FUNCTIONAL NETWORKS OF THE ANESTHETIZED RAT BRAIN AT REST

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Purpose: To examine the spatio-temporal dynamics of low-frequency hemodynamic fluctuations (LFF) of the anesthetized rat brain.

Background: Resting-state functional magnetic resonance imaging (fMRI) examines temporal correlations in the blood-oxygen-level-dependent (BOLD) signal in the absence of a specific task. It is believed that the coherence in the spontaneous low-frequency baseline fluctuations (0.01-0.1 Hz) arises from neurovascular mechanisms regulating blood flow, and is presumed to reflect intrinsic functional and structural connectivity of the brain[1]. Using a seed-voxel analysis strategy, examination of physiological fluctuations in BOLD signals of rats has revealed substantial inter-hemispheric synchrony across the caudate putamen and the primary somatosensory and visual sensory networks[2].

Hypothesis: There exist functional resting-state networks of the anesthetized rat brain beyond those that have been reported using seed-region correlation techniques. These methods test very specific hypotheses and the functional connectivity maps greatly depend on the choice of the seed voxel and the threshold used. Using a model-free analytical strategy, we expect to reveal persistent cortical and subcortical networks beyond those that have been shown using seed-region techniques.

Materials and Methods: Twenty Long-Evans rats were anesthetized with isoflurane (1%, N=10) or ketamine/xylazine (50/6 mg/kg/hr, N=10) and imaged at 9.4 T with no stimulation parameters or task for 5-10 min. Functional images were acquired with a single-shot EPI sequence (matrix size=64 X 64, FOV=25.6 x 25.6 mm, 10-13 slices, TR=1s, TE=15 ms). To avoid the constraints of seed-region techniques in the estimation of LFFs, the hypothesis independent, exploratory technique, independent component analysis (ICA) implemented in the GIFT software package, was applied. ICA uses a linear model to decompose independent, non-Gaussian datasets into distinct subparts[3] and has been successfully applied to functional data sets to show distinct functional network activity[4].

Results: Synchronous LFFs of BOLD signals were found to be in clustered, bilaterally symmetric regions in both cortical and subcortical structures, including: primary and secondary somatosensory cortices; motor cortices; striate cortices; posterior and anterior cingulate; hippocampi; caudate putamen; and thalamic nuclei. Somatosensory and motor cortices typically demonstrated both symmetric and asymmetric components with unique frequency profiles. Network activity was preserved under both types of anesthesia.

Discussion: The results show bilateral synchrony of the rat brain beyond that demonstrated previously. This represents the first complete exploration of the resting networks in the rat brain. It is a crucial step toward understanding the resting state functional activity of the rodent that is required if we are to truly elucidate the changes associated with stimulation, task, or disease models of animal imaging studies.

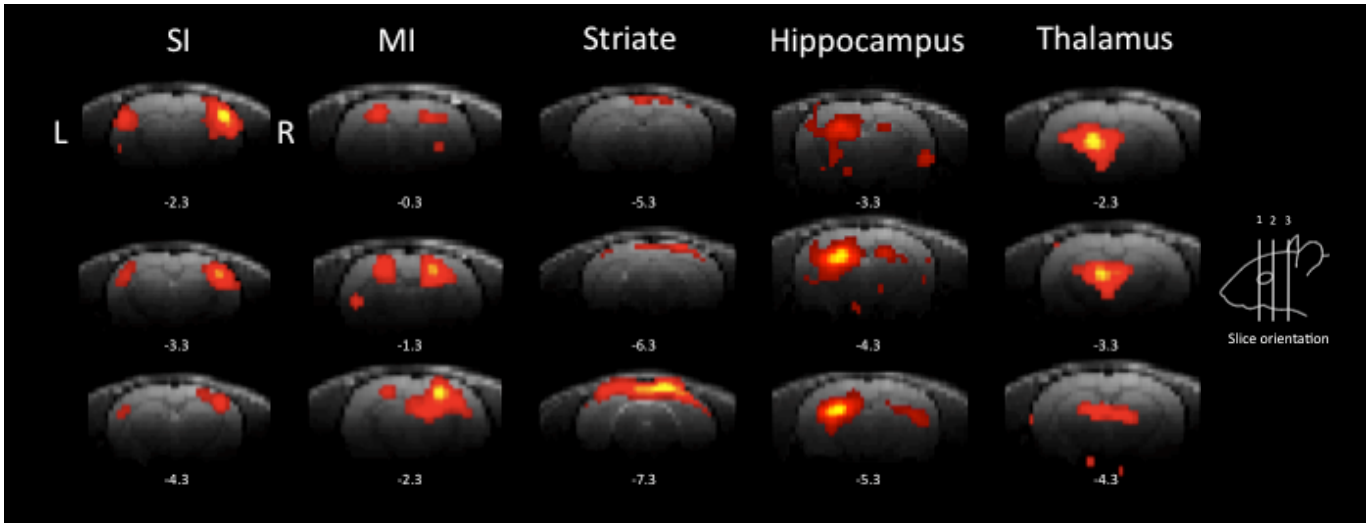

Fig 1. A selection of resting-state networks of a representative isoflurane anesthetized rat derived using independent component analysis (ICA) of BOLD functional timecourses. Component maps are overlaid on acquired anatomical images. Numbers represent the relative location of each slice relative to bregma. Inset image shows the orientation of the slices. (SI: primary somatosensory cortex, MI: primary motor cortex)

References

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