MRI mapping of hemodynamics in the human spinal cord

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Supplementary Material

Supporting Information Text

Materials and Methods

Acute Intermittent Hypoxia (AIH). AIH has been effective at improving motor function in spinal cord injured cohorts (1, 2). The data collected for the Group spinal cord vascular reactivity (SCVR) study was a part of a broader study to investigate with magnetic resonance imaging (MRI) the mechanisms of neural plasticity associated with AIH. This AIH protocol was administered after the first MRI session with a HYP 123 oxygen generator (Hypoxico, Inc., New York, NY, USA) in 15 2-minute cycles. Each cycle consisted of brief exposures to a hypoxic gas mixture (9% FiO_2, 30-60 seconds), alternating with normal room air (21% FiO_2, 60-90 seconds), targeting 85% SpO_2 during each bout. The second MRI session occurred 45-60 minutes after AIH. Note, AIH had a negligible/non-significant impact on SCVR (via a two-tailed paired t-test) and the impact of AIH was not the focus of this work.

Imaging Protocol. A high resolution anatomical T2-weighted scan, covering the brainstem to upper thoracic spine, was acquired with the following parameters: repetition time (TR)/echo time (TE)=1500/135ms, sagittal slice thickness=0.8mm, in-plane resolution 0.39mm^2, 64 slices, flip-angle (FA)=140°, field-of-view (FOV)=640mm^2. Spinal cord functional MRI (fMRI) scans were collected using a gradient-echo echo-planar imaging (EPI) sequence and ZOOMit selective excitation (TR/TE=2000/30ms, axial in-plane resolution=1mm^2, axial slice thickness=3mm, 25 ascending interleaved slices, FA=90°, FOV=128x44mm^2). The ZOOMit acquisition reduces the field-of-view around the spinal cord. The functional acquisition volume was positioned perpendicular to the spinal cord; the bottom of the volume was positioned at the bottom of the C7 vertebral level. Cervical coverage was approximately from the C4 to C7 vertebral level, but the exact coverage varied due to participant height and spinal anatomy. For each scan session, the task paradigm was displayed to participants via a mirror on the head coil, reflecting a monitor placed behind the bore of the magnet.

Physiological Monitoring. Physiological data were collected throughout the fMRI scans, including exhaled CO_2 and O_2 through a nasal cannula and breathing via respiratory belt. A pulse transducer was placed either on the dorsalis pedis artery of the foot (for the **Group SCVR** study because participants were holding hand-grips for another task) or on the right index finger (**Individual SCVR**). These signals were fed through a Gas Analyzer (CO_2, O_2 only) and PowerLab and recorded with LabChart (ADInstruments, Sydney, Australia). The scanner trigger was also recorded through the same system to facilitate alignment of all recordings with fMRI timeseries data.

Motion Correction. 2D slicewise motion correction was performed with the Neptune Toolbox (version 1.211227). Three steps of the toolbox were used to complete motion correction, including the manual definition of a “not cord” mask around the spinal cord and CSF region (#5), computation

of a Gaussian weighting mask of the spinal cord, derived from the “not cord” mask (#7), and the application of motion correction (#8). The motion correction algorithm used the Gaussian mask as a weight for each voxel, a temporal median image as the target image for the correction algorithm, and used AFNI (version 22.0.05) to compute and apply the motion parameters to the data (*3dWarpDrive*, *3dAllineate*). Temporal median filtering was de-selected. Motion corrected functional data and slice-wise X and Y motion traces were output.

Registration. A binary spinal cord mask in the functional image space was manually drawn (excluding the top/bottom slices) and is used in several steps. Segmentation and registration were performed with the Spinal Cord Toolbox (version 5.3.0). (Note, the Spinal Cord Toolbox version 6.1.0 included an update to the spinal cord segments and this new version was used to add correct labels to figures.) The anatomical T2-weighted image of each subject was segmented (*sct_deepseg_sc*) (3) and then registered to PAM50 template space (*sct_register_to_template*). The binary spinal cord mask in functional image space and anatomical-template warping field were used to inform registration of the motion corrected functional data to the PAM50 template space (*sct_register_multimodal*).

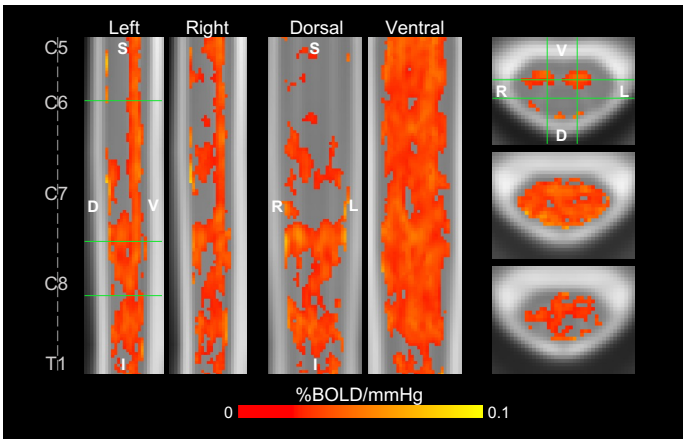

Fig. S1. Group SCVR delay-corrected amplitude map. *Delay-corrected SCVR amplitude (family-wise error rate corrected, p<0.05). Axial, sagittal, and coronal slices are the same as those shown in Fig. 1.*

SI References

1. M. S. Sandhu, W. Z. Rymer, Brief exposure to systemic hypoxia enhances plasticity of the central nervous system in spinal cord injured animals and man. Curr Opin Neurol **34** (2021).
2. A. Q. Tan, S. Barth, R. D. Trumbower, Acute Intermittent Hypoxia as a Potential Adjuvant to Improve Walking Following Spinal Cord Injury: Evidence, Challenges, and Future Directions. *Curr Phys Med Rehabil Rep* **8** (2020).
3. C. Gros, et al., Automatic segmentation of the spinal cord and intramedullary multiple sclerosis lesions with convolutional neural networks. Neuroimage **184**, 901–915 (2019).