Exploration of Functionally Connected Networks in the Rat Brain using Multislice fMRI

W. Majeed[1], M. Magnuson[1], and S. Keilholz[1]

[1]Biomedical Engineering, Georgia Institute of Technology / Emory University, Atlanta, GA, United States

Introduction: Low frequency fluctuations in T2*-weighted MR images have been used to map functional connectivity (FC) in both humans and rats [1, 2, 3, 4]. Previous studies performed on rats have demonstrated the presence of networks within somatosensory as well as visual systems [2, 3, 4]. Although multiple slices were acquired in two of the studies [3, 4], those studies focused on functional connectivity within specific functional modalities (i.e. visual and auditory systems). Multi-slice data offers greater possibility to study the functional networks, including potential connections across larger spatial distances. In this work, we utilize multi-slice fMRI data to explore networks in the rat brain.

Methods: Imaging was performed on 9.4T Bruker scanner. The rats (n = 4) were sedated using medetomidine as described in [3]. For each rat, a series of SE-EPI images was acquired of 4-5 slices with following parameters: TR = 500 ms, TE = 20 ms, matrix size = 64x64, in-plane resolution = 300-350 microns, number of repetitions =1200. The slices covered areas including somatosensory and visual cortices, caudate-putamen (CP), hippocampus and parietal association area (PrA). Slice-timing correction was performed using AFNI. Individual time-courses were filtered using a low-pass filter (f < 0.2 Hz), followed by quadratic de-trending. Gaussian blurring (3x3 kernel with σ = 2 pixels) was performed. The average signal from the ventricles was regressed out to reduce contributions from physiological noise. Seeds (3x3 pixels) were placed in different areas of brain and cross correlation maps were obtained in order to explore the networks in the brain. Regions with cross correlation greater than 0.25 were assumed to be 'connected' to the seed. Multiple reproducibly detectable networks were identified. In order to estimate dependence between networks, average time-course from each detected network was obtained and cross correlation values were obtained between average time-courses of different networks with a rat. T-test was used to detect any significant inter-network correlation.

Results: We identified four FC networks that were reproducibly seen in all four datasets: N1 - consisting of bilateral visual, parietal association and somatosensory cortices; N2 – consisting of bilateral hippocampal area; N3 – consisting of bilateral CP; and N4 – consisting of bilateral secondary somatosensory cortex (SII) and anterior primary somatosensory (SI) regions (fig 1). Fig 2 shows average time-courses for these networks for one of the datasets (50 s duration). It is very interesting to see multimodal connectivity in N1. While bilateral connectivity has been observed for somatosensory and visual cortices [2, 3, 4], correlation between these two modalities has not been explored in rats. Connectivity of somatosensory and visual areas with association cortex might indicate a network involved in multisensory integration. This explanation is supported by the existing knowledge of anatomical connections of parietal cortex with somatosensary and visual areas [5]. N2, consisting of bilateral hippocampus, might be involved in memory organization. It is noteworthy that a network consisting of bilateral hippocampus has been reported in human subjects as well, which suggests conservation of this network across these two species [6].The connectivity observed in this network may be important in the context of future experiments related to learning and memory. N3 has previously been reported by [3] and was robustly detected in our experiments. Interestingly, while N4 contains SII and frontal somatosensory areas, other areas of SI including the forepaw region are part of a different network (N1). Statistical tests showed that significant correlation did not exist between the networks with exception of N2 and N3, which exhibit weak but significant correlation (correlation = 0.1454, p-value = 0.004). This might be caused by residual noise contribution they might share. Also, inclusion of more datasets would give more reliable statistics.

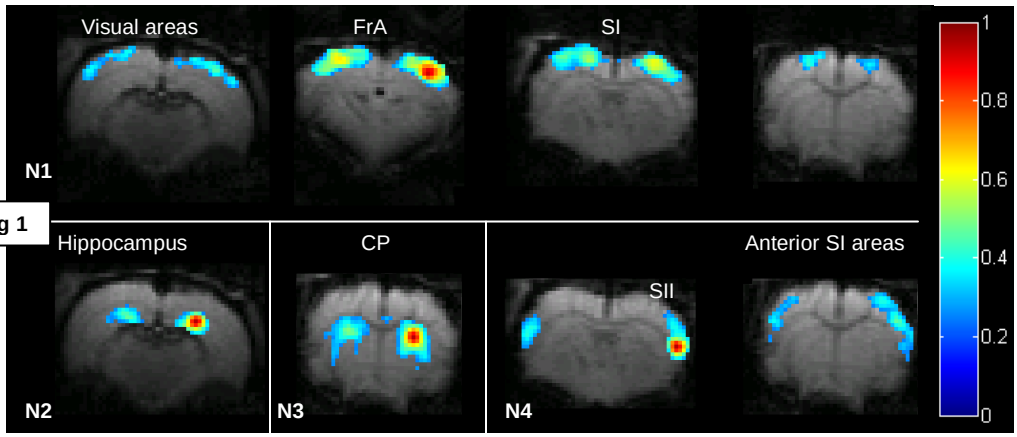

Fig 1

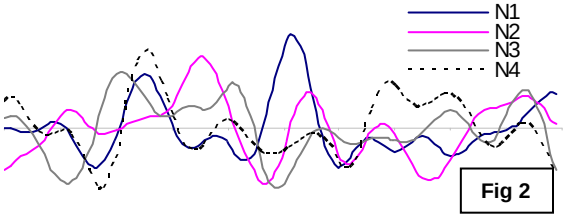

Fig 2

This work demonstrates that multi-slice data can successfully be used to detect multiple functional networks in the anesthetized rat, similar to the variety of networks observed in human studies. The excellent sensitivity achieved in this study might be attributed to high SNR, large number of repetitions and relatively low TR. Future experiments will focus on utilizing the rodent model to explore the neural basis of functional connectivity.

References: : [1] Biswal, B et al. Magn Res Med 1995; 34:537-541
[2] Williams, K et al. Proc ISMRM 14 (2006); Abstract 2119
[3] Zhao, F et al. NeuroImage 2008; 39 (1):248 -260
[4] Pawela CP et al. Magn Res Med 2008 ; 59:1021-1029
[5] Reep RL et al. Exp Brain Res 1994; 100:67-84
[6] Stein T et al. Am J Neuroradiol 2000 ; 21 :1397-1401