Combining mfVEP and VBM-OCT to Monitor the Topographic Correlation between Smoldering Inflammation and Neurodegeneration in Progressive Multiple Sclerosis

S. C. Huang[1], M. Pisa[1], S. Guerrieri[1], G. Dalla Costa[1], G. Comi[2,3], L. Leocani[1,2]

[1]Experimental Neurophysiology Unit, Institute of Experimental Neurology-INSPE, Scientific Institute San Raffaele, Milan, Italy
[2]University Vita-Salute San Raffaele, Milan, Italy
[3]Casa di Cura del Policlinico, Milan, Italy

Background: A growing body of evidence suggests that chronic inflammation is a major factor of the accumulated neurodegeneration and disability in the progressive phase of multiple sclerosis (MS). The visual system can be used as a non-invasive platform to study neurodegeneration and inflammatory demyelination and monitor their interaction as the disease progress. Neuronal/dendritic loss can be measured with optical coherence tomography (OCT) at the macula, as thinning of ganglion cell layer/inner plexiform layer (GCIPL); while inflammation/demyelination can be measured as prolonged latency in multi-focal visual evoked potential (mfVEP). Since mfVEP separates the visual field into multiple channels, with the aids of voxel-based morphometry (VBM), the GCIPL map can be divided into sectors corresponding to the mfVEP channels based on their topological relationship and perform sector-to-channel correlations. Detailed investigations of the topological relationships between inflammatory demyelination and neurodegeneration can be studied.

Methods: Two groups of newly diagnosed primary (PPMS, N = 16, age = 45.6 ± 11.1 yr, disease duration = 2.7 ± 1.0 yr) and secondary progressive MS (SPMS, N=16, age = 47.5 ± 7.2 yr, disease duration = 14.0 ± 8.8 yr, progression duration = 1.7 ± 1.4 yr) and thirty healthy subjects were enrolled. Macula volume scans were performed and the GCIPL map was segmented with Heidelberg Spectralis OCT, while mfVEP were recorded with Accumap software. The GCIPL map were divided into sectors that correspond to the central 32 channels of the mfVEP topologically. Sector-to-channel correlations were performed between the GCIPL thickness calculated from OCT and the mfVEP parameters (amplitude and latency).

Results: The patient group showed significantly lower amplitude and higher latency compared with the healthy controls. The amplitude of the PPMS group was positively correlated with the GCIPL thickness in sectors located in the central and nasal macula. On the other hand, the latencies in both PPMS and SPMS groups were negatively correlated with the GCIPL thickness, in both central and peripheral sectors.

Discussion and Conclusion: In the study, we enrolled patients with early-diagnosed progressive MS, to demonstrate that even without acute inflammatory attack, longer latency of VEP was still found in the progressive patients, implying ongoing chronic inflammation. Further, the delayed VEPs negatively correlated with the neuronal/dendritic loss quantified as thinning of GCIPL, suggesting that continuous chronic inflammation leads to neurodegeneration. The sector-to-channel correlation can be used to monitor inflammatory neurodegeneration *in vivo* and to screen for potential drugs targeting this aspect.

Key words: OCT, VEP, MS, neurodegeneration

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