Sodium MRI of Reversible Focal Brain Ischemia in the Monkey

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ABSTRACT

Stroke is the third largest cause of mortality in the United States. The introduction of thrombolytic therapy using tissue plasminogen activator (tPA) has revolutionized the treatment of acute stroke by providing an aggressive means for the reversal of the ischemic insult, albeit with potential complications that require eligibility criteria relying heavily on the time of ischemia onset. Sodium MRI has been proposed as a means to help extend the use of tPA to patients that do not meet this eligibility criteria [1]. We demonstrate the use of sodium MRI in a reversible, non-human primate model of focal ischemia. Our results indicate that tissue sodium concentration (TSC) increases steadily in the ischemic tissue shortly after ischemia onset, and that markedly different patterns of TSC accumulation ensue after restoration of blood flow.

METHODS

Data Acquisition: Sodium 3D triple/single quantum data were acquired on a 3 Tesla whole body scanner (GE MS, Milwaukee, WI), using a custom built, 22cm diameter, dual-tuned (^{23}Na/^{1}H), dual-quadrature birdcage RF coil [2]. A twisted projection imaging (TPI) sequence [3] was used to acquire TSC maps every 5.5 minutes throughout the duration of the studies. Maps of the spatial distribution of the B_1 field were obtained for correcting the TSC estimates for B_1 inhomogeneities [4]. Proton MRI scans, including diffusion weighted imaging (DWI) and magnetic resonance angiography (MRA), were also performed to document the extent and location of ischemia.

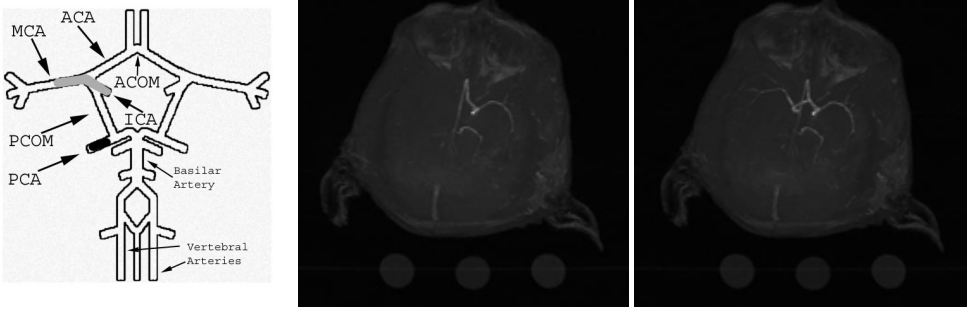

Figure 1: *(left) Diagram of the inferior view of the brain vasculature during temporary occlusion of the right MCA using a balloon catheter. The positions of the balloon (gray cylinder) and embolization coils (dark cylinder) are also shown. (center) MRA prior to reperfusion. (right) MRA after reperfusion (through deflation and removal of the balloon without removing the animal from the scanner).*

Animal Model: Reversible focal brain ischemia was induced in pig-tail monkeys (*Maccaca nemestrina*, n=3) using an endovascular approach. In this approach, ischemia is achieved using embolization coils to occlude the posterior cerebral artery (PCA) and a balloon catheter to occlude the bifurcation of the middle cerebral artery (MCA) on the right hemisphere of the animals (figure 1, left). The effectiveness of this procedure is shown in figure 1 where MRA's are shown before (center) and after (right) reperfusing the ischemic hemisphere through deflation and removal of the balloon. The animals were kept under anesthesia throughout the experiment using a fentanyl infusion, and their temperature was maintained at 37°C.

RESULTS

Figure 2 (left) presents selected partitions from sodium 3D images (top) from a monkey brain and TSC rate maps (spatial map for the slope of the TSC increase) before (middle) and after (bottom) tissue reperfusion. Notably, most of the changes in TSC accumulation rates take place in the MCA territory where a reduction in TSC increase is observed after reperfusion. These findings are consistent with the lack of TTC staining in the MCA territory on the "rough" histology sections (center and right) and seem to indicate that reperfusion of the MCA territory has been of benefit in this model.

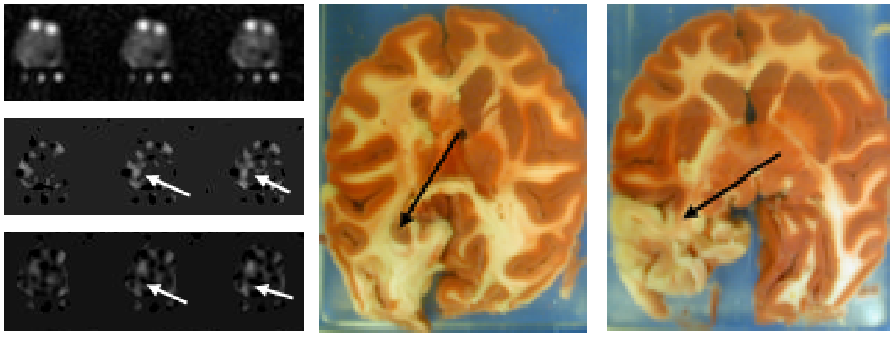

Figure 2: *Left column: (top) Selected partitions from a 3D sodium image, and their corresponding slope maps before (middle row) and after (bottom row) reperfusion of the MCA territory. Changes in the rate of TSC accumulation are clearly observed in the region corresponding to the MCA territory (arrows). Only pixels with statistically significant slopes (P<0.005) are shown in these maps. The TTC-stained sections (center and right) demonstrate ischemic damage in the PCA territory.*

CONCLUSIONS

Our results demonstrate that sodium MRI signal intensity increases in stroke shortly after ischemia onset. The TSC rise has been found to be spatially heterogeneous with a spatial distribution that changes upon tissue reperfusion and that cannot be explained through partial voluming effects. This hetereogeneity could have important implications during the clinical management of stroke.

REFERENCES

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Supported in part by NIH grant R01 NS044818.