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## Aging rat brain: a model for analyzing interactions among CSF dynamics, ventriculomegaly and the $\beta$ -amyloid retention of alzheimer's disease

Conrad Johanson\*, Stephanie Flaherty, John Duncan, Edward Stopa and Gerald Silverberg

Address: Department of Clinical Neuroscience Brown Medical School/RI Hospital 593 Eddy Street Providence, RI 02903 USA

Email: Conrad Johanson\* - Conrad\_Johanson@Brown.edu

\* Corresponding author

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### Background

Age-associated disruptions in brain barrier systems (including choroid plexus) lead to multiple problems for CSF turnover and brain interstitial fluid composition. Age is a great risk factor for Alzheimer's disease (AD). We have presented evidence that beta-amyloid ( $A\beta$ ) retention in AD is linked to decreased CSF turnover and reduced  $A\beta$  transport out of human brain. It is also known that CSF formation is reduced in aged rats (Preston et al.).

### Materials and methods

To extend this model, we sought evidence to confirm the postulated  $A\beta$  retention in the brain of old animals. Brown-Norway/Fischer (B-N/F) rats, at 3 mo (young adult) and 30 mo (advanced age), were used to characterize the presence of  $A\beta$  1–42 fragments in various regions of CNS. Immunohistochemistry was used to assess the degree and localization of  $A\beta$  1–42 both the cerebral cortex (CC) and lateral ventricle choroid plexus.

### Results

In the young adult B-N/F animals, there was negligible  $A\beta$  1–42 staining in the CC. In contrast, there was substantial amyloid staining, primarily in neurons, in the 30-mo-old CC. At the blood-CSF barrier, the choroidal epithelium displayed some  $A\beta$  1–42 staining even at 3 mo, suggesting reabsorptive clearance transport of this peptide fragment from the CSF. However, in the 30-mo rats, there was increased staining of the amyloid 1–42 in the plexus.

### Conclusion

These findings point to a greater burden of  $A\beta$  in the CNS as the result of advanced aging. Thus, this accumulating  $A\beta$  in cortical and choroidal tissues is consistent with the independent observations of a slower flow of CSF in older animals. The parallel findings of  $A\beta$  retention and CSF slowing, in aged rats vs. human AD subjects, encourage further mechanistic studies in B-N/F animals to delineate functional relationships among  $A\beta$  transport, CSF formation/volume, and  $A\beta$  retention in hippocampal and cortical regions.

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