

**P406****Oligodendrocyte apoptosis triggers peripheral immune cell recruitment into the forebrain**

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**Background:** Brain-intrinsic degenerative cascades, such as oligodendrocyte apoptosis with concomitant microglia activation, have been proposed to be an initial factor driving inflammatory lesion formation in multiple sclerosis (MS). Experimental models recapitulating this sequel of events are, however, missing.

**Objectives:** To identify primary oligodendrocyte apoptosis as a potent trigger for peripheral immune cell recruitment into the mouse forebrain and, thus, the formation of new inflammatory, demyelinating lesions.

**Methods:** Female C57BL/6 mice were fed cuprizone for one week followed by subsequent immunization with myelin oligodendrocyte glycoprotein peptide (MOG<sub>35-55</sub>). While cuprizone feeding induces primary oligodendrocyte apoptosis, MOG immunization results in the formation of myelin autoreactive T-cells in peripheral lymphoid organs. Brains were histochemically evaluated for the presence and spatial distribution of perivascular inflammatory infiltrates. Furthermore, such infiltrates were characterized in detail by immunohistochemistry.

**Results:** While inflammatory infiltrates were virtually absent in the forebrain of MOG-immunized animals (i.e. active experimental autoimmune encephalomyelitis), widespread perivascular foci were found in the forebrains of animals subjected to cuprizone prior to MOG-immunization. Peripheral immune cell recruitment induced microglia activation, astrocyte dysfunction, demyelination, and oligodendrocyte loss. Furthermore, acute axonal damage (determined by anti-APP staining) was clearly evident in these inflamed regions. White matter areas without overt demyelination (i.e. normal appearing white matter) showed as well moderate microglia activation.

**Conclusion:** This study clearly illustrates the significance of brain-intrinsic degenerative cascades (i.e. primary oligodendrocyte apoptosis) for immune cell recruitment and MS lesion formation. Further studies have to address the signalling cascades and mechanistic processes which form the top-down communication between the affected brain area, neurovascular unit and peripheral immune cells.

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