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Expression of the beta-amyloid transporter, LRP-1, in aging choroid plexus: implications for the CSF-brain system in NPH and Alzheimer's disease

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Background

The CSF system, including the choroid plexus, is an important route for removing the A-Beta peptides that, in high concentrations, injure neurons. Central retention of A-Beta peptides occurs when the blood-CSF and blood-brain barriers suffer deficits in aging and disease. LRP-1, a transporter, which actively removes A-Beta from extracellular fluid, undergoes expression changes in senescence, which is a risk factor for NPH and AD. We hypothesize that LRP-1 activity in the 'barriers' is essential for the well-being of the brain's interstitial and cerebrospinal fluids. This study has assessed the expression of LRP-1 in the choroid plexus and cerebral capillaries of aging rats in order to elucidate the state of this A-Beta clearance transporter in senescence. Faulty A-Beta disposal from the CNS may predispose to NPH and the reduced CSF turnover rate in AD.

Materials and methods

Lateral ventricle choroid plexus and cortical capillaries, for comparison, were assessed for LRP-1 expression by immunohistochemistry (IHC) and RT-PCR. Tissue specimens were taken from Brown-Norway/Fischer (B-N/F) rats at various ages from 3 to >30 mo. It was of interest to compare the time course of LRP-1 expression in the blood-CSF vs. the blood-brain barrier to obtain information about the relative abilities of these major transport interfaces to clear A-Beta from the CNS in young vs. senescent adults.

Results

LRP-1 by IHC assessment was expressed extensively in the choroid plexus epithelium of healthy young adults; expression of this A-Beta transporter was sustained even in the oldest animals. This was confirmed by RT-PCR, which showed mRNA for LRP-1 in the choroidal epithelium at all ages, with enhancement of the transcript in the oldest B-N/F animals. In contrast, LRP-1 expression in cerebral microvessels declined throughout aging, and was virtually not present at 12 mo. The IHC findings for LRP-1 in brain capillaries at various ages were in agreement with the corresponding PCR data.

Conclusion

Our findings demonstrate that the LRP-1 'barrier transporter system' that removes the potentially harmful A-Beta from the CNS undergoes a different time course in expression (choroid plexus vs. cortical capillaries) as adulthood progresses into senescent debilitation. In early adult life, the BBB may have the prominent role in protecting the brain from excessive A-Beta buildup. However, with advanced aging, the neurons may become progressively more dependent upon the choroid plexus-CSF system for maintaining A-Beta homeostasis in the

extracellular fluid of the CNS. Stabilizing (or even augmenting) the capacity of the LRP-1 transporters in the 'barriers' may be significant in slowing down the onset of NPH and/or the more severe stages of CSF-brain disruption in AD. Supported by the Rae Richter, Saunders and Brown Neurosurgery Foundations.