Longitudinal MRI of spinal cord injury in mouse: Changes in signal patterns associated with the inflammatory response

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Introduction

Current trend indicates that paraplegic murine models are increasingly used in experimental spinal cord injury (SCI) research because of the availability of genetically engineered transgenic and mutant mouse strains along with molecular tools [1]. However, it is interesting to note that the evolution of the neuropathology in injured mouse spinal cord (SC) exhibits distinctly different course than what is observed in rat [2]. Specifically, mouse exhibits a unique neuroinflammatory response, similar to the one seen in wound-healing or scarring, with typical characteristics of lesion site filling in with dense fibrous connective tissue. Magnetic resonance imaging (MRI) allows comprehensive and noninvasive assessment of the progression of injury characteristics following SCI. In the past, numerous studies have used MRI modalities to extensively investigate the SCI in rat and contributed our understanding of the lesion development and injury properties in the rat model. But similar studies in mouse are limited only to a few. Therefore, the goal of this paper is to demonstrate the evolution of the MR-observed neuropathology in wild type C57Bl/6 mice subjected to a contusion-type SCI. Longitudinal changes in the MR intensity are presented to assess the direct consequences of the initial mechanical injury in the acute phase and to visualize the spatiotemporal progression of the secondary injuries towards the chronic phase.

Materials and Methods

Seven mice were subject to injuries at the T11 level of SC. The animals were then scanned on postinjury days 1, 7, 14 and 28 while they were under isoflurane anesthesia (a mixture of 1.5% isoflurane, 30% oxygen, and air) administrated via nose mask using a 9.4 T INOVA Varian system (Varian Inc., Palo Alto, CA) and inductively coupled surface coil [3]. The physiological condition of the animal was monitored using ECG, respiratory and temperature probes that were connected to an MR-compatible small animal monitoring and gating system (Model 1025, SA Instruments, Inc., Stony Brook, NY). The temperature of the mouse was kept at 37 ^{o}C by circulating warm air with 40 % humidity using a 5 cm diameter plastic tubing fitted at the back door of the magnet bore. High-resolution anatomical images of the injured SC were acquired in sagittal and axial orientations using a spin echo (SE) sequence in multi-slice and interleaved fashion. The sagittal images were acquired using the parameters TR/TE=2500/12 ms, field-of-view (FOV) = 26 mm x 8 mm, acquisition matrix = 256 x 128, slice thickness =0.5 mm and number of experiments (NEX) = 2. The acquisition parameters for the axial images were TR/TE=2500/12 ms, FOV = 26 mm x 8 mm, acquisition matrix = 128 x 128, slice thickness = 1 mm and NEX = 2.

Results and Discussion

Longitudinal data from injured SCs were produced in sagittal and axial views on postinjury days 1, 7, 14 and 28 and quantified. Figure 1 shows representative images from one animal. The primary and secondary injuries reflect the complex neuroinflammatory mechanisms triggered at cellular and molecular levels combined with the endogenous attempts of the cord to repair itself. In mouse, the injuries were resolved by day 7and also initial fibrotic tissue deposition was observed on this day that lasted till day 28 (Fig. 2).

The current results clearly demonstrated the power of longitudinal MRI in providing additional insights into our understanding of the endogenous pathogenesis of the SCI in the wild-type mouse. Applications of advanced MRI modalities and data acquisition protocols should expand this power further and provide robust quantitative information on the spatiotemporal course of the changes in the anatomy, pathology, structure and function of the injured cords in genetically engineered mice.

References

[1] Guertin PA. Spinal Cord 2005;43 (8):459-61. [2] Kigerl KA, McGaughy VM, Popovich PG. J Comp Neurol 2006;494 (4):578-94. [3] Bilgen, M. et al. Magn Reson Med 2005;54 (5):1226-31.

Figure 1. *In vivo* sagittal and axial MRIs showing the pathology of an injured spinal cord on postinjury days 1, 7, 14 and 28 (from left to right).

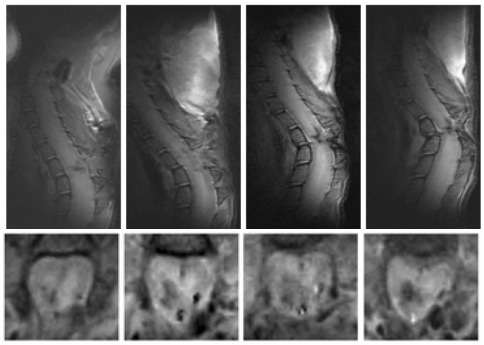

Figure 2. Comparison of a sagittal MR image of an injured SC on postinjury day 28 with the matching H&E and picrosirius red stained histology slides.