Complex Lipids in Hereditary Spastic Paraplegia

Ass Pr. Fanny Mochel, Neurometabolic Research Group, Pitié-Salpêtrière University Hospital, Paris, France

Given the crucial roles of complex lipids in cellular biology, their involvement in hereditary spastic paraplegia (HSP) is expected. In daily practice, some key lipid biomarkers are used to diagnose patients with HSP. Plasma very long chain fatty acids, cholestanol and 27- / 25-hydroxycholesterol are indeed diagnostic for adrenomyeloneuropathy, cerebrotendinous xanthomatosis and SPG5 respectively. These metabolic forms of HSP may account for up to 10-12 % of HSP of unknown etiology and are amenable to dedicated therapeutic interventions. Over the past few years, a novel, and rapidly expanding, group of inborn errors of metabolism associated with the biosynthesis of complex lipids such as phospholipids, sphingolipids and long chain fatty acids has been identified and frequently presents with spastic paraplegia. In my talk, I will particularly highlight the clinical and neuroimaging presentation of HSP patients harboring mutations in genes involved in the synthesis and remodeling of phospholipids (*DDHD1*, *DDHD2*, *NTE*, *CYP2U1*) and sphingolipids (*FA2H*, *GBA2*, *B4GALNT1*). Although these diseases were identified using next generation sequencing, the possibility to analyze the plasma lipidome of these HSP patients may facilitate the discovery, diagnosis and monitoring of this novel class of inborn errors of metabolism.