Postischemic Hyperperfusion: the Insight from a Multi-parameter MRI Study

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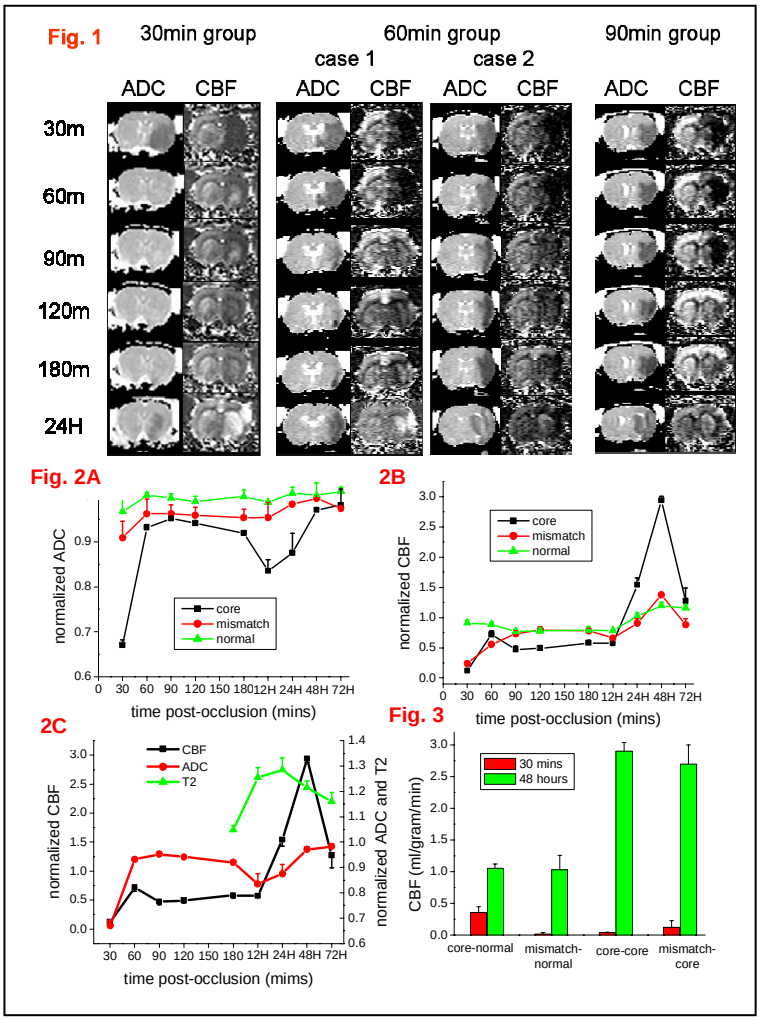
INTRODUCTION Hyperperfusion after ischemic brain injury has been sparsely and inconsistently reported in the literature (1, 2). The conditions under which hyperperfusion is elicited in stroke remain unclear. There is no consensus as to whether hyperperfusion has beneficial or detrimental effects on tissue outcome. In this study, we investigated hyperperfusion after focal ischemia in three different occlusion durations (30min, 60min, and 90min MCAO) in rats. Quantitative diffusion, perfusion, and T2 imaging were performed every 30-min up to 3 hrs after stroke onset (acute phase), and again at 24 hrs. For 30-min MCAO group, some animals (n=4) were also imaged at 12 hrs, 48 hrs and 72 hrs post-occlusion.

METHODS Twenty-three male SD rats (300-350g) were subjected to transient (30-min (n=8), 60-min (n=6), and 90-min (n=9)) MCA occlusion using intraluminal suture occlusion method (3). Quantitative diffusion, perfusion and T2 imaging were performed at acute and sub-acute phase. Normal, mismatch, and core pixels were identified based on the acute data at 30 mins after occlusion using the ISODATA automated clustering method (3). Final lesion was defined based on ISODATA analysis of T2 and ADC maps the last imaging time point. ADC and CBF were quantified as a function of time after stroke onset and normalized with respect to the normal non-ischemic hemisphere for comparisons. To investigate if the hyperperfusion is beneficial or detrimental, four different types of tissue were tracked and their CBF values were obtained: 1) pixels that migrated from core (defined at 30-min) to normal (defined at endpoint); 2) core to core; 3) mismatch to normal; 4) mismatch to core.

RESULTS Figure 1 shows ADC and CBF maps at different time points for the three MCAO groups. Hyperperfusion was observed at 24, 48 and 72 hrs post-occlusion in all rats in the 30-min MCAO group, 2 of 6 rats in the 60-min MCAO group, and none in the 90-min MCAO group.

The remaining analysis focused on the 30-min MCAO group. Normalized ADC and CBF evolutions for core, mismatch and normal pixels defined at 30-min time point are plotted in **Figure 2A-B**. No hyperperfusion was seen for normal tissues. Mismatch tissues showed slightly lower ADC and mild hyperperfusion at 48 hours post-occlusion. In contrast, the CBF of core tissues showed significant hyperperfusion 24 hrs post-occlusion and peaked at 48 hrs (290 ± 19 % of normal value). Normalized ADC, CBF and T2 evolutions of the core pixels are summarized in **Figure 2C**. ADC transiently returned to normal after reperfusion, decreased to its lowest at 12 hrs post-occlusion, and pseudo-normalized at 48-72 hrs. T2 value showed a biphasic response which does not mean that tissue recovered, as reported previously (4).

To investigate if the hyperperfusion is beneficial or detrimental, four different types of tissue were tracked and their CBF values were obtained: 1) core to normal; 2) core to core; 3) mismatch to normal; 4) mismatch to core. The results (**Fig. 3**) showed that subsequently salvaged tissue has normal CBF (no hyperperfusion) whereas tissue destined to infarct showed hyperperfusion.



DISCUSSION & CONCLUSION The key findings of this study are: 1) hyperperfusion was observed predominantly in the core 24 hrs post-occlusion in all rats of the 30-min MCAO group and some in the 60-min MCAO group, but none in the 90-min MCAO group, 2) no significant hyperperfusion was observed in the normal tissues at all time points imaged in all MCAO groups, 3) significant hyperperfusion was observed in tissues which subsequently became infarcted, but not in those which were salvaged. In some human studies, post-ischemic hyperperfusion has been reported to be a harmless and even perhaps beneficial phenomenon (5, 6). In contrast, in most experimental studies (7, 8), post-ischemic hyperperfusion was demonstrated to be not beneficial and even detrimental because it could accumulate by-products (such as free radicals) that result in delayed neuronal damage. Heiss (7) stated that forced reperfusion by reopening of the MCA cannot salvage already irreversibly damaged tissue but may cause additional damage by inducing edema, and that this latter effect may be aggravated by severe and prolonged hyperperfusion in paralyzed vessels. It seems unlikely that active recruitment of more CBF is needed in the core 24 hrs after stroke. Thus, we conclude that hyperperfusion at the chronic phase under our experimental conditions is likely due to changes in blood-brain permeability (9) which leads to increased CBF in the already infarct regions.

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