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Distribution pattern of amyloid beta peptides and aquaporin 4 proteins in Alzheimer's disease and associated transgenic mouse models

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The amyloid cascade hypothesis postulates that accumulation of Aβ is an initial event in the pathology of Alzheimer's disease (AD) and represents overall one of the two main histopathological features. This study aimed at investigating the distribution and clearance of amyloid beta peptides in AD brain tissue as well as in two associated mouse models — APPSL and 5xFAD. We histologically quantified various parameters: first, we evaluated the absolute distribution pattern of amyloid beta peptides; second, we investigated the occurrence of cerebral amyloid angiopathy (CAA) and third, we examined the localization of aquaporin 4 (AQP4) water channels. We immunofluorescently labelled sections from human AD patients at different Braak stages (I/II, III/IV and V/VI) and brain sections from the two transgenic mouse lines across different time points. Quantifications of labelled tissues revealed that overall amyloid-beta intensity, significantly increased in humans at advanced Braak stages and both transgenic mice during aging. Evaluation of CAA, which is defined as amyloid-β deposition in vascular walls, was technically challenging in human tissue. However, APPSL and 5xFAD transgenic mice developed severe CAA with increasing age. Finally, studying AQP4 protein distribution as a major participant of the glymphatic system involved in the clearance of amyloid beta revealed that in AD, parenchymal AQP4 increased with disease progression, while perivascular AQP4 was decreased at early AD stages and returned back to baseline levels at late stages. Furthermore, AQP4 protein was accumulated in close proximity to amyloid beta plaques. A similar result was observed in APPSL and 5xFAD mouse brain tissue. Together, these data show that these two mouse models are valuable to study amyloid-beta related pathways in AD.

Biography

Magdalena Temmel is currently a PhD student of Natural Sciences at the Karl-Franzens University of Graz, Austria. In her PhD thesis, she focuses on investigating high-fat diet induced changes in the A53T-mutated alpha-synuclein expressing mouse model of Parkinson's disease. She is performing all her project-associated works at QPS Austria Neuropharmacology, which is a leading CRO focusing on central nervous system, orphan and mental disorders. The research presented here was part of her Master's thesis that was performed as a cooperation project between several universities.

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