Quantitation of Brain Tissue Swelling Using MRI

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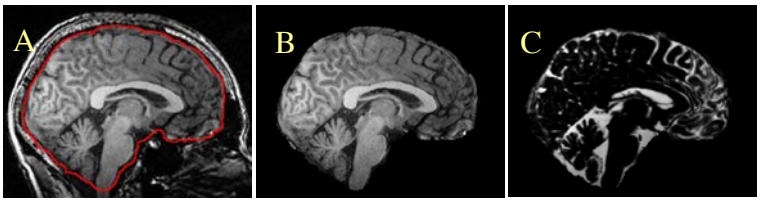
Introduction:

Many cerebral disease processes are characterized by brain swelling. The ability to quantify this swelling would allow a better characterization of the disease process as well as providing insights into normal physiological changes in cerebral parenchymal volume. Based on the Munro Kellie doctrine, that given a fixed intracranial space, the volume sum of all the intracranial tissues must remain constant, any changes in brain tissue volume will be reflected as changes in cerebrospinal fluid (CSF) or cerebral blood volume. Cerebral blood volume accounts for only a small fraction of the intracranial volume (approx 4%), however changes in CSF volume are readily detectable. The Poisson ratio for brain matter is of the order 0.45 (with 0.5 being completely incompressible) thus CSF volume changes provide an accurate reflection of the changes in brain parenchymal volume. We describe a method to quantify CSF volume with MRI, and use this to detect and quantify brain swelling. To test this we made repeated measures of CSF volume in normal volunteers (control group, n=3), and also following 40 minutes of 12% FiO2 hypoxia - a stimulus expected to cause minor cerebral swelling (hypoxia group, n=10).

Several standard segmentation analysis routines such as SPM and FSL, are available to characterize cerebral tissues based on their MR signals. Typically these use a T1-weighted sequence as a single reference for tissue segmentation, producing probability maps that represent what portion of each voxel is assigned to white matter (WM), grey matter (GM), or CSF. These analysis routines produce improved results when additional MRI volumes are included with alternative types of contrast (e.g. T2-weighted and proton density). However, these methods will routinely underestimate CSF quantities since voxels with partial volumes of CSF may be misclassified as GM and WM. To quantify CSF specifically, we utilize a heavily T2-weighted FSE sequence, with GM and WM signal minimized using a long TE and long Echo Train Length (increasing magnetization transfer effects). Remaining intracranial signal in our T2-weighted volume represents CSF, with lower signal values corresponding to CSF partial volumes. Integrating the signal over the intracranial volume provides a measure of intracranial CSF volume.

Methods:



Data were collect on a GE EXCITE Twinspeed 3T system. The Initial 3D acquisition was a high-resolution T1-weighted volume of the whole head using a FSPGR sequence (TR/TE/TI = 7.9 / 3.1 / 450 ms, matrix 256 x 256 x124, resolution 1 x 1 x 1.2mm, ~8 mins). Subsequent volumes used a heavily T2-weighted FSE sequence (TR/TE/ETL = 3000 / 400 ms /128, same resolution, ~12 mins). All volumes were coregistered. A coarse brain mask was created using FSL's Brain Extraction Tool (BET) on the T1-weighted volume (fig A). The mask was grown by 5 pixels and adjusted to ensure it included all intracranial CSF - bounded caudally by the Foramen Magnum (fig B). The mask was then applied to the heavily T2-weighted volume. The signal was thresholded to remove spurious pixels due to noise, and normalized relative to the intraventricular CSF signal (fig C). An estimation of the noise was made by measuring the mean signal in a ROI outside of the head. The normalization factor was estimated from the signal of a ROI placed in the ventricles. Empirically, the best noise rejection was found using a threshold 1 s.d. above the mean noise, and the best normalization using a cutoff 1 s.d. above the mean ventricular CSF signal. The thresholded, normalized intracranial signal was integrated to generate the CSF volume.

Results:

Mean resting CSF for all subjects was: Male = 200ķ50 ml (n=6, age 32ķ5 years), Female = 203ķ54 ml (n=7, age 35ķ10 years). Three repeated CSF measures in the control group (n=3, 2 male, 1 female, age 36ķ5 years) were 195ķ58 ml, 198ķ58 ml, 190ķ57 ml ($p = 0.23$). Repeated measures during hypoxia (n = 10, 4 male, 6 female, age 34ķ9 years) showed significant CSF volume loss i.e. brain swelling ($p < 0.0001$); normoxia 207ķ59 ml, 20 mins hypoxia 203ķ58 ml, 40 mins hypoxia 192ķ57 ml. This was significantly different than the changes in the controls (significant group x time interaction, $p < 0.05$ one tailed). Mean change in CSF volume with hypoxia= -4.7ml (-2.3%) after 20 mins, and -16.5ml (-8.1%) after 40 mins. Mean coefficient of variation within control subjects = 2%.

Discussion:

Measuring CSF volume provides a sensitive indication of brain tissue swelling. Despite a large variation in resting CSF volume across subjects, our method for quantifying CSF using a repeated measures design allows us to detect small changes in CSF, and hence in brain swelling. We have used this method to demonstrate very early brain swelling as a normal physiological response to 12.5% FiO2 hypoxia. The method is very sensitive to motion – as the added ghosting artifacts elevates the MR signal with overestimates of CSF volume, which limits its utility in some patient and subject groups. The choice of noise threshold has only a small effect on the CSF quantitation. The method is sensitive to the choice of normalization factor (signal intensity for a voxel containing 100% CSF). Empirically we found 1 s.d. above the mean ventricular CSF signal an appropriate value across many subjects, however a more formal determination of this cutoff is still needed. (Supported by AHA-0665027Y, AHA-054002N, NIH-HL081171, NIH-M01RR0827)