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Aging rat brain: a model for analyzing interactions among CSF dynamics, ventriculomegaly and the β -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 β) retention in AD is linked to decreased CSF turnover and reduced A β 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 β 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 β 1–42 fragments in various regions of CNS. Immunohistochemistry was used to assess the degree and localization of A β 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 β 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 β 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 β in the CNS as the result of advanced aging. Thus, this accumulating A β 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 β 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 β transport, CSF formation/volume, and A β retention in hippocampal and cortical regions.

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