Resting state spinal cord functional connectivity at 3 Tesla

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Introduction

We recently reported our ability to detect resting state functional connectivity in the human spinal cord at 7 Tesla via measurements of robust correlations between blood oxygenation level dependent (BOLD) signals between left and right ventral (motor) horns, as well as between left and right dorsal (sensory) horns [1]. At high field no significant group-level correlations were observed between spinal cord gray matter and surrounding white matter regions, providing confirmation that gray matter correlations were not dominated by spatially correlated physiological noise [1]. The goal of this work is to evaluate whether similar resting state correlations can be characterized at 3 Tesla with the goal of translating our high-field methodology to the clinic. We hypothesize that while the BOLD contrast-to-noise ratio (CNR) may be decreased at lower field, the increased fidelity of B_0 and B_1 field, and the smaller impact of physiological noise coupled with improved pulse sequence design, may offer a unique opportunity to study connectivity. Furthermore, the establishment of protocols for the acquisition and processing of resting state spinal cord functional magnetic resonance imaging (fMRI) data at 3 T would facilitate widespread adoption of spinal cord functional connectivity into clinical applications where it may provide new insights into disruption of normal cord function in diseases of the central nervous system.

Methods

Images were acquired on a Philips Achieva 3 T scanner with a dual-channel transmit body coil and a 16-channel neurovascular coil for signal reception covering the brain and cervical spinal cord. Healthy volunteers were scanned under a protocol approved by the institutional review board. Resting state BOLD fMRI data were acquired with a 3D gradient-echo sequence with the following parameters: in-plane field of view = 150 × 150 mm, slice thickness = 5 mm, voxel size = 1 × 1 × 5 mm^3, 12 slices, repetition time = 40 ms, echo time = 8.0 ms, flip angle = 8°, echo train length = 7, sensitivity encoding [2] reduction factor = 2.0 (left-right), partial k-space scan factors = 0.714 × 0.8, volume acquisition time = 2.64 seconds (220 ms/slice), number of volumes (after 5 'dummy' scans) = 455 (20 minutes). Functional data were processed as described in [1] except the slice-by-slice functional-to-anatomical affine registration (3dAllineate [3]; step #8 in [1]) registered each functional to its corresponding anatomical using five cost functions ('ls', 'crM', 'crA', 'crU', and 'lpa' [3]), and then applied the median transform to all volumes. These cost functions were empirically observed to produce reliable results, and use of the median value protected against possible errant transformations.

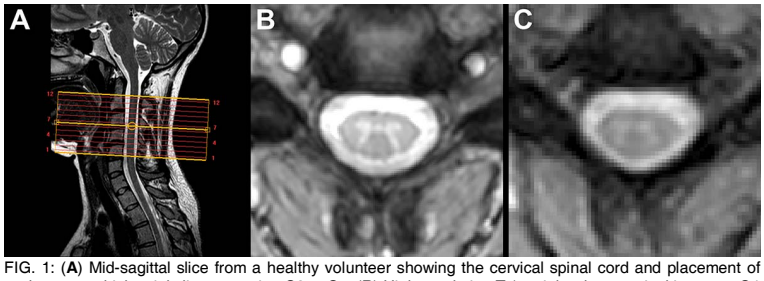

FIG. 1: (**A**) Mid-sagittal slice from a healthy volunteer showing the cervical spinal cord and placement of twelve 5-mm thick axial slices covering C2 to C5. (**B**) High-resolution T_2*-weighted anatomical image at C4 acquired with 0.65 x 0.65 x 5 mm^3 voxels and interpolated to 0.29 x 0.29 x 5 mm^3 clearly shows the butterfly-shaped gray matter column. (**C**) Functional image of the same slice interpolated to the final resolution of the anatomical. This T_2*-weighted sequence acquired 12 slices with 1 x 1 x 5 mm^3 voxels every 2.64 seconds (220 ms/slice). Functional images show minimal geometric distortions.

Results

Figure 1 presents data from a healthy volunteer (female, 25 years old). Axial slices were planned perpendicular to the cord to obtain coverage of four vertebrae (C2 to C5). High-resolution (0.65 × 0.65 mm^2) averaged multi-echo gradient echo (mFFE) [4] T_2^*-weighted axial images (Fig. 1B) clearly show the characteristic gray matter butterfly, and a similar pattern is observed in T_2^*-weighted fMRI data (Fig. 1C). For this subject, median temporal signal-to-noise ratio (TSNR) in spinal gray matter increased by only 13% (from 24.5 to 27.7) after physiological noise correction (steps #11 and #12 in [1]); at 7 T, the TSNR increase was 30% across subjects, suggesting an approximately linear decrease in physiological noise with decreasing field. Figure 2 displays a seed-based analysis of functional connectivity using AFNI's 'InstaCorr' function [3]. The correlation threshold was set to $p < 3 \times 10^{-6}$ to protect against type I errors, and no cluster thresholding was used to reveal all correlations within gray and white matter. A seed placed in the left ventral (motor) horn displays significant positive correlations with the right ventral horn and central gray matter on the same slice and adjacent slices, but not surrounding white matter.

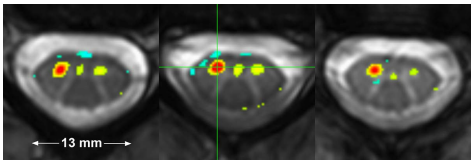

FIG. 2: A seed-based analysis of functional connectivity at 3 T using data from a single resting state run. A voxel selected in the left ventral horn in C4 (marked with a green crosshair) displays significant temporal correlations with the right ventral horn and central gray matter in the same slice, as well as the left and right ventral horns and central gray matter in adjacent slices.

Discussion

This abstract demonstrates the viability of obtaining high-resolution resting state spinal cord fMRI data at a clinical field of 3 T. The primary advantage of fMRI at 7 T is the greater-than-linear increase in BOLD CNR with increasing field, but the well-known challenges of 7 T fMRI include T_2^* blurring, power deposition (specific absorption rate), and B_0/B_1 inhomogeneities. These challenges are less problematic at 3 T, and the decrease in BOLD CNR at a lower field can be partially recovered by imaging for a longer period of time. In this initial study, we acquired 20-minute runs to investigate the temporal correlations over what may be considered the longest feasible time to acquire a resting state run during a clinical examination. Future work will study the temporal dynamics of the BOLD signal during this time and determine the minimum required run length to reliably detect functional connectivity. We will also use the developed methods to investigate and characterize differences in spinal gray cord matter connectivity between healthy controls and cohorts of patients with central nervous system diseases.

Acknowledgments – This research was primarily supported by NIH grants 5R21NS081437-02 and 1K99EB016689-01A1, but also by grants 1R01EY023240-01A1 and 1R21NS087465-01. The authors thank Benjamin N Conrad for assistance with subject recruitment.

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