

Role of oligodendrocyte progenitors in Multiple System Atrophy

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Research question and background

Multiple system atrophy (MSA) is a rare and fast progressing atypical parkinsonian disorder characterized by alpha-synuclein aggregation within mature oligodendrocytes leading to their dysfunction. The widely distributed oligodendrocyte progenitor cell (OPC) population represents an endogenous source for replacement of such dysfunctional mature oligodendrocytes. OPCs are capable to proliferate, migrate, and differentiate in demyelinated brain areas ultimately (re-)myelinating responsive axons.

However, studies investigating the biology of OPCs in MSA patients are rare. Thus, our goal is a comprehensive analysis of OPCs in MSA post-mortem tissue. Such an approach is of particular importance for understanding the role of OPCs in disease progression and for evaluating these cells as a potential target for interventional strategies as a therapy for MSA is currently not available.

Methods and tissues used

We aim to characterize the OPC population in distinct, severely affected brain regions of MSA patients with predominant parkinsonism, i.e. putamen, substantia nigra, and medulla oblongata, in comparison to age- and gender-matched controls (n=6). We plan to analyze different maturation stages of OPCs, e.g. proliferative PDGFR α -positive progenitors, activated Olig2/Nkx2.2 oligodendrocyte precursors, and mature (pre-)myelinating NogoA-positive oligodendrocytes. The paraffin-embedded post-mortem tissue obtained from the Netherlands Brain Bank is currently processed for immunohistochemical evaluation and results will be obtained within the next months.