

Investigation of venous effects in spinal cord fMRI using hypercapnia

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Introduction

An effective non-invasive method of assessing spinal function would be of great clinical importance. However, a better understanding of neurovascular coupling in the spinal cord is needed for a reliable use of the BOLD technique in a clinical context. In recent studies, hypercapnia was used as a control stimulus to study the sensitivity of BOLD responses in the spinal cord [1,2]. Hypercapnia is known to cause large increases in perfusion and subsequently in BOLD signal [3]. In this study we built further on this investigation by (i) comparing responses to hypercapnia in the spinal cord and the brain, (ii) adding a motor task to the protocol and (iii) acquiring susceptibility weighted images (SWI) to investigate the spatial concordance of the most significant responses with large veins.

Methods

Data acquisition. Functional MRI acquisitions were conducted on six subjects in a 3T MRI system (Siemens Medical Systems) using a spinal coil, a neck coil and a 12-channel head coil combined. Axial slices covered the brain and the whole cervical cord, with slices positioned in the middle of each vertebral body to limit susceptibility artifacts. The sequence used was gradient echo EPI with GRAPPA acceleration factor 2 (TR/TE = 3000/30ms, alpha = 70°, slice thickness = 4mm with a 5mm slice gap, matrix size = 128x72, in-plane resolution = 1.5x1.5 mm). To study the spatial distribution of responses, SWI data were acquired with the same slice prescription (TR/TE = 28/20ms, in-plane resolution = 0.5x0.5mm). Standard MPRAGE was also acquired with 1x1x1.5 mm³ voxel size.

Functional protocol. Both hypercapnia and motor tasks were performed in a block-design fashion (4 blocks of rest, 4 blocks of task, 60 s each). Hypercapnia was induced using a computer-controlled system that allows targeting of specific end-tidal CO₂ values (+5 mmHg). The motor task consisted of squeezing a ball with the dominant hand, inducing activity in motor and sensory units at levels C5-7. Data were analyzed using the general linear model with standard parameters.

Results

Hypercapnia-induced signal changes were observed for all subjects in the brain and spinal cord (Fig 1,2). This signal was predominant in large veins (Fig 2). A motor stimulus similarly elicited signal changes (Fig 3) with good spatial correspondence of signal increase around C6.

Discussion

In this study as in some others [4,5], highest BOLD signal changes were sometimes recorded at the periphery of the spinal cord. These large signal increases may occur in draining veins around the cord (Fig 2), as observed in the brain (Fig 1). This is consistent with studies in brain showing that BOLD responses at 3T typically show the highest amplitude in large veins [6], particularly at high spatial resolutions such as that used in the present study. This signal from draining veins may account for some inter-subject variability as it may arise as a result of individual differences in vascular anatomy. The dominance of venous washout signal in spinal cord BOLD fMRI shown here further suggests the use of other types of contrasts such as blood volume imaging with superparamagnetic contrast agents (e.g. MION) when high spatial resolution is needed [5]. Furthermore, spinal cord functional studies offer great challenges in terms of analysis techniques and their shortcomings prevent firm interpretation of results. The difficulties experienced here in correcting motion arising from respiration, swallowing and the motor task highlight the shortcomings of standard motion correction algorithms and suggest the need for spinal-dedicated approaches [7]. Further difficulties arise from the large variability associated by physiological variations in respiration depth rhythm and cardiac cycle. Though these sources of variation are not accounted for here, future work will integrate an improved framework for accounting respiratory and cardiac variance when modeling spinal cord time series, as proposed in [8]. Because of these detrimental factors affecting sensitivity, it is likely that only the stronger large vein responses remain readily detectable in the spinal cord, although weaker parenchymal responses may well be present.

References

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- [8] Brooks et al., *Neuroimage* 2008; 39: 680-692.

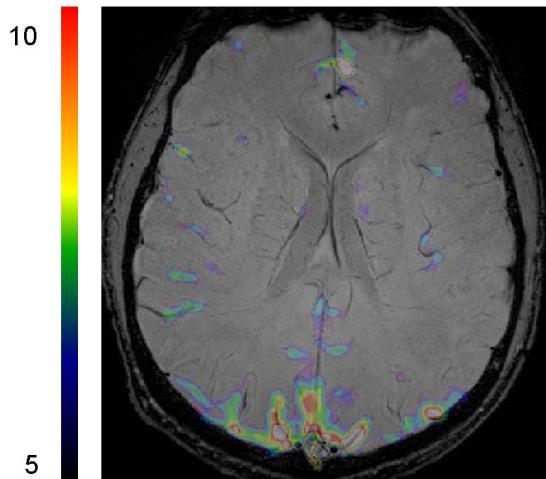


Fig 1. Overlay of BOLD t-map over a brain SWI. At 3T, highest BOLD signal from large draining veins in brain, seen as dark voxels in the SWI. A threshold of $t=5$, corresponding to a corrected peak p value of 0.05 was chosen to highlight the high signal from veins.

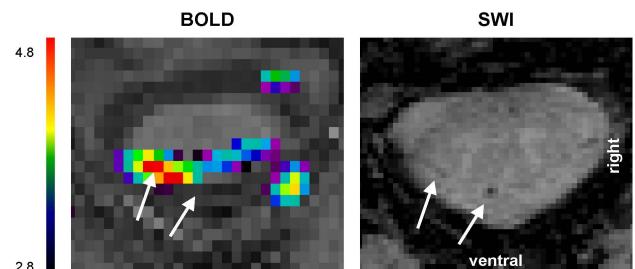


Fig 2. Overlay of BOLD t-map over anatomical image and comparison with SWI in spinal cord. Even though distortions cause displacement of activation, activation pattern seems to follow that of large veins. $T = 3.13$ corresponds to a cluster p value of 0.05.

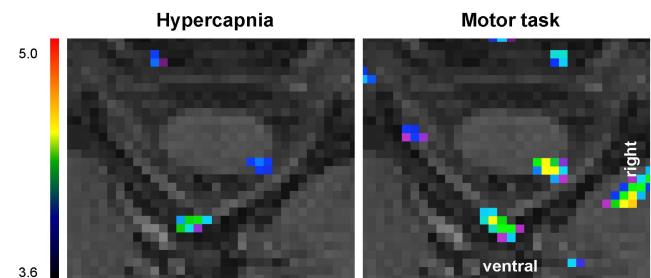


Fig 3. Overlay of BOLD t-maps for hypercapnia and motor stimuli. There is a good spatial correspondence of activations over large veins. $T = 3.13$ corresponds to a cluster p value of 0.05.