Alterations in Cortical Sensorimotor Connectivity following Complete Cervical Spinal Cord Injury: Evidence from Resting-State fMRI

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Introduction: Previous studies with task-based functional magnetic resonance imaging (fMRI) have demonstrated changes in brain cortical activation patterns in patients with spinal cord injury (SCI). However, similar alterations in activation patterns during the resting state, when patients are not engaged in voluntary movements remains unclear. We undertook a prospective resting-state fMRI (rs-fMRI) study to explore changes in cortical activation maps in SCI patients.

Methods: With IRB approval, 7 subjects with complete cervical SCI (more than 2 years post injury) and 7 controls were scanned using a whole-body 3.0 T Signa GE scanner. Participants were positioned supine on the gantry of the scanner with the head in a midline location in a purpose built multi-channel head coil. High-resolution anatomical images using T1-weighted spoiled gradient-recalled (SPGR) pulse sequence with TR = 8.2 ms, TE = 3.2 ms, slice thickness = 1 mm with no gaps were obtained. Functional images were acquired using gradient-echo EPI pulse sequence with TR = 2000 ms, TE = 25 ms, slice thickness = 3.5 mm with no gaps, voxel resolution = 4 x 3.75 x 3.75 mm^3 and repetitions = 240.

The rs-fMRI data was pre-processed using Analysis of Functional NeuroImages (AFNI) software**.** Slices in each volume were corrected for systemic, slice-dependent time shifts. Signal spikes were removed by interpolation of a weighted-average value of the adjacent time points. Rigid body correction for head motion along three translational and three rotational parameters was performed using the default iterated least-square minimization with higher-order Fourier interpolation. Detrending was done to remove mean, linear and quadratic trends. Signals from white matter and cerebrospinal fluid were regressed out followed by regression of whole-brain signal averaged over a fixed region in the atlas space [1]. A temporal band-pass filter was applied to allow for low-frequency fluctuations within 0.015 - 0.1 Hz frequency range and data was smoothed spatially (FWHM = 6-mm) [2].

A region of interest (ROI) based analysis was performed using pre-central and post-central gyrus as seed regions [3]. The average BOLD signal time course of selected ROI was used as an input for correlation to time-course of individual voxels from the entire brain using the Pearson cross-correlation (r) to create functional 'connectedness' maps. Whole-brain functional connectivity maps were generated for each subject representing the strength of correlated resting state BOLD signal fluctuations for each seed volume. Pearson correlation coefficients values were converted to z values using Fisher's transformation to yield normally distributed values. Two-sampled t-test was carried to check for significant differences between the two patient groups (p-value less than 0.05).

Results: SCI patients showed decreased functional connectivity in motor and sensory cortical regions when compared to normal controls. The decrease was noted on both ipsilateral and contralateral hemispheres. In addition, the thalamus showed increased connectivity bilaterally in the SCI group.

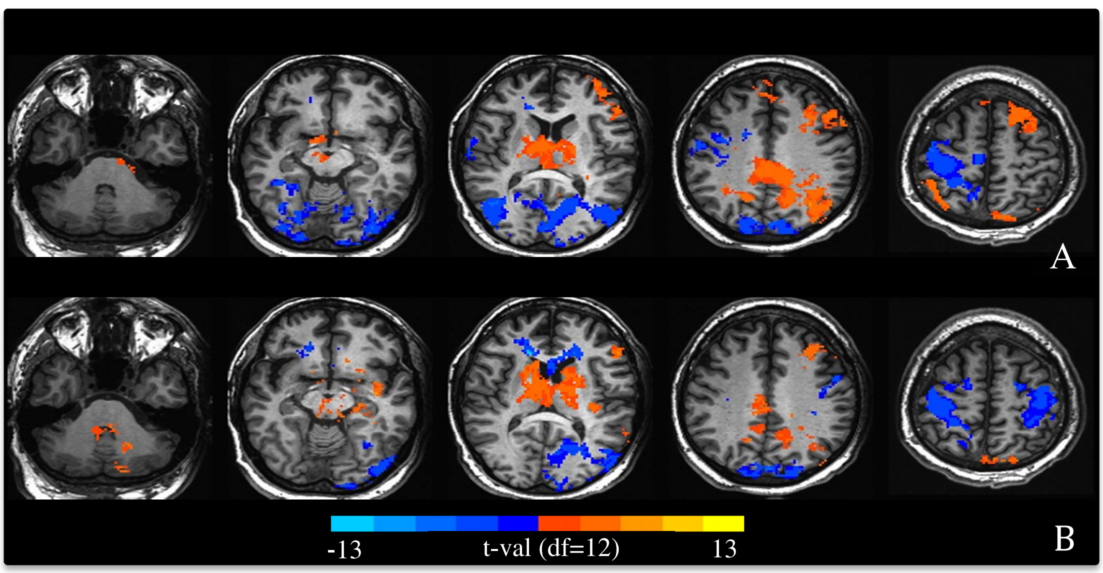

Figure 1: Differential resting-state functional connectivity network pattern for (**A**) left pre-central gyrus and (**B**) right pre-central gyrus, between spinal cord injury (SCI) patients and controls. Normally distributed group maps were compared using t-tests ($P<0.05$, two-tailed, min cluster size = 681.5 contiguous voxels). T-test involved subtraction of controls from SCI patients. Hence, blue color signifying negative t-values indicates SCI patients have lower connectivity compared to controls and vice versa. Color bar is presented with t-val (t-value), df (degrees of freedom).

Conclusion: rs-fMRI demonstrated significant differences in sensorimotor cortex functional connectivity between SCI patients and controls in both cerebral hemispheres. Notably, there is decreased connectivity in sensorimotor cortex in the SCI patients in the resting state. The decrease is observed in both the cerebral hemispheres and is suggestive of alterations in inter-hemispheric communication. Our results suggest that cortical circuits undergo dynamic reorganization following SCI for significant periods of time after injury suggesting ongoing neural plasticity in the central nervous system.

References

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