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Optical Coherence Tomography (OCT): a window to the central nervous system

Optical coherence tomography (OCT) is being used more and more by optometrists as a means to directly assess the cells of the retinal and the axons of the optic nerve. Optical coherence tomography is a non-invasive imaging technology that has been compared to ultrasound. It uses light waves rather than sound waves to take cross-sectional images of the transparent layers of the retina to a resolution of up to 15 microns (a human hair is 40 to 120 microns thick). OCT imaging provides diagnostic and treatment guidance for disorders of the retina, such as DR, macular degeneration and glaucoma.

There is now a body of research showing that OCT assessment of the eye can also provide useful information for early diagnosis of neurodegenerative diseases including Parkinson's disease, multiple sclerosis and Alzheimer's disease. In this issue of Primary Eye Care we present an overview of new findings from three studies which investigate thinning of the retinal nerve fibre layer (RNFL) in patients with Alzheimer's disease, fibromyalgia, and hereditary spastic paraplegia.

Previous studies have shown that axonal loss in the retinal nerve fibre layer (RNFL) correlates with the extent of functional disability in multiple sclerosis and Parkinson's disease and evidence of retinal nerve fibre layer thinning in Alzheimer's disease (AD) has been observed in a number of histological, imaging, and electroretinogram (ERG) studies over the past two decades.

In 1996 Blanks et al. found extensive neuronal loss in the retinal ganglion cell (RCG) layer of patients with severe Alzheimer's disease when compared to a control group.

Danesh-Meyer et al (2006) used scanning laser ophthalmoscopy to show the reduction of optic nerve fibres in AD patients compared to age -matched controls. OCT analysis has been employed in other research to evaluate and measure retinal nerve fibre layer (RNFL) thickness in the eyes of AD patients with interesting results.

For example, one study showed that the mean macular RNFL thickness and the mean total macular volume measured by OCT are significantly lower for patients with mild cognitive impairment (MCI), mild AD, and moderate to severe AD when compared to age-matched controls (Paquet et al., 2007). Also, the RNFL thinning is significantly greater in the moderate to severe AD group than for those with mild cognitive impairment. The conclusion is that reduction in total macular volume is related to the severity of cognitive impairment and RNFL thinning may be a useful proxy measure for monitoring disease progression in AD patients.

Later work by Lu et al. in 2010 suggested that patterns of retinal damage may yield additional information over and above simple disease progression. The finding that retinal damage due to AD may be localised preferentially to the vertical quadrants has raised the possibility that localised thinning of the RNFL could be specific to certain forms of neurodegenerative disease rather than part of a generalised change associated with any neurodegenerative process.

Hereditary spastic paraplegia (HSP) offers a perfect model to address the question of whether RNFL thinning represents a non-specific affection in all neurodegenerative disorder or whether it might retain some specificity. Researchers from the University of Tubingen proposed that since HSP preferentially affects the longest axons of the corticospinal tracts the RNFL would be spared if RNFL thinning is a general marker of all forms of neurodegeneration (Wiethoff et al., 2012). There were 28 HSP patients in the study group, 6 of complex phenotype (HSP-c) and 22 of pure phenotype (HSP-p) with disease causing mutations known for 17 of the patients. The control group consisted of 28 healthy subjects matched for gender with mean age of 38 years.

HSP patients demonstrated a tendency to reduced foveal thickness and thinning of overall RNFL but neither reached statistical significance compared to the control group. Changes in RNFL were not uniform with increased RNFL thickness seen in the temporal superior and nasal superior sectors compared to healthy controls. On the other hand, a slight reduction in RNFL thickness in HSP patients was observed in temporal, nasal, nasal inferior, and temporal inferior sectors.

Overall, greatest change observed in HSP patients was foveal total retinal thickness measurement.

Patients with pure HSP showed neither significant reduction of global RNFL nor thinning in any of the individual sectors. Only total retinal thickness at the fovea was significantly thinner in patients with pure HSP.
In patients with complex forms of HSP the RNFL thickness was significantly reduced within temporal and temporal inferior sections. Despite the small sample size, this study added weight to the suggestion that RNFL loss is not merely a general change in any neurodegenerative disease but may emerge in specific patterns depending on the underlying pathology and its expression.

A Spanish study in 2016 (Garcia-Martin et al.) which evaluated RNFL parameters in patients with Fibromyalgia (FM) using OCT analysis, documented the presence of axonal damage in the optic nerve of FM patients, even in the early stages of the disease. The study also found further evidence of specific patterns of localised thinning of the retinal nerve fibre layer across sub-groups of patients with the disease.

Fibromyalgia patients were evaluated according to Giesecke's fibromyalgia sub-groups, the Fibromyalgia Impact Questionnaire (FIQ), and the European Quality of Life-5 Dimensions (EQ5D) to enable disease profiles to be constructed. A total of 116 FM patients and 144 age and sex matched controls were assessed using OCT. Age, sex and intraocular pressure did not differ significantly between FM and control groups but FM patients had significantly reduced RNFL thickness. Analysis with Spectralis OCT revealed significant differences in the nasal and temporal sectors of FM patients and significant thinning of the papillomacular bundle. The researchers noted that although other sectors showed a clear tendency toward RNFL thinning the differences were not statistically significant.

Further sub-group analysis was undertaken using the Fibromyalgia Impact Questionnaire (FIQ) to identify 68 patients with severe FM (FIQ ≥ 60) and 48 patients with mild FN (FIQ score < 60). Both subgroups showed statistically significant thinning of the RNFL in the temporal inferior sectors compared with controls. Further, the RNFL temporal inferior sector thickness was significantly reduced in patients with severe FM compared to those with mild FM.

Despite the intergroup differences detected between patient sub-groups, the direct correlation between FIQ and RNFL parameters did not demonstrate prognostic utility.

Comparing patient sub-groups based on Giesecke's classification - biologic FM (n=26), depressive FM (n=34), and atypical FM (n=56) – it was shown that statistical differences existed between patients with biologic FM compared to the other FM patients when the thinning of RNFL in the temporal inferior and temporal superior sectors were compared.

Given that FM currently lacks a specific and definitive diagnostic test the results of this study open the possibility of facilitating the diagnosis of FM by using OCT to evaluate the optic nerve. RNFL thinning is a clear indicator of the presence of the disease and this has been demonstrated even in early stages of FM.

This will be useful for general practice since OCT tests are non-invasive, fast and comfortable for the patient, and relatively inexpensive.

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