Comparison of Spontaneous Electrophysiological and fMRI Fluctuations during Rest in Rat Brain Cortex

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ABSTRACT Resting state fMRI has been used to demonstrate that the spontaneous hemodynamic resting state fluctuations (RSF) are spatially synchronous among the functionally related brain regions (e.g., bilateral sensorimotor cortex). This finding has been interpreted as evidence of neural connectivity between discrete brain regions.[1] And thus far, the synchronous low-frequency phenomena have been utilized by many, mainly to visualize the functional connectivity between various brain regions and to determine the spatial disruption of connectivity in neural diseases.[2,3] Despite these advances, the relevance of RSF to overall neural activity and functional connectivity remains unclear. In this study, we plan to use electrophysiological measurements to detect the presence of resting state electro-cellular activity, so as to provide a basis for understanding whether these fluctuations are derived from synchronous neuronal modulation or are the result of a direct vascular response.

MATERIALS AND METHODS Four normal healthy Sprague-Dawley rats (~300g) were used for the RSF acquisition by electrophysiological recording and resting state fMRI. Electro-cellular activities were recorded at the cortical level for detecting electrophysiological RSF (n=2). The local field potential (LFP) was recorded at the sampling rate of 2000 Hz for 90 sec. Two one-dimensional electrodes, each with multiple contacts (23 contact points with 0.1mm separation between each contact) spanning through the entire cortical depth, were used bilaterally for simultaneous recordings from both left and right sensorimotor cortices (Figure 1). Each LFP time course obtained from a single contact point was low-pass filtered (< 80Hz) for further analyses. In different sets of animals (n=2), resting state BOLD fMRI activities were using echo planar imaging (EPI) pulse sequences (9 x 1mm slices: TR/TE = 3700/15 ms) at 9.4 T. During both the electrophysiology and the fMRI sessions, mechanically ventilated rats were anaesthetized with the continuous infusion of alpha-chloralose and pencuronium. Prior to the correlation analysis, each voxelwise fMRI time course was detrended to the third order and bandpass-filtered between 0.02 and 0.25 Hz.

RESULTS AND DISCUSSION Our goal was to determine the electro-cellular source of resting state functional connectivity by confirming bilateral signal synchrony and/or interference patterns using resting state electrophysiological recordings at the cortical level. Fig. 1 shows a typical correlation map derived from resting state BOLD fMRI time courses, exhibiting voxels that are temporally synchronous with neighboring voxels. The significantly correlated regions are predominantly distributed in bilateral cortices (Fig. 1). For the analysis of electrophysiological signals, spectral density was calculated to reveal frequency components of LFP. Fig. 2a shows the representative Fourier transform of a typical LFP time course measured from the middle of cortex (contact depth ~ 1-2 mm). Multiple peaks demonstrate the presence of spectral components below 2 Hz, revealing quantifiable low-frequency electrical activities. Moreover, cross-correlation coefficients between multiple cortical layers in both left and right hemispheres were calculated to reveal whether the inter-hemispheric connectivity is based on electro-cellular activity (Figure 2b). The cross-correlation analysis between LFP time courses showed significant inter-hemispheric interactions. Fig. 2b depicts correlation coefficients between left and right sensorimotor cortices and between time courses acquired from each contact point (i.e., 23 from left x 23 from right), showing specific cortical layers that either positively (red) or negatively (blue) correlate with other cortical layers in the opposite hemisphere. Such significant inter-hemispheric correlation patterns throughout the entire cortical depth were consistent in two rats. Although further studies are warranted for unraveling direct sources of RSF, the current results imply that electro-cellular activities at one sensorimotor cortex may significantly affect the distant sensorimotor cortex in the other hemisphere, suggesting a neural basis of resting state functional connectivity.

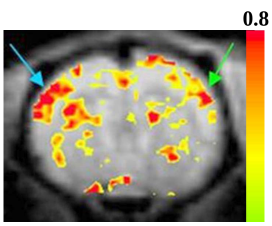

Figure 1. Functional map of coherent RSF activity using the BOLD signal time course band-pass filtered between 0.02 and 0.25 Hz. Blue and green arrows indicate bilateral sensorimotor cortices where the electrodes were inserted.

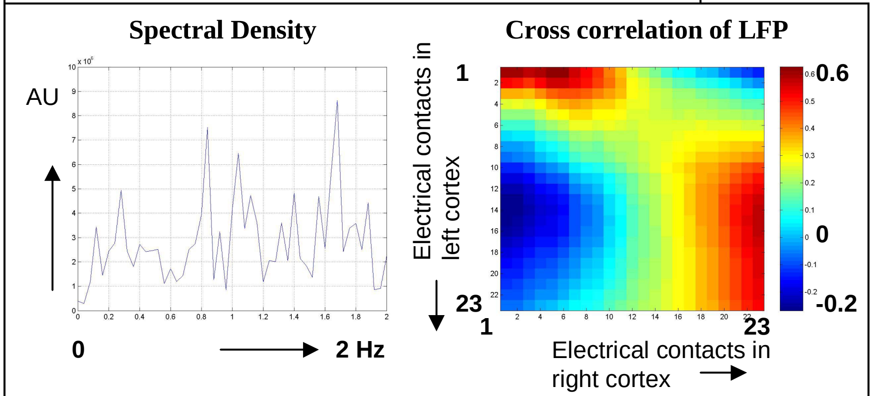

Figure 2. Frequency spectrum of resting state LFP time courses **(a)** and correlation coefficients between the left and right sensorimotor cortices using 23 electrode contact points (1 - near the cortical surface and 23 – deep cortical layer with 0.1 mm separation between each contact) spanning the entire cortical depth (~2.5 mm) **(b)**: sampling frequency and duration - 2000 Hz and 90 sec.

REFERENCES

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