Spinal fMRI of Spinal Cord Injury in Human Subjects

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Synopsis
The reliability of spinal fMRI methods for detecting areas of activity in spinal gray matter has been demonstrated. Here, spinal fMRI is applied to the first study of spinal cord injury. The lumbar spinal cord was studied inferior to the injury in order to investigate tissues that were undamaged by the original injury. Neuronal activity was consistently detected, and demonstrated diminished sensory activity but apparently enhanced activity related to motor reflexes to withdraw from the sensation. However, the signal intensity change response to different temperatures was essentially identical to that observed in non-injured subjects.

Introduction
Functional magnetic resonance imaging of the spinal cord, Spinal fMRI, has been developed over the past 4 years, and optimized methods which vary from those used for brain fMRI have been established (1,2,3,4). This work has demonstrated that spinal fMRI can be used to accurately demonstrate areas of neuronal activity in the spinal cords of healthy subjects. The signal intensity change in the spinal cord has also been shown to have a graded response to stimuli of different intensities, with a considerably higher response to noxious stimuli. Based on this preceding work to establish the reliability of the spinal fMRI method, in the present work we present the first study of spinal cord injured (SCI) patients. The purpose of this study is to further develop spinal fMRI as a clinical tool for assessing the injured spinal cord, and to continue to verify the spinal fMRI method.

Methods
Spinal fMRI studies were carried out at 1.5 T (General Electric, Signa Horizon LX) with subjects supine, using a phased-array receiver coil. Functional time-course data were obtained using a single-shot fast spin-echo sequence (TE = 38 msec), and sets of 5 slices spanning the lumbar spinal cord segments were imaged every 8.25 seconds. Slices were oriented transverse to the spinal cord and were aligned with either the intervertebral discs or the centers of the vertebrae according to established methods (1,2,3). Thermal stimulation was applied with a Medoc® TSA-II thermal sensory analyzer. The thermal probe was placed against the skin on the calf to stimulate the 4th lumbar dermatome. In each experiment, images were acquired repeatedly while the stimulator was cycled between 32°C for the baseline and 10 °C for stimulation. Baseline conditions were held for 49.5 to 66 seconds and stimulation periods were maintained for 33 seconds. In separate experiments the time for the transition from 32°C to 10°C was 8.25 sec, 24.75 sec, or 41.25 seconds. Studies were repeated with the stimulus applied to each leg. Data were analyzed using custom-made software written in IDL (Interactive Data Language, Research Systems Inc., Boulder Co.) using a correlation method with a p-threshold of 0.05. The paradigm was defined with the signal higher during stimulation than during the baseline conditions. Only data acquired during the constant temperature periods were used for calculating the correlation to the model paradigm, and no model was assumed for the transitions.

Results
Spinal fMRI studies of the lumbar region were carried out with 25 volunteers with cervical or thoracic spinal cord injuries. Of these, 16 had complete injuries and could not feel the cold stimulus on either leg. The average time since the injury was 18 ± 9 years. Activity was detected in the lumbar spinal cord upon thermal stimulation of the leg, in all subjects. Those with complete SCI had considerably reduced activity in the ipsilateral dorsal horn (sensation and pain areas), compared to that observed in healthy subjects. Motor areas in the central and ventral gray matter were also observed to be active ipsilaterally, as in non-injured subjects, but were considerably reduced activity in the ipsilateral dorsal horn (sensation and pain areas), compared to that observed in healthy subjects. Neuronal activity was consistently detected, and demonstrated diminished sensory activity but apparently enhanced activity related to motor reflexes to withdraw from the sensation. The signal intensity change response to different temperatures was essentially identical to that observed in non-injured subjects.

Discussion and Conclusions
Spinal fMRI results obtained in SCI subjects demonstrate neuronal activity in the spinal cord decades after the injury occurred, even when the subjects could not feel the stimulus. The diminished activity in the dorsal horn is presumed to reflect the loss of ascending axonal pathways, with the continued function of axons projecting to elsewhere within the spinal cord segment or adjacent segments. Conversely, the increase in activity observed in motor areas both ipsilateral and contralateral to the stimulus is presumed to demonstrate motor reflex activity in the absence of inhibitory input from descending axonal tracts. The signal change response in the spinal cord as a function of temperature demonstrates that although the distribution of activity in the spinal cord is altered inferior to an injury, the activity that is maintained is similar to that in non-injured subjects.

Figure 1: Fractional signal changes observed in the lumbar spinal cords of healthy subjects (circles) and subjects with complete spinal cord injuries (squares), as a function of stimulation temperature, compared to baseline at 32 degrees C.

References