Temporal Evolution of the Diffusion/Perfusion Mismatch in a Rat Model of Focal Cerebral Ischemia

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Introduction

Diffusion-weighted imaging (DWI) detects early ischemic abnormalities related to reduction of the apparent diffusion coefficient (ADC) of brain water. Perfusion-weighted imaging (PWI) provides information about the hemodynamic status of brain tissue and detects regions with impaired cerebral perfusion. Clinical reports have demonstrated that the impaired perfusion region is typically larger than the lesion detected by DWI early after stroke onset. The difference between the PWI and DWI abnormalities was termed the diffusion/perfusion mismatch, and the DWI lesion usually enlarges over time until it coincides with the region of perfusion deficit. The mismatch region may represent potentially salvageable brain tissue with timely and appropriate therapy. The diffusion/perfusion mismatch evolution has not been well characterized during the first few hours in individual patients, nor in animal models. The aims of this study were to evaluate the evolution of the DWI/PWI mismatch in a permanent and 60 minutes temporary focal experimental ischemia rat model.

Methods

Twelve Sprague Dawley rats weighing 300-350g were subjected to permanent and 60 minutes temporary ischemia using the intraluminal middle cerebral artery occlusion (MCAO) method (n=6 each group). MR experiments were performed on a 4.7-T/40-cm horizontal magnet. A surface coil (2.3-cm ID) was used for brain imaging and an actively-decoupled neck coil was used for CBF labeling. Anatomical images were acquired with TR=2s, 8 echo trains, TE effective=65ms, matrix = 256x256, FOV=2.5x1.9cm^2 , seven 1.5-mm slices and 4 averages. ADC was measured using spin-echo EPI with matrix=64x64, FOV=2.5x1.9cm^2 , and six 1.5-mm slices, TE=40ms, TR=1.5s, 4 averages, b = 5, 1504 s/mm^2 along each of the 3 principle axes. CBF was measured using the continuous arterial spin-labeling technique with single-shot, gradient-echo EPI, with parameters similar to the ADC measurement except TE=17ms, and TR=2s, and 100 pairs of images were acquired for averaging. DWI and PWI were acquired at 30, 60, 90, 120 and 180 min after occlusion in both the permanent and temporary occlusion models. In the transient ischemia group, reperfusion was done at 60 min after occlusion, and DWI and PWI were acquired before and after reperfusion at this time point. ADC maps and CBF maps were used to calculate the lesion volume (mm^3) for each time point. The rats were sacrificed at 24 hours after MCAO and infarct volume was determined by 2,3,5-triphenyltetrazolium chloride (TTC) staining.

Results

The lesion volume on the ADC maps was significantly smaller than that on the CBF maps through the first 60 minutes after MCAO in the permanent ischemia group. At 90 minutes after occlusion, the mean abnormal perfusion volume was 23 mm^3 larger than the mean abnormal diffusion volume. By 180 minutes, the ADC- and CBF-defined volumes were almost identical. The ADC-defined lesion at three hours was highly correlated with the 24-hour TTC-derived infarct volume. With 60 minutes of transient ischemia, the PWI and DWI mismatch was similar to permanent ischemia before reperfusion. After reperfusion the lesion volumes on PWI and DWI became much smaller (Fig. 1). There was a significant difference in 24-hour infarct volumes between the two groups (244.5 ± 45.4 mm^3 in the permanent group and 139.8 ± 32.2 mm^3 in the 60 minute transient occlusion group, $p<0.01$)

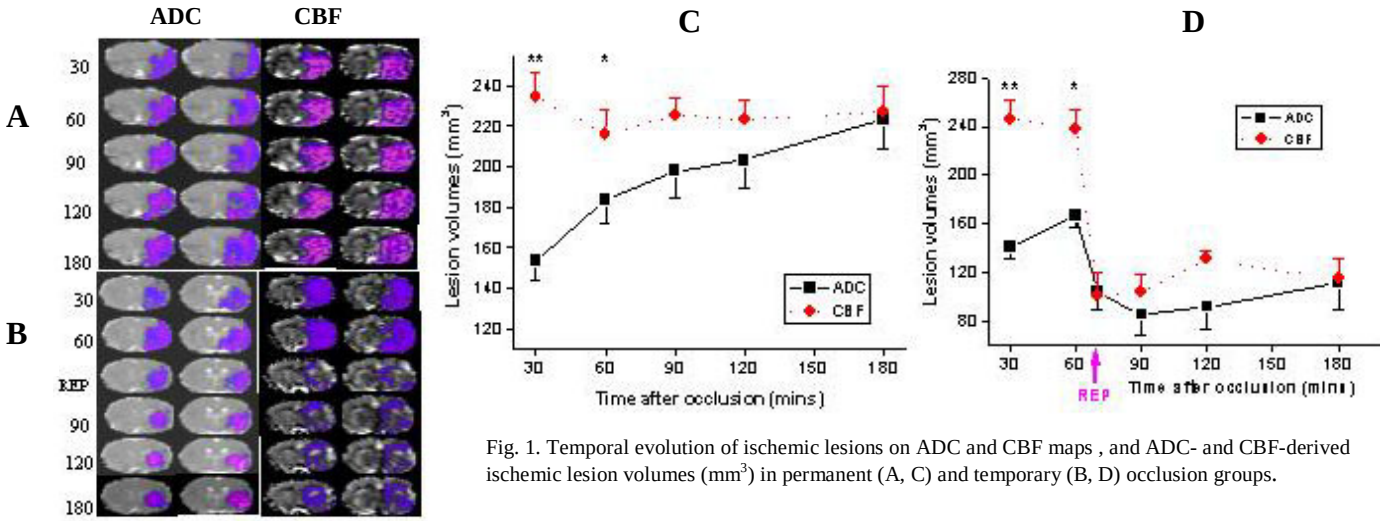

Fig. 1. Temporal evolution of ischemic lesions on ADC and CBF maps , and ADC- and CBF-derived ischemic lesion volumes (mm^3) in permanent (A, C) and temporary (B, D) occlusion groups.

Discussion and Conclusion

We demonstrated that a significant mismatch exists between DWI and PWI lesion volumes up to 60 minutes after MCAO, and that the mismatch diminished gradually and disappearing by three hours after MCAO in this permanent occlusion model. Reperfusion at 60 minutes prevented the mismatch region from further progression to ischemic damage, implying that early reperfusion therapy can impede ischemic lesion expansion when a DWI/PWI mismatch is present. The study of diffusion/perfusion mismatch provides a volumetric estimate of the putative ischemic penumbra and the duration of its temporal existence, information that could be useful for defining an effective therapeutic window.

References

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