

## Multi-Echo Independent Component Analysis (ME-ICA) of High Frequency Resting-State fMRI Data

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**Introduction:** Resting-state functional connectivity magnetic resonance imaging (fcMRI) has emerged as a popular approach to characterize functional connectivity of the brain at rest. Conventional resting-state fcMRI analysis usually retains only temporal frequencies lower than 0.1Hz by applying a low-pass filter to the time series and thus removes high temporal frequency information. Due to the recent emergence of simultaneous multi-slice acquisitions that are able to easily capture whole brain functional MRI data with low TRs, there has been an increased interest in resting-state networks in frequency bands greater than 0.1Hz<sup>1-5</sup>. Even though these studies report detecting high frequency resting-state networks, in most cases it is unclear if they are BOLD networks. One study<sup>5</sup> acquired multi-echo data and showed that the resting amplitude fluctuations scaled linearly across echoes, i.e. the networks had BOLD weighting, but this was only shown for a few networks. Here, we would like to investigate more generally the occurrence of whole brain high frequency BOLD networks, using a multi-echo independent component analysis<sup>6</sup> (ME-ICA) method that can automatically decompose resting-state data into BOLD and non-BOLD networks, and a multi-echo simultaneous multi-slice (MESMS) acquisition<sup>7</sup> that allows for acquisition of resting-state networks with low TRs.

**Methods:** Resting-state fMRI data were collected from twelve subjects on a 3T GE MR750 system with a 32 channel receive coil (Nova Medical). The MESMS resting-state acquisition (10 minutes per run; eyes open; fixation cross) used a 1.33-fold in-plane acceleration. The resolution was 3.75x3.75x4mm<sup>3</sup> and had whole brain coverage (FOV 24cm, 64x64 matrix, 36 slices). A blipped-CAPI echo planar imaging (EPI) k-space trajectory<sup>8</sup> was used, with 3 sagittal slices per RF excitation. Other acquisition parameters were: TR=0.87s (fs/2=0.57Hz), 690 volumes, TE=[13.8, 32.5, 51.2]ms, and FA=56°. To reconstruct the images, we used a SENSE reconstruction with a fast Conjugate Gradient Toeplitz-based iterative algorithm and a spatial roughness penalty<sup>9</sup>. ME-ICA analysis was run on the MESMS data and temporally filtered MESMS data. We used both a high-pass filter (HPF: fpass>0.19Hz; 37-tap FIR) and low-pass filter (LPF: fpass<0.19Hz; 37-tap FIR). For the ME-ICA analysis, each dataset had their 3 echoes optimally combined<sup>10</sup> (OC) and then decomposed first using principle component analysis (PCA), for data dimensionality reduction, followed by independent component analysis (ICA). For both the PCA and ICA steps, each resulting OC component time series was fit to the original multi-echo data and the resulting spatial maps were statistically tested for BOLD and non-BOLD properties<sup>6</sup> on a per voxel basis. A spatially averaged goodness of fit metric for both properties was then used to automatically find BOLD and non-BOLD networks. Using this procedure, PCs that were deemed to be BOLD, non-BOLD, or both were accepted for ICA decomposition, and ICs from that analysis were categorized as BOLD (accepted) or non-BOLD (rejected) using the same procedure.

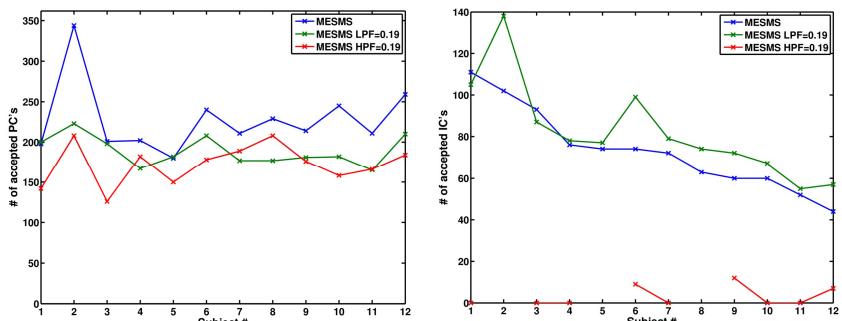


Figure 1: Number of accepted PC's (Left) and ICs (Right) from running ME-ICA on MESMS, MESMS HPF and MESMS LPF. Both plots show the number of accepted components per subject ordered from highest to lowest number of accepted ICs for MESMS.

**Results & Discussion:** Figure 1 (Left) shows the number of accepted PCs across subjects from the ME-ICA analysis of all datasets. It shows that by filtering, there is a significantly lower number of accepted PCs across subjects as compared to the unfiltered MESMS data (LPF:  $t(11)=-3.99$ ,  $p<0.003$ ; HPF:  $t(11)=-5.62$ ,  $p<0.0003$ ), although no significant difference was detected between the two filtering methods. This reduction in the number of accepted PCs is expected, since filtering reduces the time series degrees-of-freedom and hence its data dimensionality. Figure 1 (Right), shows the number of accepted ICs across subjects from the ME-ICA analysis of all datasets. There is a stark difference between MESMS LPF and MESMS HPF. While MESMS LPF has a higher number of BOLD ICs as compared to MESMS ( $t(11)=2.57$ ,  $p<0.03$ ), MESMS HPF has nearly no BOLD ICs. For the twelve subjects, ICA failed to converge for three subjects, no BOLD ICs were detected for six subjects, and relatively small numbers of BOLD ICs (9, 12, and 7 BOLD ICs for subjects 6, 9 and 12 respectively) were detected for the remaining three subjects. Overall, our results show that even though the MR signal dimensionality (number of accepted PCs) is similar between the MESMS LPF and MESMS HPF time series, ME-ICA analysis indicates that high frequency BOLD resting-state networks are rarely encountered. This observation casts doubt on findings related to resting-state BOLD networks at frequencies higher than 0.2Hz. Furthermore, it suggests that imaging slow BOLD hemodynamic signals at higher temporal frequencies may be of principal benefit for denoising purposes, and that emerging reports of high-frequency resting BOLD networks may require closer examination.

**References:** [1]Boubela et al, Front Hum Neurosci 2013. [2]Lee et al, Neuroimage 2013. [3]Gohel et al, Brain Connect 2014. [4]Kalcher et al, PLoS One 2014. [5]Chen et al, 20th OHBM 2014. [6]Kundu, et al, PNAS 2013. [7]Olafsson et al, ISMRM 2014. 4139. [8]Setsompop et al, MRM 2012. [9]Fessler et al, IEEE TSP, 2005. [10]Posse et al, MRM 1999.