Significant changes in brain water diffusivity observed under hyperosmolar conditions

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INTRODUCTION

One important and unresolved question in MR diffusion research is what determines the changes in tissue water diffusivity observed during cerebral ischemia. Many hypotheses have been advanced that implicate events associated with the failure of the energetic metabolism; they include changes in the relative size of the intracellular and extracellular compartments, and in the membrane's permeability to water. Since in ischemia there are simultaneous changes in cell metabolism, and intra- and extracellular volume, it is difficult to identify the factor that is primarily responsible for the observed changes in tissue water mobility. In an attempt to separate these effects, Sevick (1) used a model of water intoxication to induce intracellular edema without metabolic impairment. However, the resulting 8% decrease of the ADC was very small in comparison to those observed during ischemia. By subjecting living brain tissue to hyperosmolar conditions, we can examine the effect on the measured diffusion coefficient of selectively reducing extracellular volume.

METHODS

Cats under 2% isoflurane anesthesia underwent surgery for placement of femoral arterial and venous catheters. After the animals were centered in the magnet, we obtained a set of baseline DWIs as normal saline was infused. Subsequently, we infused a hypertonic 18% NaCl solution intravenously at a rate of 20 ml/hr. Periodically, we monitored blood serum Na^+, K^+, osmolarity, pH, glucose, lactic acid, pCO_2, and pO_2 levels. All variables were maintained at physiological levels with the exception of serum osmolarity, which we maintained at different steady-state levels over a period of approximately 8 hours. During this time we acquired 6 sets of 25 interleaved spin-echo EPI DWIs (2) in which diffusion gradients of varying strengths (3-32.5 mT/m) were applied along 6 non-collinear directions. Post-mortem DWIs were also obtained.

Experiments were performed on a 2-T GE/Bruker animal system using a birdcage quadrature coil. Sequence parameters were pixel matrix size=128×128, FOV=80mm. TE=74 ms, and TR=2-3s (cardiac gated to one slice per heart beat, 4 slices), diffusion gradient duration=15ms, diffusion time=45ms. Images were Fourier transformed, as well as phase and navigator echo corrected (2). Then, for each set of DWIs (including the baseline DWIs) a diffusion tensor was estimated in each voxel (3). The principal diffusivities and their sum (the scalar invariant) Trace(D), were then calculated for each voxel (3).

RESULTS AND DISCUSSION

Figure 1 shows an enlargement of the CSF space with an increase in serum osmolarity, and a concomitant reduction in Trace(D). Although not shown, amplitude images also show a progressive intensity reduction in both grey and white matter with an increase in serum osmolarity. Figure 2 shows a plot of Trace(D) and amplitude (T_2-weighted signal) vs. serum osmolarity in the grey matter of a representative animal. Even for a moderate increase in osmolarity (350 mOsm), the reduction of both values was significant (15-20%). Since it is reported that at 360 mOsm the brain loses about 50% of the extracellular water with no changes of the intracellular volume (4) and that metabolic impairment does not occur below 400 mOsm (5), we conclude that the size of the extracellular compartment is likely to contribute significantly to the measured water diffusivity in the brain.

At higher osmolarity (490-580 mOsm) the reduction in both amplitude and Trace(D) in grey matter was about 60%. Post-mortem, the amplitude remained relatively constant at 40% of the control value, consistent with no changes in the total amount of water, whereas Trace(D) increased to 60% of the control value. We are not aware of any other conditions in which water diffusivity is found to increase post mortem. Our tentative interpretation of this result is that live brain cells actively maintain intracellular volume at the expense of the extracellular volume, whereas post-mortem, water is passively redistributed between compartments with a resulting increase in extracellular volume.

In the white matter, the reduction of Trace(D) was smaller (30% at the highest osmolarity) while the decrease in amplitude was similar to what we observed in grey matter. We observed a relatively small percentage decrease of Trace(D) in the white matter because the largest principal diffusivity (i.e., parallel to the fibers) did not decrease significantly. This finding suggests that the reduction in the extracellular space does not increase the tortuosity significantly in the direction parallel to the fibers.

Figure 1: Trace(D) maps of the cat brain acquired with serum osmolarity of 310 mOsm {left} and 470 mOsm {right}.

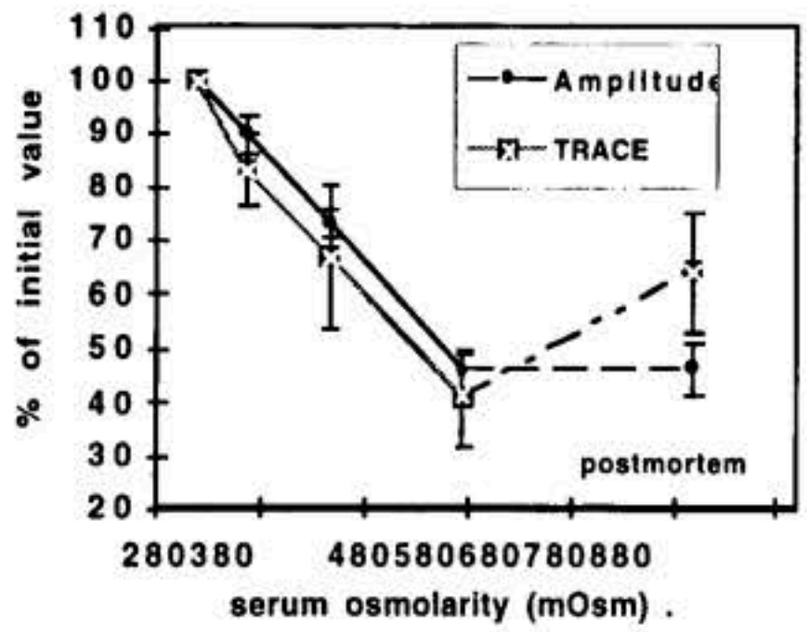

Figure 2: Plot of Trace(D) (stippled line) and amplitude (T_2-weighted) signal (solid line) as % of control value vs. serum osmolarity. Post-mortem values are also reported.

CONCLUSION

Our results suggest that the volume of the extracellular compartment is the most significant factor in determining the diffusivity of water in the brain measured by MRI.

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