Resting-state fMRI at 4 Hz

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TARGET AUDIENCE Scientists interested in studying resting-state hemodynamic correlations at frequencies above 0.1 Hz.

PURPOSE Resting-state fMRI[1] studies using BOLD contrast[2] investigate hemodynamic fluctuations below 0.1 Hz, because 1) the canonical hemodynamic response has much spectral power <0.1 Hz, and 2) under the constraint of getting 3-4 mm spatial resolution, typical full-brain echo-planar imaging (EPI) has about 0.5 Hz sampling rate. Here, we hypothesize that resting state fMRI can detect interregional correlations even at frequencies above 0.1 Hz . We used whole-brain[3] MR inverse imaging (InI)[4] with 10 Hz sampling rate and approximately 5-mm spatial resolution at cortex, to study the correlation of narrow-band power envelope between bi-hemispheric primary sensorimotor (SM1)[5] and primary visual cortices (V1) at frequencies ranging between 0.1 Hz and 4 Hz.

METHODS Seventeen subjects, giving informed consent, were instructed to lie still in a 3T MRI scanner (Tim Trio, Siemens Medical Solutions, Erlangen, Germany, 32-channel head coil array) with their eyes open during a 4-minute InI measurement. A fully gradient encoded reference scan, required for the subsequent volumetric image reconstruction, was first measured before the accelerated InI images, where partition-encoding steps along the coronal direction were left out in order to achieve the 10 Hz sampling rate. The imaging parameters were: TR=100 ms; TE=30 ms, flip angle=30°. High-resolution anatomical images were also acquired using a 3D T1-weighted (MPRAGE) pulse sequence.

Using the reference scan data from all channels of an RF coil array, volumetric InI images were reconstructed at every 100 ms using the minimum-norm estimate[3]. The fMRI time series from each subject were morphed to a standard brain template based on the high-resolution anatomical images in a spherical coordinate system[6]. To remove potential confounds in the time series, we used a Bayesian method[7] to dynamically monitor and suppress the cardiac and respiratory fluctuations in the fMRI signals, which were also high-pass filtered at 0.025 Hz to remove very slow variations. The band-limited power envelope of each fMRI time series was calculated using a Morlet wavelet filter: $m(t)=\exp(-2\pi j f_0 t)\exp(-t/2\sigma^2)$, where t denotes time, f_0 denotes the central frequency of our interest and σ^2 controls the spectral resolution. We used seed-based correlation to study the functional connectivity of the resting state in visual and sensorimator cortices. We manually selected the SM1 and V1 and used them as the seed regions-of-interest (ROI's), whose band-limited power envelop across the 4-minute scan was used to calculate the correlation coefficients (CC's) throughout the brain. The frequency f_0 was changed between 0.1 and 4 Hz. To average across subjects, CC's were transformed to the Z-score via Fisher's transformation, and Z-scores were averaged across subjects.

RESULTS Figure 1 upper panel shows spatial distribution of the Z-scores of the CCs at 0.1 Hz and 4.0 Hz using two seed ROIs (SM1 at left hemisphere or V1 in the right hemisphere; see green areas in the figure inlet). Consistent with previous findings, contralateral SM1/V1 showed strong correlations around 0.1 Hz. Significant correlations (Bonferroni corrected $p<0.01$) were also observed around 4.0 Hz. Figure 1 lower panel shows the quantitative results (Z-score.means and standard deviations). The right SM1 has average Z-score of 11.71 at 0.1 Hz and 8.12 at 4 Hz. The left V1 has average Z-score at 14.97 at 0.1 Hz and 8.22 at 4.0 Hz.

DISCUSSION Contrary to the prevailing view based on conventional resting-state fMRI studies limited to very low sampling rates, our results show showed significant inter-hemispheric correlations even at frequencies above 0.1 Hz. Considering the power spectral density of a canonical hemodynamic response function, our results suggest that at 4 Hz, either the noise and signal are decreased in parallel, or other physiological signal exists, such that the contrast-to-noise ratio (quantified by the Z-score of the correlation coefficients) is still 60% of that at 0.1 Hz. While the spatial resolution of InI is somewhat limited in the InI-encoded direction, the present recordings had full gradient encoding along the left-right axis and therefore unambiguously differentiated between the hemispheres. Further validation by, for example, contrasting between task-induced and resting states, could help ascertain if the observed correlation is related to the resting state physiology. Our observation also motivates further development of fast fMRI methods in order to observe frequencies above 5 Hz, the Nyquist frequency in this study, to reveal more detailed physiological information embedded in hemodynamic signals.

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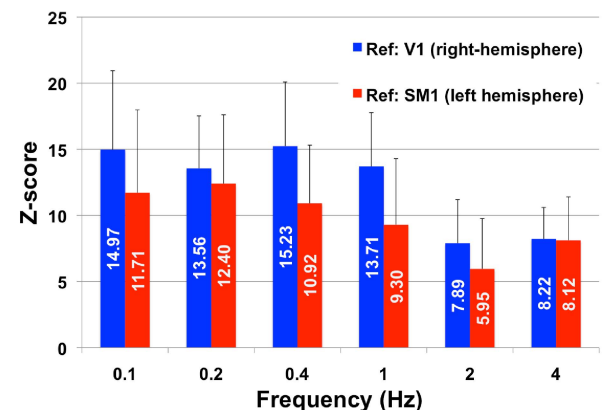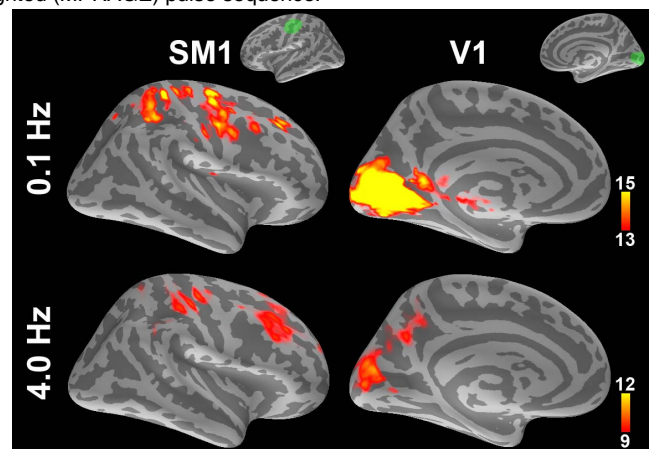
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