Spinal cord and brainstem activation in carpal tunnel syndrome patients in response to noxious stimuli: a spinal fMRI study

J. K. Leitch[1], C. M. Cahill[2,3], N. F. Ghazni[1], C. R. Figley[1], and P. W. Stroman[1,4]
[1]Centre for Neuroscience, Queen's University, Kingston, Ontario, Canada, [2]Pharmacology & Toxicology, Queen's University, Kingston, Ontario, Canada, [3]Anesthesiology, Queen's University, Kingston, Ontario, Canada, [4]Diagnostic Radiology & Physics, Queen's University, Kingston, Ontario, Canada

Introduction:

When tissue damage or noxious insult occurs, the pain we feel serves a purposeful function by eliciting a behavioural response to minimize damage and promote rest to speed the healing process.[1] However, 2-3% of North Americans suffer from neuropathic pain[2] which is both chronic and maladaptive. Many studies, including functional imaging studies, have shown that chronic pain is processed differently than physiological, purposeful pain, both in terms of the subjective reporting of pain and in neuronal activation of pain pathways. For example, patients suffering from chronic pain show altered activation in the anterior cingulate and prefrontal cortices.[2] However, most studies determining changes in neuronal activity concentrate on higher areas of brain function, with little to no attention paid to areas that modulate pain transmission within the spinal cord and brain stem regions. Recent functional magnetic resonance imaging (fMRI) studies in our laboratory compared healthy subjects to an experimental model of neuropathic pain to demonstrate differences in neuronal activation in brain stem nuclei; notably, in the periaqueductal grey (PAG), thalamic-midbrain border, and medulla regions.[3] In this study, we aim to show the neuronal activity in such regions in a neuropathic patient population. Carpal tunnel syndrome (CTS) is a common form of neuropathic pain caused by compression of the median nerve. Here we show the pain response in patients diagnosed with CTS using a combination of blood oxygenation level dependent (BOLD)[4] and signal enhancement by extravascular water protons (SEEP)[5] fMRI effects to detect neuronal activity in the brain stem and spinal cord.

Materials & Methods:

Functional MRI studies of the spinal cord and brain stem were carried out in 3 (2 female, 1 male) subjects diagnosed with CTS in a 3T Siemens Magnetom Trio. To examine the activity caused by noxious touch, von Frey filaments were applied to the area on the volar forearm above the median nerve at a frequency of 1 Hz (pain threshold was determined during psychophysical testing 24 hours prior to imaging). Stimuli were applied in a block paradigm consisting of three stimulation periods of 56 seconds, interleaved with baseline periods of 140 seconds, for a total of 11 min 12 seconds for each experiment. After each block, volunteers were asked to rate the pain and unpleasantness on a numerical 11 point scale, where 0 indicates no pain and 10 indicates worst possible pain.[6]

Functional imaging data were acquired with a half-fourier single-shot fast spin-echo (HASTE) sequence. TE=38 msec and TR=1 sec per slice, in order to obtain primarily proton-density weighted images. Signal intensity changes observed in the image data upon a change in neuronal activity were the result of SEEP and BOLD effects. Sagittal image slices were selected to span from the C7/T1 disc to the superior edge of the thalamus, with a 20 cm x 10 cm FOV, a 192 x 96 matrix, in fourteen 2 mm thick contiguous sagittal slices spanning the entire width of the spinal cord and brainstem. Spatial suppression pulses were applied to eliminate aliasing and signal anterior to the spine. The peripheral pulse was recorded continuously during each study and a general linear model was used to improve the discrimination between physiological motion and signal intensity changes arising from neuronal activity.[7] Analysis was completed using custom-made software, written in MatLab.

Results & Conclusions:

In CTS subjects, our findings show areas of neuronal activity in the ipsilateral ventral horn (VH), the region proximal to the gracile and cuneate nuclei, the PAG and the substantia nigra in response to a noxious stimulus. Interestingly, in a model of neuropathic pain, similar structures showed activity when noxious touch stimuli was applied to the volar forearm, which was previously sensitized by capsaicin application.[3] Further, these structures appear to differ from regions of neural activity shown in healthy controls, namely, in the pontine reticular formation (PRF), the anterior pons, and the thalamic midbrain border.[3] Currently, we are continuing our examination of the transmission pathways associated with the pain response by varying the noxious stimuli used. The etiology of CTS is largely idiopathic, therefore we must tailor the noxious stimulus to one that induces the most typical pain for each individual. By evoking the specific pain that corresponds to the individual's daily experience, we can isolate the structures in the transmission pathways associated with chronic pain.

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