Visualization of mouse corticospinal tract by manganese-enhanced magnetic resonance imaging

Z. Huang[1], Y-Y. He[1], and M. Bilgen[1]

[1]High Field MRI Research Laboratory, Hoglund Brain Imaging Center, The University of Kansas Medical Center, Kansas City, Kansas, United States

Introduction

In the central nervous system, corticospinal tract (CST) consists exclusively of axons that originate from motor neurons of the cerebral cortex and project anterogradely through the spinal cord (SC). Spinal cord injury (SCI) damages the CST and causes paralysis below the site of the injury in all species. Thus, the reorganization and regeneration of the neuronal fibers in the CST is the centerpiece in SCI studies [1-3]. Conventional magnetic resonance imaging (MRI) is unable to distinguish CST from its surrounding tissue. Recently, we have performed intracortical injection of paramagnetic manganese (Mn) in rats followed by electrical stimulation and accomplished MRI visualization of the CST [4]. The increased introduction of transgenic mouse models into the SCI research necessitates the use of MRI to detect the mouse CST.

Methods

Surgeries on the motor cortex, Mn injection and electrical stimulation were conducted on 10 C57BL/6 mice of 25 to 32 g using modified procedures to what had been done on rats [4]. In SCI model, these procedures were performed 2-5 days after the injury made by contusion [5]. The mouse was scanned using a 9.4 T horizontal Varian scanner approximately 15 h after the electrical stimulation. MRI data were acquired using two protocols: proton density weighted spin echo (SE) for anatomical imaging (T_R/T_E = 4000/10 ms) as well as inversion-recovery (IR) T1-weighted SE imaging for localizing the Mn-labeling. Axial IR imaging was emphasized and obtained with $T_R/T_E/T_I$ = 2000/10/500 ms, number of excitations (NEX) = 4-16, image matrix = 128 X 128 and slice thickness = 1-2 mm. The excised sample with intact spine was imaged ex vivo using an inductively coupled surface coil [6].

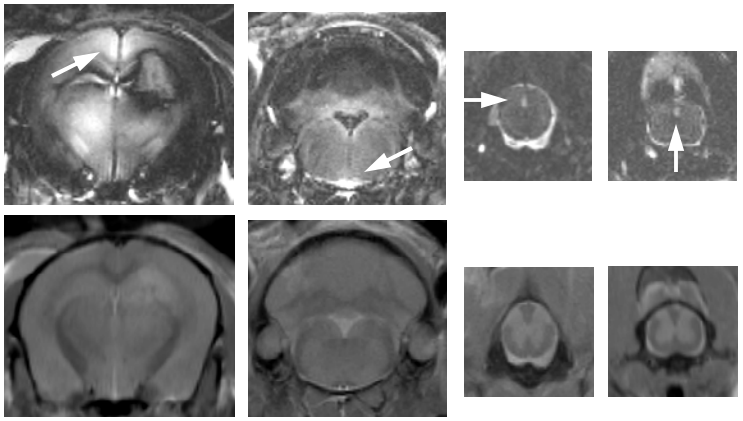

Figure 1. Axial inversion recovery (top) and corresponding proton density (bottom) images along the mouse corticospinal tract. All scans were conducted using a volume coil over a thickness of 1 mm. From left to right, arrows point to the Mn enhancements at thalamus, pyramidal tract, cervical and thoracic spinal cords.

Results

Mn-labeling was clearly observed in the axial IR images acquired at the thalamus, pyramidal tract, and cervical and thoracic spinal cords along the CST pathway (Figure 1). These IR images were obtainable for up to 24-48 hours post injection. The Mn-tracing was even more intense and convincing when the spine was imaged ex vivo at higher resolution (Figure 2). This offered the possibility of detecting the continuity and connectivity of CST fibers in injured SC.

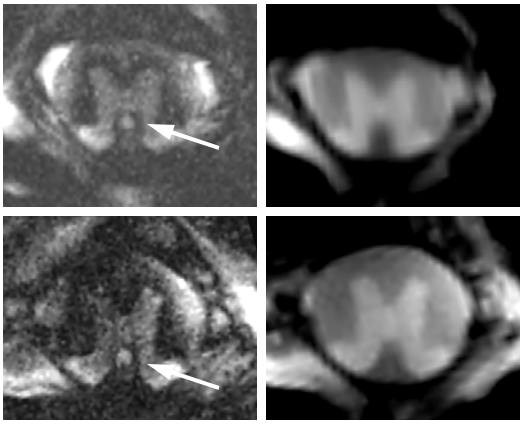

Figure 2. Mouse corticospinal tract (CST) imaged at lower thoracic level. Axial IR (**left**) and the corresponding PD (**right**) images were obtained at T9 (top) and T12 (bottom) using a surface coil over areas of 5×5 mm^2 and 4×4 mm^2, respectively. Arrows point to the Mn enhancements.

Conclusion

Due to the morphological differences between mouse and rat, the tracing of mouse CST requires higher experimental skills and different scanning strategies. Our results have demonstrated the fasibility of *in vivo* MRI of the mouse CST by intracortical Mn injection, electrical stimulation and IR imaging. This development broadens the perspective to combine MRI with a variety of transgenic mouse models in SCI research.

Acknowledgments

The study was supported by grants NS052610 and NS054019.

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