Optical Coherence Tomography in Multiple Sclerosis

Subjects: Clinical Neurology

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Multiple sclerosis (MS) is an inflammatory and neurodegenerative, potentially disabling disease of the central nervous system. OCT (Optical Coherence Tomography) and OCT-A (Optical Coherence Tomography with Angiography) are imaging techniques for the retina and choroid that are used in the diagnosis and monitoring of ophthalmological conditions.

Keywords: multiple sclerosis ; optical coherence tomography ; optical coherence tomography with angiography

1. Introduction

Multiple sclerosis (MS) is a chronic autoimmune disorder of the central nervous system (CNS) characterised by inflammation, demyelination, and extensive axonal loss [1]. Although certain factors, such as Epstein–Barr virus (EBV) infection, smoking, childhood obesity, low levels of vitamin D, and ultraviolet B light (UVB) exposure, have been implicated in the pathogenesis of the disease, the definite underlying cause remains uncertain [2].

Visual symptoms and optic neuritis (ON) are the most common ocular manifestations, occurring in up to 25% of people with MS (pwMS) [3]. Post-mortem studies have shown that 90% of pwMS present degeneration and axonal loss in their optic nerves, regardless of ON history [4][5].

Given that the diagnosis of MS relies on a combination of clinical and magnetic resonance imaging (MRI) findings [6], an expensive and time-consuming method, the introduction of sensitive, low-cost biomarkers that can be used in the screening and monitoring of pwMS remains of vital importance.

The introduction of two commonly used ophthalmic imaging modalities, optical coherence tomography (OCT), and the more recent OCT with angiography (OCT-A) has revolutionised people's understanding of the underlying pathophysiological mechanisms in MS, as they can indirectly provide information about the CNS. The imaging techniques OCT and OCT-A are fast, non-invasive, and inexpensive and provide anatomical and microvascular cross-sectional images of the retina, respectively. Their main application in ophthalmology is in the diagnosis and monitoring of diseases, such as age-related macular degeneration, retinal vascular disorders, and glaucoma. However, given that the retina is an extension of the brain, its use has expanded in the study of neurological and neuro-ophthalmological conditions [7].

The ganglion cells of the retina are located in the ganglion cell layer (GCL) and their axons form the retinal nerve fibre layer (RNFL). Both layers can be easily assessed using the aforementioned techniques, thus allowing the evaluation of potential neuronal and axonal degeneration in people.

2. Optical Coherence Tomography in Multiple Sclerosis

The imaging technique OCT was first introduced in 1991 and uses light waves to obtain cross-sectional retinal images. The RNFL and the GCL-inner plexiform layer complex (GC-IPL) are the two most commonly studied layers in MS. According to the current literature, the thickness of the RNFL and GC-IPL is found reduced in pwMS, and there is an inverse relationship with the disease duration [8][9][10]. Despite several theories, the pathophysiological mechanisms underlying these findings remain unclear [11].

Furthermore, ON is the most typical ocular manifestation, characterized by gaze-evoked retro-orbital pain and reduced visual acuity, and occurs in a significant number of pwMS [12]. Retrograde degeneration leading to axonal loss is the most probable pathological mechanism causing RNFL and GC-IPL thinning. Nevertheless, in patients with no history of ON, these findings could be either due to primary degeneration caused by the disease itself or even to retrograde degeneration after one or more subclinical episodes of ON [13].

Since MRI is the most common imaging modality used in the diagnosis of MS, many studies have focused on associating the relevant findings with those of OCT [14][15][16]. In fact, in a study by Saidha et al., GC-IPL atrophy mirrored atrophy in the white matter, brainstem, grey matter, thalamus, and the whole brain. However, a recent study by Glasner et al. suggested no correlation between white matter plaques and RNFL or GC-IPL thickness [17]. Nevertheless, grey matter atrophy seems to be the most sensitive marker of progressive MS [14]. Additionally, studies have correlated the progression of GC-IPL thinning with the development of new T2 lesions [10], damage to the optic radiations [18], and the formation of contrast-enhancing lesions [14]. One study showed that there was greater thinning in the temporal RNFL in patients with newly formed lesions in the optic radiations [19].

Several studies suggest that OCT may be used as a marker for estimating disability [20][21]. More specifically, RNFL and GC-IPL thinning were independently associated with long-term disability worsening in a recent study by Lambe et al. [22]. These findings were recently supported by Skirkova et al., who found a correlation between peripapillary RNFL values, disability, and brain MRI volumetric parameters [23]. The risk of progression can be three times higher in patients with initial RNFL thickness < 88 μm [24].

Visual acuity and contrast sensitivity are affected in patients with ON and several studies have managed to show that there are in accordance with the OCT findings [8][25][26]. GC-IPL and RNFL thinning parallel low-contrast visual acuity, and according to Lampert et al., dyschromatopsia and GC-IPL thickness are interconnected in pwMS and no history of ON [27].

Thinning of the RNFL and GC-IPL is not specific to MS; however, OCT might be helpful in differentiating it from disorders of the same spectrum. In neuromyelitis optica spectrum disorders (NMOSD), RNFL thinning tends to be more evenly distributed, whereas the temporal quadrant seems to be more affected in patients with ON MS [28]. In addition, both RNFL and GC-IPL are much more severely reduced in NMOSD than in MS. According to Brandt et al., OCT parameters may be valuable in distinguishing MS from Susac syndrome, a rare condition characterized by the triad of branch retinal artery occlusion (BRAO), encephalopathy, and hearing loss [29]. Research has shown that in patients with Susac syndrome, OCT displays scar-like pathological patterns that are strictly confined to the inner retinal layers, sparing the outer nuclear layer and the photoreceptors, thus clearly differentiating it from MS [30].

In 2008, Toledo et al. were the first to correlate OCT findings with cognitive impairment. Researchers have linked reduced RNFL thickness to cognitive disability as measured by the symbol digit modality test, a gold standard measure of information processing speed [31]. These findings were later supported by Sedighi et al., who showed that only 20% of pwMS with cognitive impairment had normal OCT findings [32]. In another study, Coric et al. noted that cognitively impaired pwMS with no history of ON had significantly reduced mean peripapillary RNFL (pRNFL) and mean macular GC-IPL (mGC-IPL) thicknesses compared to cognitively healthy pwMS [33]. Although these results may seem promising, further studies are required to support these findings.

Moreover, OCT has been used to study responses to different therapeutic options. In 2016, Pul et al. found no significant association between interferon beta (IFNβ-1b) treatment and RNFL thinning [34]. However, when Button et al. compared the effect of glatiramer acetate, natalizumab, and interferon-β-1a with the rate of GC-IPL thinning, they found that the natalizumab-treated group had a significantly lower rate of GC-IPL reduction compared to the other two [35].

Visual evoked potentials (VEP) are electrical signals generated by the visual cortex of the occipital lobe in response to visual stimuli. Klistorner et al. studied the relationship between OCT parameters and multifocal VEP (mfVEP) in patients with acute ON and found a significant reduction in RNFL thickness and mean mfVEP, particularly in the temporal quadrant [36]. Additionally, in an earlier study, researchers associated the VEP amplitude with the loss in RNFL thickness in patients with ON and noted that the main mechanism behind this loss is axonal degeneration [37].

One study examined the pupillary light response in patients with MS and found that attenuation of the melanopsin-mediated sustained pupillary constriction response was significantly associated with thinning of the GCL-IPL in pwMS with a history of ON [38].

A recent paper described peripapillary hyper-reflective ovoid mass-like structures (PHOMS) as a novel OCT finding that might be noted in people with early MS. Their presence suggests disease progression; however, more research is needed to support these results [39].

In recent years, artificial intelligence (AI) and machine learning have proven useful in medicine. In a recent study, researchers developed a system based on a convolutional neural network that can classify the disease according to the thickness of the OCT scans, thus assisting in the early diagnosis of the disorder [40]. Machine learning has also been successfully used to predict disability progression in pwMS by analysing RNFL thickness [41].

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