Wavelet Coherence Analysis of Functional Connectivity within Default Mode Network Employing Simultaneous MultiSlice (SMS) Resting-state fMRI

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Purpose: Resting state fMRI (rsfMRI) has been increasingly used to study functional connectivity between neuronal processes[1]. However, most rsfMRI studies are based upon a static description of functional connectivity and implicitly ignore the temporal variability in neuronal activation within the length of imaging. One of the main limitations of investigating the dynamics of functional connectivity is the poor temporal resolution in typical rsfMRI studies (TR>2 s). At this sampling rate, higher frequency physiological fluctuations (such as respiratory and cardiac pulsation) are aliased into the low-frequency band typically used for rsfMRI studies (0.01-0.1 Hz). This effect confounds the neuronal signals, making the dynamic analysis of the rsfMRI challenging. Recent advancements in data acquisition and multiband imaging techniques[2,3] have enabled whole-brain fMRI scanning at sub-second temporal resolution. This significant improvement in rsfMRI bandwidth un-aliases the respiratory and cardiac components and provides the opportunity to study the functional connectivity that may present in components of the rsfMRI signal above 0.1 Hz[3]. In an effort to study the dynamics of functional connectivity, we studied the time-frequency dynamics of the default mode network (DMN) at a temporal sampling rate of 350 ms at two frequency bands: 0.01-0.1 Hz and above 0.1 Hz using the wavelet coherence approach. Wavelet coherence is a method for analyzing the coherence between two time series as a function of both time and frequency[4,5].

Methods: Six healthy volunteers (36±15 years; range 25-62) were included in this study. Subjects were scanned at 3T (GE Discovery MR750) using a 32-channel head coil (NOVA Medical). Resting-state data were scanned using a Simultaneous MultiSlice (SMS) EPI with blipped CAIPI sequence[3] with a TR/TE= 350/30 ms, multiband acceleration factor 6, CAIPI FOV shift of 3, FOV= 22x22·cm^2, matrix size =70x70, total number of acquired slices = 30, slice thickness = 4 mm, scan duration 2:55min (500 volumes). EPI images were preprocessed using FSL, including motion correction, spatial smoothing (6mm FWHM), and nonlinear normalization to MNI atlas space. Subsequent data preprocessing consisted of the removal of linear trends, rigid body motion parameters, white matter, and CSF time-courses by linear regression. Data were then temporally filtered into two bands: 1) 0.01-0.1 Hz and 2) >0.1 Hz, with the exclusion of cardiac (0.8-1.2 Hz) and respiratory (0.2-0.35 Hz) components. Four nodes in the DMN were chosen for the analysis: medial prefrontal cortex (red in Fig.1), posterior cingulate cortex (green in Fig.1), right and left angular gyri (yellow and blue in Fig.1). Masks for these nodes were created using group ICA analysis (Fig.1)[6]. For wavelet coherence analysis, Morlet mother wavelet (ω_0=6) was used, as it provides a good tradeoff between time and frequency localization[5]. The statistical significance level of the wavelet coherence was estimated using a Monte Carlo simulation on an ensemble of 1000 bootstrapped surrogate time series pairs[5].

Results: Wavelet coherence between four nodes of the DMN for a subject at two temporal filtration bands is shown in Fig.1a and 1b. The colored boxes on the top of each graph represent the nodes involved. Black contours represent areas in the time-frequency domain with coherence magnitude higher than 95% significance threshold. In these graphs, lower Fourier periods correspond to higher frequency fluctuations. For all subjects, all DMN nodes exhibit considerable modulation of coherency across the time-frequency plane using both temporal filtration bands (0.01-0.1 and >0.1 Hz). Significant coherence was often focal in time, particularly above the 0.1 Hz filtration band. Variability in coherence over time was not uniform across subjects.

Discussion: Our results indicate that functional connectivity occurs at multiple frequency bands – including those above 0.1 Hz that are commonly ignored in rsfMRI studies (Fig1b) – and exhibits dynamic changes within time scales of seconds to minutes, which is in line with evidence from electrophysiology[7]. These changes are not apparent from stationary analyses. The observed variability in coherence may be attributed to modulation of the cognitive state. However the contribution from residual physiological noise needs to be further studied. These results suggest that full frequency band analyses and measures of variability typically ignored when characterizing resting-state networks provide significant information, complementing common quantities measured in rsfMRI,

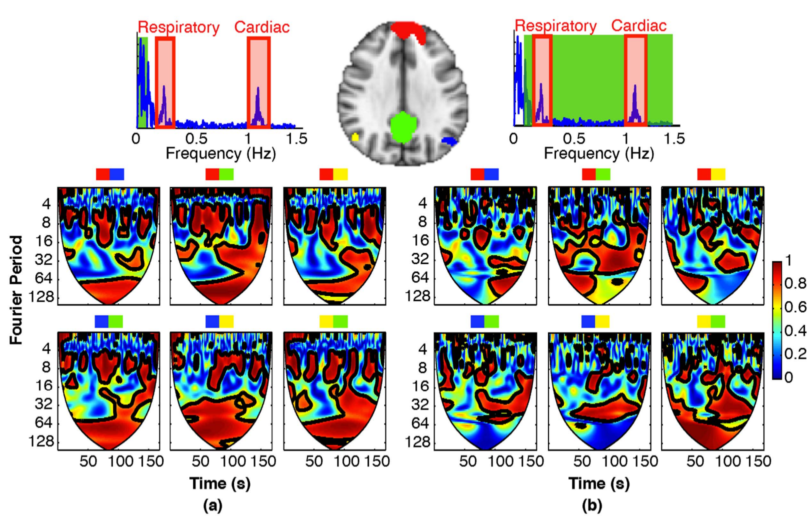

Figure 1. Cross wavelet transform between four nodes of the DMN for a representative subject in two different temporal filtration bands: **(a)** 0.01-0.1 Hz **(b)** above 0.1 Hz with the exclusion of respiratory and cardiac pulsation bands. Lower Fourier periods correspond to higher frequency fluctuations. DMN nodes used for the analysis are: medial prefrontal cortex (red), posterior cingulate cortex (green), right and left angular gyri (yellow and blue). Color boxes on top of each graph represent the DMN nodes involved.

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