Novel Assessment Of The Effects Of Spinal Cord Injury In Patients By Means Of Spinal FMRI

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Introduction

Assessment of the condition of the spinal cord in patients after spinal cord trauma is essential, both for treatment planning and for monitoring outcomes. Functional MRI of the spinal cord (spinal fMRI) is a sensitive and reliable method for mapping function in the human spinal cord, and has been shown to have the potential to be a highly valuable clinical tool. A significant challenge for all MRI methods applied to the spinal cord is the poor field homogeneity caused by magnetic susceptibility differences, and this is further confounded by metallic fixation devices used to stabilize the spine after trauma. Another challenge for such clinical applications of fMRI is to be able to develop a method that is practical in a clinical setting, both in how it can be applied and the time required, while ensuring that it provides sufficient information for diagnostic purposes.

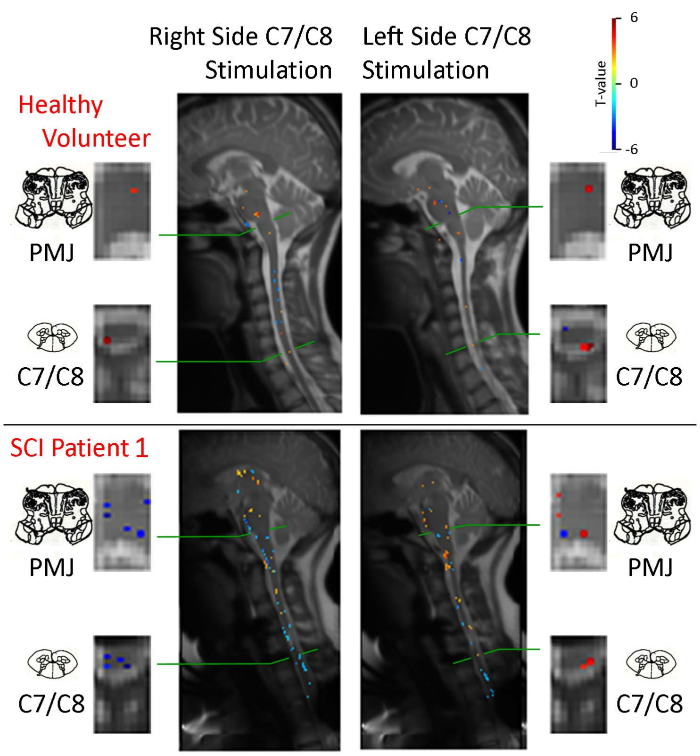
Here, we present a novel method of stimulating 4 sensory dermatomes simultaneously, in order to map function on both the right and left sides of the cord, as well as at two segmental levels; above and below the injury site. Thermal stimuli are used because they are passive, and involve spinal cord pathways involved with sensation, pain responses, and a component of motor responses. The stimuli are applied in 4 distinct block paradigms that are linearly independent to permit detection of distinct responses to each of the 4 stimuli. Data are presented from cases of spinal cord injured patients to demonstrate the clinical value, and practicality.

Methods

Functional MRI studies of the injured spinal cord were carried out with a 3 T Siemens Magnetom Trio using a phased-array spine receiver coil with subjects lying supine. Initial localizer images were acquired in 3 orthogonal planes using a fast gradient-echo imaging sequence. Functional MRI data were then acquired spanning the spinal cord, centered at the injury level, in contiguous 2 mm thick sagittal slices, with a 28 cm x 21 cm FOV, and a 192 x 144 acquisition matrix. A half-fourier single-shot fast spin-echo sequence (HASTE) was used, with the echo time set at minimum (38 msec) and a repetition time of 1 second per slice, to provide high SNR and optimal image quality in the spinal cord, even in close proximity to metallic fixation devices on the spine. Signal intensity changes observed in the image data upon a change in neuronal activity level were the result of signal enhancement by extravascular water protons (SEEP), as described previously[1]. Spatial suppression pulses were applied to eliminate signal from anterior to the spine, and flow compensating gradients were applied in the head-foot direction. The peripheral pulse was recorded continuously during each study for use in subsequent data analysis. For each fMRI data set the 3D volume was imaged 45 times, in a total of 6 min 45 sec.

Thermal stimulation of 4 different sensory dermatomes was applied by means of a custom-made device that is entirely automated, requiring only the press of a button to initiate the stimulation sequence. This device controls heating and passive cooling of four thermodes to a preset stimulation temperature of 44 °C during stimulation, in four linearly-independent block-design paradigms to enable the distinct response to each stimulus to be determined. The four thermodes were placed symmetrically on the right and left sides, on sensory dermatomes corresponding to approximately 2 spinal cord segments above, and below, the injury level.

Spinal fMRI analysis was carried out using custom software written in MatLab as described previously[2], with modifications to be almost entirely automated when used with the four pre-set stimulation paradigms. The resulting three-dimensional image data were reformatted to permit smoothing only along the long axis of the cord anatomy, and were normalized to a consistent coordinate space for all studies to facilitate group comparisons of results[3]. Time series analysis was carried out by means of a general linear model with inclusion of terms to model the cardiac-related confounds.



Results and Conclusions

Results obtained in every spinal cord injured participant to date demonstrate little to no image distortion or signal loss in the spinal cord near fixation devices. Activity is seen both above and below the level of injury on the right and left sides, corresponding to the placement of the thermodes. Comparisons with data from healthy volunteers demonstrate changes in function as a result of the spinal cord injury, in good agreement with clinical tests. In addition, preserved sensory functions and evidence of descending modulation of activity have been detected, providing clear evidence of preserved pathways through the level of injury.

The results to date demonstrate that the method we have developed is a sensitive and practical means of assessing spinal cord function. This method can be applied in any modern clinical MRI system, with no modifications, and minimal extra training of clinical personnel needed either for data collection or analysis.

Figure 1 Example of spinal fMRI results from a healthy control volunteer (top), and an age-matched volunteer with an incomplete cervical spinal cord injury at the C5 vertebral level (bottom). Maps of activity are shown in two selected sagittal slices and selected transverse slices (at the C7/C8 spinal cord segments and pontomedullary junction), to demonstrate the responses detected with right- and left-hand stimulation at 44 °C. The areas of activity are indicated in colour (representing the significance, T-value, of the response), overlaid onto the functional imaging data.

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3 P. W. Stroman, *et al.,* Magn Reson. Imaging (2008).