Mapping Cellular Architectonics of Rat Hippocampus using Manganese-enhanced and Diffusion Spectrum Imaging

J-C. Weng[1], J-H. Chen[1], P-F. Yang[1], L-W. Kuo[1], V. J. Wedeen[2], W-Y. I. Tseng[3]

[1]Interdisciplinary MRI/MRS Lab, Department of Electrical Engineering, National Taiwan University, Taipei, Taiwan, [2]Martinos NMR Center, Massachusetts General Hospital, Harvard Medical School, Charlestown, MA, United States, [3]Center for Optoelectronic Biomedicine, National Taiwan University College of Medicine, Taipei, Taiwan

Introduction

Manganese-enhanced magnetic resonance imaging (meMRI) and diffusion spectrum imaging (DSI) both have the potential to probe the neuroarchitecture based on the different biological mechanisms. However, application of these two methods simultaneously and non-destructively in rat hippocampus has never been demonstrated yet. Lauterbur first indicates the usefulness of paramagnetic ions for altering contrast [1]. The contrast of T1WI between neural cells and other tissue is provided by the changes in T1 relaxation time due to the manganese ions. On the other hand, the DSI method was first proposed by Wedeen [2] and then has been validated and mapped complex fiber architecture in rat brain [3]. By applying diffusion-sensitive magnetic gradients to tag translational motion of water molecules, 3D probability density function (PDF) of molecular displacement can be reconstructed from the measured DSI data.

Therefore, the purpose of this paper is to realize the neuroarchitecture of rat hippocampus using meMRI and DSI in 3T MRI. We tested when the maximum signal of neuronal architecture in rat hippocampus could be measured using manganese-enhanced T1WI (meT1WI) after IV administration of manganese chloride ($MnCl_2$) solution. Then we combined meMRI with DSI index that can quantify DSI anisotropy (DA) of PDF [4] to indicate the consistency of the two tools. The results indicate that neuronal architecture of rat hippocampus can be visualized and has high consistency in a systemic administration of Mn^{2+} and water molecular diffusion.

Materials and Methods

Adult Wistar rats were anesthetized with ketamine. $MnCl_2$ ($MnCl_2$-$4H_2O$, Osaka, Japan) was given by infusing 2 ml of a 128 mM $MnCl_2$ solution at a rate of 2 ml/h through the femur vein. Rat temperature was maintained at 37°C using warm water circulation during and after infusion. To avoid suffocation, atropine was injected subcutaneously after the $MnCl_2$ infusion. Rats were scanned 12 h, 24 h, and 36 h after $MnCl_2$ administration.

The data were acquired on a 3T MRI Biospec system (Bruker, Germany). A multislices multiechoes spin echo sequence was performed to obtain T1WI. T1WI images were acquired with in-plane resolution of 78 μm, slice thickness of 1 mm. 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

In the study of optimum scan time after IV administration of $MnCl_2$ solution, four adult Wistar rats 12 h, 24 h, and 36 h after $MnCl_2$ administration and control were used. In results, we found that 24 h after IV administration of $MnCl_2$ solution was the best time to acquire T1WI in rat hippocampus. Cellular architectonics of rat hippocampus can be visualized by meT1WI and DA index derived from DSI. In meT1WI, the CA1, CA2 and CA3 were enhanced but dentate gyrus was not enhanced yet (Fig. 1a). When DSI vectors were superimposed with meT1WI (Fig. 1b), they 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 dentate gyrus. Fig. 1c showed the brightest region of meT1WI (in black) was superimposed with DSI max vectors color map. The enhanced cell layers in the CA1 to CA3 (in black) and neural fibers (in green) were arranged in layers. In Fig. 1d, layered structures of hippocampus were also found in the DA map. Fig. 1e showed the brightest region of meT1WI (in black) was superimposed with the brightest region (most anisotropic structure) of DA map (in green). Layered arrangement of the enhanced cell layers in the CA1 to CA3 (in black) and neural fibers (in green) was clearly shown.

In discussions, because Mn^{2+} can enter neural cells via voltage-gated calcium channels to enhance excitable cells and trace neural pathway [5], it provides an opportunity to investigate the functional mapping of the brain. Cortical development and plasticity couple strongly with alteration of connectivity and underlying cytoarchitecture. In view of foreseeable potential of combining high resolution MEMRI and DSI in neuroscience research, further study is required to develop robust MRI techniques to map structure and function of rat brain.

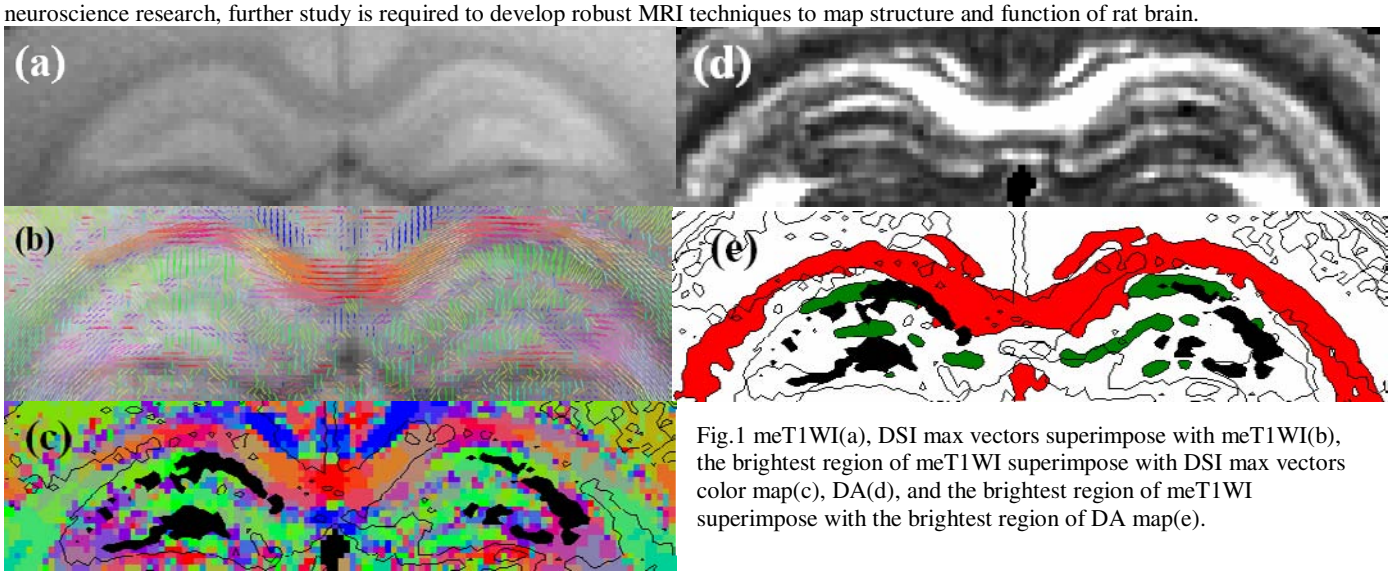

Fig.1 meT1WI(a), DSI max vectors superimpose with meT1WI(b), the brightest region of meT1WI superimpose with DSI max vectors color map(c), DA(d), and the brightest region of meT1WI superimpose with the brightest region of DA map(e).

Conclusions

In this study, we have demonstrated that meMRI enhanced the cellular layers of rat hippocampus and diffusion anisotropy of DSI highlighted the fibrous layers. Combining both techniques allows investigation of derangement involving both cellular and fibrous structures of the hippocampus.

References

[1] P. C. Lauterbur, Nature 242, 190. 1973. [2] V. J. Wedeen, ISMRM 82. 2000. [3] C. Lin et al., NeuroImage 19, 482. 2003.
[4] L. Kuo et al., ISMRM 592. 2003. [5] I. Aoki et al., NeuroImage 22, 1046. 2004.