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Enhanced expression of the LRP-1 transporter at the blood-CSF interface in chronic hydrocephalus

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Background

Reduced CSF formation in chronic hydrocephalus (NPH) prompts the question of how the expression of choroid epithelial transporters is altered when flow is disrupted. In the Kaolin model of communicating hydrocephalus, we previously demonstrated that choroid plexus chloride transport (proportional to CSF production) is significantly decreased [1]. To investigate the expression of other choroidal transporters that effect CSF homeostasis, we have now analyzed the time course of LRP-1 expression in the plexus at various stages of hydrocephalus. LRP-1 is a transporter that mediates efflux of A-Beta peptide from the CSF. We postulate that LRP-1 in choroid plexus has a key absorptive role that stabilizes A-Beta in the CNS.

Materials and methods

In 15 Sprague-Dawley (SD) rats at 12 mo of age, we injected Kaolin into the cisterna magna to induce an NPH-like hydrocephalus. Animals were analyzed at 2, 6 and 10 weeks post-induction. Ventriculomegaly was confirmed by 4.7 Tesla MRI. Choroidal tissues were removed from the lateral ventricles and immunostained with antibody against LRP-1 or analyzed by quantitative (q) PCR to determine LRP-1 transcript levels. 4–5 rats were analyzed at each stage.

Results

Compared to controls, there was enhanced immunostaining of LRP-1 in the choroidal epithelium at 2 wk and 6 wk post-induction. At 10 wk, LRP-1 staining was even greater than at 2 and 6 wk, being especially marked at the apical (CSF-facing) pole of the epithelium. Apically-located LRP-1 can actively remove A-Beta from the CSF [2]. The immuno-histochemistry findings were corroborated by qPCR. Thus, LRP-1 transcript in choroid plexus, compared to control, was augmented even at 2 wk. Upregulated LRP-1 mRNA in the plexus was sustained at 6 and 10 wk. For comparison, we analyzed LRP-1 mRNA in human choroid plexus from patients with Alzheimer's disease (AD), a condition in which NPH often coexists. LRP-1 expression was also maintained in AD choroid plexus (i.e., the blood-CSF interface), unlike the cortical microvessels in AD, which lose LRP-1 [3].

Conclusion

When comparing NPH and AD with aging responses, there are contrasting differences in the expression patterns of LRP-1 at the blood-CSF vs. blood-brain interfaces. The ability of choroid plexus to sustain, and even increase, LRP-1 expression in chronic hydrocephalus suggests that the blood-CSF transport interface may help to cover deficient LRP-1 expression in cerebral capillaries in aging, NPH and AD.

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