Manganese-enhanced MRI of Perilesion Cortex in Subchronic Focal Brain Ischemia

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INTRODUCTION: Rescuing the ischemic penumbra from infarction is the mainstay of acute stroke therapy (1). Yet, to date, little is known about the subchronic/chronic events of recovery mechanisms in the brains, which are equally important in determining and improving the functional consequences of brain lesions. Our previous Mn-enhanced MRI (MEMRI) study had demonstrated the transient brain changes in the early recovery period after focal brain ischemia (2). In this study, MEMRI was employed to investigate into the late changes in Mn²⁺ enhancement in subchronic focal brain ischemia, with emphases on the temporal evolutions in different subregions of the perilesion cortex.

MATERIALS AND METHODS: Animal Preparation: Adult Sprague-Dawley male rats (200-250 g, N=18) were prepared and were divided into 4 groups. The first 3 groups (n=4 each) were subjected to focal cortical photothrombotic lesions (PCI) in the center of motor cortex of one side of the brain using the rose bengal techniques (3), while the other animals in Group 4 (n=6) were untreated and served as control. Two and 6 days after surgery, animals in Groups 1 and 2 were respectively administered with an intraperitoneal injection of MnCl₂ solution (45mg/kg, 100mM), while Group 3 received no Mn²⁺ injection. MRI was performed to the ischemic animal s at 3, 7, 14, 21 and 28 days after ischemia. For (2). In this study, MEMRI was employed to investigate into the late changes in Mn²⁺ enhancement in subchronic focal brain ischemia, with emphases on the temporal evolutions in different subregions of the perilesion cortex.

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MRI Protocols: All MRI measurements were acquired utilizing a 7 T Bruker scanner. Under inhaled isoflurane anaesthesia (3% induction and 1.5% maintenance), animals were kept warm under circulating water at 37°C and were imaged using a receive-only surface coil. 2D T1-weighted RARE sequence was acquired with FOV = 3.2 x 3.2 cm², matrix resolution = 256 x 256, slice thickness = 1 mm, number of slices = 10, TR/TE = 400/7.5 ms, RARE factor = 4 and NEX = 16; T2WI was performed under the same dimensions with TR/TE = 4200/65 ms, RARE factor = 12 and NEX = 2; Signal intensities (SI) in the ipsilesional cortex, including the ischemic core, ventral rim, lateral rim, and parietal cortex were obtained using ImageJ v1.42q, and were normalized with the SI in the contralesional cortex (Fig. 1, bottom left). The SI in the ipsilesional dorsal thalamus was normalized with the contralesional dorsal thalamus. Two-tailed paired t-tests were compared between ipsilesional cortical/subcortical regions and the contralesional cortex/thalamus in the same groups. Results were considered significant when p<0.05.

RESULTS AND DISCUSSION: As shown in Figures 1 and 2, Mn injection to the ischemic animals at Days 2 or 6 led to a transient increase in SI in the lateral rims (Fig. 1, solid arrows) surrounding the hypointense ischemic core at Days 3 and 7 (p<0.05) in consistency with our previous study (2). Interestingly, in the ventral rim, a delayed enhancement was found at Day 14 (Fig. 1, open arrows) (p<0.05), which remained observable at later time points. Significant T1W enhancement was observed in the lateral rim at Day 7 without Mn injection, yet no apparent enhancement was found in the ventral rim at Day 14 (Fig. 1) (p<0.05). In Figure 3, the T1W hyperintensity appeared to colocalize with the enhanced GFAP, MnSOD and GS expression at the ischemic core, oxidative stress and glutamate excitotoxicity, respectively.

CONCLUSION: Previous studies suggested that after acute stroke, the rescued penumbra may be affected by selective neuronal loss and microglial activation, which may hinder functional recovery (1). Our results on the Mn detection of the differential temporal changes in the perilesion cortex may provide a new tool for in vivo monitoring of the evolutionary changes of salvageable tissues and hence represent potential new therapeutic targets for improving the functional consequences after stroke.