

Oral Presentation

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Changes in pTau in CSF and brain relating to chronic hydrocephalus

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Background

Changes in CSF circulation, as seen in adult chronic hydrocephalus (CH), can result in changes in CSF content, neurodegeneration, a loss of neurological function, and death. The microtubule-associated protein, Tau has been implicated in the pathogenic mechanisms of dementia and neurodegenerative disorders through accumulation in CSF and brain. To date, the relationship between the CSF circulation changes in CH and the levels of tau in CSF and brain has not been studied.

Materials and Methods

This study used an experimental model of chronic obstructive hydrocephalus developed in our laboratory to investigate whether changes in CSF circulation could have an effect on the level of Tau protein in CSF and brain. The degree of CH-CSF impairment was determined on the basis of changes in CSF volume, pressure and turnover. CSF levels of Tau were quantified using standard ELISA technique at baseline (pre-CH) and sacrifice (post-CH). To determine the level of Tau protein in brain, immunological and histological methods were used to identify neurons and glial cells, and stereologic cell counting procedure was used to determine the density of Tau+ cells in the brain.

Results

Chronic hydrocephalus was surgically induced in 12 adult male canines where the baseline levels of ICP (range 5–16 mmHg) and ratio of ventricle to brain (range 1.14–4.43 × 10³) increased 22.2% and 660% respectively. CH also resulted in an average 22.9% decrease in the rate of CSF clearance. In 8 of 12 cases the level of CSF Tau increased an average 52.3%, however in 4 animals a decrease (14.1%) was observed. Overall, the level of Tau in CSF did not significantly correlate with changes in CSF volume, pressure, or turnover. The density of Tau+ cells was

assessed in 7 animals (4 CH, 3 CTL) and was significantly higher in the cortex of animals with CH lasting <30 days (25%) and >30 days (18%) when compared to experimental controls ($P = 0.05$). The density of Tau+ cells was also higher in white matter for animals with CH (3–33%).

Conclusion

Our preliminary findings suggest that CSF circulation may play a physiologically significant role in the pathophysiology of Tau protein clearance, and in turn may influence brain parenchymal tau levels. These results reinforce the suggestion that Tau may play a role in the dementia of chronic hydrocephalus as has been considered in other dementias. Measures of Tau may be important in developing future diagnostic and/or treatment methods in CH.