Manganese-Enhanced and Diffusion Spectrum MRI of Hippocampal Cytoarchitecture in Epileptic Rats

J-C. Weng[1], C-Y. Lee[2], H-H. Liou[2], J-H. Chen[1], and W-Y. I. Tseng[3]

[1]Interdisciplinary MRI/MRS Lab, Dept. of Electrical Engineering, National Taiwan University, Taipei, Taiwan, [2]Dept. of Pharmacology, National Taiwan University College of Medicine, Taipei, Taiwan, [3]Center for Optoelectronic Biomedicine, National Taiwan University College of Medicine, Taipei, Taiwan

Introduction

The hippocampus is a critical structure for learning and memory formation. It is easily injured by diverse neuropathologies such as epilepsy. Recently the neuroarchitecture of hippocampal damage has been investigated by manganese-enhanced magnetic resonance imaging (MEMRI) [1] and diffusion tensor imaging (DTI) [2] respectively due to different abilities of these two techniques. In our pervious study [3], we demonstrated the application of MEMRI and diffusion spectrum imaging (DSI) simultaneously and non-destructively in the healthy rat hippocampus. Base on the pervious study, we tried to characterize activity-dependent plasticity in hippocampus after intraperitoneal pilocarpine injection and to compare it with healthy brain using MEMRI and DSI in 3T MRI. To improve detection sensitivity to the full extent of Mn^{2+} concentrations and to optimize detection of low concentrations of Mn^{2+}, R1 map was implemented [4]. To quantify the diffusion anisotropy of probability density function, DSI anisotropy (DA) index was used [5]. Our results indicate that MEMRI and DSI can both be used to detect specific changes at the cellular level during activity-dependent plasticity, and the signal changes in R1 and DA map can serve as an imaging marker for epileptogenesis.

Materials and Methods

Male Wistar rats were injected with pilocarpine (300-380 mg/kg, intraparentally) to induce status epilepticus (SE). The behavioral seizures were evaluated according to Racine's score [6]. SE was defined with continuous convulsions with score 4 to 5 for at last one hour. Adult healthy (N=2) and epileptic (N=3) Wistar rats were anesthetized with intraperitoneal injection of sodium pentobarbital. $MnCl_2$ was given by intraperitoneally injecting 2 ml of a 128 mM $MnCl_2$ solution. Rat body temperature was maintained at 37°C using warm water circulation after infusion. To avoid suffocation, atropine was injected subcutaneously after the $MnCl_2$ infusion. Rats were scanned 24 h after $MnCl_2$ administration.

The data were acquired on a 3T MRI Biospec system (Bruker, Germany). A multislice multiechoe spin echo sequence was performed to obtain T1WI. T1WI images were acquired with in-plane resolution of 78 μm, slice thickness of 1 mm. R1 mapping images were acquired by the same sequence with 23 points sampled along the recovery with TR/TE = 300~6000/10 ms and with in-plane resolution of 156 μm. Images of DSI were acquired with a spin echo pulsed gradient sequence, in-plane resolution of 156 μm, slice thickness of 1 mm. The diffusion-encoding scheme constituted 515 diffusion-encoding directions. We obtained diffusion attenuated images with b values changing from 0 to 26,700 s mm^{-2}.

Results and Discussions

Hippocampal cellular architectonics of healthy and epileptic rats can be visualized by T1WI and R1 map 24 h after Mn^{2+} injection. In the control rats, the CA1, CA2 and CA3 were enhanced by Mn^{2+} but dentate gyrus (DG) was not enhanced yet (Fig. 1a, b). In the epileptic rats, the DG and the CA3 subregion were enhanced obviously (Fig. 2a, b). An increase in the number of manganese-enhanced pixels in the DG and CA3 subfields was found in the epileptic rats compared with the control rats, possibly reflecting the underlying pathophysiology involving cell loss and gliosis in CA3, and mossy fiber sprouting in DG. When DSI vectors were superimposed with T1WI map (Fig. 1c, e), the hippocampus of the control rats clearly showed neural fibers projecting from the enhanced cell layers in the CA1 to CA3, as well as from the non-enhanced cell layers of DG. Layered arrangement of the cell layers in the CA1 to CA3 (dark region, least anisotropic structures) and neural fibers (brightest region, most anisotropic structures) was clearly shown in the DA map (Fig. 1d). In the DA map of epileptic rats, however, the hippocampus showed less-organized fiber orientations (Fig. 2c, e) and indistinct layered structures (Fig. 2d). The averaged DA value calculated from the hippocampus of the epileptic rats was lower than that from the control rats. These findings implied that the hippocampal cellular architecture of the epileptic rats became disordered.

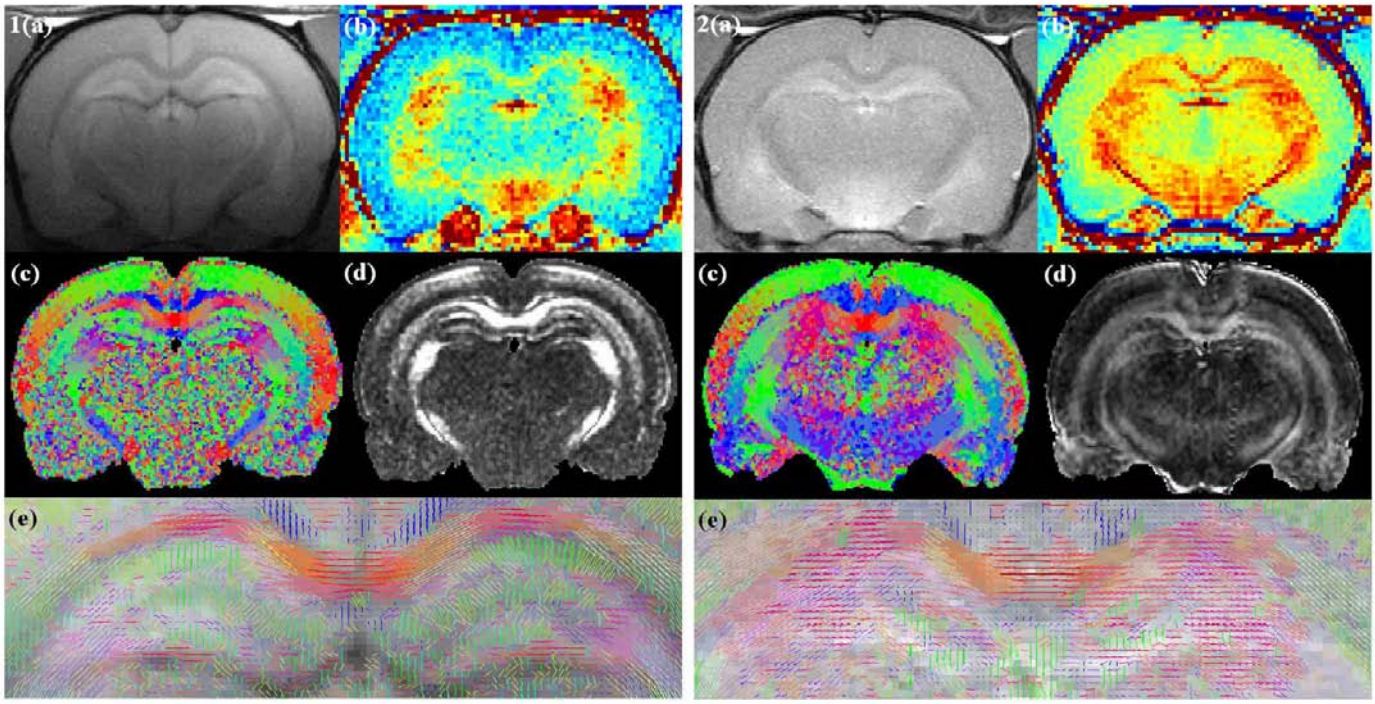

Fig. 1 Manganese-enhanced T1WI (a), R1 mapping (b), color map of DSI max vector (c), DA map (d), and DSI max vector (e) of a healthy rat brain.
Fig. 2 Manganese-enhanced T1WI (a), R1 mapping (b), color map of DSI max vector (c), DA map (d), and DSI max vector (e) of an epileptic rat brain.

Conclusions

In this study, we have demonstrated that MEMRI and DSI can be used simultaneously to detect specific changes at the cellular level during activity-dependent plasticity. Our results also suggest that the signal changes in R1 and DA map can serve as an imaging marker for epileptogenesis. Combining both techniques allows detection of alteration in both cellular and fibrous structures of the hippocampus.

References

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