Frequency Dependence of the Developing Brain Functional Network: MRI-EEG?

W. Gao[1], H. Zhu[2], K. Giovanello[3], K. Smith[4], D. Shen[5], J. Gilmore[6], and W. Lin[5]

[1]Department of Biomedical Engineering, University of North Carolina-Chapel Hill, Chapel Hill, North Carolina, United States, [2]Department of Biostatistics and BRIC, University of North Carolina-Chapel Hill, [3]Department of Psychology and BRIC, University of North Carolina-Chapel Hill, [4]Department of Radiology, University of North Carolina-Chapel Hill, [5]Department of Radiology and BRIC, [6]Department of Psychiatry, University of North Carolina-Chapel Hill

Introduction

While resting state functional MRI (rsfMRI) has been utilized to delineate brain functional connectivity, most of the studies to date have concentrated on signal < 0.08 Hz. Frequency-based brain network analysis on rsfMRI may offer new insights into frequency dependence of brain functional network [1]. In this study, healthy pediatric subjects at age of 2 wks to 2 yrs were recruited and rsfMRI was obtained, aiming to delineate the emerging and developing trajectory of brain functional connectivity at different frequencies of interest in a critical time period of early brain development.

Methods

71 normal subjects including 20 neonates (9M, 24 ± 12 days (SD)), 24 1-year-olds (16M, 13 ± 1 months), and 27 2-year-olds (17M, 25 ± 1 months) were included in this study. All subjects were at sleep during the imaging session. None of the subjects was sedated. Informed consent was obtained from the parents and the experimental protocols were approved by the institutional review board.

For the rfcMRI studies, a T2*-weighted EPI sequence was used with TR = 2sec, TE = 32 ms; 33 slices; and voxel size = 4x4x4 mm^3. 150 volume data were acquired to provide time series images. Anatomical images using a 3D MP-RAGE sequence were acquired with TR = 1820ms; TE = 4.38 ms; inversion time = 1100ms; 144 slices; and voxel size = 1x1x1mm^3. MP-RAGE images were used for co-registration across subjects in each age group.

The BOLD time series images were preprocessed, including time shifts, rigid body correction for head movement, and spatial smoothing (6-mm FWHM Gaussian kernel), followed by data reduction using PCA. Subsequently, the infomax algorithm was applied for ICA analysis to obtain a set of aggregate independent components for each age group. The number of components for each age group was 28, 31 and 27 for neonate, 1yr and 2yr groups, respectively, determined using the minimum description length criteria. GIFT software proposed by Calhoun et al [4] was used for group ICA.

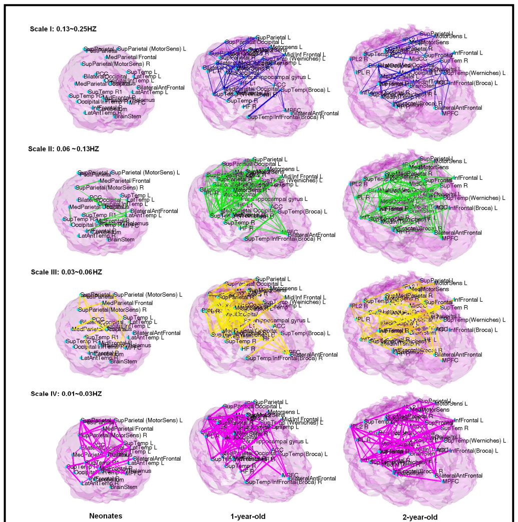
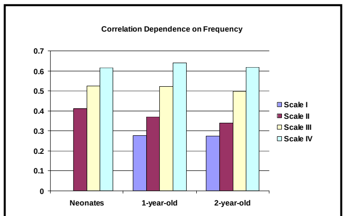
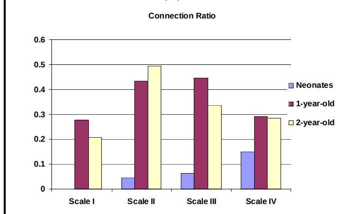


Fig.1. Brain networks at different frequency scales.



(a)



(b)

Fig.2. The mean connection strength (a) and connection ratio (b) are shown for all groups.

After removing the components associated with CSF, motion and vessels through visual inspection, ROIs were defined based on spatially un-connected regions (Z>1) in the remaining components. The mean time course of each ROI was extracted from each individual subject separately and discrete wavelet transform was applied on each regional mean time series. A correlation matrix was then calculated based on the wavelet coefficients at the first 4 scales (SI: 0.13-0.25Hz; SII: 0.06-0.13Hz; SIII: 0.03-0.06Hz; and SIV: 0.01-0.03Hz). After Fisher's Z-transform of the correlation value, one-sample t-test (two-tailed) was performed on the group mean value for each connection to determine significance at each wavelet scale. The false discovery rate (FDR) approach was applied to correct for multiple comparisons at $\alpha<0.05$.

Results

Fig.1 shows the connectivity patterns of the entire brain at different frequency scales across the three age groups. A much sparser connection is observed in neonates when compared with the remaining two age groups across all frequency scales while the differences between 1yr and 2yr olds are less evident. More quantitative assessments regarding the frequency dependence on the connection strengths (mean correlation coefficient, Fig. 2a) and connection ratio (# significant connections/# all possible connections, Fig2b) are shown in Fig. 2. The connection strength is inversely proportional to the frequency scales for all groups. In addition, the connection strengths are rather similar for each frequency scale with the exception of neonates where no connection was observed for SI. In contrast, the relation between the connection ratio and frequency is less clear. The connection ratio of neonates increases from SII to SIV. However, the relation for 1yr and 2yr groups is a bell shape with the 1yr old group exhibiting the highest connection ratio at SIII and at SII for the 2yr old group. Finally, the dependence of connection strength on frequency and anatomical distance (Euclidian distance between region centers) is shown in Fig.3. In this figure, the connections in each wavelet scale are further decomposed in to 5 different categories as those only appear at each specific scale and those appear consistently across all scales. With the exception of scale I and II in neonates, connection strengths at different scales are all significantly different from each other (p<0.05 after correction). More interestingly, the connections appeared in all frequency scales exhibit higher connection strengths and a shorter Euclidian distance.

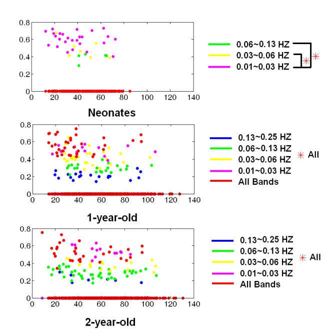


Fig.3. Dependence of connection strength on anatomical distance and frequency.

Discussion

Unlike the typically employed rsfMRI where signal<0.08 Hz is analyzed together, discrete wavelet transform was employed to determine frequency dependence on functional connectivity. Our results suggest a frequency dependence on the brain network, including the connection patterns, connection strengths and connection ratios across all ages. In addition, with the exception of neonates, both 1yr and 2yr olds exhibit cortical connectivity in SI (0.13-0.25Hz) where signal is typically disregard in previously reported studies. To the best of our knowledge, this is the first reported results on the frequency dependence of functional connectivity in the developing brain.

References

[1] Achard et al., *J Neuroscience,* 26(1), 63-72, 2006. [2] Calhoun, et al, *HBM*, 14, 140-151, 2001. [3] Bassett and Bullmore, *Neuroscientist*, 12, 512-523, 2006.