# Resting-state Functional Connectivity Altered by Complete and Partial Corpus Callosotomy in Rats

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## INTRODUCTION

The spontaneous fluctuations in the BOLD signal of fMRI reveal functional connectivity networks in brain during rest [1]. This so-called resting-state functional connectivity MRI (rsfMRI) has been increasingly used in the diagnosis of a variety of brain diseases including Alzheimer's, schizophrenia and autism [2]. However, the exact underlying mechanism of the spontaneous fluctuations in rsfMRI signals is still under debate. Thus the interpretation of changes in connectivity becomes a critical issue. One assumption is that functional connectivity may reflect the anatomical connection via axonal projections through corpus callosum (CC). Human studies with callosal agenesis and corpus callosotomy (in a single patient) reported the reduced and loss of interhemispheric correlation in rsfMRI, respectively [3, 4]. Recently, our group has examined the role of CC in interhemispheric functional connectivity using a rat model of complete corpus callosotomy and showed loss of intercortical connections [5]. In this study, we investigated the effects of complete, and more importantly, partial transection of corpus callosum on rsfMRI signal.

## MATERIALS AND METHODS

***Animal Preparation:*** Adult Sprague-Dawley rats (220~250g, 3 months, N=26) were divided into 4 groups. Group 1 (N=8): complete transection of the CC, Group 2 (N=6): anterior partial transection from genu to the central body of CC, Group 3 (N=6): posterior partial transection from posterior CC body to splenium, Group 4 (N=6): skull opening only. At 7 days after surgery, animals were MRI scanned under mechanical ventilation with isoflurane anesthesia (1%). ***MRI Protocols:*** All MRI experiments were conducted using a 7 T Bruker scanner with a surface coil. Six resting-state fMRI acquisitions were performed using a single-shot GE-EPI sequence with TR/TE=1000/18ms, flip angle=30°, FOV=32×32mm$^2$, 64×64 matrix, nine 1-mm-thick contiguous slices and a total of 280 data points. RARE T2W images were acquired using TR/TE=4200/36ms as an anatomic reference for EPI data. ***Data Analysis:*** All rsfMRI data was slice-timing corrected, co-registered, detrended and temporally low-pass filtered. Group independent component analysis (ICA) was performed using GIFT v1.3h Toolbox. The number of components was set at 37 and the spatial maps of independent components were scaled to z scores with a threshold of z>2 (correlation coefficient >0.35).

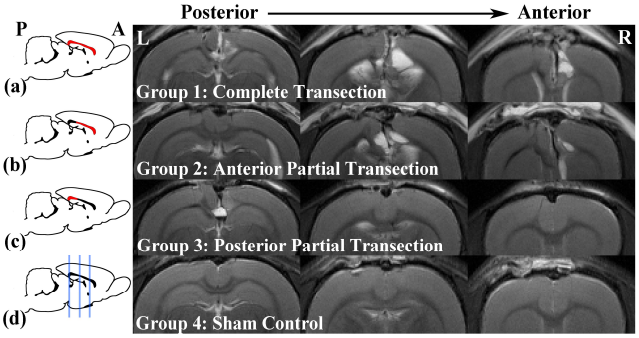


**Fig.1** Representative T2W images from the animals with complete (**a**), anterior partial (**b**), posterior partial (**c**) transection of corpus callosum (CC) and sham control (**d**). The disrupted part of CC was indicated in red color in the sagittal plane with the blue lines indicating the corresponding locations of T2W slices in the right panel.

## RESULTS

Fig. 1 shows the T2W images for the representative animals in each group. Fractional anisotropy (FA) maps (obtained from DTI protocol - not shown) indicated the fiber disruption in corresponding CC regions, validating the surgery. Fig. 2 shows the two typical sets of functional connectivity maps with the components covering somatosensory cortex and visual cortex, respectively, from one animal in each group. In animals from Group 1, the interhemispheric correlations in both networks that were present in the sham animals from Group 4 were prominently absent (Figs. 1a and 1d) while the intrahemispheric connections were preserved. The loss of intercortical connection in somatosensory network was found in animals from Group 2 (Fig. 2b left). However, such loss was not observed in Group 3 animals (Fig. 2c left). In contrast, the connection in visual cortex remained intact for the Group 2 animals (Fig. 2b right), while this interhemispheric correlation diminished in rats from Group 3 (Fig. 2c right).

## DISCUSSION AND CONCLUSION

The corpus callosum contains interhemispheric connections for the somatosensory and visual cortices [6], the two spatially independent connectivity networks examined in this study. Therefore, the loss of interhemispheric correlations in these two networks after complete CC transection indicates the crucial role of CC in the spontaneous neural activity within the two hemispheres. Moreover, histological study showed that different cortical regions are connected via different parts of CC [7]. For example, somatosensory cortex projects fibers through the anterior CC body while axons from visual cortex pass through the large portion of the CC as well as splenium. Therefore, our findings that partial CC transection disrupted only the specific intercortical functional connection that is known to be anatomically connected through CC further suggest that the spontaneous fluctuations in rsfMRI signal largely reflect the anatomical connections. Further studies combining fiber tracking using DTI or/and histology are needed to assess the correlation between axonal projections and functional connectivity. In conclusion, the experimental results of this study provide direct evidence for the essential role of CC in spontaneous neural activity detected by resting-state fMRI.

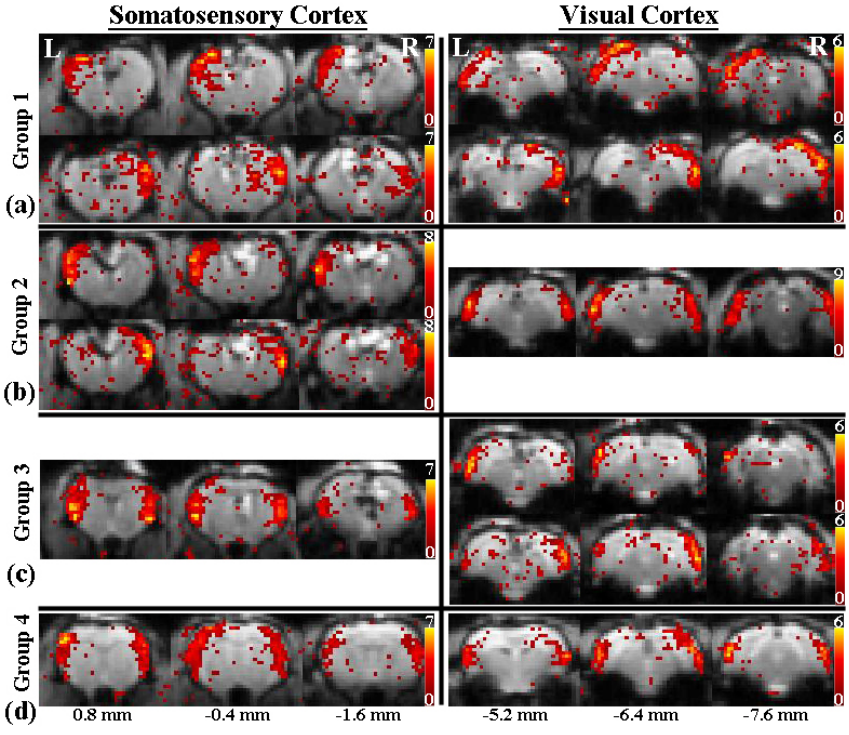


**Fig.2** Typical functional connectivity maps with the components covering somatosensory cortex and visual cortex, respectively, from animals with complete (**a**), anterior partial (**b**), posterior partial (**c**) transection of CC and sham control (**d**). Distance to Bregma for each slice is labeled at bottom.

## REFERENCES

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