DIFFERENTIAL EXPRESSION OF PERILIPINS IN HUMAN BRAIN DURING NORMAL AND PATHOLOGICAL AGING

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Introduction: Lipids are the most abundant organic molecules found in the brain, where play a particularly important role for its functions. Alterations of lipid homeostasis and metabolism may contribute to the development of neurodegenerative diseases, as well as cerebral neoplasm. Lipids are stored within lipid droplets (LDs), dynamic organelles characterized by a core of neutral lipids (triglycerides and cholesterol esters) and surrounded by a phospholipid monolayer decorated with several proteins. Under physiological conditions, a low amount of LDs is present in the brain. In recent studies, an increased level of LDs has been found in neurodegenerative diseases, such as Alzheimer's (AD) and Parkinson's diseases, as well as peripheral neuropathy. The regulation of LD homeostasis depend on proteins present on the surface of LDs. Among these, the most abundant are Perilipins (Plins), a family of five proteins (Plin1-Plin5), sharing sequence similarity and the capacity to binds LDs. Plins are expressed in many metabolic tissues, such as skeletal muscle and liver, with a specific expression pattern. An abnormal expression of Plins is associated with a deregulation of LDs metabolism and the development of several metabolic diseases in liver and skeletal muscle. Moreover, we have observed that Plin2 expression levels in skeletal muscle increase with aging. In contrast, the role of Plins in the brain is still poorly understood, in both normal and pathological conditions, as well as aging.

Methods: We characterized the expression of Plins in different representative areas (frontal and temporal cortex, cerebellum and hippocampus) of the brain obtained from 12 subjects of different age (33-104 years). Moreover, we analyzed samples from 3 AD, 1 Lewy Body dementia and 1 cap CAA patients.

Results: Plin1 and Plin4 are not expressed in any of the considered areas of the healthy subjects, while Plin5 is ubiquitously expressed. Plin2 is expressed in the neurons of the cortex grey matter, hippocampus and *nucleus dentatus* cerebellum. At variance, Plin3 is expressed in the white matter. With age, Plin2 and Plin3 increase in the considered areas, while Plin5 remains stable. In the pathological samples Plin2 is unexpectedly decreased, while Plin3 is apparently less affected.

Interestingly, in AD neurons a weak Plin1 positivity is evident. Further analyses on dissected white and grey matter are ongoing.

Conclusions: This study provides for the first time an overview of Plins expression in the brain, and suggests that Plins (in particular Plin2 and Plin3) are possible markers/targets of aging and neurodegenerative processes.