ポスター

[1P]F. 神経系の疾患 2

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[1P-200]パーキンソン病モデルマウスにおけるシヌクレイン病理に対するミクログリア介在性神経炎症の影響

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Parkinson's disease (PD) is a neurodegenerative disorder pathologically characterized by the accumulation of intracytoplasmic Lewy bodies and progressive degeneration of dopaminergic neurons in the substantia nigra (SN). α-synuclein, a 140-amino acid protein, is the major filamentous component of Lewy bodies. Several findings in animal models have implicated cell-to-cell propagation of α-synuclein, which seed aggregation of endogenous α-synuclein in recipient cells resulting in dopaminergic neuronal loss, as a significant contributor in PD pathology. Intra-parenchymal inoculation of exogenous α-synuclein, mainly α-synuclein fibrils, is one of the most common animal models used for studying α-synuclein accumulation, aggregation and propagation. On the other hand, previous clinical and experimental research suggests that neuroinflammation, an inflammatory response within the central nervous system, plays a central role in the dopaminergic neuronal loss in PD. Some studies showed that overactivated microglia induce severe neurotoxic effects and neuroinflammation in PD. In addition, aging is a known risk factor in PD and many studies show that aging disrupts the control of microglia-mediated inflammation. In this study, we evaluated the effect of microglia-mediated neuroinflammation on PD pathology using α-synuclein fibrils-inoculated senescence accelerated mice. The senescence accelerated mouse prone 8 (SAMP8) is a widely used rodent model of aging and senile dementia, while the senescence accelerated mouse resistant 1 (SAMR1) that does not show these senescence-related phenotypes is commonly used as control. We injected α-synuclein fibrils into the SN of SAMP8 mice (N=10) and the control group, SAMR1 mice (N=13). At 24 weeks after fibril injection, we assessed PD pathology and dopaminergic neuronal loss in the SN of both groups by immunohistochemical analyses. We observed that SAMP8 mice showed more widespread PD pathology and progressive degeneration of dopaminergic neurons in the SN compared to SAMR1 control mice. We further found that the number of Iba1-positive cells, indicative of activated microglia, in the SN of SAMP8 mice increased compared to that of SAMR1 mice. These findings suggest that microglia-mediated neuroinflammation plays an important role in PD pathology and aging exacerbates these processes.