

Original Article

Noninvasive assessment of the injured human spinal cord by means of functional magnetic resonance imaging

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Study design: A magnetic resonance imaging technique that enables indirect detection of neuronal activity has been developed for the spinal cord. In the present study, this method, spinal functional magnetic resonance imaging (fMRI), is applied to the first study of the injured spinal cord, with the goal of better clinical assessment of the entire cord.

Objectives: The objectives of this project are: (1) to investigate the neuronal activity that can be detected in the spinal cord caudal to a chronic injury by means of spinal fMRI, and (2) to develop spinal fMRI as a clinical diagnostic tool.

Setting: Institute for Biodiagnostics, National Research Council of Canada, Winnipeg, Manitoba, Canada.

Methods: fMRI of the spinal cord was carried out in 27 volunteers with cervical or thoracic spinal cord injuries (SCIs). Of these volunteers, 18 had complete injuries, and nine had incomplete injuries. Spinal fMRI was carried out in a 1.5 T clinical MR system, using established methods. Thermal stimulation at 10°C was applied to the fourth lumbar dermatome on each leg, and images were obtained of the entire lumbar spinal cord.

Results: Areas of neuronal activity were consistently observed in the lumbar spinal cord in response to the thermal stimulation, even when the subjects had no awareness of the sensation. The pattern of activity was notably different compared with noninjured subjects. In general, subjects with complete SCI showed absent or diminished dorsal gray matter activity, but had enhanced ventral activity, particularly contralateral to the stimulation.

Conclusions: Spinal fMRI is able to provide a noninvasive assessment of the injured spinal cord that does not depend on the patient's perception of the stimulus being applied. This work was carried out on a standard clinical MRI system without modification, and so is readily applicable in most MR units.

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Introduction

Standard assessment of the condition of the spinal cord after an injury, or when affected by disease, is limited to the information that can be revealed by external signs such as whether or not the patient can feel light touch or pin-prick, or can move a particular muscle group.¹ This method of assessment, and the assessment scale defined by the American Spinal Injury Association, is a proven and effective means of determining the function retained

by a patient after trauma to the spinal cord. However, it does not reveal the full extent of the condition of the cord, or how the condition changes over time, unless a change in the cord's condition is revealed by external signs. The purpose of the work we are carrying out is to develop a noninvasive method of mapping neuronal function, anywhere in the spinal cord, by means of functional magnetic resonance imaging (fMRI).

Information about the full extent of the cord's condition, and any changes as a result of clinical interventions, is becoming increasingly valuable as new methods of treating spinal cord injury (SCI) are being

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developed.²⁻⁶ Significant recovery from SCI has been shown to be a reality in animal models, and is expected to be realized in human patients in the not-too-distant future. The new treatment methods that are being developed generally involve implantation of natural or synthetic materials into the spinal cord, in order to create an environment that promotes axonal regeneration while impeding scar formation. The implant materials that have been used so far include fetal tissue, stem cells, Schwann cells, polymer hydrogels, and combinations of polymer matrices and tissue cells.⁷⁻⁹ The intention with most of these treatments is to create a bridge of implant material between healthy tissues to cause axonal growth and sprouting, release of nerve growth factors, development or migration of astrocytes, and growth of new blood vessels into the implant material. For this spinal cord regeneration to be effective at improving the patient's condition, it is therefore critical that there is functional, healthy, spinal cord tissue on both sides of the implant site. Similarly, it is essential that the surgeon know the number and location of all damaged sites that need to be 'bridged' in this fashion.

The method we have developed for fMRI in the spinal cord (spinal fMRI), has been proven in healthy volunteers to demonstrate neuronal activity in the spinal cord in response to sensory stimulation and motor tasks.¹⁰⁻¹³ Here we present the first spinal fMRI study of spinal cord-injured patients, and demonstrate the clinical applicability of this method on a standard clinical MR system. Spinal fMRI demonstrates neuronal function indirectly via the changes in the blood flow and blood oxygen-level that occur in close proximity to gray matter with increased oxygen uptake. The blood oxygenation-level-dependent (BOLD) contrast that has been proven to be dominant in fMRI of the brain,¹⁴⁻¹⁶ is based on the fact that deoxygenated hemoglobin in the blood acts as an MR contrast agent and causes the MR signal to decay, or 'relax' more quickly. When the spiking rate of neurons increases, the nerve cell bodies take up more oxygen, and hemodynamic changes occur resulting in an overabundant increase in the blood supply to the neurons, resulting in a local decrease in the concentration of deoxygenated hemoglobin. The consequence of this sequence of events with respect to MRI is that the signal is slightly stronger when it is recorded because it has not decayed as quickly. The MR image intensity, or brightness, is therefore slightly higher in the region spanning the neurons whose spiking rate has increased. Clearly, this method therefore shows only relative changes in neuronal function and requires a careful design of the fMRI study, so that the 'active' and 'rest' conditions that are compared can be accurately interpreted. In the course of the development of spinal fMRI, a second important contrast mechanism has been identified that also depends on the blood flow increase to active neural tissues. When the blood flow increases, the intravascular pressure also increases, particularly on the arterial side of the capillary network. This change in pressure slightly alters the normal fluid balance, and the

usual flux of water across the blood vessel walls into the extracellular space is increased slightly, resulting in a slightly more extravascular fluid in close proximity to the active neural tissue.^{17,18} The MR image signal arises primarily from water protons, and so is also increased as a result. We have therefore termed the effect 'signal enhancement by extravascular water protons' or 'SEEP', and have proven it to be the dominant contrast mechanism in our spinal fMRI method.¹⁹⁻²¹

The spinal fMRI method is therefore able to demonstrate areas of increased activity in spinal cord gray matter, in response to a stimulus or task performed by the subject. White matter tracts that are involved are not demonstrated, but the method is equally sensitive to active gray matter whether primary neurons or interneurons, etc. The magnitude of the signal change that is detected in the MR images is typically <8%, and has been observed to depend on the intensity of the external stimulus, and therefore on the spiking rate of the neurons being stimulated.²² The method has thus been demonstrated to reflect neuronal activity accurately in the spinal cord, including primary input and reflex responses. Here we apply this method to the first complete study of the injured spinal cord, caudal to the site of injury, in subjects who have no awareness of the stimulus being applied, and we demonstrate the function that is retained in the injured spinal cord.

Methods

Subjects

A total of 27 subjects with SCI in the cervical or thoracic regions were studied (23 male/4 female); 18 with complete injuries (ASIA level A), and nine with incomplete injuries. All subjects provided written consent prior to entering the MR system. The mean age of the subjects was 40 ± 10 years, and the average time since the injury had occurred was 16 ± 8 years. The minimum time since the injury had occurred was 4 years, and all subjects were in stable condition and in otherwise good health. Of the subjects with complete injuries, eight were involved in motor vehicle accidents, three had diving accidents, one fell from a height, one was impacted by a falling object, one was involved in a sledding accident, one was injured during a hockey game, and three did not report the mechanism of injury. Out of the nine subjects with incomplete injuries, four had diving accidents, one had an injury similar to a diving injury while performing gymnastics, one had a hyperextension injury from a low fall, one was in a motor vehicle accident, and one fell from a tire being pulled behind a vehicle over ice.

These results are compared with those obtained previously from 15 healthy volunteers (8 male, 7 female). The mean age of this group was 37 ± 11 (SD) years and no subject had any history of neurological or major medical disorder. The experimental protocol was reviewed and approved by our institute's Human Research Ethics Board.

MR data acquisition

Spinal fMRI studies were carried out with a 1.5 T clinical MR system (General Electric, Signa Horizon LX) with subjects supine. A dedicated phased-array spine coil was used for signal detection, whereas a body-coil was used for transmission of uniform radio-frequency pulses. Functional time-course data were obtained using a single-shot fast spin-echo sequence with an echo time of 34 ms, and sets of five slices spanning the entire lumbar spinal cord and the 12th and 11th thoracic segments were imaged every 8.25 s. Slices were oriented transverse to the spinal cord and were aligned with either the intervertebral discs or the centers of the vertebral bodies according to our established methods.^{10,11} The imaging field of view was 12 cm and data were obtained in a 128 × 128 matrix yielding a roughly 0.9 mm in-plane spatial resolution. Flow compensation gradients were applied in the through-slice direction, and spatial saturation pulses were applied to eliminate the signal from surrounding regions anterior and to the right and left of the spine. This was to eliminate aliasing and reduce motion artifacts from the abdomen.

Thermal stimulation paradigm

Thermal stimulation was applied with a Medoc[®] TSA-II thermal sensory analyzer controlled from a personal computer. The temperature probe was 3 cm × 3 cm and was placed against the skin on the inner calf to stimulate the L4 dermatome. In each experiment, images were acquired repeatedly, while the stimulator was held constant at 32°C for 49.5 s, then ramped to 10°C and held for 33 s, after which the temperature was returned to 32°C for another 49.5 s. The 10°C cold stimulation was applied a second time for 33 s and was followed by another 66 s at 32°C. In separate experiments the time for the transition from skin temperature to 10°C was 8.25 s, 24.75 s, or 41.25 s. Studies were repeated with the stimulus applied to each side of the body. Control experiments with non-injured volunteers were carried out in a preceding set of studies with the stimulus applied to only the right leg.

Data analysis

Data were analyzed using custom-made software written in IDL (Interactive Data Language, Research Systems Inc., Boulder, CO, USA), consistent with that used in the previous studies with non-injured subjects. The data analysis included rigid-body registration of the images to reduce any effects of motion during the data acquisition. The image alignment was performed only on a sub-region of the images containing the spinal canal to avoid the effects of changes in the tone or position of the surrounding muscle. A model paradigm was defined for correlation to the signal intensity changes in order to identify regions of the spinal cord that changed intensity in response to the stimulation.²³ The paradigm was defined with the signal higher during

stimulation than during the baseline conditions with the probe at 32°C. However, only data acquired during the constant temperature periods were used for calculating the correlation to the model paradigm. No model was assumed for the signal intensity changes occurring during the temperature transitions. Those image regions undergoing signal intensity changes correlated with the pattern of stimulation with a correlation coefficient >0.35 (corresponding to $P < 0.05$) were assumed to be regions of neuronal activation related to the stimulation.

The activity maps obtained for individual subjects were combined to create maps showing the consistent areas of activity in the spinal cord for each group. These combined maps were constructed by first manually aligning the spinal fMRI results from each individual subject with an anatomical reference image. The same anatomical reference was used in all cases to facilitate comparisons of results between groups. The co-aligned maps were then summed, smoothed with a 3 × 3 filter in each slice to reduce the effects of the alignment process being imperfect (due to intersubject variations in anatomy), and were then thresholded so that only voxels with activity in three or more subjects are displayed as being active. The resulting combined activity maps demonstrate the three-dimensional distribution of consistent spinal cord activity in each group, and are displayed in Figure 1 as a series of five two-dimensional slices for each group. The color scale indicates the number of subjects showing activity at each voxel, with the greatest degree of consistency shown in red, decreasing in order through orange, yellow, and then green.

Results

Spinal fMRI results consistently demonstrated activity in the lumbar spinal cord in response to thermal stimulation of the skin on the inner calf (L4 sensory dermatome), in all spinal cord-injured subjects. Compared with the pattern of activation observed in healthy subjects (Figure 1a), subjects with complete SCI consistently demonstrated diminished, but not absent, activity in the ipsilateral dorsal gray matter (Figure 1b). In contrast, activity in the ventral regions appeared to be increased on both the ipsilateral and contralateral sides of the cord. Subjects with incomplete injuries, but who could not feel the cold stimulus applied to the leg, also showed diminished activity in the ipsilateral dorsal gray matter compared with healthy control subjects (Figure 1c). Ventral activity, both contralaterally and ipsilaterally, was similar or diminished compared with healthy subjects, and so was noticeably less than that observed in subjects with complete SCIs. Those subjects who could feel the cold stimulus, or at least had some altered sensation to it, although they had incomplete SCIs, had patterns of activity that were quite similar to that observed in healthy subjects (Figure 1d). There was consistent activity in the ipsilateral dorsal horn of the gray matter, extending up into the central and ventral regions, as well as contralateral ventral activity.

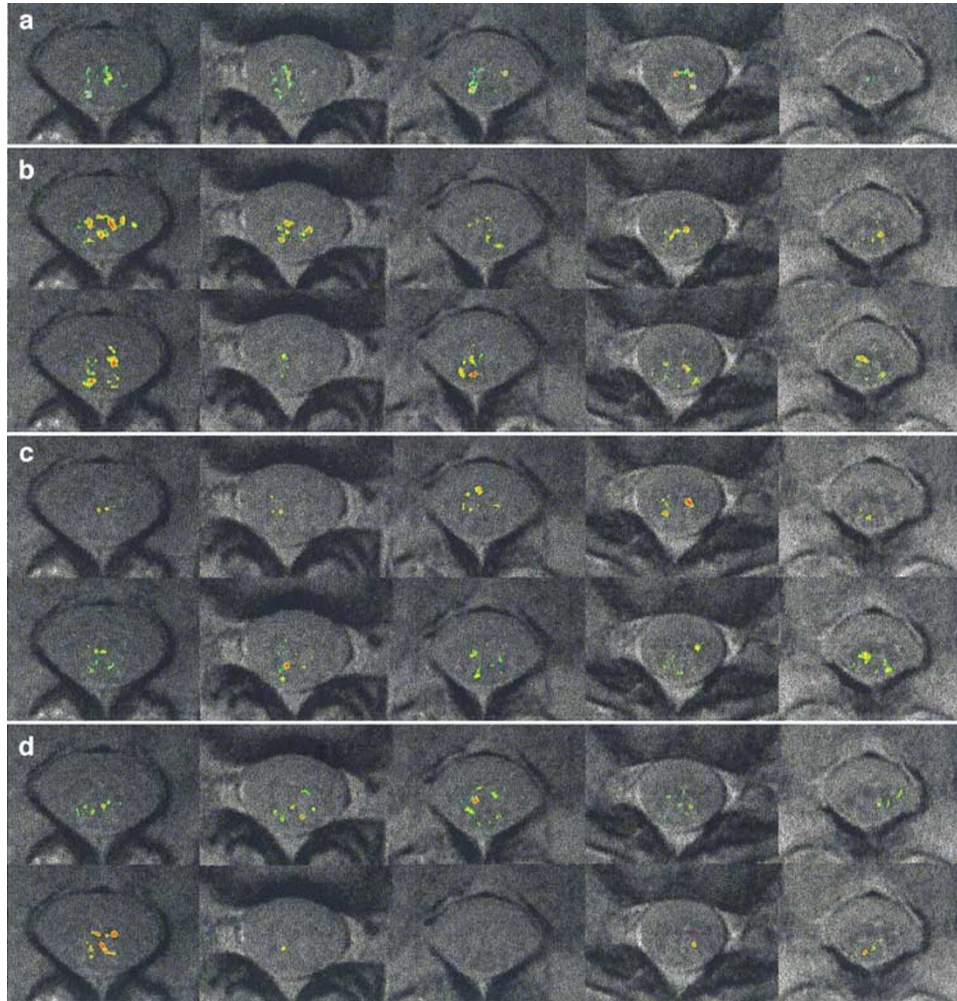


Figure 1 Combined spinal fMRI results from the lumbar spinal cord showing the activity response to 10°C thermal stimulation of the L4 dermatome. For healthy subjects (**a**), only the right leg was stimulated, whereas for SCI subjects (**b–d**) results with the right-leg stimulation are shown in the top row and the left leg in the bottom row. (**a**) Healthy subjects ($n = 13$); (**b**) subjects with complete SCIs ($n = 18$); (**c**) subjects with incomplete SCIs and who could not feel the cold sensation ($n = 5$ right, $n = 6$ left); and (**d**) subjects with incomplete SCIs and who could feel the cold sensation ($n = 4$ right, $n = 3$ left). Images are in radiological orientation with the right side of the body toward the left side of the image, and dorsal is toward the bottom. From left to right the slices span approximately through the following spinal cord segments: fifth/fourth lumbar; third lumbar; second/first lumbar; 12th thoracic; and the 11th thoracic. The color scale shows red at points with the greatest consistency across subjects, through orange, yellow, and then green indicating that only three subjects showed activity

Plots of the percent signal intensity change as a function of the stimulation temperature demonstrate the same biphasic pattern as that observed in healthy subjects, and was not observed to depend on whether the injuries were complete or incomplete. Signal intensity changes were between 2% and 3% with temperatures between 29 and 15°C, and increased markedly to $\approx 8\%$ with the temperature reduced to 10°C. (Figure 2)

Discussion

Spinal fMRI maps of active areas obtained for individual subjects demonstrate (indirectly via hemody-

amic changes) where the activity level of a group of neurons has changed in response to a stimulus. In the image data, the tissue is divided into image volume elements (voxels) which, in the present studies, span $0.9 \text{ mm} \times 0.9 \text{ mm} \times 7.5 \text{ mm}$, with the largest dimension parallel to the long axis of the cord. The signal changes that are detected and that reflect neuronal activity changes are therefore averaged over each voxel. The maps do not demonstrate the proportion of the neurons in each volume that underwent a change in activity, nor the amount of change in activity. However, it has been shown in the brain with conventional fMRI that the fractional signal change (as in Figure 2) corresponds closely with the change in neuronal spiking rate,²⁴ and

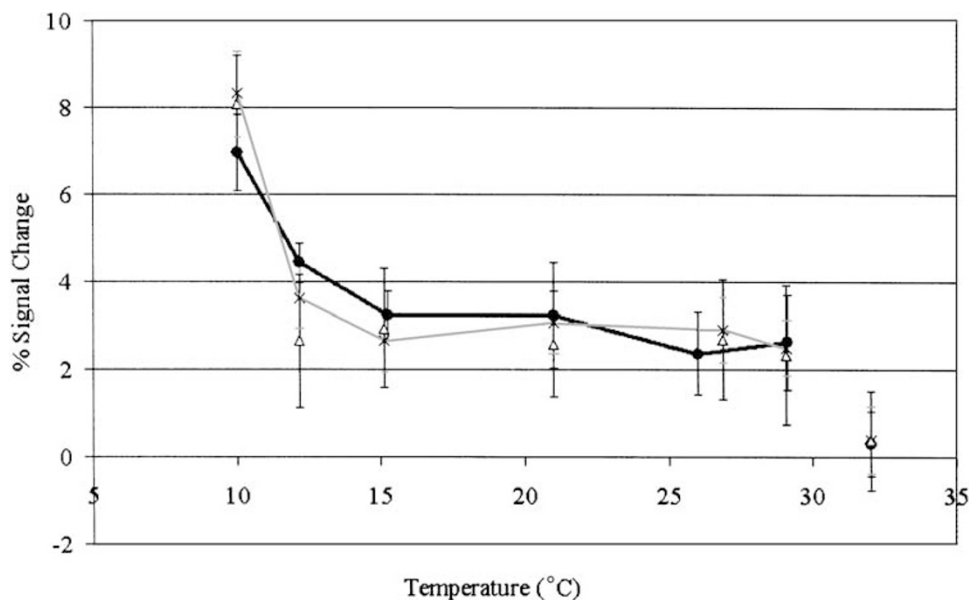


Figure 2 Spinal fMRI signal intensity response in the lumbar spinal cord to stimulation of the L4 dermatome over a range of temperatures. Black circles indicate results from healthy volunteers, (×) symbols indicate results from subjects with complete SCIs, and triangles indicate results from subjects with incomplete SCIs. Signal intensity changes are relative to the baseline temperature at 32°C

our previous studies suggest this in the spinal cord as well.²² The combined maps of active areas for a group of subjects (Figure 1) demonstrate the location and extent of spinal cord gray matter regions that were consistently observed to be active, with the colors indicating the degree of consistency. Areas of activity with greater levels of consistency across the group are therefore interpreted as having more activity related to the stimulus, or as being more likely to show activity each time the stimulus is applied and so containing neurons that are more closely linked to the activity. A greater spatial extent of an active region in the spinal gray matter, or a greater number of contiguous active voxels, is also interpreted as showing more neuronal activity related to the stimulus, because it reflects a greater volume containing a significant number of neurons that are closely linked to the activity. The combined activity maps shown in Figure 1 are displayed as a series of five sequential image slices depicting the three-dimensional distribution of activity in the spinal cord. Therefore, the spatial extent must also be viewed three dimensionally. The images are then interpreted as reflecting more activity where the consistency, and/or three-dimensional spatial extent of an active region is increased relative to the healthy control data (Figure 1a). Conversely, less neuronal activity is concluded where the three-dimensional spatial extent and/or consistency is reduced, relative to that in healthy controls.

Thermal stimulation of a single sensory dermatome is known to elicit neuronal activity in the dorsal gray matter of the corresponding spinal cord segment, as well as in adjacent spinal cord segments via interneurons, resulting in a roughly gaussian distribution of activity

along the cord.^{13,25} If the thermal stimulation is noxious or painful, then activity becomes more pronounced in Rexed's laminae I and II at the tip of the dorsal horn. Interneurons also project to motor areas in the ventral gray matter regions, both ipsilaterally and contralaterally, and form the reflex arc to withdraw from the noxious sensation.²⁵ In all 27 of the spinal cord-injured subjects that we studied, neuronal activity was detected in the lumbar spinal cord, caudal to the injury site, in response to 10°C thermal stimulation of the fourth lumbar sensory dermatome. It is already established that there is activity in the spinal cord caudal to an injury as evidenced by leg spasms that are known to involve motor reflex arcs through the spinal cord.^{26–28} However, we have now observed the level and extent of activity in the spinal cord, and the activity related to sensory input, even when the subject has no awareness of the sensation. This information provides a more complete clinical picture of the condition of the injured spinal cord, beyond what can be obtained from the ASIA assessment scale.

Distribution of neuronal activity

While there are similarities between the pattern of activity observed with thermal stimulation of the L4 dermatome in spinal cord-injured subjects compared with noninjured subjects, there are a number of notable differences as demonstrated in Figure 1a and b. One such difference is that subjects with complete SCI (Figure 1b) had diminished dorsal activity, which relates to sensation or pain. While the input to the cord from the cold receptors or nociceptors in the skin on the leg

is not expected to have been altered by a thoracic or cervical SCI, it is clear that the activity within the cord has been altered. The difference then presumably reflects the disruption of ascending white matter tracts. Following injury of white matter tracts, there is a fairly well-defined sequence of events resulting in demyelination and then deterioration of the damaged tracts.²⁹ The nerve cell bodies of these axons lie in the gray matter of the spinal cord and so either no longer function to produce an action potential to propagate upward along the axon, have deteriorated, or due to plasticity of the CNS have made different connections with nearby neurons.³⁰ In any case, they no longer contribute to the signal changes observed with fMRI. However, also within the gray matter are interneurons that continue to function and project to other gray matter regions within the spinal cord segment, or project to adjacent spinal cord segments. The interneurons that continue to function can therefore account for the remaining activity that is observed in the dorsal horn of the gray matter.

Interneurons can also explain a second difference in the pattern of activity observed for subjects with complete SCIs, (relative to non-injured subjects), which is that the ipsilateral and contralateral ventral activities appear to be increased. The ventral regions relate to motor activity, and so the activity we observe appears to relate to reflex motor activity to withdraw from the cold sensation, as was observed in the noninjured subjects. The explanation for the increased ventral activity is actually suggested by the results obtained from subjects with incomplete injuries, but who could not feel the thermal stimulus. In these subjects, there was apparently less ventral activity than in the noninjured subjects, and so very much less than in the subjects with complete SCIs. This strongly suggests that the cause is a lack of descending inhibitory input from the brain to mediate the motor reflex, in subjects with complete SCIs. This is quite well known from studies of the polysynaptic withdrawal reflex in spinal cord-sectioned animals. In contrast, some of the white matter tracts that have been spared in subjects with complete injuries may carry this descending inhibition that can help to mediate the reflex responses.

Of the 18 subjects we studied with complete injuries, most sustained severe lateral impact injuries. Almost half of these subjects were involved in motor vehicle accidents and so were likely impacted ventrally. In contrast, more than half of the subjects we studied with incomplete injuries were involved in diving accidents where the impact would cause a longitudinal force along the spine and a burst fracture in most cases. It is known from the ASIA assessment that in the subjects with incomplete injuries, some white matter tracts, particularly ascending tracts, have been spared. It is therefore reasonable to expect that some descending tracts have also been spared, and may contribute to mediating the withdrawal reflex. The subjects with incomplete injuries, and who could not feel the stimulus, are therefore expected to have less activity in both the dorsal and ventral regions because they have lost the ascending

sensory tracts, but may still have some descending tracts to mediate the withdrawal response. Consistent with this interpretation, it is also noticeable in Figure 1 that subjects with incomplete injuries and who could feel the stimulus had a pattern of activity that was quite similar to the noninjured subjects, as would be expected.

Signal intensity response to graded thermal stimulation

Spinal fMRI data showing the percent signal intensity change with different temperatures of cold stimulation demonstrated a response pattern that was essentially identical to that observed in noninjured subjects (Figure 2). In fMRI of the brain it has been demonstrated that the signal intensity change relates to the spiking rates of neurons.²⁴ Previously, we have shown that the pattern of response in the spinal cord to different temperatures of stimulation is very similar to that of electrophysiological recordings made in the spinal cords of cats. The signal change response to thermal stimulation at different temperatures was observed to be essentially identical in the injured and noninjured spinal cord. This demonstrates that the neurons that are continuing to function, respond to sensory input in the same manner as those in the spinal cords of the noninjured subjects. Hence, although it is clearly demonstrated that the pattern of activity is altered caudal to the injury site, the activity of the neurons that remain appears to be unchanged.

Individual case studies – clinical relevance of spinal fMRI

The interpretation of results from single trials is slightly different from that of grouped results because the former demonstrate the spatial extent of activity for a particular experiment, and so can vary from one trial to the next. Factors such as random noise, subtle motion, etc, can influence whether or not some voxels containing only a relatively small number of active neurons, or neurons with a relatively small change in activity level, are detected as being active. It is also possible that the observed response is not identical in repeated trials because of physiological variables such as changes in the sensory response of the skin to a thermal stimulus, changes in mediating input from the brain, etc.

The subject selected for one case study suffered an incomplete SCI as a result of a diving accident at the level of the fifth and sixth cervical vertebrae. This subject can walk with a cane and is classified as ASIA D. The ASIA assessment showed active movement against some resistance or full resistance in motor groups innervated by the right lumbar region, and weaker function on the left. Light touch was preserved but impaired on both sides, and pin-prick sensation was absent on the right, but impaired on the left, in the lumbar dermatomes. The subject reported some sensation with the thermal stimulation, and that it was stronger on the right than on the left, at the time of the study. Spinal fMRI results from this subject, shown in Figure 3, demonstrate dorsal and ipsilateral ventral

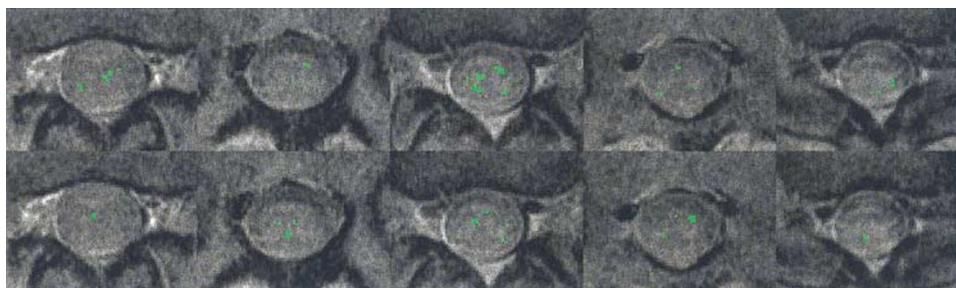


Figure 3 Spinal fMRI results for case study 1 spanning the lumbar spinal cord (same slices as in Figure 1), with stimulation of the right leg (top row) and the left leg (bottom row). Images are in radiological orientation with the right side of the body to the left of the image, and dorsal is toward the bottom. This subject had an incomplete injury in the cervical spinal cord (ASIA D) as a result of a diving accident, and reported more thermal sensation on the right leg than on the left

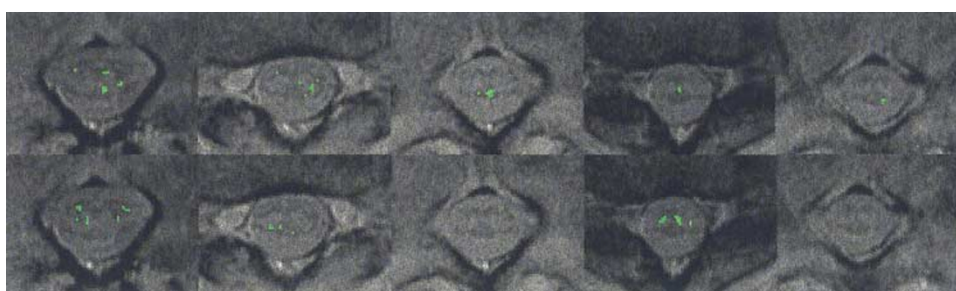


Figure 4 Spinal fMRI results for case study 2 spanning the lumbar spinal cord (same slice locations as in Figures 1 and 3), with stimulation of the right leg (top row) and the left leg (bottom row). Again, images are in radiological orientation with the right side of the body to the left of the image, and dorsal is toward the bottom. This subject suffered a complete injury (ASIA A) 7 years ago at the first thoracic vertebral level, and so had no temperature sensation in either legs

activities with right-side stimulation (top row). This pattern is fairly similar to that observed in noninjured subjects, with the exception of possibly greater contralateral ventral activity. With left-side stimulation (bottom row) the dorsal activity was very minimal, and the most notable areas of activity were ventral and near the central canal, consistent with the withdrawal reflex. This pattern shows retained sensory function and related ascending tracts on the right side, probably deteriorated ascending tracts related to the left-side sensation, and also deteriorated descending tracts leading to the left motor areas. This is consistent with the pattern recorded for the retained motor function with the ASIA assessment and also with the sensation reported by the subject at the time of the study.

The subject selected for a second case study was injured 7 years ago at the first thoracic vertebral level as a result of a motor vehicle accident, and is paraplegic. This subject's injury is classified as ASIA A and so there is no residual sensation or motor activity related to the lumbar spinal cord. Spinal fMRI results, shown in Figure 4, demonstrate no activity in the right dorsal or ventral areas in response to stimulation of the right leg (top row). However, this stimulation did cause activity on the contralateral side, and around the central canal, consistent with the withdrawal reflex. Stimulation of the

left leg (bottom row) produced activity in an almost mirror pattern to the right-leg stimulation, except that some ipsilateral activity was seen centrally and ventrally, and more ventral activity was apparent. This pattern is consistent with our interpretation of the general results, as reflecting loss of both descending and ascending white matter tracts, but with retention of interneuron activity in the lumbar cord, and consistent with the ASIA A rating.

Conclusions

Spinal fMRI has been demonstrated to be an effective and noninvasive means of mapping function in the injured spinal cord, even caudal to a site of injury. The results of this first study of spinal cord-injured subjects have shown that there is a considerable amount of activity remaining in the injured spinal cord even decades after the injury occurred. Moreover, the activity recorded is independent of the subject's perception of the thermal stimulus applied. The pattern of activity observed in the injured spinal cord also demonstrates changes in function that occur as a result of loss of ascending and descending white matter tracts. Although the changes we have shown in spinal cord-injured subjects are not surprising, and are expected based on

studies carried out in spinal cord-injured animals, until now it has only been assumed that the effect of injury in spinal cord-injured humans was the same. Finally, the results of selected individual case studies serve to demonstrate the clinical applicability of the spinal fMRI method that we have developed.

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