Editorial

Usefulness of the new Spectral-Domain Optical Coherence Tomography (SD-OCT) devices in the study of degenerative dementias

Utilidad de los nuevos dispositivos de tomografía de coherencia óptica de dominio espectral para el estudio de las demencias degenerativas

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Neurodegenerative diseases group a family of cognitive disorders such as multiple sclerosis or Alzheimer, Parkinson or Creutzfeldt-Jakobs. Said cognitive disorders are due to an increase in cellular death processes and are associated to changes in behavior and alteration of many bodily activities including balance, movement, speech, breathing and cardiac function. Alzheimer's disease is the most frequent cause of dementia in old age. It is estimated that in our country 500,000 people have this disease and, due to the progressive aging of our population, this number could quadruple in the next 50 years with devastating consequences not only for the sufferers and their families but also to the very stability of our health system. Alzheimer's disease is characterized by the presence in the brain of patients of 2 aberrant structures, senile plates and neurofibrillary tangles, loss of synapses (mainly between hippocampus and cortical neurons) and axon deterioration.

In Parkinson's disease there is a selective loss of dopaminergic neurons, mainly through brain basal ganglia. Mammal retina contains dopaminergic neurons which are in charge of regulating the receptive field of ganglionic cells to provide contrast sensitivity and chromatic vision. Previous studies have demonstrated that the extension of dopamine in retinal cells is lower in patients with degenerative diseases.

The pathogenesis of multiple sclerosis is not entirely defined, although the majority of authors agree that it is caused by the concurrence of inflammation, demyelination and axon damage processes. Said axonal damage appears in the early stages of the disease and can be monitored by studying the retina nervous fiber layer (RNFL). This layer is formed by the axons of ganglionic cells and therefore does not contain myelin.

There is no specific evidence to diagnose degenerative dementias. Symptoms can vary from one individual to another and could be similar to those of other diseases, particularly in the early stages. The diagnostic criteria are different in each hospital even though some are standardized such as the Poser and McDonald criteria for multiple sclerosis in which clinical findings must be associated to the presence of specific signs in neuroimaging tests. At this point in time, none of the standardized criteria for degenerative diseases include neuro-ophthalmological explorations even though a

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substantial number of authors suggest that, on the basis of the usefulness demonstrated by RNFL analysis for the diagnostic and follow-up of these diseases, optic coherence tomography (OCT) should be included in the diagnostic criteria. Previous studies with time domain OCT (Stratus, Carl Zeiss Meditec, Dublin) have registered acceptable specificity and sensitivity values for diagnosing said neurodegenerative diseases.\textsuperscript{6,7} However, to date no sensitivity and specificity data have been published for the new spectral domain OCT instruments. A preliminary study carried out with Cirrus HD OCT (Carl Zeiss Meditec, Dublin) and Spectralis OCT (Heidelberg Engineering Inc, Heidelberg, Germany) observed that both devices sample high sensitivity (90% with Cirrus and 93% with Spectralis) with an acceptable specificity (85 and 87%, respectively) for diagnosing multiple sclerosis.

The higher performance of spectral domain OCT devices compared with the previous time domain OCT devices is beyond doubt because the quality, resolution and reproducibility of its images and measurements have increased. However, some ophthalmologists have pondered about the improvements provided by spectral domain OCT for studying said neurodegenerative diseases. In this regard, it is to be pointed out that the advantages in this field of ophthalmology are quite remarkable:

- In the first place, new spectral domain OCT devices apply highly developed technology that allows simultaneous measurement of echoes and noise reduction, producing images with less artifacts, greater reproducibility and enhanced definition of the retinal structures and layers. The Cirrus HD OCT device is capable of taking measurements with a resolution of 5/1000 mm and over 67 million different information points with the use of infrared technology. On the other hand, Spectralis OCT simultaneously analyzes multiple wavelengths of the reflected light spectrum at a speed of over 100 times faster than the previous time domain OCT and capturing about 40,000 sections per second. One of the main differences between Spectralis OCT and Cirrus OCT is the combination with confocal scanning (Confocal Scanning Laser Ophthalmoscope) that provides simultaneous images with enhanced image contrast and detail as well as exclusively analyzing the focal point information. Another significant difference is that the Eye Tracking technology of the Spectralis device is able to recognize ocular movements and guide the scanner as it allows control of the image during acquisition.

- The majority of spectral domain OCT allow three-dimensions reconstructions of retina and optic nerve images.

- Some OCT, such as Spectralis, allow the operator to regulate the scanner in order to adapt it to the size of the eye. This translates into the acquisition of high quality images and reliable measurements in highly myopic eyes in which time domain OCT could hardly focus on the retina.

- The software of most spectral domain OCT devices includes a follow-up function in which the device marks anatomical references of each eye. This allows operators to carry out subsequent scans at exactly the same location to detect whether during the follow-up of patient pathology modifications have occurred in the measurements and structures of each retina area or sector. As previous time domain OCT devices did not have said function, it was commonplace to observe retinal thickness changes which did not match true changes but could be caused by slight movements of the eye or head of the patient, by repeating the scan in a different anatomic location or by changes in the scanning circle location.

- The new spectral domain OCT devices enable the acquisition of volume cross sections. By analyzing each one of the data contained in volume information it is possible to study any section in that area and not only the recorded tomographic section. This technology exhibits clear advantages vis-à-vis radial sections made with time domain OCT devices because the volumetric scan controls all the areas in detail and prevents the exclusion of any area in the monitoring and follow-up of pathologies.

- Some spectral domain OCT devices include protocols with specific application in Neuro-ophthalmology (Fig. 1). At present, there is only one application of this type included in clinic: the NSite axonal analysis application of Spectralis OCT that provides among others the RNFL-N pattern in which the acquisition of images during scanning starts and ends in the nasal quadrant of the optic nerve head, so that in the temporal sector the reproducibility and reliability of these measurements are increased. The importance in this scanning change lies in that the temporal quadrant is precisely that which exhibits early alterations in neurodegenerative diseases.\textsuperscript{8} Other protocols included in the NSite Axonal Analytics application of Spectralis OCT are the PMB pattern which focuses on the papillomacular bundle and the nervous fibers surrounding the macula, performing an isotropic scanning that has the drawback of requiring high acquisition times and good patient cooperation but yields a vast amount of information about the thickness of the main bundle that transmits the stimuli collected in the macula photoreceptors (Fig. 1); the OHN-N Pattern, utilized to display papillary edema with 3-D reconstructions and is particularly useful for studying optic neuritis; the volume-in-vertical pattern in which scans are captured at right angles to the nervous fibers, allowing a cross section view, and finally the Enhanced Depth Imaging pattern that carries out a special analysis of the optic disc displaying the lamina cribrosa and therefore the area where axons are covered by myelin.

At this point in time there is no efficient treatment for degenerative dementia, even though dozens of labs all over the world are actively pursuing the identification of new genes and risks involved in these pathologies which could contribute to clarify the physiopathological background and to identify new therapeutic targets. One of the main current problems in neurodegenerative diseases, particularly Alzheimer’s and Parkinson’s, is that when the diagnostic is reached the brain has already suffered extensive and irreparable damage. For this reason, it is urgent to find biomarkers to detect the disease at significantly earlier stages, even prior to symptoms, when any therapeutic strategy would have greater possibilities of success. And in this regard, neuro-ophthalmological exploration can play an important role as a useful tool for
diagnosing and following up said neurodegenerative pathologies.

Some studies have evidenced a good correlation between numerological dysfunction in patients with ME, measured with the EDSS scale (Expanded Disability Status Scale) and RNFL defect measured with OCT. However, the association between RNFL thickness measurements and the characteristics of neurological diseases has not yet been studied with spectral domain devices. In a preliminary study carried out on 30 eyes of Parkinson’s patients, we have observed a significant correlation between the Mini-mental cognitive dysfunctions test score (Mental State Examination) and the mean and temporal RNFL thicknesses measured with the RNFL-N Pattern of the Nsite axonal application of Spectralis OCT. However, we have not observed an association between the Mini-mental test score and RNFL thickness measurements made with the classic glaucoma protocol of Spectralis RNFL or with those taken by Cirrus OCT. We have also observed that the RNFL-N and PMB patterns of the Spectralis Nsite Axonal application are more sensitive than the RNFL protocols of Spectralis and Cirrus to detect defects in RNFL secondary to neurodegenerative diseases.

Some authors suggest that OCT could substitute nuclear magnetic resonance as the “princeps” test for assessing patients with neurodegenerative diseases. However, many neuro-ophthalmologists regard this assertion as excessively ambitious because OCT only assesses a very small part of the central nervous system (SNC), specifically that corresponding to the retina ganglion cells, and even though neurodegenerative diseases tends to affect the SNC in a diffuse manner, considerable variability has been observed between the areas exhibiting greater axonal deterioration depending on said different pathologies as well as great individual variability. Accordingly, we found patients with multiple sclerosis in incipient stages with significant RNFL thickness reduction (e.g. if they have exhibited inflammatory outbreaks at the optic nerve level). Even so, we have observed subjects with the same disease in more advanced stages or progressive forms that hardly exhibit any RNFL thickness reduction.

In conclusion, the new protocols designed by OCT manufacturers that include specific applications for neuro-ophthalmology could provide significant advantages in the assessment of said patients, allowing neurologists to base some of the diagnostic and therapeutic techniques on neuro-ophtalmological exploration, leading to a consultation of
important synergies between neurology and ophthalmology services in hospitals.

REFERENCES