, and keywords included "multiple sclerosis,""optic neuritis,""visual function,""optical coherence tomography," and "optometry." Articles focusing on visual dysfunction, assessment tools, and management strategies relevant to optometry were prioritized. Emerging evidence highlights the utility of optical coherence tomography (OCT) and visual evoked potentials for detecting subclinical optic nerve damage, while functional deficits such as impaired contrast sensitivity, reduced stereoacuity, and visual field loss significantly impact daily activities. Through comprehensive eye examinations, monitoring of visual performance, and identification of red flags requiring neurological referral, optometrists play a central role in early detection. Recent studies also emphasize low-vision rehabilitation, prisms, and tailored visual aids as effective strategies to improve quality of life in affected patients. Visual dysfunction is a common and often under-recognized component of MS, and optometrists are well positioned to provide functional support, detect early signs, and collaborate in multidisciplinary management. Integrating advanced imaging, functional testing, and low-vision strategies into routine optometric care may improve both visual outcomes and patient quality of life. The present review summarizes pathophysiological mechanisms, clinical manifestations, diagnostic tools, and rehabilitation approaches, while new advances in OCT, OCT-angiography, and artificial intelligence-based analytics are discussed.

Keywords: Multiple sclerosis, optic neuritis, visual function, optical coherence tomography, optometry, low vision

Introduction

Multiple sclerosis (MS), a chronic immunemediated demyelinating disorder of the central nervous system that primarily affects young adults with peak onset between 20 and 40 years, is characterized by multifocal lesions, inflammation, demyelination, and neurodegeneration in brain, spinal cord, and optic nerves, and often leads to progressive neurological dysfunction (1). As of 2023, MS affected ~2.9 million individuals globally, with females more commonly affected than males (2), and visual disturbance is often an early sign reflecting the disease's predilection for the optic nerves and visual pathways (3).

Visual impairment in MS encompasses a broad spectrum, ranging from acute optic neuritis (ON) to chronic, subclinical dysfunction. ON presents as the initial symptom in about one fifth of MS cases, and up to half of patients experience at least one episode during the disease course (4,5). Persistent visual deficits, including reduced contrast sensitivity, color desaturation, visual field defects, diplopia, or ocular motility disorders, are also common often impairing daily functioning even when high contrast visual acuity (HCVA) remains relatively preserved (6,7).

Beyond acute inflammation, MS produces chronic retinal neurodegeneration even in eyes without clinical ON. Optical

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coherence tomography (OCT) demonstrates thinning of the retinal nerve fiber layer (RNFL) and ganglion cell-inner plexiform layer (GCIPL), correlating with both visual dysfunction and global central nervous system changes (8,9). These findings reinforce the value of visual system biomarkers for assessing disease activity and monitoring progression.

This review aims to integrate recent findings (2018-2025) on visual impairment in MS and to outline the clinical implications for both optometric and neurological practice.

Methodology

Search Strategy and Selection Criteria

A comprehensive literature search was conducted across PubMed, Scopus, Web of Science, and Google Scholar for publications between January 2018 and September 2025, using the keywords "multiple sclerosis," "optic neuritis," "visual dysfunction," "low contrast acuity," "retinal nerve fiber layer," "OCT," "OCT-angiography (OCT-A)," "visual rehabilitation," and "artificial intelligence (AI) in MS," with Boolean operators ("and," "or") applied to combine terms. Studies were included if they comprised (a) peer-reviewed original research articles, systematic reviews, or meta-analyses, (b) English-language publications, and (c) work focusing on visual or ocular manifestations of MS. Exclusion criteria consisted of (a) case reports, conference abstracts, or commentaries lacking primary data; (b) non-English articles, and (c) studies unrelated to visual outcomes. Reference lists of included papers were also screened to identify additional relevant studies. From a total of 136 publications, 92 met the inclusion criteria and were used to inform this review.

Epidemiology and Clinical Context

Visual disturbances are a hallmark of MS and commonly constitute one of its earliest clinical manifestations. ON represents the most frequent acute visual event, functioning as presenting symptom in ~20% of patients and occurring in nearly half during the disease course (4,10), while subclinical optic nerve damage is even more widespread (11,12).

The global burden of MSrelated visual impairment is substantial: more than 60% of patients report visual symptoms—including acute ON, persistent low contrast loss, blurred vision, or diplopia—at some stage (13). These impairments occur across both relapsing and progressive forms, including secondary progressive MS and primary progressive MS (14).

Demographically, onset usually falls between ages 20 and 40 with a marked female predominance (~3:1), and visual symptoms follow similar distributions (2,15). When ON presents after age 50, alternative etiologies such as ischemic or inflammatory non-MS causes are more likely (16).

ON and Risk of Multiple Sclerosis

Prognostic Significance

The ON treatment trial demonstrated that about 50% of individuals with isolated ON develop clinically definite MS over ~15 years (5,17), and risk rises markedly when white matter lesions are present on brain magnetic resonance imaging (MRI) at presentation. Patients with at least one demyelinating lesion have ~72% chance of conversion (5,18). Under the 2017 McDonald criteria, ON is incorporated as diagnostic evidence when MRI or cerebrospinal fluid findings are supportive, enabling earlier diagnosis and earlier initiation of disease-modifying therapies (DMTs) (19).

Clinical Course and Recovery

Recovery after ON is variable: highdose IV corticosteroids accelerate restoration of vision, particularly contrast sensitivity and visual fields, but they do not improve long term HCVA outcomes (5,17,20). Oral prednisone alone is contraindicated because of elevated risk of recurrence (17). Even after apparent recovery occurs, persistent deficits in contrast sensitivity, color perception, and visual fields are common, reflecting incomplete remyelination or axonal injury (21).

Neuroimaging Correlates

MRI is central in evaluating ON, with acute ON typically showing optic nerve T2 hyperintensity and frequently gadolinium enhancement during active inflammation (17). Brain white matter lesions not only support the diagnosis but predict both conversion and future disability. Advanced techniques such as diffusion tensor imaging (DTI) and magnetization transfer imaging (MTI) detect microstructural changes in optic nerve and retrochiasmal pathways even in eyes without clinical ON (22).

Chronic Visual Dysfunction Beyond ON

Persistent visual deficits are experienced by many MS patients even without a history of ON, and up to ~40% exhibit low contrast letter acuity (LCLA) deficits that are missed by highcontrast tests (7,20). These chronic impairments include reduced contrast sensitivity, color desaturation, visual field irregularities, motion perception anomalies, and reading fatigue (6,21).

Structural retinal changes account for much of this dysfunction: OCT demonstrates RNFL and GCIPL thinning in both ON affected and unaffected eyes, and these correlate with quality-of-life measures such as the National Eye Institute Visual Function Questionnaire-25 (NEI VFQ25) (22). RNFL thinning in eyes without ON is also associated with greater disability (as per Expanded Disability Status Scale) and brain atrophy (8,9,23,24), reinforcing the value of routine visual function monitoring as a component of MS assessment.

Pathophysiology of Visual Dysfunction in MS

ON and Demyelination

ON involves perivascular inflammation with disruption of the blood-brain barrier, immune cell infiltration, and demyelination of optic nerve axons. Clinically, patients typically present with subacute unilateral vision loss accompanied by pain with eye movement, color desaturation, reduced contrast sensitivity, and a relative afferent pupillary defect (25,26). In demyelination, visual evoked potentials (VEPs) (pattern and multifocal) demonstrate prolonged latency together with reduced amplitude (27-29).

Axonal Injury and Retinal Neurodegeneration

Significant axonal loss begins early, and ON may result in loss of up to ~40% of optic nerve axons within weeks (30,31). Even when eyes appear clinically unaffected, OCT reveals progressive thinning of the RNFL and GCIPL, correlating with visual deficits, brain atrophy, and disability scores (8,9,12,25,32).

Subclinical Visual Pathway Damage

Eyes without clinical ON frequently demonstrate deficits in lowcontrast acuity, motion perception, and binocular vision (20,33,34), and multifocal VEPs show delayed responses or reduced amplitudes in these unaffected eyes (27,35). Lesions in optic radiations or visual cortex contribute to visual field defects, slowed processing, and interactions with cognitive impairment (36).

Mechanisms of Retinal Injury

Retinal damage can occur independently of optic nerve inflammation: histopathology demonstrates microglial activation, retinal ganglion cell loss, and retinal atrophy even without clinical ON (8,37). A subset of patients develops microcystic macular edema (MME), which is associated with worse visual function and inflammatory disease activity. Proposed mechanisms include Muller cell dysfunction, disruptions of bloodretina barrier and retrograde degeneration (38,39).

Inflammation and Neurodegeneration: A Dual Framework

Inflammation and demyelination account for acute events such as ON, whereas chronic retinal thinning and visual pathway damage reflect ongoing neurodegeneration. This dual framework has therapeutic implications: immunomodulatory therapies reduce relapses and ON frequency but do not prevent longterm axonal loss or retinal thinning (33,40).

Clinical Features and Diagnostic Evaluation

Clinical Features of ON

• ON typically presents with subacute unilateral vision loss evolving over hours to days and is frequently accompanied by pain on eye movement (41).

• Color desaturation, particularly of red hues, and contrast sensitivity deficits are common (42,43).

• Visual field defects are often central or centrocecal. Optic disc swelling is seen in ~35% of cases, whereas the optic disc remain normal in retrobulbar ON (44,45).

Other Ocular Manifestations

• Diplopia from internuclear ophthalmoplegia (medial longitudinal fasciculus involvement), nystagmus or gazeevoked oscillations to brainstem or cerebellar lesions (46,47).

• Homonymous visual field defects arise from optic radiation or occipital lesions.

• More subtle deficits: motion perception, reading fatigue, or binocular dysfunction (34).

Diagnostic Tools

A wide range of diagnostic tools is available to assess visual function in MS, each offering distinct clinical insights. These methods allow detection of both structural and functional abnormalities, from subtle visual deficits to significant neurodegenerative change, and Table 1 presents a comparative overview of the most commonly used techniques, highlighting their utility in diagnosis, monitoring, and prognosis.

- **High Contrast Visual Acuity (HCVA)**

Measures central vision clarity and remains the standard clinical test, although it is less sensitive to subtle visual deficits in MS patients (7,20).

- **Low Contrast Letter Acuity (LCLA)**

Measures contrast sensitivity deficits and detects impairments even when HCVA is preserved; LCLA correlates with RNFL and GCIPL thinning, and is a sensitive functional measure in MS (22,33,48).

- **Color Vision Testing**

Assesses color desaturation, particularly relevant during or after episodes of ON (44).

- **Visual Field Testing**

Detects scotomas and central or peripheral visual field defects, providing lesion localization within the visual pathways (45,36).

- **Optical Coherence Tomography (OCT)**

Measures structural parameters including RNFL and GCIPL thickness and detects MME; OCT is a sensitive biomarker for both acute inflammatory and chronic neurodegenerative damage in MS (8,12,39,40).

- **VEPs and multifocal VEPs**

Evaluate latency and amplitude of visual signal transmission and reveal demyelination and conduction delays even in subclinical cases (27,35,49,50).

Table 1. Comparative summary of major diagnostic tools

Diagnostic tool	Primary parameter assessed	Clinical advantages	Limitations	Relevance in MS-related visual dysfunction
OCT	RNFL and ganglion cell complex thickness	Non-invasive, quantitative, sensitive to axonal loss	Limited correlation with cortical demyelination	Standard tool for detecting retinal neurodegeneration
OCT-A	Retinal microvasculature and perfusion	Visualizes microvascular impairment; complements structural OCT	Motion artifacts; limited field of view	Emerging biomarker for neurovascular coupling and disease activity
VEP	Electrical response of visual cortex to stimuli	Detects subclinical demyelination, functional measure	Influenced by fatigue, non-specific to lesion site	Essential for early detection and monitoring of optic pathway damage
MRI	Demyelinating plaques and optic pathway lesions	Whole-brain visualization, correlates with disease burden	Expensive, less sensitive to subtle retinal changes	Gold standard for diagnosing and staging MS
AI-based image analysis	Multimodal pattern recognition (OCT, MRI)	Automated detection, predictive analytics	Requires validation, potential for algorithmic bias	Promising adjunct for precision diagnosis and prognosis

OCT: Optical coherence tomography, OCT-A: OCT-angiography, VEP: Visual evoked potentials, MRI: Magnetic resonance imaging, AI: Artificial intelligence, RNFL: Retinal nerve fiber layer, MS: Multiple sclerosis

- **Magnetic Resonance Imaging (MRI)**

Detects lesions, active inflammation, and optic radiation involvement; advanced techniques such as DTI and MTI provide microstructural information. MRI remains the gold standard for diagnosis and prognosis in MS (17,22,36).

- **Patient Reported Outcomes (e.g., NEI VFQ-25)**

Capture quality of life and real-world visual impact, providing an essential complement to objective clinical testing (22).

Treatment of Visual Dysfunction in MS

Acute Management of ON

High dose intravenous corticosteroids (e.g., methylprednisolone 1 g/day for 3-5 days with taper) shorten time to visual recovery, particularly contrast, fields, and color perception, although they do not improve long term HCVA (5,17,20). For severe or steroid non-responsive cases, plasma exchange is reserved.

Disease-Modifying Therapies (DMTs)

DMTs (interferon beta, glatiramer acetate, fingolimod, ocrelizumab, cladribine) reduce ON recurrence and suppress MRI inflammatory activity, yet their effect on slowing retinal thinning and neurodegeneration remains modest (46,47,51).

Neuroprotective and Remyelinating Strategies

Strategies under investigation include:

- Phenytoin, which has been shown to reduce RNFL loss in acute ON cohorts (44,45).

- Clemastine fumarate, anti-LINGO1 antibodies, neurotrophic and antioxidant therapies all of which remain in study phases (45).

Symptomatic and Supportive Therapies

- Lowvision aids, magnifiers, electronic reading devices to assist reading and mobility.

- Prism therapy for diplopia and oculomotor exercises with vision therapy for improving gaze stability.

- Vision rehabilitation and occupational therapy further support and maximize independence (46).

Digital Monitoring and AI Integration

Smartphonebased tests for visual acuity and contrast sensitivity correlate with OCT metrics and may enable remote follow-up (46). AI/machine learning models that combine OCT, VEP, MRI, and biomarkers (serum neurofilament light chain) show growing promise for prediction of disease progression and for personalized treatment planning (33).

Rehabilitation of Visual Dysfunction in MS

Visual rehabilitation plays a central role in improving functional outcomes and quality of life in MS-related visual impairment. Conventional strategies such as contrast sensitivity and reading training are now complemented by contrast enhancement filters, digital magnification, and adaptive lighting systems to optimize residual vision, while occupational therapy emphasizes mobility and orientation training for safe navigation and spatial awareness. Adaptive software solutions, including screen-reading programs, speech-to-text converters, and AI-assisted visual scene interpreters, significantly enhance patient independence. Multidisciplinary rehabilitation models integrating neurologists, optometrists, and low-vision specialists are increasingly recommended to deliver holistic, goal-oriented care.

Illustrative Case Example: A 34-year-old woman with relapsing-remitting MS reported fluctuating vision and difficulty with contrast discrimination. OCT revealed thinning of the RNFL, while OCT-A demonstrated reduced vessel density in the superficial plexus. A customized rehabilitation plan involving contrast filters, adaptive magnification, and mobility training resulting in a 25% improvement in LCLA and increased

subjective quality-of-life scores on the NEI VFQ-25 scale after 12 weeks, illustrating the functional impact of integrating structural assessment with rehabilitative care (52).

Emerging Research and Future Directions

Growing evidence supports OCT-A as a sensitive biomarker in MS, detecting reduced retinal vessel density—particularly in macular and peripapillary regions—which may precede structural damage and help distinguish ON-affected eyes.

Parallel research has accelerated development of AI and machine learning models capable of predicting MS progression using OCT, VEP, MRI, and clinical data, with increasing emphasis on model explainability for clinical adoption (12).

An expanding literature also highlights sex differences and lifestyle influences: although MS is more common in women, men may experience greater visual decline, and modifiable factors such as smoking, vitamin D, diet, and physical activity are under investigation for their effects disease progression and visual outcomes.

Explainable Artificial Intelligence in MS-Related Vision Research

Artificial intelligence has substantial potential for early detection and monitoring of optic nerve and retinal changes in MS, but translation to clinical use depends on transparency and interpretability. Explainable AI frameworks aim to demonstrate which image features or biomarkers drive predictions, increasing diagnostic confidence, reducing bias, and supporting ethical integration of AI systems into multidisciplinary MS care. Ongoing research should prioritize clinician-interpretable AI models for OCT and MRI analysis to ensure real-world applicability.

Conclusion

Visual dysfunction in MS is multifactorial, involving acute inflammatory injury (ON), chronic neurodegeneration, and subclinical visual pathway damage. Diagnostic tools—OCT, VEP, MRI—permit early detection and longitudinal monitoring. Current DMTs lessen ON recurrence and reduces relapses but provide limited protection against long term axonal loss and retinal thinning. Emerging strategies, including neuroprotective and remyelinating therapies, AI-based predictive tools, OCTA vascular metrics, and structured rehabilitation, are increasingly important for preserving vision and quality of life. Personalized multimodal monitoring together with early intervention holds the greatest promise for improving outcomes.

Footnotes

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