DFA Dirección de Formación Académica

CENTRO DE INVESTIGACIONES EN OPTICA, A.C.

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Tesis: "IMAGING APPROACHES FOR THE STUDY OF DEMYELINATION PROBLEMS IN H-ABC TUBULINOPATHY"

Resumen:

Hypomielination with atrophy of the basal ganglia and cerebellum (H-ABC) is a central neurodegenerative disease due to mutations in the tubulin beta 4a gene. Diagnosis is made by integrating clinical data, magnetic resonance imaging of the brain and genetic analysis.

In this work we have used three different imaging approaches for the study of the central nervous system affected by H-ABC: magnetic resonance imaging (MRI), second harmonic generation (SHG) microscopy and fluorescence microscopy. Our experiments were performed in the taiep rat, which is the only spontaneous tubulin beta 4a mutant available for the study of this pathology.

The pathological signs presented by taiep rats and the morphological changes we found by our longitudinal MRI study were similar to those of patients with mutations in TUBB4A. Using the novel label free SHG microscopy, we identified microstructural differences between the central nervous system of taiep rats compared to control animals. We contrasted our MRI and SHG findings with images of fluorescently labeled tissue from taiep and control rats. The fluorescence microscopy results corroborate the hypomielination of taiep rats in the corpus callosum, the cerebellum and the striatum. On the other hand, the comparison of fluorescence with SHG microscopy results, indicate that microtubules from oligodendrocytes were the source of abnormal signal, which was clearly localized in white matter regions.

The importance of this work stems from the demonstration that nonlinear optics can be used not only to study and advance the understanding of the pathophysiology of tubulinopathies, but that it also has the potential to represent a new diagnostic approach to the medical problem. Demyelinating disorders are difficult to diagnose, and therefore new complementary techniques could be helpful for the description of those features of the disease that could potentially be used as clinical markers.

A diverse readership may benefit from the information detailed in this work, whether they are from scientific areas involved in the study of the cell cytoskeleton, the development of optical imaging devices or interested in the study of neurobiology and neurodevelopmental disorders.