Specific versus Nonspecific Connectivity: A Transition of the Resting Network from Light to Deep Anesthesia

X. Liu[1,2], X-H. Zhu[1], Y. Zhang[1], and W. Chen[1,2]
[1]CMRR, radiology, University of Minnesota, Minneapolis, MN, United States, [2]Biomedical Engineering, University of Minnesota, Minneapolis, MN, United States

Introduction Coherent spontaneous hemodynamic fluctuations have been widely observed in many brain networks of different species, and they were hypothesized to reflect underlying "functional connectivity" [1] of the brain and imply many "resting networks" [2]. Since it is known that the anesthesia can significantly affect brain activity and state; it can probably also influence these resting networks. Previous studies [3-4] have demonstrated that the magnitudes of spontaneous blood-oxygen-level-dependent (BOLD) and cerebral blood flow (CBF) fluctuations in deeply anesthetized rats decreased as the isoflurane concentration increased. However, the significance of these studies was limited by the narrow range of anesthesia depths (1.8~2.2% isoflurane). To better understand how the depth of anesthesia can affect spontaneous hemodynamic fluctuation, BOLD signals were acquired from rats under a much wider range of anesthesia (1.0 to 1.8% isoflurane) in the present study; and the modulation of the resting networks at different anesthesia levels were examined base on the spatiotemporal correlations of spontaneous BOLD fluctuations.

Methods All experiments were performed on a 9.4T horizontal animal magnet (Magnex Scientific, UK) interfaced with a Varian INOVA console (Varian Inc., Palo Alto, CA). Five consecutive gradient-echo planar image (GE-EPI) slices covering somatosensory cortex (Bregma -4.3 to 0.7 mm [5]) were acquired (FOV = 3.2×3.2 cm^2; TR/TE = 612/16.5 ms; 64×64 matrix size; 1 mm thickness, and 550 image volumes) when rats were in uniform darkness (regarded as the resting-state). For each anesthesia level of ~1.0%, ~1.5%, and ~1.8% isoflurane (we defined as ISO 1.0, ISO 1.5, and ISO 1.8 conditions, respectively), the GE-EPI data acquisition was repeated 3 ~ 4 runs. For each run, three correlation maps were created with respect to three different reference regions: the left and right S1FL (primary somatosensory cortex, forelimb region) and the right S1BF (primary somatosensory cortex, barrel field) [5]. Each correlation map within a region of interest (ROI) covering left-hemispheric cortex was projected (by averaging) to a line orthogonal to the brain midline, therefore we can obtain a profile describing how the correlation to a reference region changes along this line under various conditions.

Results Nine correlation maps and the BOLD time courses of the corresponding reference regions from a representative rat are demonstrated in Fig. 1. Under ISO 1.8 condition with deep anesthesia, the correlation maps show very strong temporal correlations over the whole cortical regions, as well as some sub-cortical regions; and the relocation of the reference region did not change the pattern of correlation map. The BOLD time courses show some triangle-shape bumps, which are highly synchronized over different reference regions; and it is similar to the CBF signals acquired in previous studies under the same anesthesia level [3-4]. In contrast, the BOLD correlations under ISO 1.0 condition become much more specific within particular networks. The correlation map with respect to the right S1BF reference mainly covers the bilateral S1BF regions, while those with respect to the bilateral S1FL is limited to more centralized S1FL regions. The BOLD signals still show strong spontaneous fluctuations but with distinct temporal characteristics among different networks. In terms of specificity, the correlation map under ISO 1.5 condition seems to sit between ISO 1.0 and ISO 1.8 conditions, however, the fluctuation magnitude of BOLD signals was smallest.

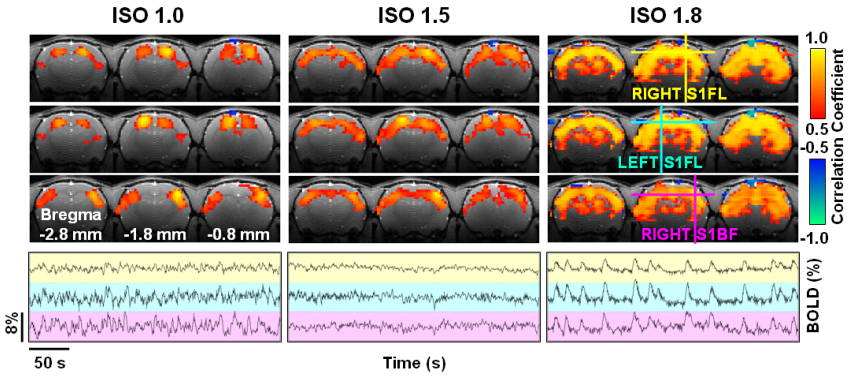

Fig. 1 BOLD correlation maps and time courses from a representative rat. The top three rows are correlation maps with respect to the bilateral S1FL (yellow and blue cross) and the right S1BF (magenta cross) regions, respectively. The BOLD time courses of these reference regions are plotted on backgrounds with corresponding color at the bottom row.

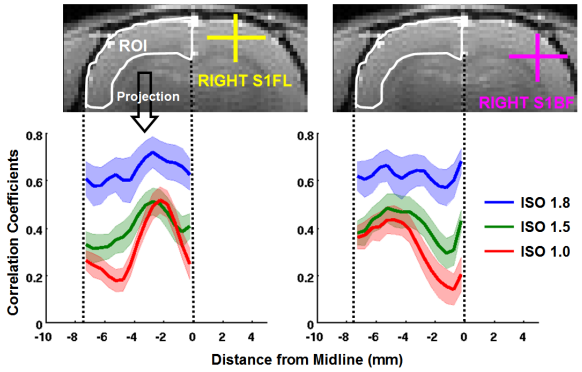

Fig. 2 Correlation map profiles along a line orthogonal to the brain midline with respect to the S1FL (left panel) and S1BF (right panel), respectively. Shadows represent the standard errors.

Figure 2 summarizes the correlation profiles along the direction orthogonal to the midline (central fissure) averaged over all four rats. The profiles are quite uniform under ISO 1.8 condition across a large cortical region, but show well-defined, sharp peaks at the position symmetric to the reference regions under ISO 1.0 condition. This result is consistent with the observations in Fig. 1.

Discussion In this study, a specific-to-nonspecific transition of the resting network from light to deep anesthesia was observed in rat sensorimotor cortical regions. This observation is partially supported by a previous electrophysiological study [6], which demonstrated the deeply anesthetized brain will response to external stimuli globally and non-selectively. According to a new theory [7], deep anesthesia can disrupt the repertoire of neural activity patterns and thus limit the brain's information capacity, even though the information may still be integrated globally. Our results support this theory from a spatial perspective by showing that the deep anesthesia disrupted the specific patterns of the resting networks, even though the global synchronization is actually increased. They also suggest that both temporal BOLD correlation and map specificity are essential for understanding "functional connectivity" under various physiological conditions.

Acknowledgement This works is supported in part by NIH grants NS41262, NS57560, P41 RR08079 and P30NS057091; and the KECK foundation.

References [1] *Biswal B. et al. MRM 1995* [2] *Mantini D. et al. PNAS 2007* [3] *Liu X. et al. ISMRM 2008 p755* [4] *Liu X. et al. ISMRM 2009 p123* [5] *Paxinos G et al, The Rat Brain in Stereotaxic Coordinates 1998* [6] *Hudetz AG.et al. Anesthesiology 2007* [7] *Alkire MT. Et al. Science 2008.*