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VEGF-R2+ activation in the caudate: an adaptive angiogenic response to hypoxia in chronic hydrocephalus?

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Background

Chronic hydrocephalus (hydrocephalus) is characterised by impaired gait, and associated with decreased cerebral blood flow and oxygen delivery. We investigated the role of chronic hypoxia in the caudate which is a known motor nucleus involved in gait control. Also, increased ICP and vascular compression as the result of enlarged ventricles may be directly responsible for the gait problems in hydrocephalus. VEGF, which is triggered by ischemic/hypoxic events causes associated adaptive angiogenesis and also plays a critical role in neuronal protection. Previously, using an experimental model of hydrocephalus, we have shown decreased cerebral blood flow, oxygen delivery and increased capillary density. Here we investigated whether neuronal and glial VEGF-R2 expression is associated with an adaptive angiogenesis in the caudate.

Materials and methods

We investigated the relationship between the duration and severity of hydrocephalus and the percentage expression of VEGFR2+ neurons, glia and blood vessels (BV) in the periventricular and deep layers of the caudate. Hydrocephalic animals were divided into Short Term (ST, n = 5) and Long Term (LT, n = 5) and compared with Surgical Controls (SC, n = 5). The density of blood vessels and cellular VEGF-R2+ was estimated using stereological cell counting methods. Values were expressed as %VEGF-R2 + cells to the total number of cells in each region.

Results

Overall, there was approximately 300–400% increase in %VEGF-R2+ neurons, and approximately 10–15% increase in %VEGFR-R2 glia in the caudate of hydrocephalic animals compared to SC. Specifically, %VEGFR-R2+ neurons were significantly greater in LT (55–60%) than SC (10–25%). Similarly, %VEGF-R2+ glia were significantly higher in hydrocephalic animals (55–60%), then SC (15–25%). BV density was found to decrease in hydrocephalic animals than SC. Overall, we found that the BV density decreased 60% in the periventricular caudate and 20% in the deep caudate compared to SC. BV density was not significantly correlated with ICP or CSF ventricular volume. Finally, caudate volume was not significantly different in hydrocephalic animals compared to SC.

Conclusion

The 300–400% increase in %VEGF-R2+ neurons and glia in hydrocephalus indicates a stimulated VEGF response that may be related to hypoxia in the caudate. The observed increase in VEGF-R2+ was not associated with angiogenesis, however may play a role in neuroprotection. Modulation of VEGF receptors may be important in our understanding of the role of hypoxic in the pathophysiology of hydrocephalus and lead to adjunct treatments.