Sustained postischemic hyperperfusion is associated with reversal of ADC abnormalities following transient focal cerebral ischemia in rats

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Introduction

Diffusion-weighted magnet resonance imaging (DWI) is a useful tool for the early detection of brain ischemia. Ischemic hyperintensity on DWI occurs within minutes after the onset of ischemia and is due to a reduction of the apparent diffusion coefficient (ADC) of water. The initial ADC reduction may revert to preocclusion values if the interrupted blood flow is restored after brief periods of focal cerebral ischemia. However, the role of hemodynamic changes after reperfusion is still not fully understood, and it remains unclear whether postischemic hyperperfusion has a beneficial or even harmful effect on the reperfused tissue. The purpose of the present study was to evaluate if the pattern of postischemic cerebral blood flow (CBF) differs between brain regions with persistent and temporary ADC abnormalities after 60min middle cerebral artery occlusion (MCAO) using serial DWI and perfusion-weighted imaging (PWI).

Materials and methods:

Transient focal brain ischemia was induced in 7 male SD rats using the intraluminal MCAO suture model (1.5% Isoflurane); reperfusion was performed at 60min post-occlusion by withdrawing the occluder while the animals were in the magnet. MRI data was acquired at 30, 60, immediately after reperfusion, 90, 120, 180min, and 24hr after occlusion. The brains were removed at 24hr for TTC staining. All MRI data was acquired with a Bruker 4.7-T/40cm (Billerica, MA) and a 20-G/cm gradient insert (ID=12cm, 120µs rise time). For all imaging acquisition below, the common parameters were: matrix=64x64 FOV=2.5x1.9cm, seven 1.5-mm slices. ADCav was obtained by averaging three ADC maps acquired separately with diffusion-sensitive gradients applied along the x, y or z direction (TR=2s, TE=43ms). Quantitative CBF was measured using the continuous arterial spin-labeling technique with single-shot, gradient-echo EPI (TE=15ms, TR=2s, 100 pairs of images for signal averaging). MRI data analysis was performed using codes written in Matlab and Stimulate software. Three ROIs in the ischemic hemisphere were defined as follows: (1) no ADCav abnormalities (no lesion=nL), (2) permanent ADCav lesion (permanent lesion=pL, present at 60 and 180min post-occlusion), (3) transient ADCav lesion (transient lesion=tL, present at 60min, but not at 180min). Lesion volumes were determined using the ADC viability threshold established previously (30±2% reduction of the mean ADC of the left hemisphere at each timepoint).

Results:

Physiological parameters were within normal range during the entire study period. Representative CBF and ADC maps from one animal are shown in Fig. 1. Mean ADC defined lesion volume slightly increased from 30min (168±41mm3) to 60min (201±32mm3), decreased immediately after reperfusion (125±43mm3 at 70min), and remained stable up to 180min (134±54mm3). ADC lesion volumes at 180min showed an excellent correlation with the TTC infarct volumes at 24 hours (140mm3). During occlusion, CBF was significantly lower in the regions with reduced ADC values (pL and tL), as compared to left hemisphere (LH, $p<0.01$). Immediately after reperfusion, CBF markedly increased in all regions examined. In the tL region, postischemic CBF remained high during the whole observational period, whereas a gradual decline in CBF was observed in all other regions, particularly in the pL region. The difference in CBF between the tL and pL region was significant at 120, 180min and 24hr ($p<0.05$). This hyperperfusion was more pronounced when compared to LH, being constantly >100% at the early phase of reperfusion and 124% and 139% at 3 and 24hr (Fig. 3). The corresponding mean ADC values expressed as percentage of the LH are shown in Fig. 4.

Fig. 1 Representative CBF and ADC maps

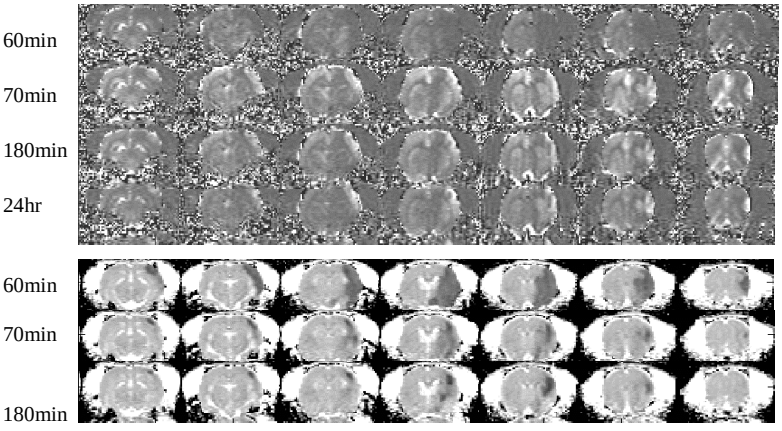


Fig. 2 Absolute CBF

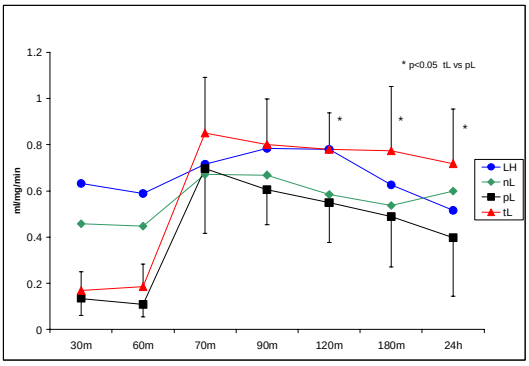


Fig. 3 Relative CBF (% of LH)

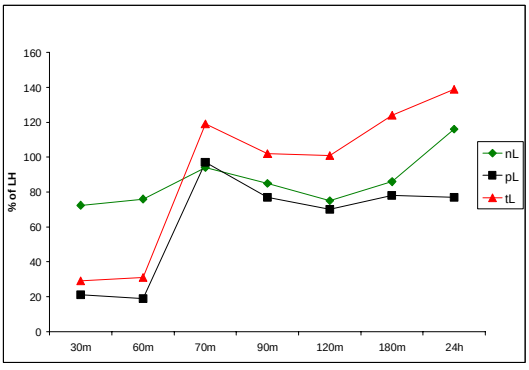
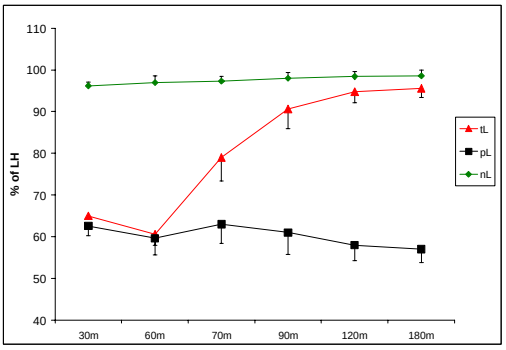


Fig. 4

Relative ADC (percentage of LH)



Discussion

Reports on the effect of early postischemic hyperperfusion on tissue fate have been contrary, and both beneficial and harmful effects have been reported, depending on severity and duration of prior ischemia. Our results do not support the latter, in contrast, reversal of ADC abnormalities was associated with a sustained hyperperfusion beginning immediately after reperfusion and lasting at least up to 24hr. In addition, the extent of hyperperfusion was more pronounced at later time points, i.e. 24hr, exceeding more than 135% of the LH. Further studies are needed to evaluate the effects of hyperperfusion after differing durations of ischemia in distinct animal models.