Functional Magnetic Resonance Imaging of the Human Spinal Cord and Brainstem During Heat Stimulation

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Introduction

The study of physiological pain responses is complex and often requires a means of studying function that is not influenced by the research subject's perception or subjective responses. With objective information about the noxious input, one may then be able to differentiate the higher brain functions that influence the subject's perception, or subjective rating of their perception. Studying pain in the spinal cord and brain stem provides a means of investigating neurological responses to pain without the modulation of attention, emotion, anticipation, etc. The spinal cord and brainstem are inaccessible in awake behaving animals or in humans, except by means of non-invasive imaging methods such as fMRI. However, conventional fMRI methods that are typically used for studying brain function are compromised by the relatively poor field homogeneity in the brain stem. The alternative is to employ fMRI methods that have been developed for use in the poor field homogeneity environment of the spinal cord, and that have been proven to be reliable. Areas related to processing of painful stimuli include the spinal cord gray matter, the medulla, and the thalamus, as these are all points along the spinothalamic tract. Ideally, one would want to study all of these areas at the same time to avoid the influence of variations in the responses to repeated applications of a stimulus. Studies have been carried out in rats using simultaneous brain and spinal cord fMRI, with very high quality results.[1] The purpose of this study was to develop a method for studying a large extent of the cervical spinal cord and brain stem, using spinal fMRI methods, for the purposes of investigating pain responses in human volunteers.

Materials and Methods

Functional MRI studies were carried out in a 3 T Siemens Magnetom Trio using a phased-array spine receiver coil with subjects lying supine. Hot and warm thermal stimulation of the palm of the hand (near the thumb) was used to elicit activity in the cervical spinal cord, by means of a Medoc® TSA-II thermal sensory analyzer. Functional image data were acquired with a half-fourier single-shot fast spin-echo sequence (HASTE) with the echo time set at minimum (38 msec) in order to obtain essentially proton-density weighted images. 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[2,3]. In separate studies image data were acquired with a 20 cm x 10 cm FOV, a 192 x 96 matrix, in 2 mm thick contiguous sagittal slices. Spatial suppression pulses were applied to eliminate signal from anterior to the spine and to eliminate aliasing. Images were positioned to span from the T1/C7 disc up to the thalamus to include the entire cervical spinal cord and brainstem. The peripheral pulse and respiration were recorded continuously during each study. The resulting three-dimensional image data were reformatted to permit smoothing only along the long axis of the cord anatomy. Analysis was done with custom-made software written in MatLab and physiological recordings were used (with a general linear model approach) to improve the discrimination between physiological motion and signal intensity changes arising from neuronal activity.

Figure: Example of a sagittal slice along the spinal cord and brainstem, up to the thalamus

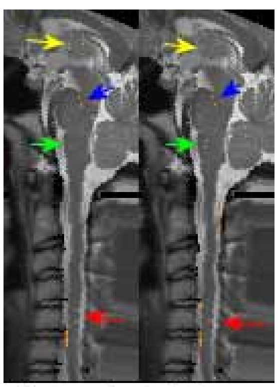

Figure: Example of results showing activity in the dorsal SC (red), medulla (green), pons (blue) and thalamus (yellow) in 2 contiguous slices

Results

Spinal fMRI data consistently demonstrated areas of activity in the spinal gray matter that correspond well with spinal cord neuroanatomy. Sensory and apparent reflex activity were demonstrated in the cervical spinal cord, and areas of activity were also consistently observed in the medulla and thalamus. Within each experiment, the combination of the areas of activity observed across areas related to sensation and noxious sensation in the spinal cord, medulla and thalamus provided confirmation of the interpretation of the results. The results thus demonstrated a clear pattern of the response in each individual trial, and changes between repeated applications of the heat stimulus could be observed. This method provides a reliable and objective means of studying pain in humans.

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