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Interaction between beta-amyloid protein and heparan sulfate proteoglycans from the cerebral capillary basement membrane in Alzheimer's disease.

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Abstract
Proteoglycans are important in the pathogenesis of senile dementia of Alzheimer type (SDAT) by participating in amyloidogenesis. Knowledge about specific proteoglycan subtypes in SDAT may be of therapeutic advantage. In this study, we examined proteoglycan constituents of SDAT brains with reference to hyaluronic acid, heparan sulfate (HS), dermatan sulfate and chondroitin sulfate subtypes. Total proteoglycans showed a 1.6-fold increase in the hippocampus and 4.3-fold increase in the gyrus frontalis superior compared to non-demented elderly subjects. The HS subtype showed a 9.3-fold increase in hippocampus and a 6.6-fold increase in gyrus frontalis superior. Immunohistochemical studies of senile plaques revealed the expression of heparan sulfate proteoglycan (HSPG) in a portion of the core of typical plaques. beta-amyloid expression was positive in senile plaques and the degenerated neuronal processes and capillary basement membrane, but was negative in endothelial cells. Microglial cells adjacent to senile plaques were positive for HLA-DR expression, and astroglial cells positive for glial fibrillary acidic protein were scattered around the microglial cells. Immunoelectron microscopic examination showed an electron-dense reaction for HSPG in the thickened basement membrane adjacent to the endothelial cells of capillary vessels, but not inside the endothelial cells. These findings suggest that a markedly increased HSPG in SDAT brains is most likely caused by HSPG from the blood capillary basement membrane and that the degenerated processes around senile plaques may arise from microglial or astroglial cells.

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