Cerebrospinal Fluid Research

BioMed Central

Oral presentation

Open Access

Clearance of amyloid-beta in experimental neonatal hydrocephalus

Kelley Deren Kelly*[1,2], Jennifer Forsyth[1], Petra Klinge[3], Gerald Silverberg[4], Conrad Johanson[5] and James P McAllister[1,2]

Address: [1]Division of Pediatric Neurosurgery, 100 North Medical Drive, Suite 1475, Salt Lake City, UT 84113, USA, [2]Department of Neurosurgery (Anatomy and Cell Biology), Wayne State University, 550 East Canfield St., Lande MRB 048, Detroit, MI 48201, USA, [3]Neurosurgical Department, International Neuroscience Institute Hannover, Alexis-Carrel-Str. 4, Hannover, 30625, Germany, [4]Department of Neurosurgery, Stanford University, 300 Pasteur Dr. Rm. 155, Palo Alto, CA 94304, USA and [5]Department of Neurosurgery, Rhode Island Hospital and, Brown University, 593 Eddy Street, Providence, RI 02903, USA

Email: Kelley Deren Kelly* - Deren@hsc.utah.edu

* Corresponding author

from 52nd Annual Meeting of the Society for Research into Hydrocephalus and Spina Bifida
Providence, RI, USA. 11–14 June 2008

Published: 3 February 2009

Cerebrospinal Fluid Research 2009, **6**(Suppl 1):S26 doi:10.1186/1743-8454-6-S1-S26

This abstract is available from: http://www.cerebrospinalfluidresearch.com/content/6/S1/S26

Background

In hydrocephalus, interruptions in normal CSF flow pathways create a deficiency in the ability of the CSF to clear toxic substances from the brain. One important substance known to be affected by impaired clearance is amyloid-β (Aβ). The accumulation of Aβ causes dementia commonly found in patients with normal pressure hydrocephalus (NPH) and Alzheimer's diseased (AD) due to deficiencies in Aβ transport proteins: low density lipoprotein receptor-related protein-1 (LRP-1) and receptor for advanced glycation end products (RAGE). Although the prevalence of neonatal hydrocephalus is relatively high, no studies have examined protein clearance mechanisms in children with hydrocephalus or immature experimental animals with this disorder. We hypothesized that impaired clearance of Aβ occurs in the neonatal hydrocephalic brain and is accompanied by alterations in Aβ transporters. Additionally, studies have shown a correlation between astrocytes and Aβ in cases of NPH and AD. Because astrocytes help maintain the blood-brain barrier and therefore may be involved in Aβ clearance, we speculated that there would be an association between Aβ and astrocytes with the progression of hydrocephalus.

Materials and methods

Rats received intracisternal kaolin injections on post-natal day one and developed severe ventriculomegaly over a three-week period. Age-matched control animals were included for comparison. MRI was performed to confirm or rule out ventriculomegaly. Animals were sacrificed on day 21 and tissue was processed for immunohistochemistry to visualize cellular morphology and the presence of LRP-1, RAGE, Aβ, and GFAP. Adult hydrocephalic tissue was also analyzed for a positive control. Additional animals were sacrificed at day 21 and fresh tissue was taken for quantitative real time RT PCR.

Results

The amount of labelling for Aβ, RAGE, and LRP-1 was reduced in 21 day hydrocephalic animals in the cortex and hippocampus compared to adult hydrocephalic animals. Comparing 21 day hydrocephalic to 21-day saline control animals, no change was detected in Aβ, RAGE, and LRP-1 in the cortex, hippocampus and choroid plexus. The labelling of GFAP in the 21 day hydrocephalic group was dramatically elevated in the cerebral cortex and hippocampus.

Conclusion

Minimal expression of the transporter proteins could have been due to immature clearance mechanisms in young animals, or the severity of hydrocephalus could have caused decrease blood flow leading to a deficiency in transporters.