Mismatch between the apparent diffusion coefficient of water and manganese accumulation on manganese-enhanced MRI (MEMRI) in experimental focal ischemia

Y. Inoue[1], Y. Mori[2], I. Aoki[2], C. Tanaka[2], T. Ebisu[3], Y. Osaka[4], T. Houri[4]

[1]Department of neurosurgery, Kyoto Prefectural University of Medicine, Kyoto, Japan, [2]Meiji University of Oriental Medicine, Hiyoshi-cho,Funai-gun, Kyoto, Japan, [3]Nantan General Hospital, Yagi-cho, Funai-gun, Kyoto, Japan, [4]National Maizuru Hospital, Maizuru, Kyoto, Japan

Introduction

The mismatch between abnormal perfusion-weighted MRI (PWI) and normal diffusion-weighted MRI (DWI) observed in humans has been suggested to possibly indicate a treatable area. However, the DWI/PWI mismatch has also been reported to be an imperfect approximation of the true tissue penumbra. Actually there are some reports describing DWI hyperintensity was also partially salvageable. In other words, the exact prediction of infarction growth remains extremely difficult because there is currently no optimal modality indicating ischemic core. Any mismatch between decreased apparent diffusion coefficient (ADC) and manganese accumulation could be still salvageable. In our recent report, the enhanced region on manganese-enhanced MRI (MEMRI) was smaller than the area with the subsequent reduction of ADC. However, in this report there was time difference between image findings, because increased signal intensity on MEMRI may reflect manganese accumulation immediately after ischemia onset, approximately 47 minutes earlier than DWI measurements. In this study, to resolve this methodological limitation, we established a remote embolic ischemia model in a magnet bore and compared these image findings. The goal of this study was to test the hypothesis that mismatch between the decreased ADC and manganese accumulation on MEMRI is observed in the super-acute stage of experimental focal ischemia.

Materials and Methods

Ten male Wistar rats (350–420 g) were anesthetized with 2.5% isoflurane and then ventilated. The right common carotid artery was ligated and a polyethylene tube was inserted into the right internal carotid artery (ICA). After the operation, the rats were placed into the magnet bore. A glycerin solution (1g/kg, 100 mg/ml) was infused from the femoral vein at the rate of 10 ml/kg/h to prevent brain swelling due to rapid osmotic changes after the opening of the blood-brain barrier (BBB). Then, D-mannitol dissolved in warm saline (25%, 5 ml/kg) was injected from the right ICA. Ten minutes after the mannitol injection, a manganese chloride ($MnCl_2$) solution (2 mM, 0.5 ml) was infused from the right ICA and T_1-weighted MRI (T1W) scanning was performed before ischemia as a control. Three TiO_2 macrospheres were then remotely injected through the tube and DWI followed by subsequent T1W was measured 2 minutes after the injection. The MRI acquisitions were performed on a 4.7-T horizontal MRI scanner (CSI-II-Omega, Bruker, Germany). A 30 mm Litz coil (Doty Scientific Inc., USA) was used. Body temperature was maintained at approximately 37.5 ºC by hot-water circulation during MRI scanning in the magnet bore. The regions of interest (ROI) were set up in the bilateral caudate-putamen (CP) and cortex (CT). The normalized signal intensity and apparent diffusion coefficient (ADC) values, divided by initial values before vascular occlusion, were calculated to compensate for individual differences in animals and measurements independent of pathologic changes.

Results and Discussion

The ADCs in the ipsilateral ROI were significantly decreased ($P < 0.0001$) after embolic stroke (Fig 1). In contrast, the manganese-enhancing region was much smaller than the area with decreased ADC. No significant increase of average signal intensity in the ipsilateral ROI was observed on MEMRI (Fig 2). These findings were consistent with the hypothesis that mismatch between the decreased ADC and manganese accumulation is present in the acute focal ischemia. In previous report, Mn2+ may enter ischemic glia cells and/or neurons through ligand-gated or voltage-gated Ca2+ channels in terminal anoxic deporalization. Manganese-enhancing region in the ischemic brain may be the ischemic core, irreversible brain damage.

Figure 1

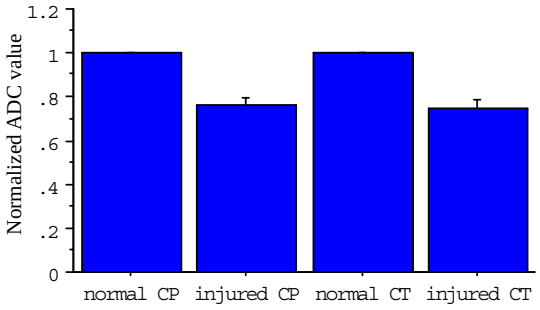

Figure 2