Frequency specificity of regional homogeneity in the resting-state human brain

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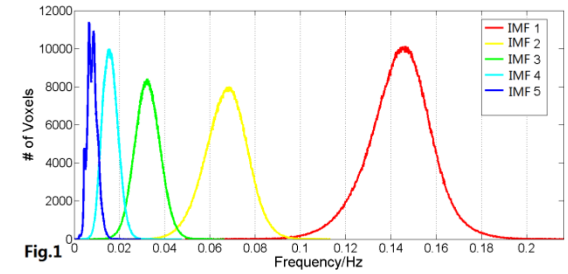
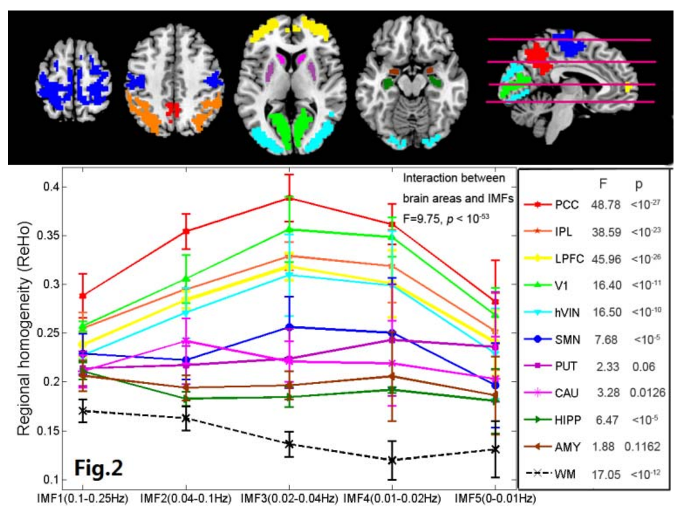


TARGET AUDIENCE. Neurologists and researchers in the field of Neuroimaging.

INTORDUCTION AND PURPOSE. In blood-oxygenation-level-dependent fMRI (BOLD-fMRI) studies, the synchronization between distant brain regions are usually measured with functional connectivity (FC), while the local coordination of brain activity can be characterized by the Regional Homogeneity (ReHo)[1]. ReHo quantifies the synchronization of the time courses of a certain voxel and its adjacent neighboring voxels. Electrophysiological studies found that gamma-band neural activity contributes to local BOLD signals, whereas low-frequency rhythms predominantly contributed to inter-areal BOLD correlations [2]. These observations implied that the neural origins of FC and ReHo may not be exactly the same. Previous studies have investigated the frequency-specific characteristics of FC; however, very few studies have explored the frequency-specific characteristics of ReHo. The purpose of this study is to decompose the original BOLD signal into distinct frequency bands in a data-driven manner and investigate the frequency-specific characteristics of ReHo.

METHODS. *MRI Data Acquisition.* FMRI data were acquired from the open source website (http://fcon_1000.projects.nitrc.org/fcpClassic/FcpTable.html). The resting state fMRI scans of all 198 healthy subjects (18-26 years, 122 females) were analyzed. Imaging was performed using a 3.0-Tesla scanner (Siemens TRIO TIM). The participants were instructed to rest with their eyes closed and not to fall asleep. A gradient echo T2*-weighted EPI sequence was used for acquiring functional images (TR/TE = 2s/30ms, matrix 64x64, FOV 240x240 mm^2, 51 axial slices, thickness/gap=3.5/1.2mm). *fMRI Data Processing.* The first 5 volumes were removed; the remaining 220 volumes were preprocessed with SPM8. A data-driven method, Empirical mode decomposition (EMD)[3], was applied in a voxel-wise fashion to adaptively decompose the time course of each voxel into several time series termed intrinsic mode functions (IMFs). Each IMF occupies a unique frequency range. The first 5 IMFs were considered here since they covered nearly the whole bandwidth of 0~0.25Hz. We then calculated ReHo in each IMF of each voxel and got five ReHo maps for each subject. A k-means clustering method was applied to the 5 ReHo maps of each subject to classify voxels into different classes. The Five ReHo values for each voxel were used as features when performing k-means clustering analysis, assigning each voxel a frequency-specific ReHo signature. Masks of different brain regions were created from the resulted clusters. The ReHo values were averaged across all the voxels within each of these masks for each subject. Group mean and standard errors (SE) of ReHo for each IMF were then determined across the 198 subjects. For comparing the group mean of ReHo in the five frequency bands (IMFs), a balanced one-way ANOVA was performed for each of the selected brain areas. For testing the effects of two factors, brain areas and frequency bands, on ReHo, a balanced two-way ANOVA was performed to examine whether there was interaction between these two factors.



RESULTS. **Fig.1** shows the frequency properties of IMFs. The histograms of frequency distribution for IMF1 to IMF5 show that each IMF occupies a unique frequency range: IMF1 (red) occupies 0.1-0.25Hz; IMF5 (blue) occupies 0-0.01Hz; with other IMFs in between. **Fig.2** shows the selected clusters and the frequency-specific ReHo in these clusters.Abbreviations: posterior cingulate cortex/precuneus (PCC), bilateral inferior parietal lobule (IPL), lateral prefrontal cortex (LPFC), primary visual area (V1), higher-order visual network (hVIN), sensory motor network (SMN), putamen (PUT), caudate (CAU), hippocampus (HIP) and amygdala (AMY). **DISCUSSION.** Our results showed that cortical areas consistently possess higher ReHo than subcortical regions across the whole frequency band. While BOLD oscillations of 0.02-0.04Hz mainly contributed to cortical ReHo, the ReHo in limbic areas involved a wider frequency range and were dominated by higher-frequency BOLD oscillations (>0.08Hz). The frequency characteristics of ReHo are distinct between different parts of the striatum, with the frequency band of 0.04-0.1Hz contributing the most to ReHo in CAU, and 0-0.02Hz contributing more to ReHo in putamen. We inferred that both the synaptic linkage types and the underlying neural activities were more diverse and heterogeneous in the brain areas for complex functions, and these diversities lead to a less homogeneity within these areas. The difference in ReHo properties between cortical and subcortical areas may hence arise from the difference in synaptic/functional/cytoarchitectonic complexity**CONCLUSION.** We have provided a new method of analyzing local activity in the frequency domain, which could reveal more information and might be more sensitive to different tasks or pathophysiological states. To the best of our knowledge, this is the first study to clarify the frequency specificity of ReHo in different brain areas. Our findings may advance the understanding of the neural-physiological basis of regional structural-functional specificity and its relationship with regional homogeneity.

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