The blood-cerebrospinal fluid barrier: the primary site for inflammation in multiple sclerosis
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Research question and background
The current view on the first route of leukocyte infiltration into the central nervous system during multiple sclerosis (MS) has recently been challenged. Data from experimental models implies that the passage of leukocytes across the brain vasculature (blood-brain barrier; BBB) is preceded by their traversal across the blood-cerebrospinal fluid barrier (BCSFB) of the choroid plexus. Our data indicate that experimental animals with an impaired BCSFB experience a more rapid onset of disease and a more severe disease course of experimental autoimmune encephalomyelitis (EAE) and enhanced inflammation within the choroid plexus. Although it is yet unknown whether in MS patients a similar sequence of events occurs, the correlation between the presence of leukocytes in the CSF and the number of MS lesions already suggests that inflammation at the choroid plexus plays a dominant but yet undefined role in disease pathogenesis.

Methods and tissues used
To study this, we have now gathered sufficient amounts of human choroid plexus tissues from MS patients as well as non-neurological controls (n=13) from the NBB. Initial data indicate that in MS choroid plexus tissues inflammatory markers (e.g. adhesion molecules, chemokines) are highly induced whereas the barrier markers (e.g. tight junction molecules) are severely diminished. Therefore, we hypothesize that alterations at the blood-CSF-barrier in MS contribute to disease onset and progression. We are currently identifying molecular networks that underlie disease-mediated blood-CSF-barrier alterations by gene profiling the choroid plexus in MS.