# A hemodynamic response function for functional MRI of the cervical spine using motor and nociceptive paradigms

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## INTRODUCTION

Over the past five years, functional magnetic resonance imaging (fMRI) of the human spinal cord has been developed and proven effective for localizing areas of neuronal activity within the spine in response to sensory stimuli [1]. However, fMRI of the spinal cord is currently not as reliable as fMRI of the brain because of several spine-specific issues. Breathing and heart-rate, as well as movement of the spinal cord within the vertebral column induce motion artifacts. In addition, the flow of cerebrospinal fluid, and the close spatial proximity of neural and vertebral tissues can lead to falsely identified areas of activation. Experimental techniques have been developed to address these issues and optimize fMRI of the human spinal cord [2]. However, to date, most fMRI scans of the human spinal cord have used a brain derived hemodynamic response function in analysis, and it has not been demonstrated that this approach is optimal for data analysis. Using both motor and nociceptive tasks, this study aims to derive a spinal hemodynamic response function (HRF) for the purpose of optimizing spinal fMRI for clinical and research use.

## METHODS

Spinal MR images were obtained with subjects supine using a 3T MRI scanner (General Electric Lx rev 8.3, Milwaukee, WI) in conjunction with a surface coil receiver (General Electric 8 phased array, receive only) and a body coil to transmit uniform Rf excitation pulses. Functional images were obtained using a T2* gradient echo spiral out sequence (TE 38msec, TR 1sec, effective TR 2 sec, 16cm x 16cm FOV, 128x128 matrix) [3]. Twelve to thirteen contiguous 7.5mm axial slices were acquired of the cervical spine from the top of C5 through the bottom of segment C8. Cardiac and respiratory functions were monitored using the scanner's built-in respiratory belt and photoplethsmograph. Immobilization of the head and neck were performed with padding and medical tape. Thermal stimuli were delivered to the thenar eminence (C6 dermatome) using a Medoc TSA-II thermal sensory analyzer and thermal probe. Each subject conducted 3 block design functional experiments, each lasting 8 minutes. 1) thirty seconds of fist clenching alternated with thirty seconds of rest. 2) thirty seconds of 48°C tonic noxious stimulus alternated with thirty seconds of 40°C baseline 3) thirty seconds of 48°C phasic noxious stimulus oscillating from 40°C to 48°C at 10°C/sec alternated with thirty seconds of 40°C baseline. Data were analyzed with Brain Voyager. Activation maps were computed to identify active voxels. For each subject, event related averages (ERAs) were computed from regions of interest (ROIs) of the spinal cord showing activity at $p<0.05$ and a clustering threshold of 4 voxels. ERAs were averaged for each subject and between subjects, then deconvolved to determine individual response functions, and a generalizable spinal cord HRF.

## RESULTS

Activity for the fist clenching task was observed at spinal segments C5-C7, bilaterally in the dorsal horn in response to unilateral motion of the hand. (Fig. 1) Activity may be localized to the dorsal horn due to sensory stimulation of the palm. For the spinal cord HRF derived from ERAs of the fist clenching task, time-to-response-peak=8sec, time-to-undershoot-peak=25sec, and response-undershoot-ratio=6. Data from both the tonic and phasic noxious stimuli paradigms is preliminary. Activations for these tasks were seen in the dorsal horn, but also in the ventral horn. Activations may be seen in the ventral horn because of projections to motor neurons involved in reflexive withdrawal. The spinal cord HRFs derived from ERAs of the tonic and phasic noxious stimuli tasks were unconventional in shape and plausible explanations for this abnormality will be discussed below.

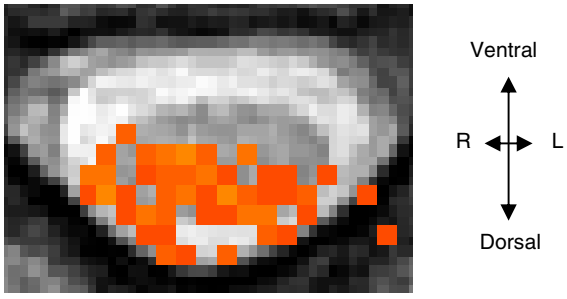


Figure 1. Representative example of an activation map at C6, generated with the fist clenching task. $p<0.01$, uncorrected

## DISCUSSION

Previous studies have demonstrated that in the brain the HRF has a time-response-peak = 5sec, a time-to-undershoot-peak = 15sec, and a response-undershoot-ratio = 6. Although our findings from the fist clenching task suggest that the undershoot-ratio is similar between brain and spinal cord, the difference between time-to-response-peak, and time-to-undershoot-peak suggest that the HRF is of a considerably longer duration in the spinal cord that in the brain. This result will be useful for optimizing the analysis of future MRI studies conducted on the human cervical spine. The deconvolution analysis conducted to derive the HRF from ERA data assumes that during block conditions of the functional scan there is a temporally invariant level of neural activity. Experimentation on animal models suggest that for noxious stimuli this assumption may prove to be invalid, and that pain fibers respond with a quickly adapting or slowly facilitating response, rather than a temporally invariant response[4]. Because pain fibers exhibit a temporally varying response, conventional MRI methods of convolving an HRF with a block design may be inappropriate for the analysis of nociception, and unconventional response functions such as those recorded in this study, may prove useful for further MRI studies investigating the sensation of painful stimuli.

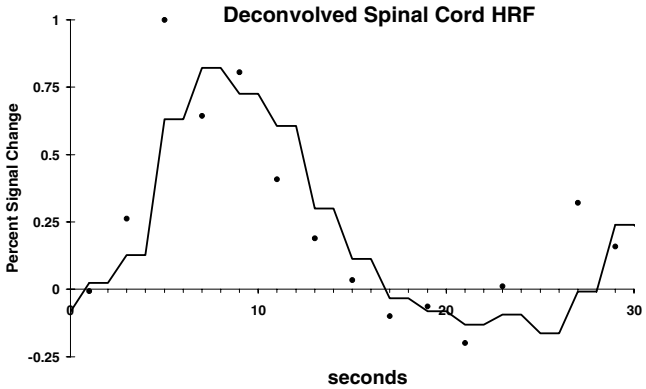


Figure 2. BOLD hemodynamic response function deconvolved from event related averages of 23 distinct ROIs obtained from 5 subjects. Trend line represents a moving 4-point average of the data points.

## REFERENCES

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