GCI-induced neurodegeneration and synucleinopathy in non-human primates

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Résumé

Aggregation of α-synuclein has been implicated in several neurodegenerative diseases, termed synucleinopathies, which include Parkinson's Disease (PD), Dementia with Lewy Bodies (DLB) and Multiple System Atrophy (MSA). These synucleinopathies are characterized by the deposit of α-synuclein aggregates in intracellular inclusions in neurons and/or glial cells. Unlike in PD and DLB, where these aggregates are located predominantly in neurons, MSA is associated with cytoplasmic inclusions of α-synuclein in oligodendrocytes. These glial cytoplasmic inclusions (GCIs) are the pathological hallmarks of MSA and are associated with neuroinflammation, demyelination and, ultimately, neurodegeneration.
This study aimed at determining the potential to induce MSA pathology in non-human primates. To this end, we inoculated MSA-derived GCI fractions into the striatum of baboon monkeys that were terminated 2 years later. Extensive histochemical and biochemical analyses were performed on the whole brain and biological fluids to evaluate pathological markers known to be affected in MSA. We characterized neurodegeneration in these GCI-injected

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monkeys by describing the pattern of dopaminergic loss, as well as loss of oligodendrocytes, in the striatum and in the substantia nigra. We also characterized the regional distribution and variations of α-synuclein immunoreactivity in several brain structures (i.e. within hippocampus, striatum, substantia nigra, and cortex), as well as its pathological state (i.e. S129 phosphorylation). Finally, we described the demyelination, neuroinflammation and occurrence of intracellular inclusion formation in this model.
Overall, we observed region-specific alterations in several brain areas related to MSA pathology. In conclusion, this study provides a potential new non-human primate model for MSA research.

Mots-Clés: alpha, synuclein, multiple system atrophy, neurodegeneration, non, human primate