IN VIVO MRI OF THE TRANSIENT AND THE FACILITATED REPAIR OF THE LESION IN SEVERED RAT SPINAL CORD

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Introduction

An intrinsic repertoire of repair mechanisms exists in the adult spinal cord; it is activated in response to injury and starts to reconstruct the cord tissue including the re-growth of severed axons and blood vessels. However, by the end of the 3rd week postinjury (PI) the natural repair is aborted and decay processes take over yielding a permanent wound gap and paralysis beyond the lesion site. This tissue decay is the primary cause for the devastating consequences of spinal cord injury: the severed nerve fibers fail to cross the wound gap, leaving the cord beyond the injury site permanently disconnected from the brain, and the related muscles remain paralyzed. Reactive astrocytes play a major role in aborting the intrinsic repair (1). Using localized radiation therapy in transected adult rat spinal cord, we found that the destructive outcome of injury can be averted and the natural repair of structure and motor function can be attained provided that at the right time (3rd wk) after injury reactive glia at the damage site are destroyed (2,3).

Here we obtained by MRI a dynamic *in vivo* view of the destructive and the repair events that take place at the lesion site of severed adult rat spinal cord. High resolution T_2–weighted sagittal images of the untreated and the irradiated severed spinal cords were acquired using a spin echo sequence, starting on day 4 after injury.

Materials and Methods

Adult Sprague-Dawley female rats, 3-6 months old were used. The spinal cord was completely transected at T10-T11; spinal cord injury and radiation therapy were described previously (3).

MRI scans of the lesion site at the spinal cord were obtained on a 4.7T/33 cm bore CSI Omega imaging spectrometer (Bruker, Fremont, CA) equipped with shielded gradients (7G/cm) and a linear birdcage coil (15 cm diameter) while the rat is anaesthetized. Images were acquired using a spin-echo sequence. High resolution T_1-weighted (TR/TE 500/16ms) and T_2-weighted (TR/TE 3500/40ms) sagittal images were obtained (1 mm thickness, 128X128 in plane-resolution, FOV 60 mm, 8 adjacent slices with a 0.25 mm gap). Imaging processing is performed on a Unix workstation using IDL (Interactive Data Language software, Research System, Inc, Boulder, Co).

Results

In the severed untreated (N=5), temporary repair proceeds through the 3rd week PI: at the first few days PI the cord tissue around the lesion site is abnormal (swollen/edema) and the cut can be discerned as a narrow dark (low signal) gap within the cord. During the 2nd and the beginning of the 3rd week PI, the cord at the lesion site seems to be almost normal with very little evidence of the initial cut. The destructive processes (localized high signal/inflammation) are noted at the end of the 3rd week, and are augmented during the 2nd month PI injury (enlarged area of high signal surrounding a wound gap) (Fig. 1A). They become more pervasive with time after injury leading eventually to a permanent wound gap. Similar permanent tissue decay processes were observed by MRI studies 2-6 months PI (4).

In contrast, in the irradiated severed cords (n=4) the natural tissue repair processes seem to continue and wound healing for the most part is accomplished. Irradiation of the lesion site during the 3rd week after the injury seems to prevent the degenerative processes: structural continuity is restored at the lesion site — the site of incision cannot be detected (Fig. 1B). However, the appearance at the 2nd month post injury of some localized inflammation (high signal) suggests that the radiation-facilitated repair is incomplete: the radiation protocols are not yet optimal.

Conclusions

The *in vivo* MRI data correlate well with the histological analysis obtained previously (2) and further support that: **i.** a window of opportunity exists during which the destructive processes could be stopped/prevented allowing thereby the natural wound healing to be accomplished; and **ii.** improving the radiation protocols might result in normal complete wound healing.

References

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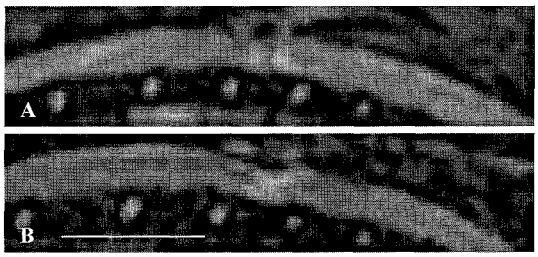

Figure 1. T_2-weighted MRI sagittal scans of the lesion site in (A) severed untreated cord 42 days PI; and in (B) severed and irradiated cord 62 days PI. Note, the wound gap in the untreated cord (A) and its absence from the treated cord (B). Radiation (10 fractions of 2.5 Gy) was given daily starting on day 12 after injury. Bar = 10 mm.