Restoration of Interhemispheric Resting-state fMRI Connectivity after Patrial Corpus Callosotomy via Intrahemispheric Reorganization

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INTRODUCTION Resting-state fMRI (rsfMRI) has been increasingly applied to the studies of brain functional organization under normal and pathological conditions[1]. Recently, it also has shown potentials in revealing the functional plasticity after brain injury and training[2,3]. Our previous study on a rat model of corpus callosotomy has directly demonstrated that disrupted rsfMRI connectivity can be partially restored atop the axonal connections as indispensable foundation[4]. However, the underlying mechanism and spatial characteristics of such plasticity in rsfMRI connectivity are yet fully understood. In this study, we further investigated the rsfMRI network reorganization after complete and partial callosotomy, aiming to identify the rewiring mechanism and topological alterations of rsfMRI networks if any.

METHODS Adult Sprague-Dawley rats (230~270g) underwent complete corpus callosotomy (N=11), posterior partial corpus callosotomy (N=8) and sham surgery (N=8), respectively. At day 7 and 28 after surgery, rsfMRI was conducted on rats that were menchanically ventilated with 1~1.5% isoflurane. rsfMRI data was acquired on a 7T Bruker scanner using single-shot GE-EPI with TR/TE=1000/18ms, FOV=32×32mm^2, 64×64 matrix and 9 contiguous 1-mm slices. All rsfMRI data was slice-timing corrected, realigned, detrended, temporally band-pass filtered and then co-registered to a common template. rsfMRI connectivity maps in primary somatosensory cortex (S1) and primary visual cortex (V1) were generated using seed-based analysis (SBA) by calculating voxel-wise correlation coefficient (r) with the mean time series from the 2×2-voxel seed in left/right S1/V1.

RESULTS At day 7, disrupted interhemispheric connectivity was observed in the specific cortical areas whose callosal connections were severed, ie. in S1 and V1 of complete callosotomy group and in V1 of posterior partial callosotomy group (**Fig.1**). At day 28, the diminished interhemispheric connectivity in V1 was restored in partial but not in complete callosotomy group (**Fig.1&2**). Increased intrahemispheric connectivity between S1 and V1 were found in both callosotomy groups using rsfMRI and intracortical EEG recording. Moreover, both callosotomy groups exhibited apparent expansions in intraregional rsfMRI connectivity as compared to sham, indicated by the increased sizes of the clusters covering the seeds (**Fig. 1**). Such expansions were directional as shown by the shift of the isocenters of the clusters covering S1/V1 seeds (**Fig. 3**).

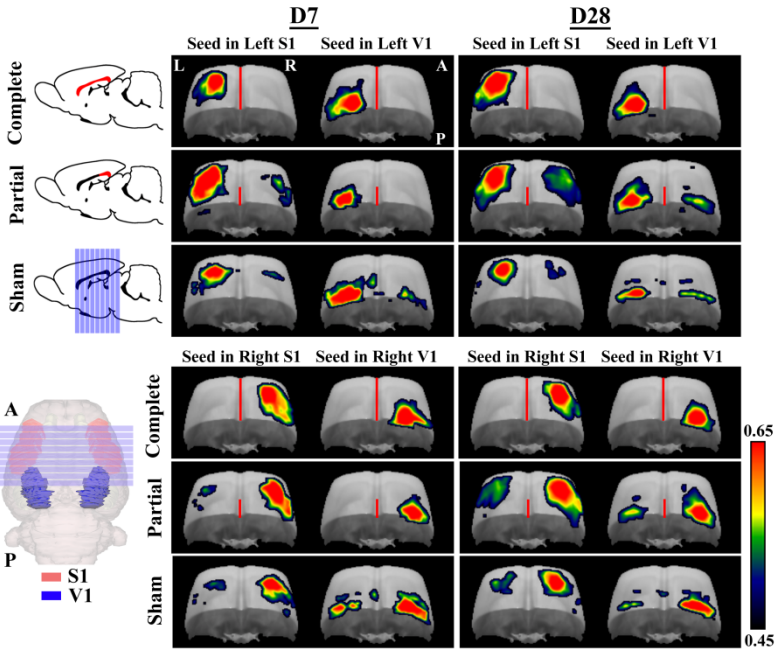

Fig. 1 3D visulization of averaged rsfMRI connectivity maps from animals with complete, posterior partial callosotomy and sham surgery at post-surgery day 7 and day 28. The seeds were centered at left/right primary somatosensory cortex (S1)/primary visual cortex (V1), respectively. The transected part of the corpus callosum is indicated in red in the sagittal planes (top left panel) and the anatomical regions of S1 and V1 are highlighted in 3D atlas space (bottom left panel). At day 28, both callosotomy groups exhibited apparent expansions in intraregional rsfMRI connectivity as compared to sham, as indicated by the increased sizes of the clusters covering the seeds.

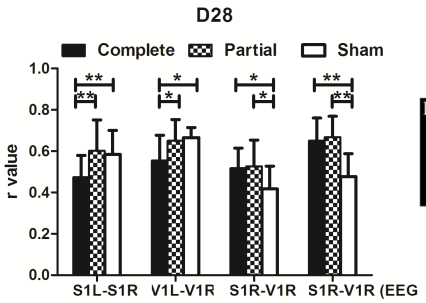

Fig. 2 Correlation coefficients calculated between the rsfMRI time courses of the seeds, showing interhemispheric functional connectivity in S1 (S1L-S1R) and V1 (V1L-V1R), intrahemispheric connectivity (S1R-V1R) and correlation analysis of wide-band power from intracortical EEG recording in S1R and V1R at post-surgery day 30. ttest*p<0.05, **p<0.01.

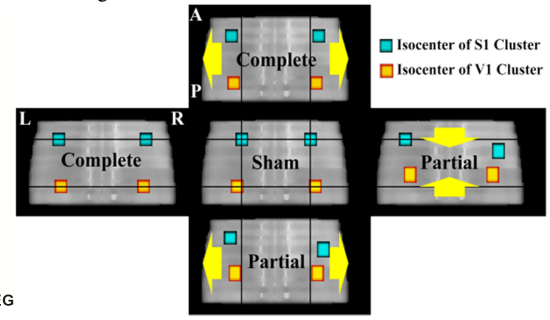

Fig. 3 The isocenters of the clusters (r>0.5) covering S1/V1 seeds in averaged rsfMRI connectivity maps were estimated to reveal any directional expanisions in the intraregional connectivity at day 28 and were overlaid on the topview of the cortical surface. Both callosotomy groups showed the lateral shift of the isocenters of S1 clusters. The partial callosotomy group also exhibited the posterior shift of S1 clusters and anterior shift of V1 clusters, indicating the two networks expanded intrahemispherically towards each other.

DISCUSSION AND CONCLUSION The restoration of disrupted interhemispheric connectivity was found in partial but not in complete callosotomy group. Given the significantly increased intrahemispheric connectivity between S1 and V1 in partial group revealed by both rsfMRI and EEG, such restoration may result from the compensation through intrahemispheric reorganization together with the interhemispheric axonal pathways crossing the remaining intact corpus callosum. This possible mechanism can be further supported by the findings of directional expansions in intraregional rsfMRI connectivity towards each other in both S1 and V1 networks. Therefore, the large-scale rsfMRI networks undergo dynamic changes and may rewire via indirect route involving not only axonal and but also synaptic connections[5]. The plasticity of rsfMRI netwroks were also found in complete callosotomy group, showing increased intrahemispheric connectivity along with lateral expansion towards the secondary somatosensory. In conclusion, our findings directly support that resting-state networks can be plastic atop the structral connections and the restoration of disrupted interhemispheric connectivity may stem from the increased intrahemispheric connectivity.

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