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MEETING ABSTRACT

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Neuroinflammatory pathways involved in the selective neurodegeneration observed in a transgenic mouse model of multiple system atrophy

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Background: Multiple system atrophy (MSA) is a fatal neurodegenerative disease characterised by widespread oligodendroglial alpha-synuclein deposits and secondary neuronal degeneration. Neuroinflammation plays a pivotal role during the progression of the pathology. Microglia, in particular, represent especially intriguing actors during these events; however, their exact role within disease progression, as well as relevant mechanisms, still need to be clarified. This study aims to analyse the pathways involved in the neuroinflammatory region-specific events occurring, over the disease course, in a transgenic mouse model of MSA.

Methods: PLP-α-Syn transgenic mice (overexpressing alpha-synuclein in oligodendrocytes under the proteolipid protein promoter, PLP) and wild type C57BL/6 controls of 2, 5 and 15 months of age were used. Immunohistochemistry was performed to observe the distribution of proteins related to specific neuroinflammatory pathways. Biochemical analysis was applied to assess levels of cytokines/chemokines. All analyses were performed on specific brain regions involved in the pathology.

Results: We show differential expression of specific cytokines and chemokines in a region- and age-specific way, which might selectively contribute to the disease pathogenesis and progression. Early microglial activation is particulalry robust in the substantia nigra of PLP-α-Syn mice compared to control animals, as assessed by different markers.

Discussion: Our findings show that the differential pathology observed in the brains of PLP-α-Syn mice is accompanied by region-specific neuroinflammatory events. Furthermore, they suggest an important role of the early, alpha-synuclein-triggered neuroinflammation for the progressive neurodegeneration of the substantia nigra in the disease. The PLP-α-Syn model provides an opportunity for a more detailed understanding of the specific pathways involved in such events, opening new possibilities for tailored therapeutic options for MSA.

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Keywords: neuroinflammation – microglia – alpha-synuclein – multiple system atrophy

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