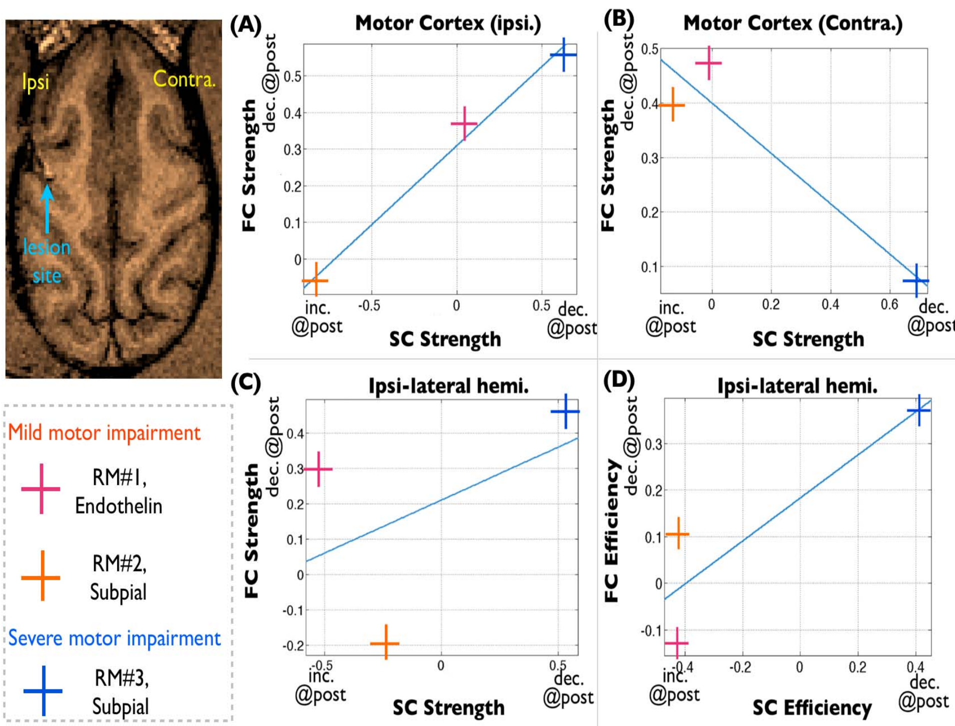
Effect of motor cortex lesions on brain connectivity of rhesus monkeys

Bang-Bon Koo[1], Mary Orczykowski[1,2], Kevin Arndt[1], Yansong Zhao[3], Tara Moore[1], and Ron J. Killiany[1]
[1]*Anatomy and Neurobiology, Boston University School of Medicine, Boston, MA, United States,* [2]*Boston University School of Medicine, MA, United States,* [3]*Philips Healthcare, Cleveland, OH, United States*

Purpose: Despite considerable efforts over the years our knowledge about how recovery of function takes place in the brain following ischemic stroke is limited. Some have postulated that the tissue surrounding the site of injury subsume the functions of the damaged region. Others speculate that recovery of function is modulated by contralateral tissues plasticity or even subcortical re-organization]. In this study, we applied an MRI based brain network approach to look for changes in the hand movement network pre and post stroke using a rhesus monkey model of ischemic stroke. Both structural and functional brain network changes were assessed at pre- and post-lesion stages using diffusion spectrum imaging (DSI) and resting functional MRI (rsfMRI).

Method: Three monkeys were used in this study. The monkeys were first trained on a fine motor tasks requiring precise opposition of the forefinger and thumb. Each monkey underwent an extensive MRI scan and then the ischemic stroke was selectively induced in the hand area of the primary motor cortex. The monkeys were then retested on the same fine motor tasks, and underwent a second MRI scanning session. To produce the lesion methods were used, the first was with mirco-suction aspiration, and the second an injection of Endothelin. In both surgeries a craniotomy was made over the primary motor cortex. The primary motor cortex region that controls the hand was identified electrophysiologically.. One monkey (RM#1) received an Endothelin injection and the other two monkeys (RM#2,3) underwent the aspiration technique. For imaging, we used following imaging protocols: *DSI*-128 half Q-scheme with 2mm iso-cubic voxel/ *rsfMRI*-155 volumes, 2sec-30msec (TR-TE) with 1-1-2mm voxel/ T1-3D TFE with 0.6mm iso-cubic voxel from 3T *Philips Achiva* scanner. Whole-brain structural and functional connectivity matrix was reconstructed (for detailed descriptions, please see *Koo et al., 2013*) and analyzed using in-house developed script based on the Brain Connectivity Toolbox (http://www.brain-connectivity-toolbox.net/). Scanning occur before training on the motor task and 12-14 weeks following surgery upon the completion of testing.



Results: RM#1 and RM#2 showed only mild, long-lasting impairment on the motor task (figure 1., left top panel) suggesting recovery had taken place, while RM#3 showed severe long-lasting impairment suggesting that little to no recovery was present.Significant differences between monkeys based upon the amount of recovery was related to the network based connectivity strength assessment in both the ipsilateral and contra-lateral primary motor cortex networks. In the ipsilateral network a losses in both the structural and functional network connections was related to poor behavioral outcomes (Fig1A). Interestingly however, in the contra-lateral side, the monkeys with the best recovery show a significant decrease in functional connectivity although their structural connections had almost no changes (Fig1B). In terms of global connectivity assessments, the severeness of the functional impairment was well explained by connectivity strength (Fig1C) and efficiency (Fig1D) in the ipsilateral hemisphere network model. The subjects with the best recovery had increased strength and efficiency in the ipsilateral hemispheric structural connections and less changes in their functional connectivity. Global connection patterns in both whole-brain and contra-lateral hemisphere didn't reveal any patterns related to recovery.

Conclusions: In this study, we affirmed the notion that stroke and the recovery process can induce widespread indirect effects on regions beyond the site of overt damage. Both direct and indirect effects on the brain can be successfully imaged and assessed by the brain network analysis methods applied in this study.