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The impact of multiple sclerosis on vision and ocular motility. The role of ophthalmologists, orthoptists, and optometrists in patient management and treatment

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HIGHLIGHTS

In multiple sclerosis, ocular symptoms occur in approximately 85% of patients, with 50% experiencing them during the initial phase of the disease.

ABSTRACT

Multiple sclerosis has numerous adverse effects on vision and can lead to significant visual impairment. Beyond the well-known symptom of optic neuritis, multiple sclerosis can cause various eye movement disorders, with bilateral internuclear ophthalmoplegia being the most common. This paper explores the range of visual disorders associated with multiple sclerosis, emphasizing ocular motility issues and the crucial role of eye care professionals in managing these patients.

Key words: multiple sclerosis, orthoptic and ocular symptoms, ocular motility

INTRODUCTION

Multiple sclerosis (MS, lat. *sclerosis multiplex*) is an autoimmunological and inflammatory chronic disease of central nervous system manifesting in demyelination, gliosis and axon loss [1]. This disease affects mostly brain, spinal cord, and nerves. The abnormal nerve conduction is caused by loss of myelin in medullary sheath and production of sclerotic layer. In case of inflammation some biochemical changes occur as well [2]. The disease can develop asymptomatically for many years. The causes for MS have not been thoroughly understood. Risk factors are related to a latitude, tobacco use, vitamin D level and Epstein–Barr virus occurrence. Likewise, infectious mononucleosis increases the risk of the disease [3]. Risk factors in combination with genetic predisposition play an important role in patomechanisms leading to the development of the disease. MS is one of the most frequent neurodegenerative diseases in central nervous system, mostly relating to women. It occurs usually in third decade of life. Walton et al. [4] indicate that there are about 2.8 million people in the world living with MS. Authors emphasise that since 2013 frequency of disease occurrence has increased in every world region. Thus, undoubtedly, this disease constitutes a significant medical and social issue. This paper will focus on discussion of the impact of MS on vision, especially ocular motility, and the role of vision specialists in diagnostics and treatment of the disease.

SYMPTOMS AND DIAGNOSIS

Multiple sclerosis begins before any first clinical symptoms appear. The most frequent initial symptoms include: tingling of the limbs, tremor, neuralgia, cramps, dysarthria, fatigue, pain and optical nerve inflammation. Partially demyelinated axons can defuse spontaneously, which causes sensory disturbances. Increased mechanical sensitivity causes signs invoked by movement, including light flashes provoked by eye movement, as well as electrical sensation in one's spine (Lhermitte's sign). Signs of MS can be divided into several groups, depending on what area is seized: in the brain, in the brainstem, in the cerebellum, in the spinal cord or in the optic nerve [5]. MS diagnosis consists of imaging study, especially magnetic resonance imaging (MRI), lumbar puncture, evoked potentials (EP), serological tests, and oligoclonal bands test. Precise diagnostic criteria of MS were included, among others, in McDonald's criteria from the year 2023 [6]. The disease usually develops gradually, for years, and it can have variable progress. Nevertheless, the disorders progression is constant. Figure 1 illustrates the process of demyelination and the formation of sclerotic lesions, which are responsible for the disruption of nerve impulse transmission.

FIGURE 1

A simplified conception of MS formation mechanisms.

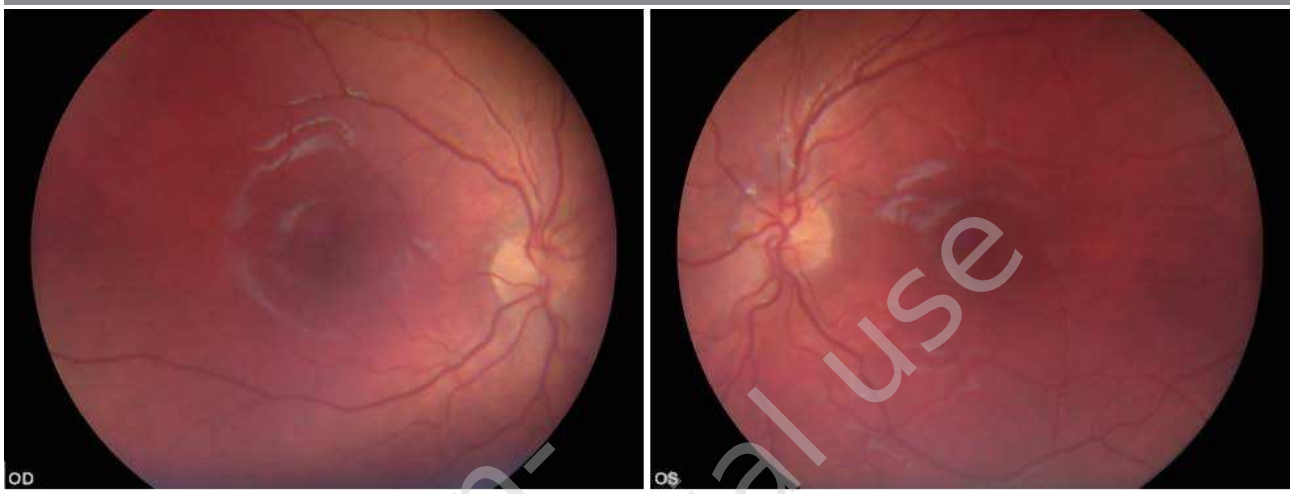
MOST FREQUENT DISEASES AND DISORDERS OF VISION

Multiple sclerosis has multiple, negative impact on vision. It is a consequence of damaging of afferent pathway of vision (sensory nerve) and efferent pathway of vision, which controls ocular motility. Ocular symptoms in MS occur in 85% of patients on average and in the initial disease phase 50% of patients suffer from it [2]. The frequency of occurrence of eye diseases and vision impairments can be encapsulated in this order: internuclear ophthalmoplegia (INO) 53%, optic neuritis 21–46%, nystagmus 15–48%, diplopia 9–38.6%, decreased visual acuity, ocular motility disorders, visual perception disorders, optic neuropathy, filed of view disorders, difficulties in reading and hand-to-eye coordination [7]. First ophthalmic sign is undoubtedly optic neuritis, which occurs in extraocular section in about 25% of patients [8]. Optic neuritis can manifest in unilateral, painful visual acuity decrease, scotoma, anisocoria, RAPD (Relevant Afferent Pupillary Defect) positive symptom, colour vision deficiencies, decreased contrast perception. Optic nerve can be pale, sometimes swollen [5], in VEP (visual evoked potentials) test one might observe the extent of wave latency [9]. Patient can have the impression of object curving in motion (Pulfrich's phenomenon), or Uhthoff's sign can manifest, which is correlated with decrease of visual acuity as a result of hyperthermia. It is worth to emphasise that the majority of optic neuritis cases is caused by idiopathic inflammatory demyelination, which can occur in isolation or as an MS manifestation. In these cases, indirectly can also occur vascular membrane inflammation or an inflammation of a partial part of vascular membrane (*pars planitis*). Importantly, optic neuritis may not show any changes on fundus examination, as it often occurs retrobulbarly (fig. 2).

Uveitis in MS is a rare ophthalmic sign, but one should remember that it can include: hemmorheas and retinal neovascularization, wet macular oedema, and paravenous inflammation [11].

FIGURE 2

Optic nerve inflammation as an MS sign.



ORTHOPTIC SIGNS

Barnes and McDonald [12] classified ocular motility disorders in MS, and these include:

- abnormalities in pursuit eye movement in free phase
- abnormalities of any eye movement type: ocular dysmetria and unstable eye fixation, damages to medial longitudinal fasciculus, vertical eye movement palsy, "one and a half" syndrome, dorsal midbrain syndrome, skew deviation
- isolated oculomotor nerve palsy
- nystagmus: horizontal, vertical, rebound, intermittent alternating
- paroxysmal eye motility disorders: ocular flutter, square wave jerks, opsoclonus.

Many authors emphasise that the best known clinical disorder of ocular motility in MS is bilateral internuclear ophthalmoplegia. Often one can observe as well conjugated gaze disorders, including extent of saccade latency, decrease of saccadic velocity, inaccurate saccades and broken pursuits. As a result of axonal hyperactivity, short diplopia attacks can occur. Bacler et al. describe additional presence of nystagmus evoked by gaze, which is jerky with a slow drift in one direction and a resetting saccade in the other direction.

Morris and Rowe [13] described ocular motility disorders in MS, depending on their localization (tab. 1).

It is important to stress that isolated cranial nerves palsy can be symptoms of multiple sclerosis and most frequently affect VI nerve. What is more, slow pursuit eye movements often are impaired in MS patients and their intensity correlates with a degree of neurological disorder. Other atypical oculomotor dysfunctions were described by de Seze et al. [14] and they might manifest in a form of bilateral III nerve palsy, opsoclonus, and Horner's syndrome.

TABLE 1

Ocular motility disorders and their localisation in the brain.

Type of disorder	Demyelination localisation
Cranial nerve palsy, paretic squint	cortical
Intranuclear ophthalmoplegia	brainstem (mainly medial longitudinal fasciculus)
Parinaud's syndrome	brainstem (dorsal midbrain)
"One and a half" syndrome	brainstem (nucleus of the nerve VI and medial longitudinal fasciculus)
Horizontal gaze palsy	brainstem (nucleus of the nerve VI)
Vertical deviations	brainstem, tegmentum of midbrain
See-saw nystagmus	brainstem, midbrain, interbrain
Upbeat nystagmus	brainstem, midbrain, medial nucleus
Rebound nystagmus	brainstem and cerebellum, as well as their projections
Intermittent alternating nystagmus and downbeat type	cerebellum
Inaccuracy of saccades and slow pursuit eye movement	cerebellum

Some disorders can be of a very subtle nature and thus, as it is emphasised by Józefowicz-Korczyńska and Pajor [15], electrooculography is a highly useful test in detecting any subclinical cases, because results are not impacted either by test paradigm or patient's age. It is worth highlighting here that as far as ocular symptoms in MS are common, those connected with pharmaceutical treatment occur very rarely [16].

CHARACTERISTICS OF CHOSEN OCULARMOTILITY DISORDERS

Cranial nerve palsy, paretic squint

In multiple sclerosis disease there can occur cranial nerves impairment, including as well oculomotor impairments. Most frequently, palsy manifest in nucleuses and neural bundles. As it is highlighted by Bet-Shlimon and Etienne, among the isolated cranial nerves palsy in MS, the most frequent one is of nerve V (trigeminal): 4.8%, next of nerve VII (facial): 3.7% and nerve VI (trigeminal): 1.0% [17]. The abducens nerve palsy is a relatively rare sign of MS, both during the development of the disease, as well as in its exacerbation. It is worth noticing that the statistics on frequency of abducens nerve palsy occurrence are very diverse, and some research report that MS can be a reason of this nerve palsy, even in 24% of cases [18]. Patients with the abducens nerve palsy usually manifest esotropia and bilateral horizontal vision, which resolves after an eye occlusion. In case of paretic squint, a full orthoptic diagnostic is essential, with a particular consideration of tests in 9 gaze directions, with measuring of primary and secondary angles, as well as assessment of binocular functions. It should be added that MRI may not detect changes in brainstem in all cases of VI nerve palsy, and differential diagnostics should incorporate diagnostics for mass lesions, Lyme disease, viral infection, syphilis, sarcoidosis, and vascular disease [18].

Intranuclear ophthalmoplegia

INO is characterised by limited or slowed adduction in the affected eye, which is possible to observe especially during saccadic eye movements. It is usually accompanied by nystagmus in abduction in contralateral eye and in a maintained vergence reflex. The frequency of INO occurrence in MS patients is about 25% [19]. Patients can sometimes have no symptoms or complain of diplopia, oscillopsia or other subjective conditions present in duction. Bilateral INO can manifest with substantial exotropia, so called WEBINO syndrome (walleye), resulting in horizontal diplopia, but can also be connected with vertical eye movement disorders, such as skew deviation (described further in the paper). Similarly to other signs, INO is a result of medial longitudinal fasciculus impairment, midbrain impairment in the vicinity of nucleus of nerve III, demyelination or infarction [19, 20]. In seniors, INO most commonly occurs as secondary to ischemic stroke, whereas in case of young patients, their diagnostics should be oriented to demyelination diseases. Symptoms of INO initially can be subtle during eye movement tests and they tend to get undetected by an inexperienced examiner, especially in case of myasthenia gravis, which can imitate INO. It should be stressed that intranuclear ophthalmoplegia symptoms may resolve spontaneously with time or after the administration of IV steroids [19].

"One and a half" syndrome

It is connected with biliteral INO and horizontal gaze palsy. For eye movement in horizontal plane abduction can be maintained on the contralateral side. Upgaze movement is maintained. The reason to the "one and a half" syndrome is invasion of medial longitudinal fasciculus, paracentral reticular formation, as well as nucleus in nerve IV in a homonymous side to the brainstem [20]. It is a rare syndrome of neurological sings. But along with INO it can be a frequent sign of MS initial phase [21].

Parinaud's syndrome

This syndrome is also called dorsal midbrain syndrome or cerebral aqueduct (Sylvian aqueduct). It constitutes of many clinical signs, of which the most characteristic is upgaze paralysis [22]. Other clinical manifestations of the syndrome are:

- vergence-retraction nystagmus with a spasm of extraocular muscles during gaze upwards
- squint, especially oblique strabismus and esotropia
- vergence palsy or spasm
- pupil reaction disorders, which may be medium wide and poorly react to light, but remain reactive during vergence
- Collier's sign – lid retraction in primary position [20].

This syndrome is most frequently associated with pineal gland and midbrain tumours, hydrocephaly, ischemic lesions or less frequently with metabolic, drug-induced, degenerative, infectious, and inflammatory causes [22]. Frequency of dorsal midbrain syndrome occurrence among MS patients is hard to asses.

Vertical deviations

Known as well as skew deviations. It is an acquired vertical deviation, which is not a result of single oculomotor muscles or nerves disorders. Similarly to "one and a half" syndrome in MS patients, it is most frequently correlated to INO. Hypertropia usually is present on the affected side and can be a result of supranuclear fibre nerve disruption, moving through medial longitudinal fasciculus, but can also be unrelated to them, for example, in case of brainstem, cerebellum or thalamus lesions. Skew deviation manifests subjectively in vertical diplopia, which can be reduced with vertical prisms. However, with time, this disorder can transform into torsional strabismus with compensatory head posture. Both concomitant features, as well as paretic can be observed in this type of deviations [23]. In case of ischemia aetiology and demyelination, as in MS patients, this disorder frequently has an intermittent characteristics with an observable spontaneous regeneration [24].

See-saw nystagmus

Nystagmus can occur in MS disease too. Typically, it is a horizontal nystagmus, but can be vertical, alternating and, among other types, see-saw type, depending on damaged brain structures. Most frequently they give an impression of trembling objects, decreased vision, eye exhaustion, perceptive and coordination disorders. See-saw nystagmus is rare, but worth noticing, kind of nystagmus. The name refers to sequence of inaccurate eye movements, which causes one eye goes upwards and the other downwards. Apart from alternating opposing vertical movements one experiences ocular rotation. Eye move synchronically up and down. The eye going upwards presents incyclorotation, and the eye going downwards excyclorotation [25].

Chosen paroxysmal eye movement disorders

In this group of oculomotor disorders most frequent are:

1. **Opsoclonus** as spontaneous, uneven, fast eye movements both in vertical, as well as horizontal planes, which can escalate in a fixation attempt. They occur as conjugated saccades of big amplitude in every gaze direction. Opsoclonus is often accompanied by myoclonus, which can take the form of paraneoplastic origin [26].
2. **Myokymia**, meaning, paroxysmal spams, which can manifest as trembling rebound eye movement, but also face muscles trembling. MS is characteristic of spontaneous myokymias of superior oblique muscle, innervated by trochlear nerve (IV), characterized by high frequency and small amplitude. They last few seconds and can repeat again and again during day. Usually they manifest in hard to spot unilateral nystagmus with coexisting diplopia, oscillopsia and blurred vision. In some cases, myokymia can be precede IV nerve palsy [20].

VISION PROGNOSES AND TREATMENT

Treatment of MS patients should be maintained interdisciplinary, which has a considerable meaning in the process of treatment. Decrease and withdrawal of ocular symptoms is hard to predict. In some patients difficulties of ocular nature can completely resolve, though in others only partially. Morris and Rowe [13] point out, after many other authors, that the improvement of vision may occur in 6 weeks. What is interesting, Smith and McDonald [27] note that the restoration of nerve conduction is supported by short internodes preceding demyelination area and small diameter of axon. Undoubtedly, systematic ophthalmic control is important, the same with following doctor's advice. In some patients' healing process it is helpful to use appropriate optic or non-optic help, as well as vision therapy. Physiotherapy and, of course pharmacotherapy, are extremely important aspects in rehabilitating MS patients. In case of centripetal pathway damage and vision loss, bilateral in nature, patients may experience visual hallucinations known as *Charles Bonnet syndrome*. Then treatment should consist of psychiatric care as well, for this syndrome occurs because of visual cortex activity without stimulation from the eyes. In this case proper dosages of olanzapine may be helpful [28]. As to this day the cure for MS has not been found, its treatment focuses mainly on stopping disease progression, stopping relapses and easing ailments, as well as delaying progression of disability.

THE ROLE OF SPECIALISTS OF EYE PROTECTION IN MULTIPLE SCLEROSIS TREATMENT

The meaning of professional ophthalmic, orthoptic and optometric care in MS patients is not to be underestimated. It can be divided into 3 realms: screening eye tests, eye disease diagnostics and bilateral vision, as well as vision therapy with selection of ophthalmic help.

First aspect of support means monitoring vision by regular check-ups, especially aimed at fundus examination screening, for example, by direct or indirect fundoscopy or picturing of fundus with funduscamera. Each MS patient manifesting visual signs, such as strabismus, nystagmus, diplopia, should obligatory have full orthoptic examination done. As highlighted by Rowe [2] orthoptic diagnosis depends on the type of ocular motility disorder, which can include paralysis of one or many extraocular muscles, nystagmus, saccadic disorders, pursuit movement impairment, as well as vestibular-ocular disorders, gaze palsy and skew deviation. Other necessary test is vision acuity test, because, as it was stressed by Hickman et al. [29], up to 72% of MS patients have decreased visual acuity up to 20/30.

Apart from standard ophthalmic diagnostic it is worth to perform test on contrast sensitivity, colour vision, and field of vision, because due to frequent optic nerve impairments, disorders in parametric tests are a common occurrence. The role of orthoptists and optometrists may also mean a selection of proper ocular correction, prims or other visual aids. Jenkins [30] points out that in 34% of patients there was an improvement after applying a dedicated orthoptic treatment. This refers to the cases with vergence deficiency and applying a prism mainly in vertical and paretic strabismus. Tinted lenses may be helpful as well, for example the blue ones, or filters of neutral density for patients with movement perception impairment [2].

Although some people need an administration of *Botulinum* toxin or surgical procedure, there are many strategies, which can help improve the vision, such as: eye movement, accommodation, stereoscopy, hand-to-eye and balance coordination exercises. Research done by Tarakci et al. [31] showed that a group training of MS patients contributes to balance improvement, decrease in spasticity and ex-

haustion. This may suggest a potentially beneficial effect of chosen vision therapy elements. As Beer et al. [32] point out, vocational rehabilitation of MS patients requires employers' commitment, as well as involvement of a multidisciplinary team and contributes to enhancing the patients' quality of life.

CONCLUSION

Multiple sclerosis is a common disease; its characteristics are progressiveness and it contributes to adults' disability in productive age [33]. Despite the known risk factors, the essence of the disease has not been fully discovered. In most of the patients, clinical symptoms affect locomotor, sensory, visual, and autonomic systems. About three quarters of MS patients suffer from vision and oculomotor problems. These are caused by the impact of demyelination on visual pathways, which control eye movements. Barnes and McDonald [12] note that practically all types of oculomotor disorders in multiple sclerosis have been described, but the most common are bilateral intranuclear ophthalmoplegia, abnormalities resulting from cerebellum damages, and rebound nystagmus. Currently MS is incurable, but in the past 2 decades many medicaments appeared and they positively modify the course of the disease [34]. There are many methods that can help improve the functioning for MS sufferers too.

The key role to this improvement have specialists of vision care as they implement screening tests, eye disease diagnostics, help with visual aids, such as diplopia reducing prisms and (if justified) conduct a vision therapy.

Figures: ORTO-OPTICA's own materials.

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