Analysis of High Frequency Resting State Networks in the Human Brain

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TARGET AUDIENCE: MR scientists and clinical researchers in the fields of neurology.

PURPOSE: Mapping of intrinsic low frequency (< 0.3 Hz) signal variations has emerged as a powerful adjunct to task-based fMRI for simultaneously mapping functional connectivity within and between dozens of resting state networks (RSNs)[1-7]. Recent advances in high-speed fMRI method development [8-16] that enable un-aliased sampling of physiological signal fluctuation have considerably increased sensitivity for mapping functional connectivity and for detecting dynamic changes over time[17-19]. As several recent studies have show, the frequency spectrum of resting state fluctuations exhibits time dynamic changes and connectivity may be detected at frequencies greater than 0.3 Hz, predominantly in visual and motor cortex. In this study we use multi-slab echo volumar imaging with 136 ms temporal resolution to compare resting state connectivity in 6 major RSNs at frequencies below 0.3 Hz and at frequencies between 0.5 and 3.6 Hz.

METHOD: Multi-slab echo volumar imaging (MEVI) data were collected in 3 healthy subjects and a patient with epilepsy (informed consent was obtained) using a 3T Siemens Trio scanner (TR/TE 136/28 ms, 5 min scan time). Data were analyzed using custom built MATLAB tools and TurboFIRE software (v5.12.4.0.2). The heart rate was determined either through Biopac data collected during the scan or from an independent component analysis of the unfiltered data. A highpass 8^{th} order Butterworth filter with 0.5 Hz cutoff frequency and a comb filter that removed the 1^{st}, 2^{nd} and 3^{rd} harmonics of the cardiac pulsation was applied. Standard preprocessing steps were applied: motion correction, spatial normalization, spatial smoothing using an $8mm^3$ Gaussian spatial filter, 8s sliding window. Six RSNs were selected using seed locations based on a group ICA study [6]: attention (ATN), auditory (AUN), default mode (DMN), frontal (FRN), sensorimotor (SMN) and visual (VSN). SCA was performed using sliding window seed-based correlation with cumulative meta-statistics [7], which as our previous studies show minimizes the effects of confounding signal changes [8] and does not require the regression of these confounds. In addition, data processed without frequency filters, using a 4 s moving average time domain filter and a 30 s sliding window with meta-statistics to map low frequency connectivity.

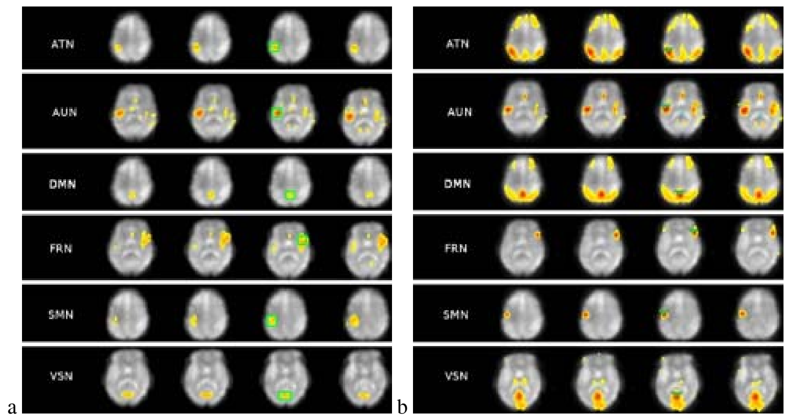

Fig. 1: Representative resting state connectivity maps in 4 consecutive slices around the seeded slice. (a) High frequency connectivity and (b) low frequency connectivity in 6 resting state networks: attention, auditory, default mode, frontal, sensory-motor, and visual. The green box indicates the seed region. Correlation threshold was set to 0.4 for all images.

RESULTS: The high frequency connectivity in the brain corresponds strongly to connectivity observed within the low frequency RSNs. However, its spatial extent appears to be much smaller than that of low frequency connectivity, which may be due to the low SNR at high frequencies. Unlike low frequency connectivity, the high frequency connectivity observed rarely crosses the corpus callosum and, if it does, the connectivity is very weak. Interestingly, connectivity at high frequencies in the auditory network was stronger than in the other high frequency networks, which may be related to our earlier observation that low frequency resting state connectivity in auditory cortex can be detected with sliding window widths as short as 1 s [21].

DISCUSSION: Our data suggest that high frequency connectivity does exist within all major RSNs previously detected at low frequencies in our data [Posse et al Front 2013]. As this study continues, we will develop an adaptive filter to account for dynamic changes in cardiac frequency during the 5 min scan. This is expected to enhance the signal to noise ratio and to allow inter-network connectivity analysis at these high frequencies. Further quantitative analysis across a larger number of subjects is currently underway to examine inter-subject variability and temporal stability of these high frequency resting state networks [20].

CONCLUSION: This preliminary study establishes resting state connectivity at frequencies > 0.5 Hz in multiple major RSNs, which may permit the observation of functional connectivity dynamics at even shorter time scales than currently feasible at frequencies < 0.3 Hz.

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