Glial tissue imaging at ischemic legion by MEMRI using manganese oral administration

Y. Kawai[1], M. Umeda[2], Y. Watanabe[2], T. Higuchi[1], and C. Tanaka[1,2]

[1]Neurosurgery, Meiji University of Oriental Medicine, Kyoto, Japan, [2]Medical Informatics, Meiji University of Oriental Medicine, Kyoto, Japan

Introduction

The manganese administration with intravenous injection is known as Manganese-enhanced MRI (MEMRI), it can find unique contrast change that is dependent on the cell activity or cell density. MEMRI is taken notice as one of the molecular imaging technique for nervous system. We reported the possibility of detection of signal enhancement caused by the manganese accumulation using MEMRI in the gliosis area after brain ischemia. Reactive gliosis is known as the hyperproliferation of astrocytes as a result of central nervous system injury. We reported that reactive gliosis as a result of focal ischemia can accelerate manganese uptake and accumulation due to the hyperactivity or high density of glial cells (Kawai et al, ISMRM 2007:1215). MEMRI needs for administrating the high concentration manganese solution. However, manganese is accumulated and remained for a long time, over one month. On the other hand, manganese chloride with low concentration is used for MRI contrast agent of magnetic resonance cholangiopancreatography (MRCP). Oral administration of low concentration manganese solution is hardly seen blood clearance variation. In this study, we succeeded to detect of brain signal enhancement at the ischemic lesion after oral administration of manganese as drinking water continuously after onset of ischemia.

Material and Method

We divided Male Sprague-Dawley rats (256.8 ± 10.3 g, N = 14). We made the temporary middle cerebral artery occlusion (MCAO) model under 2.0-2.5 % isoflurane with a 1:3 O_2 / room air gas mixture using a mask. MCA occlusion used silicon-coated nylon (4-0) suture and removed the sutures from the MCA for reperfusion 60 minutes after the occlusion. After MCAO, we started oral administration of manganese solution. Concentration of manganese solution was decided on the concentration of "Bothdel Oral Solution 10" (Meiji Dairies Corporation, JAPAN) which is used as contrast agent for MRCP. This concentration of manganese chloride tetrahydrate water solution was 144 mg / 1L. We made two kind of manganese solution 144 mg /1L (the same concentration as Bothdel, x1 group; n=4) and 1440 mg /1L (10 times higher concentration of Bothdel, x10 group; n=6). Control group was administrated normal water (n=4). T_1-weighted and diffusion-weighted images (b = 47, 1500 s/mm^2) were acquired 1 day, 1 week, 2 weeks, 3 weeks and 4 weeks after MCAO using a 4.7T-MRI (Bruker, Germany). Following after 4 weeks data acquisition, an $MnCl_2$ solution (50 mM, 75 mg/kg, 2ml/h) was infused via the tail vein. MRI measurements were also performed 24-hours after the administration as MEMRI.

Results and Discussion

The signal enhancement of ischemic region was confirmed in oral administration group. This signal change accorded with our previous report. The manganese which was administered orally is almost drained as feces, therefore the manganese absorption is probably a little. Because it is said that the absorption factor is 0.2~16.0 %, it seems that the absorption volume of the manganese in this study is quite 0.05~4.60 mg/day. A relative signal increase was observed in 2/4 rats of x1 group and 4/6 rats of x10 group. The difference of the signal change was not observed between x1 group and x10 group. With the method of continuous oral dosage of a little manganese, it was suggested that the manganese was accumulated and changed the contrast of the region. For the purpose of glial cell images it may be important that continuous administration of lower concentration manganese solution. This method using low concentrated manganese solution is possible to expand from animal to human. Furthermore, this method has possibility to detect the hyperproliferating cells, for example high grade tumor in human.

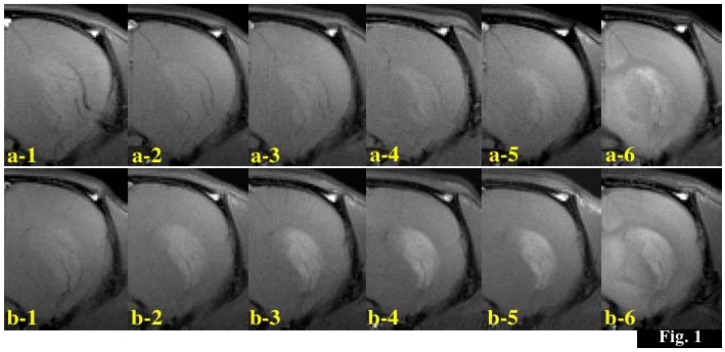
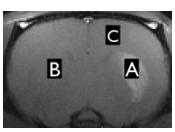


Fig. 1

Fig. 1 **Time course observation of T_1-W images**

An example of control (a) and x10 Bothdel administration (b). MCAO after 1day (1), 1 week (2), 2weeks (3), 3weeks (4), 4 weeks (5) and 50 mM $MnCl_2$ via the tail vein (6). Signal enhancement was shown in the peripheral area of ischemic region. In addition, T_1 (s) was the following values after 4 weeks. Control: area A=0.97, B=0.96, C=0.97. x10 administration: area A=0.77, B=0.99, C=1.01.



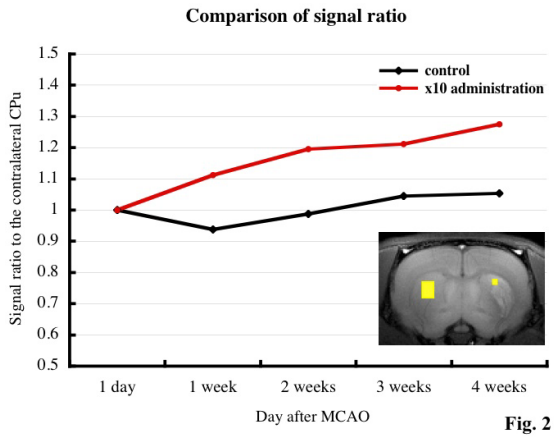


Fig. 2

Fig. 2 **Comparison of signal ratio of ischemic region**

Signal enhancement was observed in the ischemic region in comparison with contralateral side of CPu. Serial signal enhancement was observed in the x10 administration rat. The signal of the x10 administration rat was higher in comparison with the control rat.