Effects of Occlusion Duration on Infarct Volume and Tissue Fate in Ischemic Stroke

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TARGET AUDIENCE Researchers in stroke, perfusion imaging, diffusion imaging.

PURPOSE Diffusion and perfusion MRI are widely used to track the evolution of ischemic tissue fates. In this study, we evaluated initial lesion volume and endpoint infarct volume at multiple middle cerebral arterial occlusion (MCAO) durations in rats and determined the percent of the different types of tissue (i.e., apparent diffusion coefficient (ADC) lesion and diffusion/perfusion mismatch) that could be salvaged at multiple MCAO durations.

METHODS Twenty one male Sprague Dawley rats (250-300g) were subjected to 30-min (N=6), 45-min (N=5), 60-min (N=6) or 90-min (N=4) transient MCA occlusion using intraluminal suture occlusion method.[1] Animals were maintained anesthesia with ~1.2% isoflurane in air. Body temperature, PaO2 and heart rate were continuously monitored and maintained within normal ranges. MRI experiments were performed on a 7-T/30-cm magnet. Quantitative CBF (cerebral blood flow) and ADC were measured using continuous arterial spine labeling and diffusion-weighted EPI.[1] T2 maps were acquired using fast spin echo sequence[1] in day-2.

Based on 30-min (first time point) ADC and CBF maps, ischemic core, perfusion/diffusion mismatch and normal tissues were classified using automated clustering ISODATA method.[2] Initial lesion volumes were defined by the core tissue volumes. Final infarct volumes were derived from day-2 T2 maps using threshold of mean T2 value of normal hemisphere plus two times of standard deviation. Edema correction was applied.[3] Changes in infarct volume at day 2 relative to lesion volume at 30 mins were analyzed. Day-2 data was co-registered to acute phase data[4] for pixel-by-pixel tissue fate tracking. Paired t-test was used for comparison between initial lesion volume and final infarct volume. A P-value of 0.05 was taken to be statistically significant. Data showed in figures and texts are mean ± SEM.

RESULTS Figure 1 shows the initial ADC-defined lesion volume at 30 mins and final T2-defined infarct volume at 2 days after stroke and their % lesion volume changes. The initial lesion volumes of the different occlusion duration groups were *not significantly different across all occlusion groups* (P>0.05), indicating consistent and reproducible initial volume sizes.

Figure 2 shows the % of the initial ADC lesion and mismatch pixels became normal at day-2 for different occlusion duration groups

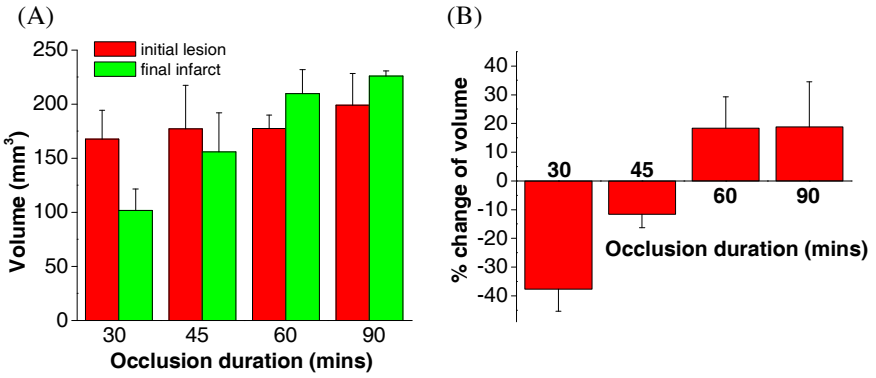

Figure 1. (A) Initial lesion (30 mins) and final infarct (day 2) volume of rats subjected to 30, 45, 60 and 90-mins MCAO. **(B)** Percent change of volume of different groups.

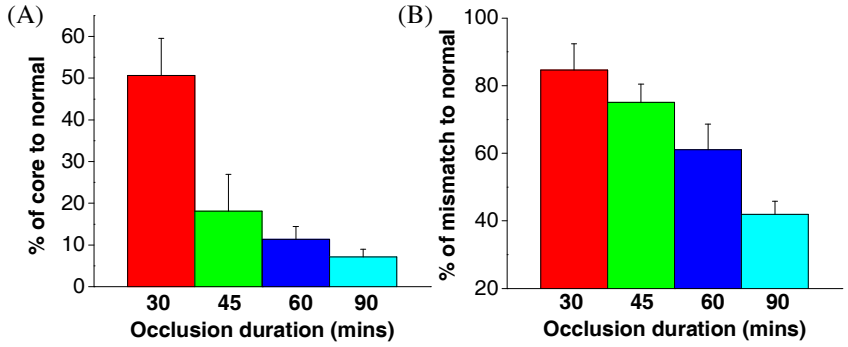

Figure 2. Percentage of core (A) and mismatch (B) tissues salvaged by reperfusion.

DISSCUSSIONS & CONCLUSIONS The final lesion volumes of the 30- and 45-min MCAO groups were smaller than the initial lesion volumes. By contrast, the final infarct volumes of the 60- and 90-min MCAO groups were larger than the initial lesion volumes, indicating that it was too late and there was apoptotic death even if ADC was transiently reversed.

In the 30-min MCAO group, half the initial ADC lesion was reversed, whereas in the 60- and 90-min MCAO groups, only about 10% of the initial ADC lesion was reversed, and there was a relatively weak dependence on duration. By contrast, the mismatch salvaged was inversed proportional to MCAO duration in roughly linear fashion.

In conclusion, this study provided insights into the types of tissue salvaged for different occlusion durations. Future studies will investigate the underpinnings of molecular and immunohistochemical changes of these tissue types.

REFERENCES: [1] Shen Q, et al, J Cereb Blood Flow and Metab 2011;31:2076. [2] Shen Q, et al, J Cereb Blood Flow and Metab 2004;24:887. [3] Tatlisumak T et al, Stroke 1998;29:850. [4] Liu ZM, et al, Magn Reson Med 2004;52:277. *Supports: NIH R01-NS45879, AHA 12BGIA9300047, CTSA 8UL1TR000149.