Sodium Diffusion in Healthy and Globally Ischemic Rat Brain

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Synopsis Endogenous Na^+ resides primarily in the extracellular space in healthy tissue and therefore may be used as a molecular marker for the motion of water in that space. This will potentially provide mechanistic insight into the as yet unexplained marked decrease in water diffusion following CNS injury. As a first step, the apparent diffusion coefficient (ADC) of total brain tissue $^{23}Na^+$ has been determined in healthy and globally ischemic rat brain. Findings indicate a total $^{23}Na^+$ ADC of 1.15 ± 0.09 μm^2/ms at a 12.7 ms diffusion time (T_{diff}) in healthy brain, and 0.33 ± 0.07 μm^2/ms at a 14.9 ms T_{diff} in globally ischemic brain.

Introduction Though changes in water ADC following injury to brain tissue are readily observed, the mechanisms responsible for this remarkable phenomenon are not well understood. Knowledge regarding the motion of species that exist in the intracellular or extracellular milieu allows inferences to be made about the motion of water in those spaces. The high concentration and compartment specificity of sodium make it an obvious molecular marker of the extracellular space. However, the short T2 and low magnetogyric ratio of $^{23}Na^+$ pose significant challenges to the basic MR diffusion measurement. We present a method to measure diffusion of total tissue $^{23}Na^+$ in the living and globally ischemic rat brain.

Materials and Methods A 4-cm, 1-turn proton surface coil was used to take scout images, plan voxels, and monitor temperature (1) *via* the chemical shift difference between water and endogenous N-acetylaspartate (NAA) (figure 1). Brain temperature was also monitored with a fiber optic probe placed in the nasal cavity. Temperature was maintained before and after sacrifice by circulating warm water under the animal. An orthogonal, two-turn, ellipsoidal (1.4-cm long axis x 1.0-cm short axis) surface coil was placed directly above the brain for $^{23}Na^+$ diffusion measurements, which were made using a modified LASER sequence (2). $^{23}Na^+$ coil dimensions were such that localization within the brain required slab selection only in the dimension parallel to the coil, thus minimizing echo time. Measurements were taken on 250 to 350-gram male Sprague-Dawley rats. Global ischemia was induced *via* sacrifice with a 1-ml bolus injection of 2-M KCl into the femoral vein. Experiments were performed at 4.7 T using a gradient system capable of producing 60 G/cm field gradients along three orthogonal directions. Sine-shaped gradients and gradient prepulses were used to minimize the effects of eddy currents resulting from the strong gradients (3).

Results Within the 1.4 x 1.0-cm cylindrical volume element with a selected 0.60 to 0.75-cm thickness, $^{23}Na^+$ ADC was found to be 1.15 ± 0.09 μm^2/ms (figures 2, 3). In a similar voxel, the water ADC was 0.83 ± 0.02 μm^2/ms at a T_{diff} of 48.2 ms. Following sacrifice, the ADC of $^{23}Na^+$ and water decreased to 0.33 ± 0.07 μm^2/ms and 0.51 ± 0.01 μm^2/ms, respectively. The two different T_{diff}'s for healthy and ischemic $^{23}Na^+$ measurements, 12.7 ms and 14.9 ms, respectively, were required to maximize signal to noise and dynamic range of the experiments. $^{23}Na^+$ T1 and T2 in the same voxel in healthy brain were determined to be 40 ± 4 and 34 ± 2 ms, respectively.

Discussion After death, Na^+ redistributes and primarily occupies the intracellular space. Following this redistribution, both the $^{23}Na^+$ and water ADC/D^{free} ratios decrease to the same value of 0.17, where D^{free} is the diffusion coefficient in free media at 37 °C (table 1). The ratios measured in the ischemic rats suggest that similar biophysical determinants govern $^{23}Na^+$ and water ADC values under conditions for which $^{23}Na^+$ and water share similar intra/extracellular partitioning. The two-fold difference between the ADC/D^{free} ratios of $^{23}Na^+$ and water observed in the living rats (column 3 of table 1) is therefore attributed to differences in intra/extracellular partitioning for the two molecules. This finding suggests that diffusion in the extracellular environment appears approximately two-fold less hindered than diffusion in the intracellular environment.

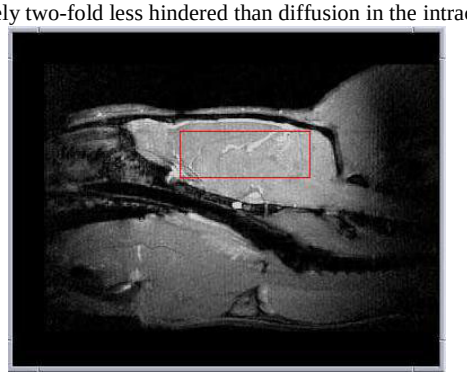

Figure 1. Sagittal, gradient-echo, proton image with the planned voxel highlighted in red.

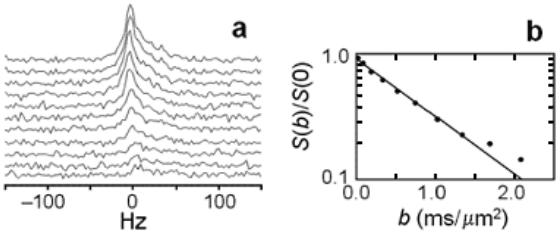

Figure 2. a. Representative array of diffusion-attenuated $^{23}Na^+$ resonances with 20 Hz line broadening (SNR=13.7 in unfiltered data). b. Semilog plot of estimated amplitudes of the time-domain data as a function of *b*-value, modeled (solid line) *via* Bayesian probability theory to a single exponential decay

$$S(b) = S(0)e^{-b*ADC},$$

where b accounts for all gradients and cross terms.

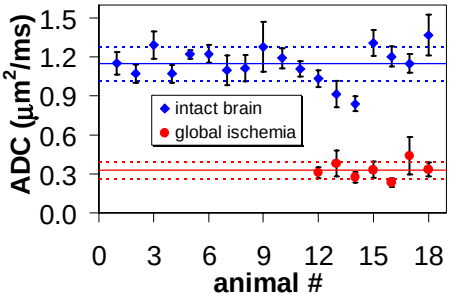

Figure 3. Total brain tissue $^{23}Na^+$ diffusion in intact and globally ischemic rat brain. Mean ± SD is indicated by dashed lines. Error bars represent the range of values encompassing one standard deviation of the probability distribution of the ADC for a given subject.

	ADC (μm²/ms)				
species	D^{free}	intact brain	% of D^{free}	global ischemia	% of D^{free}
$^{23}Na^+$	1.9	1.15	61	0.33	17
$^{1}H_2O$	3.0	0.83	28	0.51	17

Table 1. Relative ADC reduction from free diffusion of water and sodium in intact and globally ischemic rat brain.

References

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