Temporal Course of Hyperdynamic Pulsatility and Ventricular Dilation in a New Rat Model of Communicating Hydrocephalus

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Introduction

Hydrocephalus has long been described as a "plumbing problem", the consequence of an imbalance between CSF (cerebrospinal fluid) formation and resorption, or an obstruction to CSF outflow from the fourth ventricle. While this may adequately explain obstructive hydrocephalus, it fails to explain many observed facts about CH (communicating hydrocephalus). For instance, why is CH characterized primarily by dilation of the cerebral ventricles as opposed to the subarachnoid spaces[1,2]? Why is CH associated with a significant increase in CSF pulsatility? Why do many hydrocephalic patients undergoing VP (ventriculoperitoneal) shunting fail to show improvement[3,4]? A novel rat model of CH[5] has been developed to explore these and other issues; this model uses partial obstruction of the basal cistern to reduce access of CSF to the basal cistern and ventral SASs (subarachnoid spaces), which is often the cause of CH in patients. CH is characterized by quantifying VM (ventriculomegaly) and aqueductal CSF pulsatility using MRI. The temporal course of changes in VM and CSF pulsatility are presented here.

Methods

CH is induced in female Sprague-Dawley rats (n=16) by injecting 20-30 µl of 25% kaolin (aluminum silicate) suspension into the basal cistern through a 1.5 cm incision in the ventral side of the neck (controls: saline injection (n=2), intact (n=4)). Animals were imaged on a 9.4T Bruker Biospin microMRI scanner at Brookhaven National Laboratory, using a 3 cm surface coil. Anesthesia was induced using 40 mg/kg Brevital and maintained with 1-2% Isoflurane both prior to kaolin injection and prior to scanning. Ventriculomegaly is quantified by measuring ventricular volume (VV – volume of lateral ventricles, third ventricle, cerebral aqueduct and aqueductal recess) using 3D TrueFISP images (TE/TR: 2/4, 128x128x100 matrix, ST: 0.32 mm, FOV: 3 cm). These images were also used to estimate the presence of CSF in the basal cistern and ventral SAS. CSF pulsatility is assessed by measuring aqueductal stroke volume (SV – net CSF volume pulsating caudally or cranially through the cerebral aqueduct in one cardiac cycle) using phase contrast images (TE/TR: 6/10, 128x128 matrix, ST: 1 mm, FOV: 3 cm, velocity encoding: 1-2 cm/s). Animals were scanned between days 0 and 102 post CH induction. Comparisons of SV and VV were done using an unpaired Student's t-test, corrected for multiple comparisons.

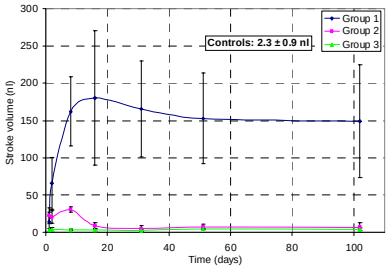

Fig. 1. CSF pulsatility, measured as the SV (in nl) at the cerebral aqueduct, over time.

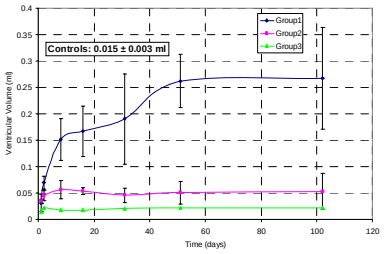

Fig. 2. Ventricular dilation, measured as the VV (in ml), over time.

Results

All rats tolerated the surgery well. Two died during anesthesia before scanning (days 2 and 4). Based on the extent of ventricular dilation and CSF pulsatility, the experimental animals were found to be clustered into distinct "pulsatility developmental" groups. Group 1 (n=6) was characterized by very severe ventriculomegaly and highly increased CSF pulsations (Fig 1 & 2). Their SV and VV both rose sharply and subsequently remained elevated ($p<0.01$ for SV & $p=0.01$ for VV, compared to control). Their SV and VV were also strongly correlated in both acute and chronic phases ($p<0.01$, Fig 3). Group 2 animals (n=3) had unexpected intermediate results. They had an initial rapid increase in SV and VV (Fig 1 & 2), although values were not as high as Group 1 ($p<0.01$ for both SV & VV). SV, however, dropped back to near control values after day 8, while VV remained elevated. Correlation between SV and VV in this group was only found in the chronic phase ($p<0.01$; Fig 3). A third group (Group 3, n=9) did not show significant changes in VV or SV above control levels (Fig 1 & 2), although their basal CSF distribution was significantly lower than control values (Fig 4, $p<0.05$). Finally, the basal CSF distribution (i.e. site of kaolin blockage) was similar in Groups 1 and 2 ($p=0.87$) and only the ventral CSF appear to correlate with the severity of the CH (Fig 4).

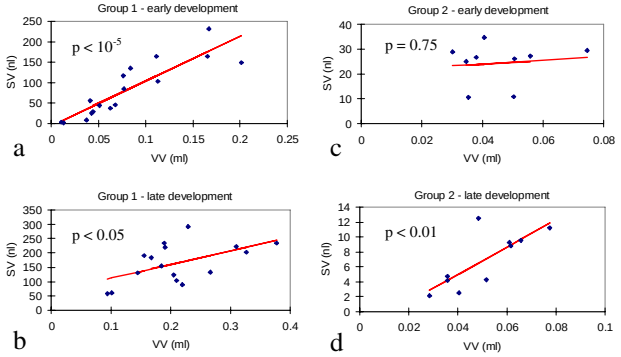

Fig. 3. SV and VV correlations within groups at different time periods. (a) and (c) represent early development (days 1-8), and (b) and (d) represent late development (days 16-102) of Groups 1 and 2 respectively. Only (c) shows no apparent correlation.

Discussion

The fact that animals clustered into distinct "pulsatility developmental" groups can have several interpretations. These might represent two different forms of CH (e.g. severe vs. mild). The abrupt drop in SV in a subset of the animals following the acute stage (Group 2) may explain some of the variability found in clinical studies of hyperdynamic aqueductal pulsations in NPH[3,4]. The strong correlation between SV and VV in Group 1 would seem to indicate a causal relationship in severe CH cases. However, we must consider that these two effects could be extraneous effects of an unrelated cause such as gliosis. The strong correlation in this group may also explain the excellent prediction of shunt success in cases of extreme hyperdynamic pulsatility. Most interestingly, Group 2 results indicate that SV is not necessarily dependent on VV. The "correction" of elevated SV in the chronic stage may indicate an active compensatory mechanism in mild CH that allows pulsatility to return to control levels, and may also play a role in preventing extreme VM in this group. These results may explain some of the difficulties found in using aqueductal pulsatility as a marker for VP shunt surgery. Finally, the CSF distributions indicate that the CSF access to the ventral SAS may be the most important factor in the development of VM in this model.

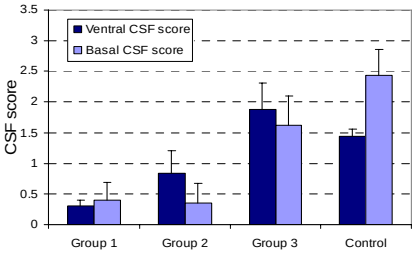

Fig. 4. CSF distribution scores in the basal cistern and ventral SASs.

References

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