Deconvolution of Compartmental Water Diffusion Coefficients in Stroke Using DW-IR MEMRI

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Introduction: The apparent diffusion coefficient (ADC) of brain water is known to decrease in ischemia.[1] Although the mechanism of the decrease is not well understood, it is thought to be related to relative changes in the intra- and extra-cellular volume fractions during ischemia.[2,3] We sought to identify the relative contributions of intra- and extracellular water ADC changes during ischemia using Mn^{2+} as an intracellular MRI contrast agent. Intracerebroventricular (ICV) infusion of Mn^{2+} results in neuronal uptake, selectively shortening the T_1 and T_2 relaxation times of intracellular water. The relative differences in T_1 or T_2 relaxation times between the two compartments can be used to selectively null the signal from one of the compartments.[4] In the first set of experiments, the average T_1 and T_2 relaxation times of water were measured in the intra- and extracellular compartments post-Mn^{2+} infusion. Secondly, diffusion-weighted inversion-recovery (DW-IR) images were acquired from each compartment by choosing an inversion time (TI) to selectively null the MRI signal from the other compartment.

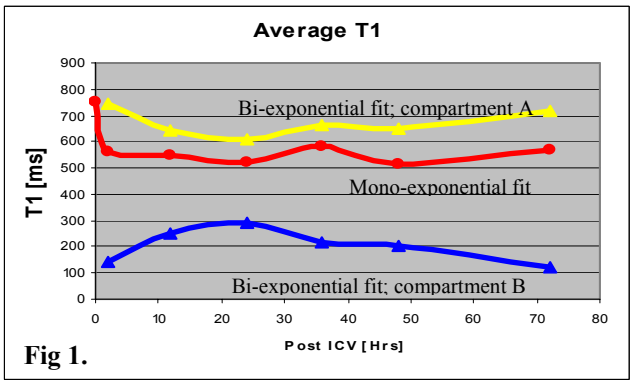

Fig 1.

Methods: All MR imaging was performed on a Bruker Biospin 2T/45 cm horizontal bore system equipped with 200mT/m gradients and a surface coil for RF transmit and receive. Two groups of rats (SD, 275-300g) were used in this study. The first group (n=5) was anesthetized with intraperitoneal injection of chloral hydrate (400 mg/kg) and immobilized on a stereotactic frame. Manganese, 50 µl of 25 mM $MnCl_2$ in saline, was infused ICV over 2 mins through a burr hole the skull (0.8 mm posterior, 1.2 mm lateral to the bregma, and 4mm below the skull). T_1 was measured using an IR sequence acquired at 2, 12, 24, 48, 72 and 96 hrs time-points post-ICV infusion of Mn^{2+}. A sech pulse was used for adiabatic spin-inversion and TI values (21) were spaced logarithmically from 14.88-5000 ms. Other imaging parameters were TR = 7.5 s, TE = 7 ms, FOV = 31 mm, 64 × 64 data matrix with an in-plane resolution of 484 microns and 5 slices of 1mm thickness. T_2 was measured using a CPMG sequence with identical resolution (TR = 5 s, TE varied in 24 steps between 4.5 ms and 108 ms). Bi-exponential T_1 and T_2 maps were calculated using Matlab.

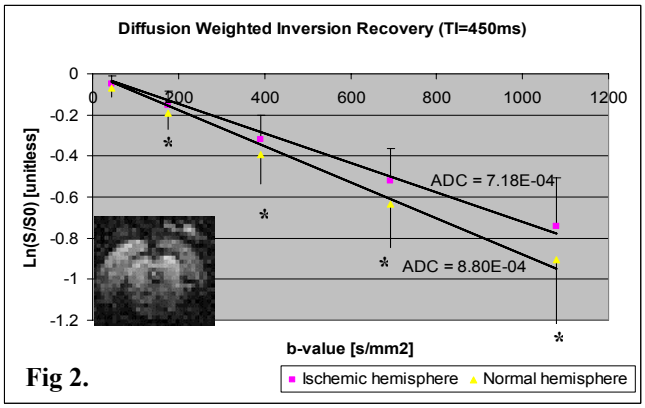

Fig 2.

In a second group (n=4), Mn^{2+} was infused (ICV) 72 hrs prior to middle cerebral artery occlusion (MCAO). MRI was performed 2 hrs post-MCAO. Eleven DW-IR MRIs were acquired with b-values from 5-1080 s/mm^2 and TR = 5 s, TE = 27 ms, FOV = 31 mm, 64 × 64 matrix acquisition (in-plane resolution of 484 microns), 5 1-mm-thick slices, $\delta = 8$ ms, $\Delta = 13$ ms and diffusion gradients applied in three directions simultaneously. TI values of 100 ms and 450 ms were used to null the intra- and extracellular water signals, respectively. Average ADC was calculated from each brain hemisphere and compared across all 5 slices. A single-tailed, paired-t-test analysis was used; $p<0.05$ was considered statistically significant.

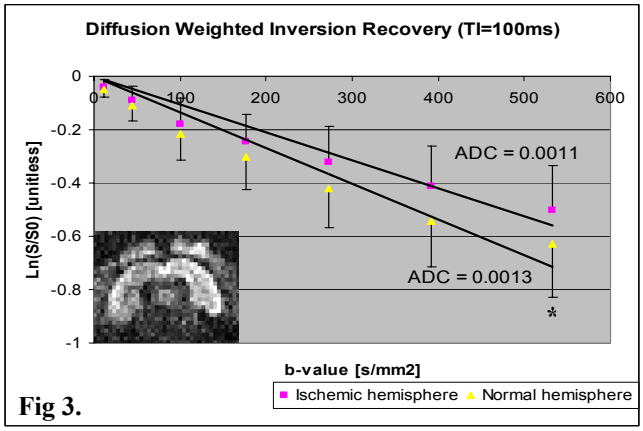

Fig 3.

Results and Discussion: T_1-weighted images acquired at various time points showed uniform enhancement in the brain at 72 hours post-ICV Mn^{2+} infusion (the time point used for all experiments). The average bi-exponential T_1 values were $T_{1a} \sim 150$ ms; $M_{0a} = 64\%$; $T_{1b} \sim 700$ ms; $M_{0b} = 34\%$ (**Fig 1**); the bi-exponential T_2 values were $T_{2a} \sim 9$ ms; $M_{0a} = 66\%$; $T_{2b} \sim 51$ ms; $M_{0b} = 34\%$. Extracellular ADC values calculated from DWIs with TI = 100 ms (intracellular water signal nulled) decreased significantly from 1.3×10^{-3} mm^2/s to 1.1×10^{-3} mm^2/s during ischemia (**Fig 2**). Similarly, intracellular ADC values calculated from DWIs with TI = 450 ms (extracellular water signal nulled) showed a significant reduction from 0.88×10^{-3} mm^2/s to 0.72×10^{-3} mm^2/s in the ischemic hemisphere (**Fig 3**). Since Mn^{2+} distribution was not uniform in all brain regions, there may be some signal cross-contamination between compartments if each component is not completely nulled at their respective TI values.

Conclusion: ICV infusion of Mn^{2+} appears to achieve sufficient intracellular concentrations of Mn^{2+} to move the inter-compartmental equilibrium water exchange into the slow-exchange regime[5]. When this is the case, it is in principle possible to separate the intra- and extracellular water signals on the basis of differences in their respective T_1 and T_2 relaxation times. The ADCs measured separately from intra- and extracellular water in ischemic rat brain showed a significant reduction during cerebral ischemia. However, the absolute values of both the intra- and extracellular ADCs are somewhat higher than the combined rat-brain ADCs measured from both compartments (~0.8×10^{-3} mm^2/s). Furthermore, the percent-ADC reduction following ischemia is not as large in these studies (~15-18%) as that observed from the combined compartments (~30-35%) under similar ischemic conditions. However, the effect of inter-compartmental equilibrium water exchange is not accounted for in either of these cases and this issue may be responsible for some of these differences.

Reference: 1) Moseley et al MRM 1990;14:330 2) Neil JJ et al MRM 1996;35:329 3) Duong TQ et al MRM 1998;40:1 4) Silva et al MRM 2002;48:826 5) Labadie et al JMR Ser B 1994;105:99