Neural Origin of the Interhemispheric Functional Connectivity Loss after Complete Corpus Callosotomy

Russell W. Chan[1,2], Iris Y. Zhou[1,2], Y. X. Liang[3], Yong Hu[4], K. F. So[3], and Ed X. Wu[1,2]

[1]*Laboratory of Biomedical Imaging and Signal Processing, The University of Hong Kong, Hong Kong SAR, China,* [2]*Department of Electrical and Electronic Engineering, The University of Hong Kong, Hong Kong SAR, China,* [3]*Department of Anatomy, The University of Hong Kong, Hong Kong SAR, China,* [4]*Department of Orthopaedics & Traumatology, The University of Hong Kong, Hong Kong SAR, China*

INTRODUCTION: Resting-state functional connectivity MRI (RSfcMRI) is the measure of spontaneous fluctuations in the BOLD signal [1]. It was reported that resting-state networks were characterized by specific electrophysiological signature [2]. Moreover, it was suggested that resting-state spontaneous fluctuations were correlated with delta oscillations using different anesthesia levels as a model [3]. Previously, a case study reported that complete transection of the corpus callosum induced loss of interhemispheric correlations in RSfcMRI [4]. However, the results were limited by the lack of any electrophysiological recordings. Therefore, it could not be excluded that the loss of interhemispheric correlations in RSfcMRI might arise due to non-neuronal physiological modulations. In this study, intra-cortical electroencephalography (EEG) signals were recorded in the complete corpus callosotomy rats to understand the neural origin of the loss of interhemispheric correlations in RSfcMRI.

MATERIALS AND METHODS: Animal Preparation: Male adult Sprague-Dawley rats (250g, 3 months, N=5) were subjected to complete transection of the corpus callosum. The sham group (N=6) were subjected to skull opening. The subjects were MRI scanned at one month post-surgery under mechanical ventilation with 1% isoflurane anesthesia. Intra-cortical EEG recordings were collected from all of the subjects three days after the MRI experiments. **MRI Protocol:** All MRI measurements were acquired utilizing the 7 T Bruker scanner using a surface coil. RSfcMRI was acquired using a single-shot GE-EPI sequence with TR/TE=1000/18ms, flip angle=30°, FOV=32×32mm^2, MTX=64×64, 9 1mm slices, and a total of 400 data points. RARE T2W images were acquired with TR/TE=4200/36ms as anatomical reference for EPI images. **EEG Procedure:** Four holes were opened in the skull at the bilateral visual cortex (6.5mm posterior to bregma and 4mm from the brain midline) and bilateral somatosensory cortex (0-0.5mm posterior to bregma and 3-3.5mm from the brain midline). One EEG electrode was inserted onto the nose of the subject, working as the ground. Four electrodes were inserted into the rat brain through the respective holes. The left somatosensory electrode was treated as the reference. EEG signals were continuously recorded for at least 20mins with 1% isoflurane anesthesia. EEG signals were sampled at 10 kHz. **Data Analysis:** All RSfcMRI data were compensated for slice timing, detrended, realigned as well as temporally low-pass filtered to obtain low frequency fluctuations. Subsequently, inter-animal co-registration was performed. The visual network was obtained using GIFT v1.3h (Group ICA Toolbox). All EEG data were notch filtered at 50 Hz and band-pass filtered into 6 different frequency bands: wide (0.1-100Hz), delta (1-4Hz), theta (5-8Hz), alpha (9-12Hz), beta (13-30Hz) and gamma (30-100Hz). Subsequently, the signals were down-sampled into 200 Hz, and Hilbert transform was applied to quantify the power of EEG signals. Lastly, the EEG signals were truncated into 400 seconds segments to match the RSfcMRI data and correlation coefficients were calculated. Statistic evaluation was conducted using t-test and results were considered significant when $p<0.05$ (*, ** and *** denote paired t-test was applied with $p<0.05$, $p<0.01$ and $p<0.001$ respectively; #, ## and ### denote heteroscedastic t-test was applied with $p<0.05$, $p<0.01$ and $p<0.001$ respectively.)

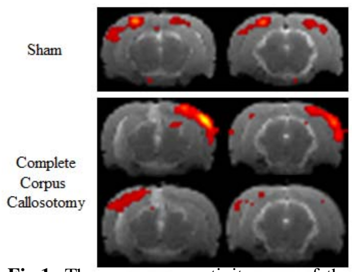

Fig.1: The mean connectivity map of the visual network obtained with ICA. It is observed that interhemispheric correlation was present in the sham group. However, it was absent in complete corpus callosotomy group.

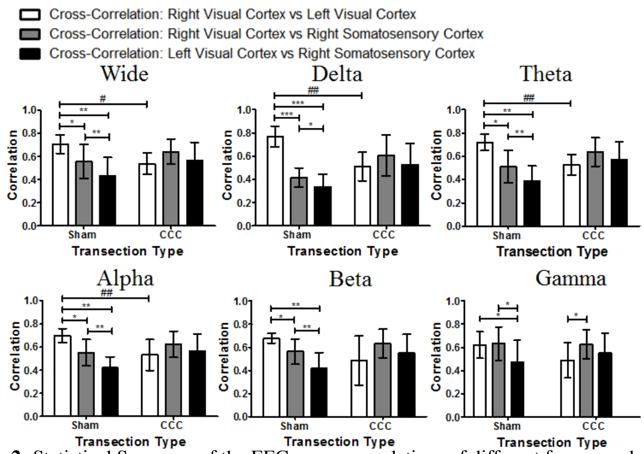

Fig.2: Statistical Summary of the EEG power correlations of different frequency bands

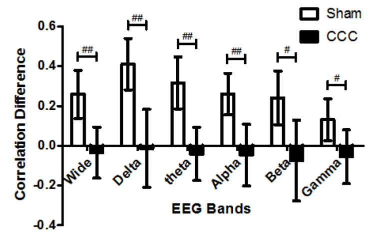

Fig.3: Statistical summary of the correlation difference between the correlation of the bilateral visual cortex and the correlation of the left visual cortex vs right somato- sensory cortex.

RESULTS: Fig.1 shows the functional connectivity maps covering the bilateral visual cortex in the sham group as well as the complete corpus callosotomy (CCC) group. The interhemispheric correlation of the bilateral visual cortex was present in the sham group. However, it was absent in the CCC group. The EEG power correlations of different frequency bands are summarized in Fig.2. The interhemispheric correlation of the bilateral visual cortex was significantly higher for the sham group in the wide, delta, theta and alpha frequency bands, compared to the CCC group. The difference between the correlation of the bilateral visual cortex and the correlation of left visual cortex vs right somatosensory cortex is shown in Fig.3. The sham group showed significantly higher correlation difference in all frequency bands when compared to CCC group. Fig.4. shows the scatter plots of EEG power correlation of the bilateral visual cortex against resting-state correlation coefficient of the bilateral visual cortex.

DISCUSSION AND CONCLUSION: Visual cortex is connected to its interhemispheric homologous via axonal connection through the corpus callosum. Disrupting the callosal connection of visual cortex led to the loss and decrease of interhemispheric correlation of the bilateral visual cortex detected in RSfcMRI and EEG respectively. Moreover, previous studies have suggested that resting-state spontaneous fluctuations are correlated with delta oscillations using different anesthesia levels as a model [3]. In this study, the results in Fig.3 and Fig.4 indicated that delta band had higher correlation with resting-state connectivity, which was similar to previous findings. Unlike previous anesthesia model, the current complete corpus callosotomy model provided drastic loss in interhemispheric correlations in RSfcMRI and could serve as an alternative model in studying the relationship between EEG and RSfcMRI. In conclusion, our results clearly supported that the loss of interhemispheric correlations in RSfcMRI reflects the changes in spontaneous brain activity and its coherence. Moreover, the results strongly indicated that resting-state spontaneous fluctuations have strongest correlation with delta oscillations.

REFERENCES: 1. Fox MD, Nat Rev Neurosci. 2007. **2.** Mantini D, Proc Natl Acad Sci 2007 **3.** Lu H Proc Natl Acad Sci 2007 **4.** Johnston JM, J Neurosci. 2008

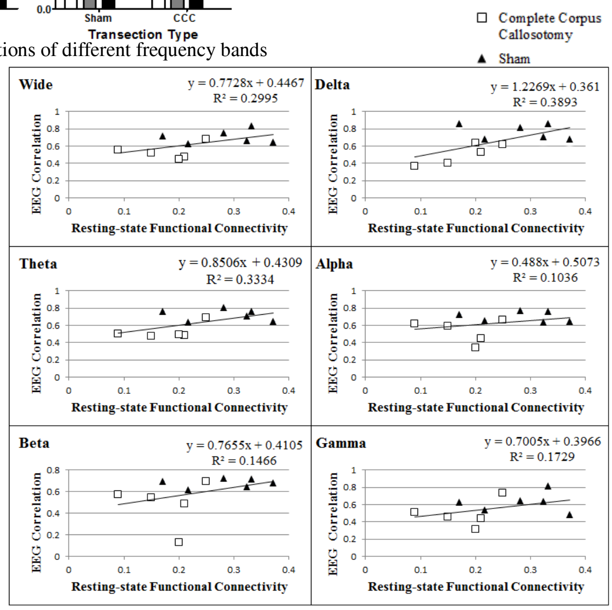

Fig.4: Scatter plots of different frequency bands of EEG power correlation against resting-state correlation coefficient of the bilateral visual cortex. Linear regression was applied and the R^2 was calculated.