A New Method of Motion-Compensated Spinal fMRI: Identifying Human Spinal Cord Function with Increased Sensitivity and Reproducibility

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Introduction

Before functional magnetic resonance imaging (fMRI) of the spinal cord can be used as a reliable tool for clinical investigation of spinal cord injury and evaluation of novel treatment strategies, the sensitivity and reliability of isolated studies must be improved. Previous research has shown that the human spinal cord oscillates in a predictable manner relative to the cardiac cycle, and can be modeled as a linear combination of three principal components (Figure 1).[1] Left unaccounted for, this motion significantly reduces the sensitivity and reproducibility of spinal fMRI data, limiting the ability to discern between small, discrete regions of neural activity within the cord. In the present study, a new data analysis method is presented: one that incorporates recent advances in modeling spinal cord motion to reduce the effects of cardiac-induced cord motion on spinal fMRI.

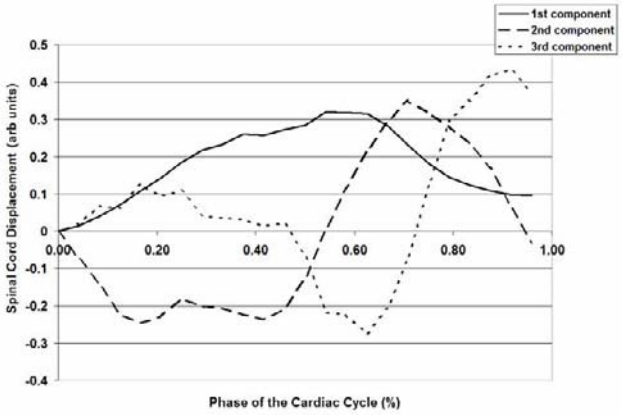

Figure 1. Principal components of spinal cord motion

Methods

All experiments were performed in a 3T Siemens Magnetom Trio with subjects lying supine. Functional MRI data were acquired from healthy subjects during interleaved periods of rest and a variety of thermal and fine-touch stimuli applied to the hand, thereby eliciting activity in the cervical spinal cord and brainstem. A half-fourier single-shot fast spin-echo (HASTE) pulse sequence was employed while the timing of peripheral pulses, external triggers and stimulus paradigm were recorded. The volume of interest (spanning from the thalamus to the upper thoracic spinal cord) was acquired in 2 mm thick contiguous sagittal slices, each having a 200 mm × 100 mm FOV (192 × 96 matrix). The TE was set to 38 ms, resulting in predominantly proton-density weighted images.

The sagittal image data were then analyzed using current methods,[2] by reformatting into cubic voxels, and re-slicing transverse to the cord in order to facilitate rostral/caudal smoothing prior to normalization. Regions of activity were identified as those having $P < 0.01$ using a general linear model (GLM) analysis. In this case, the basis sets included in the GLM were: a boxcar model paradigm, a constant function (to account for baseline intensity), a linear ramp function (to account for baseline drift), and the re-sampled peripheral pulse traces (sampled at the time of each image acquisition).

The data were re-analyzed using our new motion-compensating method: a two-stage GLM approach. First, the sagittal data were analyzed to identify and eliminate the components of signal change occurring synchronously with modeled cord motion. The motion-compensation stage employed six basis functions: a constant, a linear ramp, a model of cardiac motion (to account for the pulsatile flow of blood and cerebrospinal fluid), and each of the three principal components of spinal cord motion (sampled at the time of each slice acquisition). After fitting with the GLM, the signal time course components matching the models of cord motion and cardiac motion were subtracted from the image data on a slice-by-slice basis to account for interleaved slice timing. The resulting sagittal data was then reformatted and normalized before initiating the second stage of GLM analysis with a statistical threshold of $P < 0.01$, in order to identify voxels with time courses matching the stimulation paradigm. In this case, the basis sets included a boxcar model paradigm and its first derivative (to account for stimulus on/off ramps), as well as a constant function to account for baseline intensity.

Results

By analyzing the same data with and without the proposed motion-compensation analysis method, differences in the neuronal activity identified with the new method were demonstrated. Results show that the new method identifies the same general areas of activity in the spinal cord as determined by the current method, but with higher sensitivity (i.e. more regions appearing active) and better reproducibility (i.e. better inter- and intra-subject agreement). The results of this study demonstrate a significant development in overcoming one of the key challenges for spinal fMRI.

Conclusion

A new, motion-compensating method for spinal fMRI data analysis has been developed and validated. By including a model of spinal cord motion in a two-step GLM analysis, it is possible to discriminate between signal intensity changes arising from physiological motion and those arising from neuronal activity. By first eliminating the components of signal change ensuing from cord motion, the ability to reliably localize regions of functionally relevant signal change is improved.

References

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2. Stroman, P.W. Discrimination of errors from neuronal activity in functional magnetic resonance imaging in the human spinal cord by means of general linear model analysis. *Magn Reson. Med.* **56**, 452-456 (2006).