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Poster board C41 - Wed 07/07/2010, 12:15 - Hall 1
Session 197 - Parkinson's 3
Abstract n° 197.41
Publication ref.: FENS Abstr., vol.5, 197.41, 2010

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Title  Microglia acquire distinct activation profiles depending on the degree of alpha-synuclein neuropathology in a rAAV based model of Parkinson's disease

Text  Post-mortem analysis of brains from Parkinson's disease (PD) patients strongly supports microglia activation and adaptive immunity as factors contributing to disease progression. Such responses may be triggered by a-synuclein (a-syn), which is known to be the main constituent of the aggregated proteins found in Lewy bodies in the brains of PD patients. To investigate this we used a recombinant viral vector to express human a-syn in rat midbrain at levels that induced neuronal pathology either in the absence or the presence of dopaminergic cell death, thereby mimicking early or late stages of the disease. Microglia activation was assessed by stereological quantification of Mac1+ cells, as well as the expression patterns of CD68 and MCH II. In our study, when a-syn induced neuronal pathology but not cell death, a fast transient increase in microglia cell numbers resulted in the long-term induction of MHC II+ microglia, denoting antigen-presenting ability. On the other hand, when a-syn induced both neuronal pathology and cell death, there was a delayed increase in microglia cell numbers, which correlated with long-lasting CD68 expression and a morphology reminiscent of peripheral macrophages. In addition T-lymphocyte infiltration, as judged by the presence of CD4+ and CD8+ cells, showed distinct kinetics depending on the degree of neurodegeneration, and was significantly higher when cell death occurred. We have thus for the first time shown that the microglial response differs depending on whether a-syn expression results on cell death or not, suggesting that microglia may play different roles during disease progression. Furthermore, our data suggest that the microglial response is modulated by early events related to a-syn expression in substantia nigra and persists at the long term.

Theme  C - Disorders of the nervous system
Parkinson's disease - Animal models

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