IBS CNIR - KSMRM Joint Symposium on Animal fMRI

SY10-1

Optogenetic fMRI Dissection of Cortical Descending Inputs to Midbrain Auditory Processing

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The cortex contains extensive descending projections, yet their impact on brainstem sensory processing remains poorly understood. In the central auditory system, the auditory cortex contains widespread projections to nuclei of the auditory midbrain, called the inferior colliculus (IC), which integrates almost all ascending signals from multiple brainstem nuclei and is the origin of several important auditory processing properties. In this study, we developed a number of auditory fMRI methods to map the auditory processing functions in the IC of rodent models. We further employed these fMRI techniques, together with cortical ablation or cortical optogenetic neuromodulation, to interrogate how cortex inputs influence the IC BOLD responses to external auditory stimuli. Our experimental findings directly revealed the large-scale influences of cortical descending projections, from both auditory and visual cortices, on the IC auditory processing in the midbrain.

Keywords : -

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Cortical Plasticity of Brain Injury by Functional MRI

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Infants and children possess an incredible resilience from injury in comparison to adults owing to the powerful ability of the developing brain to modify its own structure and function in efforts to compensate for loss of function due to injury. This ability, known as neuroplasticity, is particularly active during childhood as the synaptic organization and white matter pathways are still undergoing development in the developing brain. There is growing evidence that functional recovery from injury might well be a consequence of the reorganization of the neural network and/or recruitment of new areas as a process of neuroplasticity because significant diffuse and redundant neural connections as well as the ability of new circuits to form through reorganization exist in the central nerve system (CNS); however, the exact picture of where such reorganization take place has not yet been clearly defined.

In this presentation, I will demonstrate the presence of neuroplasticity at work 1) in spontaneous recovery and 2) enhanced recovery by physical exercise after neonatal hypoxic ischemic (HI) injury, by elucidating a precise picture in which such reorganization takes place using functional MRI techniques. Severe HI brain injury was induced to postnatal day 7 (p7) Sprague-Dawley rats according to the Rice-Vannucci model (right carotid artery occlusion followed by 150 minutes of hypoxia with 8% O2 and 92% of N2).

Brain activation maps along with anatomical and functional connectivity maps related to the sensory motor function were obtained at adult (p63) using blood oxygen level dependent (BOLD)-functional MRI (fMRI), resting state-functional MRI (rs-fMRI) and diffusion tensor imaging (DTI); each of these MRI data was related to sensory motor functional outcome. In-depth investigation of the functional MRI data revealed: 1) intra-hemispheric expansion of BOLD signal activation in the contralesional undamaged hemisphere for ipsilesional forepaw stimuli to include the M2 and Cg1 in addition to the S1 and M1 wide spreading in the anterior and posterior directions, 2) inter-hemispheric transfer of BOLD signal activation for contralesional forepaw stimuli, normally routed to the injured hemisphere, to analogous sites in the contralesional undamaged hemisphere, localized newly to the M1 and M2 with a reduced portion of the S1, 3) inter-hemispheric axonal disconnection and axonal rewiring within the undamaged hemisphere as shown through DTI, and 4) increased functional interactions within the cingulate gyrus in the HI injured rats as shown through rs-fMRI. The BOLD signal amplitudes as well as DTI and rs-fMRI data well correlate with behavioral tests (tape to remove). We found function normally utilizing what would be the injured hemisphere is transferred to the uninjured hemisphere, and functionality of the uninjured hemisphere remains not untouched but is also rewired in an expansion corresponding to the newly formed sensorimotor function from both the contralesional and the ipsilesional sides.

The conclusion drawn from the data in our current study is that enhanced motor function in the contralesional hemisphere governs both the normal and damaged sides, indicating that active plasticity with brain laterality was spontaneously generated to overcome functional loss and established autonomously through normal experience via modification of neural circuitry for neonatal HI injured brain. In addition, with physical exercise after injury, much enhanced plasticity was observed both in intra-hemispheric expansion in the contralesional undamaged hemisphere and inter-hemispheric transfer to analogous sites in the contralesional undamaged hemisphere.

Keywords : plasticity, fMRI, resting state-fMRI, DTI, hypoxic-ischemic brain, developing brain

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Rodent fMRI of sensory and optogenetic stimulation

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The demand for fMRI studies in rodents have been steadily increasing with advent of transgenic and optogenetic technologies for visualizing brain activities in the entire brain and for understanding disease progressions and treatments. For animal fMRI, anesthesia is often used for reducing animal's anxiety and minimizing head motions. Various anesthetics including isoflurane were evaluated for rat fMRI studies. However, anesthetic effect to animal physiology can be dependent on species, thus the protocols obtained from rat studies cannot be simply translated into mouse fMRI. Thus, we evaluated the use of ketamine for mouse fMRI studies. In addition, we explored optogenetic fMRI responding to photic activation of channelrhodopsine in cortical and subcortical areas. Our preliminary studies show that fMRI in rats and mice can be reliably obtained under anesthesia with careful monitoring of animal anesthetic depth.

Keywords : FMRI, BOLD, Brain, Function