The influence of carbon dioxide on brain functional homotopy using resting-state fMRI
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Target Audience: Scientists and physicians who are interested in brain networks using resting state functional MRI (RS-fMRI) and its clinical applications.

Purpose: Homotopy is a fundamental characteristic of the intrinsic functional architecture of the human brain. Recently, such a high degree of interhemispheric synchrony can be estimated based on spontaneous activity by use of resting state fMRI (RS-fMRI) with blood oxygenation level dependent (BOLD) technique 1. Regional homogeneity (Reho) is another brain characteristic signifying local brain tissue synchronization, which can be measured with RS-fMRI 2. Carbon dioxide (CO2) is a potent vasodilator and has been known to cause cerebral blood flow (CBF) and BOLD signal changes. In this study, we have evaluated how CO2 breathing can influence brain functional homotopy and Reho in healthy brains in order to better understand physiologic respiratory noise of RS-fMRI data.

Materials and Methods: Fourteen healthy controls (8 male and 6 female, 27.6 ± 6.4 years old) participated in this hypercapnia study. Two 5-minute long RS-fMRI standard BOLD scans were performed at 3T MR with TR/TE=1500/25ms, FOV=220×220mm², matrix=64×64, number of slices=33, slice thickness=3mm, and 200 measurements. The first one was acquired under a normocapnia condition (breathing room air) and the second under a hypercapnia condition (breathing a mixture of 5% CO2, 21% O2, and 72% N2). Enough time was given between the two functional runs in order to allow end tidal CO2 (EtCO2) level to reach equilibrium, which was monitored and recorded throughout the experiment on a MEDRAD system. In addition, a high resolution anatomical T1 image was acquired for image co-registration and segmentation. RS-fMRI data were processed using the Configurable Pipeline for the Analysis of Connectomes (C-PAC, fcp-indi.github.com) to generate voxel mirrored homotopic connectivity (VMHC) and Reho at normocapnia and hypercapnia conditions. The average across gray matter voxels within regions defined by the MNI structural atlas 3 was taken. Values were compared using a paired Student’s t-test and a p value <0.05 was considered significant.

Results: The average EtCO2 increased significantly from the normocapnia to hypercapnia condition (40.15 ± 2.63 to 47.39 ± 2.74 mmHg, p<0.01). A significant decrease in global gray matter VMHC (Figure 1) is seen under hypercapnia versus normocapnia conditions (p<0.001) at resting state, and also in the regions indicated in Figure 2 except for thalamus, caudate, and cerebellum. A significant global gray matter decrease was also seen in Reho (p<0.002), predominantly in the frontal and parietal regions. However, was not as pronounced as changes seen in VMHC.

Discussion and Conclusion: Our observation of decreased brain homotopy (i.e. inter-hemispheric correlations) during CO2 breathing is consistent with previous reports that elevated arterial CO2 decreases brain connectivity, which may be secondary to general reduction in spontaneous neural activity or oxygen metabolic rate during hypercapnia 4. The changes of Reho found only in frontal and parietal regions indicate that the local synchronization (between nearest neighboring neurons) was affected by blood flow and/or neuronal activity changes, but the change is much less diffuse compared with VMHC. This study has implications on RS-fMRI data analysis methodology in dealing with effects of varied cardiac and respiratory patterns that can potentially influence blood flow and CO2 levels.


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