Attentional modulation of thermal sensory responses in the human spinal cord

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Introduction

Cognitive and emotional factors have been shown to modulate perceived pain or sensations in fMRI studies of the brain and brainstem [1,2]. Moreover, changes in attention focus are known to affect input to cortical and brainstem regions, which also provide modulatory input to the spinal cord. It is yet unknown, though, whether changes in attention focus can modulate activity in the spinal cord itself. Here we investigate how sensory responses in the spinal cord are altered by descending input from supraspinal structures, related to changes in attention. We hypothesize that in active regions of the cervical spinal cord the magnitude of signal change due to thermal sensory stimulation depends on a person's attention focus. This may contribute a significant source of variability between fMRI studies, but could potentially be exploited to distinguish alterations in ascending and descending pathways as a result of trauma or disease.

Methods

Functional MRI studies of the cervical spinal cord and brainstem were carried out with 9 healthy volunteers in a 3 T Siemens Magnetom Trio using a phased-array spine receiver coil with subjects lying supine. Subjects viewed a rear-projection screen via a mirror. Thermal stimulation of the right thenar eminence was used to elicit activity in the cervical spinal cord, with a Medoc® TSA-II thermal sensory analyzer. Functional image data were acquired with a half-fourier single-shot fast spin-echo sequence (HASTE) with an echo time of 38 msec and repetition time of 1 second per slice. 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 [3-5]. Other image parameters include: 1.5 mm x 1.5 mm resolution, 9 slices, 2 mm thick contiguous sagittal slices, and a 28 cm x 14 cm FOV to span the cervical spinal cord, brainstem, and mid-line cortical structures.

Thermal sensory stimulation was applied in a block paradigm with a total duration of 9 min 9 sec for each experiment, containing 4 blocks of 45 seconds of stimulation at either 18 °C or 15 °C in separate experiments, interleaved with 72 second duration baseline periods at 32 °C. Throughout each experiment, the volunteer was presented with written instructions or questions in the center of the screen, and a choice of 4 answers, one in each corner. During the 1st and 3rd stimulation periods the volunteer was instructed to focus his/her attention on the stimulus, and was prompted every 18 seconds to rate their level of discomfort due to the stimulus at that instant, by selecting one of 4 ratings. Otherwise, during the 2nd and 4th stimulation periods, the volunteer was presented with mentally-challenging multiple-choice questions, and the questions were refreshed every 18 seconds, in order to direct their attention away from the thermal stimulus. An MR-compatible eye-tracking system was used to record the responses.

The 3D image data were analyzed, and the results normalized to a consistent coordinate space to facilitate group analyses, using custom software written in MatLab [6,7].

Results

Thermal stimulation of the hand consistently produced activity in the contralateral thalamus, in the vicinity of the periaqueductal gray matter (PAG), in the reticular formation of the pons, and in the rostral ventromedial medulla (RVM). Activity was also consistently detected in the cervical spinal cord in dorsal and ventral regions, primarily at C6 and C7, in locations that are consistent with those observed in previous studies by our group. Activity in all of these regions depended significantly on whether the subject was attending to the thermal stimulation, or was focussing on answering questions. In each of these regions there was significantly more positive activity when the subject's attention was diverted from the sensation.

No significant dependences were detected in the rates of correct answers to the multiple-choice questions, on either the temperature of stimulation, or the attention focus: 69% ± 45% and 65% ± 48% during stimulation at 18 °C and 15 °C, respectively. Ratings of discomfort were enumerated from 1 to 4 (1: no discomfort to 4: worst discomfort possible), and mean values were 2.13 ± 0.80 and 2.27 ± 0.87 during stimulation at 18 °C and 15 °C, respectively. Ratings of discomfort on a visual analog scale (0: no discomfort to 10: worst possible discomfort), after each stimulus block was completed, averaged 0.46 ± 1.05 and 0.60 ± 1.49 while attending to the 18 °C and 15 °C stimuli, respectively, and 1.03 ± 2.02 and 1.51 ± 2.63, while attending to the questions.

Discussion and Conclusions

The areas of activity that were identified are consistent with the known anatomical regions involved with pain and temperature responses across the cervical spinal cord and brainstem. This includes afferent sensory input, and descending modulation via the opiate analgesia system (PAG and RVM), affective components of pain (thalamus, locus coeruleus), and regulation of motor responses (reticular formation) [1]. The magnitudes of the signal intensity changes are inferred to reflect the input to an area [8]. Both positive and negative areas of activity are therefore to be expected based on the neuroanatomy, corresponding to increased or decreased descending modulatory input in response to the subject's attention focus. Significantly greater input was observed with distraction, particularly in the vicinity of the PAG, RVM, and in the ipsilateral dGM at around C6. This implies that greater descending input to the cervical spinal cord from the analgesia system plays an important role in altering perceived sensations, with changes in attention focus.

The results of this study demonstrate that attention focus significantly influences activity detected by means of spinal fMRI in the cervical spinal cord during innocuous thermal sensory stimulation. This has implications for the use of spinal fMRI for research or clinical evaluation, because, if not controlled, it is a potential source of significant inter-trial variability. Alternatively, by intentionally varying the subject's attention focus between repeated studies, it may be possible to discriminate ascending and descending input pathways, thereby revealing important features of normal spinal cord function, as well as the effects of trauma or disease.

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