Analysis of Hemorrhagic Traumatic Axonal Injury Lesions Using Seed-Based Resting-State FMRI at 7T

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TARGET AUDIENCE: Neurologists, neuroscientists and physicists who are interested in resting-state FMRI for lesion analysis..

INTRODUCTION. Hemorrhagic traumatic axonal injury (hTAI) is associated with disruption of neural networks and loss of neurocognitive function in patients with severe traumatic brain injury. However, recent evidence from histo-radiologic correlation studies suggests that hTAI lesions may not invariably destroy axons. Rather, red blood cells may intercalate between partially injured axons, which have the potential to recover their structural integrity[1]. Resting-state FMRI (RS-FMRI) offers the potential to study how brain networks change in order to compensate for injuries. It is unclear how to optimize the placement of seeds in and around lesions. We aimed to study the effects of seed placement and identify the functional connectivity of a hTAI lesion in a patient who recovered after traumatic brain injury.

METHODS. With IRB approval, RS-FMRI was performed on a 27-year-old patient who recovered from traumatic coma (6 years post-injury) and two healthy controls (26-year-old females). The patient had diffuse axonal injury (grade 3) involving the white matter (WM) of the bilateral cerebral hemispheres, splenium of the corpus callosum and dorsolateral midbrain. We chose one hTAI lesion located at the gray-white matter junction of the right frontal lobe. Data were acquired using a 7T Siemens whole-body MRI scanner equipped with a 32-channel RF receive coil and a single-shot gradient-echo EPI sequence using FLEET[2] with TE/TR=25/3560 ms, 1.5 mm isotropic voxels, FOV=19.2 cm×19.2 cm, 60 slices, partial Fourier=7/8, GRAPPA *R*=2, BW=1776 Hz/pixel, effective echo spacing=0.56 ms, 180 time points, and total scan time=11 min. Network analyses were conducted in each subject's native space. Preprocessing of the FMRI data included motion correction, slice timing correction, temporal filtering (0.01 Hz), regression of nuisance variables (WM, CSF, movement and global signal) using FEAT[3] and smoothing to 3 mm. Seed-based analysis was performed using AFNI[4]. T_1-weighted multi-echo MPRAGE images were acquired at 0.75mm isotropic resolution. **ROI-Seed Analysis:** A hand-drawn seed-ROI covering the hTAI was registered to the healthy controls using FLIRT[3] and FNIRT[3] to warp each of the EPI to T_1-weighted image then to MNI space, respectively. The equivalent seed-ROI was obtained in the contralesional hemisphere by performing a right-left flip in MNI space. **Single-Voxel Seed Analysis:** To study the temporal SNR (tSNR) and contribution to correlation maps for single voxels within and around the ROI-seed, seeds were placed along a straight line running left-right through the center of the lesion (Fig.1). Voxels 2 and 6 are two voxels outside the lesion. Voxels 1 and 7 are four voxels outside the lesion. All images are displayed in radiological format (left side of the image corresponds to the right side of the brain).

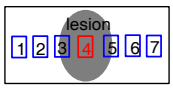

Fig.1 Position of single voxel seeds.

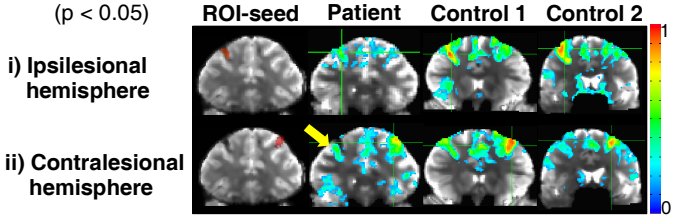

Fig.2 Seeds and correlation maps of ROI-seeding in the i) ipsilesional and ii) contralesional hemisphere in the patient and controls. The first column displays the hand-drawn ROI-seed. The yellow arrow highlights the fact that the patient's DLPFC node of the ECN is more inferolateral compared to the controls.

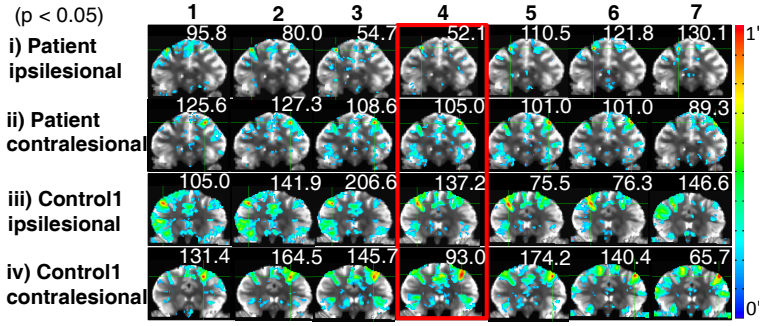

Fig.3 Correlation maps for single voxel seeds within and around i) the ipsilesional hemisphere in the patient, ii) the contralesional hemisphere in the patient, iii) the ipsilesional hemisphere in control1, iv) the contralesional hemisphere in control1. Each column number corresponds to the seed positions shown in Fig.1. Temporal SNRs of the seed at each position are shown at the top right of each map.

RESULTS AND DISCUSSION.

ROI-Seed Analysis: The correlation patterns in the patient show a similar pattern to that of controls, but with weaker correlations and smaller clusters. For the controls, correlation maps obtained by seeding in the contralesional versus ipsilesional hemispheres show similar clusters within the DLPFC nodes of the ECN. In the patient, the DLPFC node of the ECN on the ipsilesional side appears to be more inferolateral to the hTAI lesion area compared to the controls (Fig.2, yellow arrow). **Single-Voxel Seed Analysis:** The correlation maps and tSNR values for the single-voxel seeds are shown in Fig.3. The tSNR for the voxel at the center of the lesion in the patient is 62.0% lower compared to the control1 and 50.4% lower compared to the contralesional side in the patient. For the controls the ECN nodes appear for all voxel positions. For the patient, the voxel at the center of the ipsilesional ROI shows only a few small, nondescript clusters, whereas voxel 1 shows the ECN most faithfully since this voxel is closer to the apparent inferolateral location of the right DLPFC node. Contralesional correlation maps in the patient show the ECN with the exception of voxel 1 and 2.

CONCLUSION. This study suggests that RS-FMRI can potentially detect brain reorganization due to hTAI lesions. Although the absence of pre-injury RS-FMRI data precludes confirmation of network reorganization, the inferolateral location of the right DLPFC node in the patient suggests that the right DLPFC node has remapped as a result of the hTAI lesion. In addition, since a single-voxel seed at the center of the hTAI lesion has lower tSNR and does not demonstrate a recognizable network, we demonstrate the importance of seeding a larger peri-lesional region or of systematically shifting the ROI placement to identify intact and/or reorganized networks.

ACKNOWLEDGEMENTS. We thank Gary Glover and Jingyuan Chen for helpful discussions. Funding for this work was provided by: NIH NINDS R25NS065743, NIBIB K01-EB011498, CIMIT, Boston, MA, Li Ka Shing-Oxford-Stanford Big Data in Human Health seed grant Stanford Radiology Angel Funds, GE Healthcare, NIH: P41-EB015891, S10-RR026351

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