Spinal cord imaging using manganese enhanced MRI

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Introduction

Recent developments in treatment of spinal cord injury (SCI) in mice have shown promising results of functional recovery (1). However at present no in vivo method for functional visualization of SCI is available. It has been shown that manganese can serve as MRI contrast agent for neuronal activity in the cerebrum in mice (2). Here we describe a setup for manganese enhanced MRI (MEMRI) for imaging of the spinal cord (SC) in mice. We studied the time course of manganese enhancement in the SC after intraventricular injection and studied the differences of manganese uptake in the SC between injured and non healthy mice.

Methods

Animal preparation: 21 C57BL/6 mice were anesthetized using 3% isoflurane mixed with oxygen with a flow rate of 0.5 l/min. During trauma induction, isoflurane dose was lowered to 1.5% to maintain anesthesia. 10 mice were laminectomized at level Th 8/9 and SC was transected leaving only the ventral funiculus intact. 10 non-operated mice served as control, 5 without Manganese injection and 5 with injection. One non operated injected mouse was used for a time series at 0, 12, 24, 36, 72 and 120 h after injection. 250 nl 0.8 mM $MnCl_2$ was injected bilaterally in the lateral ventricle using an oocyte injector. Contrast agent was applied on the day of operation after the OP procedure. Imaging was performed 3 days after injection of $MnCl_2$. During imaging the animals were anesthetized as described above. *Imaging:* MRI experiments were performed using a 1.5 T clinical scanner (SIEMENS symphony, Erlangen, GER) and a dedicated animal volume resonator using a 3D-FLASH imaging sequence with the following parameters: TR/TE 14.0/5.22 ms, flip angle 30º, 28 partitions, partition thickness: 0,5 mm, FOV 80 mm, matrix size 512 x 512, voxel size 0.15 x 0.15 mm, 32 averages. Time series parameters: TR/TE: 35.0/4.11 ms, flip angle 70º, 60 partitions, partition thickness: 0.2 mm, FOV 51 x 29 mm, matrix size 256 x 144, voxel size 0.2 x 0.2 x 0.2 mm, 22 averages. The experiments were performed in sagittal plane for positioning (3 averages) and in axonal plane for detailed SC imaging. Total imaging time was 90 minutes for the time series and 60 minutes for the SCI experiment. *Data processing:* Images were evaluated using the scanner software package (Syngo, SIEMENS, Erlangen, GER). The SC was outlined on axial slices and mean signal was calculated. A second ROI was placed within the FOV outside the animal contours for noise measurement. Mean SNR and standard deviation (SD) were calculated for each anatomical position for each of the three groups and graphically displayed.

Results

Figure 1 shows the time course of manganese enhancement in several positions of the spine. After 2-3 days a homogeneous enhancement at level Th 7-10 is found (possittion 3-5) lasting for 36 hours after which a slow washout starts. Figure 2 shows a plot of SNR in the spinal cord. Slice 8 corresponds to level Th 8-9 where the injury was inflicted. All animals were imaged 36 hours after SCI and injection. Uninjured animals display a homogeneous SNR of about 18 without and 36 with contrast agent throughout the SC. Proximal to the injury injured mice show SNR comparable to non injured mice. Moving further distal towards the lesion SNR gradualy drops reaching background levels just at the lesion site (slice 8 corresponding to Th 8-9).

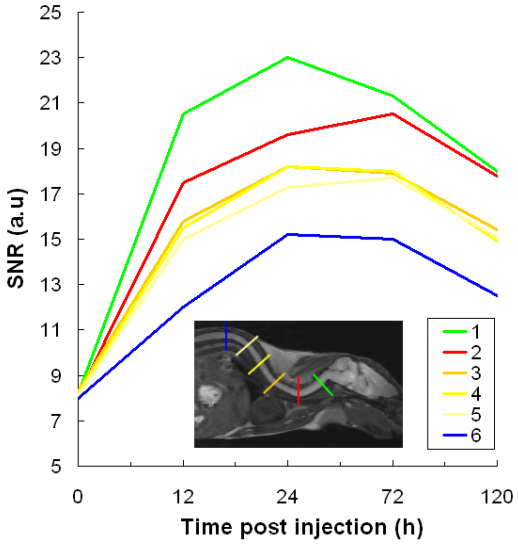

Fig. 1 Timecourse of manganese enhancement in the SC. Different Colors indicating different anatomical positions in the SC.

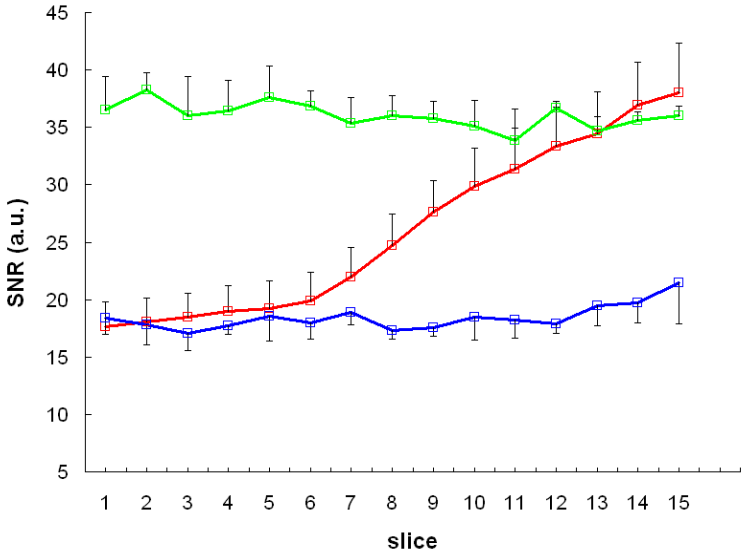

Fig. 2 SNR in the SC. Blue green and red curves corresponds to no injury/no injection, no in-jury/injection and injury/injection mean SNR and SD.

Discussion

We report of an in vivo method for functional spinal cord imaging in mice using MEMRI. Manganese was readily taken up and transported through the spinal cord though means of uptake and transportation need to be elucidated. Furthermore changes in manganese uptake profiles when comparing injured and healthy mice suggest a function dependent decrease in uptake in the injured mice. Decrease in enhancement proximal to the lesion site may correlate with dying back of axons. Decrease to baseline levels may indicate a near total loss of functional axons at these levels. Correlation with histology is underway to support this hypothesis.

References

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