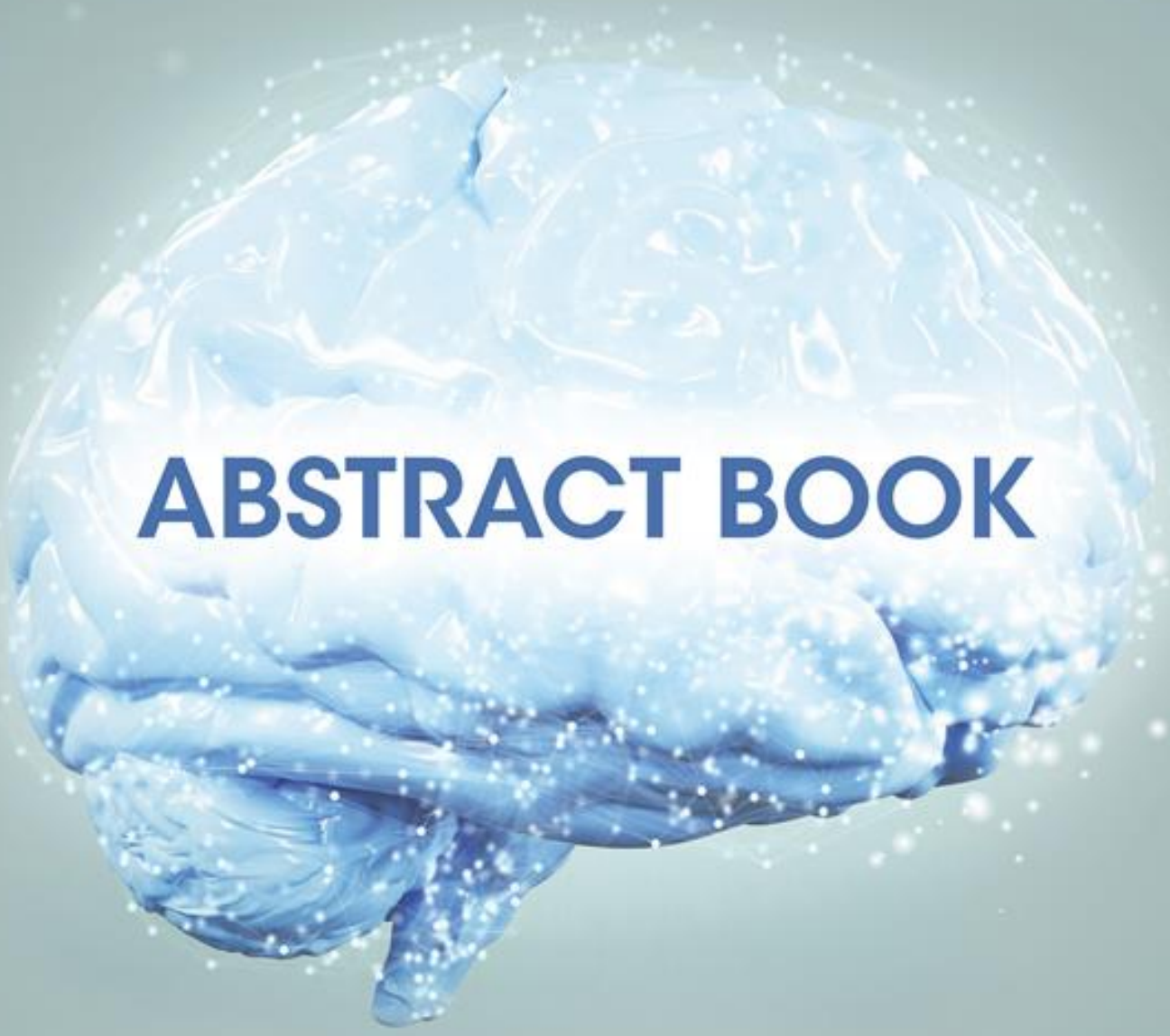
19th MEETING

3-5 November 2021

Lleida



ABSTRACT BOOK

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COMPARING ASTROGLIAL REACTIVITY IN TWO TRANSGENIC MOUSE MODELS OF TAUOPATHY

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Astrocytes are becoming crucial players in the pathology of neurodegenerative disorders, such as Alzheimer's disease (AD). Astrocyte responses have been mainly analyzed in the context of amyloid-beta (Abeta) pathology, highlighting their role in the development/progression of amyloidosis and their relationship with the microglial response. Regarding tau pathology, some studies have reported that astrocytes respond to hyperphosphorylated tau (phospho-tau) and suggested their implication on tau transmission/elimination. Here, we aimed to analyze the astroglial reactivity to tau pathology in the hippocampus of two transgenic mouse models of tauopathy, ThyTau22 and P301S. Proteinopathy was assessed by western-blotting and immunohistochemistry using phospho-tau antibodies (AT8). Inflammatory markers (GFAP, Iba-1, CD45, TREM2) were analyzed by qPCR and immunohistochemistry for bright-field microscopy; glial-phospho-tau relationship was analyzed under confocal and transmission electron microscopy. P301S mice exhibited an intense reactive astrogliosis, increasing with aging in parallel to a strong phospho-tau pathology. ThyTau22 model showed a slighter astrocyte reactivity accompanied by a lesser accumulation of phospho-tau. Astrogliosis in P301S mice closely correlated with an acute DAM-like microglial activation, not observed in ThyTau22 hippocampus. Confocal and ultrastructural studies revealed that, in both models, astrocytic processes contained phospho-tau, especially those surrounding blood vessels. Our results support that astrocytes respond to tau pathology in the absence of Abeta. This reactivity highly correlates with phospho-tau pathology and markedly depends on microglial activation. Moreover, astrocytes may play a role in the elimination/spreading of phospho-tau species through the brain. Deciphering the mechanisms underlying these processes might help to develop therapies to slow down the progression of AD.
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