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The Cross-linking non-amyloid CSVD and CAA

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Statement of the Problem: In human autopsy studies of the non-demented elderly and Alzheimer's disease non-amyloid cerebral small vessel pathology (CSVD) and cerebral amyloid angiopathy (CAA) are found in the same brain. We here hypothesize a causal link between the two CSVD entities that goes beyond just a simple co-occurrence. We therefore investigated if spontaneously hypertensive stroke-prone rats (SHRSP), a valid non-transgenic animal model of human non-amyloid CSVD, develop CAA as a function of different non-amyloid CSVD stages. Methodology: Two-photon-microscopy was performed in 21 SHSRP to assess stages of CSVD in vivo. Therefore, the fluorescent dye Dextran was used to label the cerebral vasculature, and cerebral blood flow measures (CBF) were additionally conducted. Furthermore, in 13 out of those 21 SHRSP Methoxy-X04 (Congo red derivate) was used for the intravital CAA detection. Findings: Non-amyloid CSVD progression occurs in a temporal manner, comprising the following stages: stage 0 – no CSVD pathology, stage 1A – small vessel wall damage, stage 1B – CBF reduction, stage 2 – non-occlusive/ incomplete thrombus formation and stage 3 – occlusive/ complete thrombus formation. Six out of 13 SHRSP (46%) that underwent Methoxy-X04 imaging displayed intravital β-amyloid positivity of the cerebral small vessel walls, i.e. perivascular amyloid deposits and brightly fluorescent arteriolar/small artery wall adherent plane- or circular-shaped amyloid accumulations indicative of CAA. In nearly all Methoxy positive SHRSP amyloid deposits were detected surround thrombotic arterioles characterized by (in)complete small vessel occlusions (CSVD stage 2/3). Conclusion & Significance: Advanced non-amyloid CSVD stages display a condition prone to vascular β-amyloid accumulations, in terms of CAA. Further investigations have to shed light on the pathophysiological interactions between the two small vessel disease entities, especially whether a failure of perivascular Aβ-drainage or disturbances of endothelial Aβ-transport across the blood brain barrier drives the vascular amyloid pathology found in the SHRSP.

Biography

Solveig Niklass has her expertise in basic research in the field of cerebral small vessel disease (CSVD) as a cause of acute strokes. She established the 2-photon-microscopy in spontaneously hypertensive stroke prone rats as a tool for intravital imaging of the cerebral vasculature. New dyes for in vivo imaging allow for the simultaneous detection of CSVD and cerebral amyloid pathology, defining the focus of her actual research.

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