Delayed Postischemic Hyperemia in a Rat Model of Focal Ischemia Observed by MR Perfusion Imaging Using Arterial Spin Tagging

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Introduction

Clinical and experimental transient cerebral ischemia is often followed by hyperemia, or "luxury perfusion". The mechanism underlying this is unclear, as is its role in the development of cerebral infarction. In *global* ischemia models, an initial hyperemia occurs immediately upon reperfusion, followed by delayed hyperemia 12-48 hours after ischemia in brain regions sustaining neuronal damage[1]. A similar initial hyperemia occurs in *focal* ischemia[2,3], but *delayed* hyperemia after transient focal ischemia has been less well characterized. In this study, arterial spin tagging (AST) MR perfusion imaging was used to evaluate hyperemia 24 and 48 hours after ischemia/reperfusion in focal ischemia in rat.

Material and Methods

Focal ischemia was induced in 6 male Sprague-Dawley rats by intracerebral injection of endothelin-1 (3 µl, 20 pmol/µl) just above the middle cerebral artery (MCA) distal to the striatal branches[4]. At 24 and 48 hours after ischemia, the rats were placed in a homebuilt 3 cm-diameter saddle coil in a 7T/21 cm magnet. Cerebral blood flow (CBF) was measured quantitatively using a SNAPSHOT FLASH-based AST MR perfusion imaging sequence using a 2 mm thick slice centered at the caudoputamen, 5×5 cm^2 FOV, 128×128 points, TR=4.3 ms, TE=2.3 ms, 12° flip angle, and 24 averages. A 400 ms post-tagging delay was used to eliminate intravascular artifacts[5]. Proton density images were acquired using a four-step offset gradient cycling protocol to eliminate the asymmetrical magnetization transfer effect. Perfusion images were calculated as described previously[6]. Statistical analysis was carried out using a two-tailed paired *t*-test.

Results

Figure 1 shows perfusion images obtained at 24 (A) and 48 (B) hours post-ischemia, and a T2 weighted (TE=80 ms) image of the same slice acquired at 48 hours (C). At 24 hours hyperemia was evident in the ipsilateral striatum. At 48 hours, hyperemia was pronounced in both the ipsilateral striatum and cortex. The region of hyperemia at 48 hours postischemia correlated well with the final infarction as defined by the T2 weighted image. CBF ratios (ipsilateral/contralateral) were 1.27±0.22 ($p<0.05$) and 1.72±0.52 ($p<0.01$) in the striatum at 24 hours and 48 hours, and 0.96±0.40 (N.S.) and 1.53±0.45 ($p<0.01$) in cortex at 24 hours and 48 hours (Fig 2).

Figure 1. Perfusion images obtained at 24 (A) and 48 (B) hours post-ischemia, and T2 weighted image of the same slice acquired at 48 hours (C).

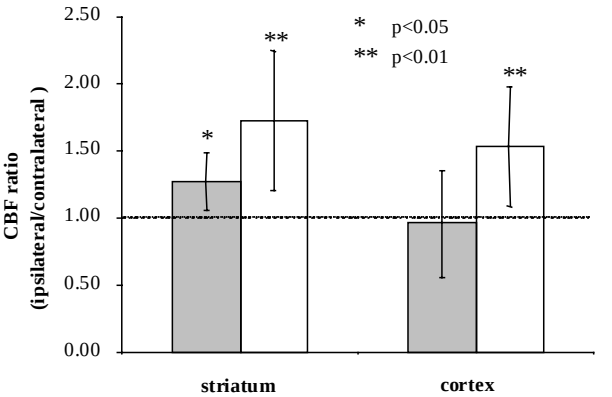

Figure 2. CBF ratios (ipsilateral/contralateral) ± SD in the striatum and cortex at 24 □ and 48 ▨ hours postischemia.

Discussion

Delayed postischemic hyperemia is apparent in the endothelin model of focal ischemia in rat. This hyperemia is distinct from the subacute initial hyperemia observed in previous studies. The time course of the development of this hyperemia is different for striatum and cortex. Whether it plays a beneficial or detrimental role in the development of the cerebral infarct is unclear, and clarifying this may direct the development of novel therapies for focal ischemia.

References

1. W. A. Pulsinelli et al, *Ann. Neurol.*, **11**, 499-509, (1982)
2. W. D. Heiss et al, *J. Cereb. Blood Flow Metab.*, **17**, 388-400, (1997)
3. L. Belayev et al, *J. Cereb. Blood Flow Metab.*, **17**, 1266-1280, (1997)
4. J. Sharkey et al, *J. Cereb. Blood Flow Metab.*, **13**, 865-871, (1993)
5. D. C. Alsop et al, *J. Cereb. Blood Flow Metab.*, **16**, 1236-1249, (1996)
6. H. Lei et al, *Magn. Reson. Med.*, in press.