Enhancement of Functional Connectivity within Contralesional Hemisphere after Recovery of Stroke

Woo Hyun Shim[1], Bruce Rosen[2], Jaeseung Jeong[1], and Young Ro Kim[2]
[1]Bio & Brain, Korea Advanced Institute of Science and Technology, (KAIST), Daejoen, Daejoen, Korea, Republic of, [2]Radiology, Athinoula A. Martinos Center for Biomedical Imaging, Charlestown, Massachusetts, United States

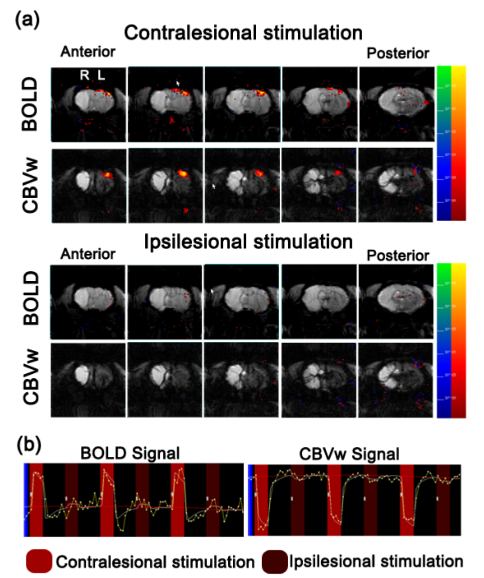

Fig 1. fMRI responses to electrical forelimb stimulation using BOLD and CBVw MRI.

INTRODUCTION: Stroke impairs brain functions and its connections, often resulting in sensorimotor function deficits. Interestingly, spontaneous recovery, though often incomplete, is commonly observed at later stages. Despite the high importance, the restorative mechanisms underlying long-term neurological recovery have not yet been determined. In this regard, task-induced functional MRI (fMRI) activities have been used for delineating factors associated with stroke recovery. More recently, resting-state MRI emerged as one of potential methods to assess overall brain connectivity and has been used for characterizing neurovascular diseases. In this work, we investigated both task-induced fMRI and resting state MRI for understanding changes in functional connectivity using the rat models recovered from impaired sensorimotor functions after severe ischemic stroke.

MATERIALS & METHODS: We used eleven Sprague-Dawley rats afflicted by severe stroke (lesion volume greater than 15% of the brain), which showed nearly full recovery of both sensory and motor functions approximately 180 days after 90 min occlusion of the right middle cerebral artery. Ten normal healthy age-matched rats were used as control. Both resting state and task-induced fMRI activities (electrical forelimb stimulations: Fig 1.) were acquired using mechanically ventilated rats that were anaesthetized with the continuous infusion of alpha-chloralose (~30 mg/kg/h). Task-induced fMRI responses were acquired for both BOLD and CBVw (i.e. using iron oxide nanoparticles) MRI. The resting state BOLD MRI time courses (Gradient EPI: TR/TE = 1000/12.89 ms; FOV = 2.5 x 2.5 cm^2; nine contiguous 1mm slices) were collected for 10 min. Each MRI time course was detrended to the second order and bandpass-filtered between 0.01 and 0.15 Hz. Seed-ROIs were selected in the contralesional hemisphere (Fig 2a), and cross-correlation (CC) values between each voxel and seed-ROI were calculated.

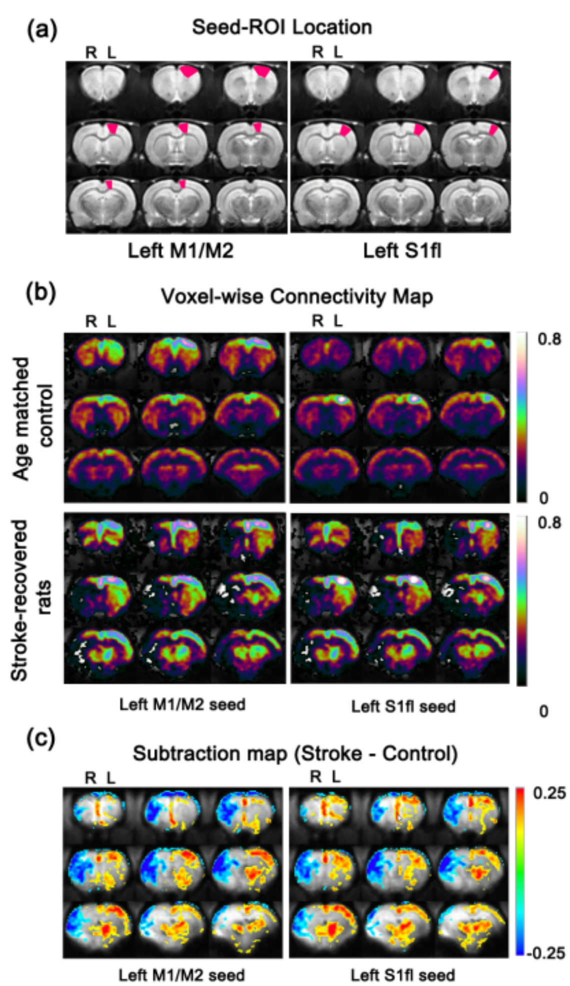

Fig 2. Seed ROI (a), averaged maps of connectivity based on CC value in control (b, upper panel) stroke (b, lower) rats, and the subtraction CC map (c).

RESULTS & DISCUSSION: Remarkably, these functionally recovered rats with the severe stroke show no fMRI responses to the electrical stimulation of affected forelimbs, in which functional reorganization was not observed, either (Fig 1). The markedly increased functional connectivity in the contralesional (non-stroke) hemisphere (L in Fig 2.) is characterized by heightened intensity as well as spatial expansion of the connectivity in comparison to the age-matched controls. In particular, strong connections between contralesional sensorimotor cortices and bilateral thalamus were also observed, which were not present in the control rats. Our findings demonstrate that fMRI response alone may not be adequate to characterize the recovery processes of sensorimotor functions. In conclusion, the data demonstrate that the restoration of sensorimotor function is associated with the increase and spatial expansion of functional connectivity mostly within the contralesional hemisphere.