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Human arachnoid membrane: active transport of amyloid-beta

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Background

Alzheimer's disease is characterized by an increase in cerebral deposition of the neurotoxic peptide, amyloid-beta (Aβ). The underlying cause of this deposition remains unknown. A suggested mechanism of Aβ accumulation in the central nervous system is an age-related decrease in clearance of Aβ, due to diminished cerebrospinal fluid (CSF) outflow or decrease in transport of Aβ via membrane transporters located within the arachnoid membrane (AM) or arachnoid granulation (AG) cells. The receptor for advanced glycation endproducts (RAGE) and low-density lipoprotein receptor-related protein 1 (LRP-1) have been previously identified in the choroid plexus and cerebral microvasculature, where they are utilized for Aβ import (RAGE) and export (LRP-1).

Materials and methods

The focus of this research is to demonstrate the transport properties of human AG cells in culture, and to characterize the presence and the functional transport abilities of RAGE and LRP-1 in primary human AG cells, in both normal and disease states. We have used conventional immunoblotting and immunostaining techniques to identify LRP-1 and RAGE expression in AG tissue sections and cultured AG cells.

Results

Previous research in this laboratory has shown that AG cells express intercellular junctional proteins characteristic of epithelial barriers and that they demonstrate fluid transport properties. In addition, both Lucifer yellow (LY) permeability and in vitro perfusion studies confirm that AG cells maintain barrier integrity and exhibit a unidirectional fluid flow consistent with CSF circulation in vivo. The existence of transporters for Aβ in both AG and AM tissue has been demonstrated by immunohistochemistry using 4 human donors. Results show positive staining for LRP-1 in AG sections and positive RAGE staining in vascular endothelial cells. Ligand binding kinetics and co-localization of Aβ with these membrane transporters are currently under investigation in both healthy and diseased states.

Conclusion

Using immunoblotting and immunocytochemistry we have confirmed the presence of RAGE and LRP-1 in primary human AG cell culture and in AM tissue lysates suggesting active transport of Aβ by the arachnoid granulations and arachnoid membrane.