Characterization of the interaction of the cellular Prion Protein (PrPC) with beta-sheet rich protein aggregates in Dementia

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Research question and background

Protein misfolding from their soluble forms into highly ordered fibrillar aggregates is a key event for the development and course of neurodegenerative diseases. Beta-sheet rich protein aggregates are thought to be the main toxic species in this process. Much attention was paid to the finding that the cellular Prion protein (PrPC) is a high affinity receptor for beta amyloid-oligomers in vitro and in vivo and signals through activation of Fyn1 kinase, although our knowledge on the occurrence of this binding in brain of demented patients is limited.

Methods and tissues used

Besides standard biochemical and morphological methods, we employed a novel binding assay to assess the interaction between beta amyloid or other beta sheet rich proteins and PrPC. Furthermore we investigated which sizes of beta amyloid-oligomers or other beta sheet rich protein-oligomers show optimal binding using size exclusion chromatography.

Results and conclusion

Binding of beta amyloid to PrPC always occurred in Alzheimer's disease brains and not in non-demented controls. In contrast to synthetic beta amyloid-oligomers, larger protein assemblies containing beta amyloid bound to PrPC in brains of Alzheimer's disease patients.