USING MULTI-ECHO FMRI TO INCREASE TASK-BASED CONTRAST-TO-NOISE AND RESPONSE STABILITY

Benjamin Gutierrez[1], Daniel A Handwerker[1], Javier Gonzalez-Castillo[1], Vinai Roopchansingh[2], Laura Buchanan[1], Peter A Bandettini[1,2]

1. Section on Functional Imaging Methods, LBC, National Institute of Mental Health, Bethesda, MD

2. Functional FMRI Facility, National Institute of Mental Health, Bethesda, MD

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INTRODUCTION

fMRI is limited by our ability to distinguish neuronally interesting signal fluctuations from artifacts and noise. A recently developed technique uses multi-echo fMRI scans to empirically remove artifacts (Kundu 2011 & 2013). In this study we show how multi-echo denoising affects the signal quality and stability of the very common fMRI block design study. We also use this data to validate the finding that nearly whole brain significant activation comes with sufficient data (Gonzalez-Castillo 2012) while testing if multi-echo imaging allows us to obtain a similar amount of data in a more practical amount of time.

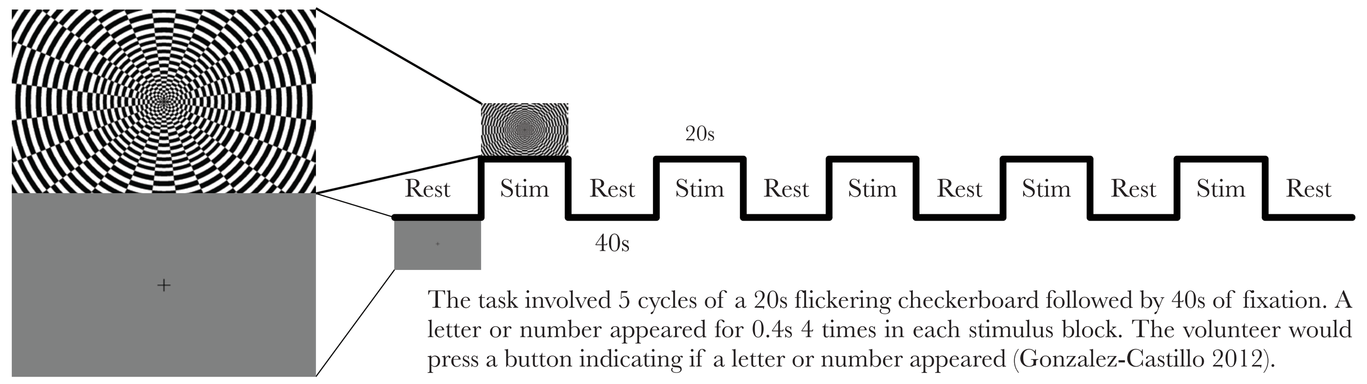
Using the same experiment design as (Gonzalez-Castillo 2012), we collected 103 runs of the same task across multiple days for a total of 9 hours of data, but acquired multi-echo rather than single-echo fMRI data. We compared results using the middle echo, an optimally combination of 3 echoes (Posse 1999), and after a modified ME-ICA denoising procedure (Kundu 2012 & 2013)

Methods

Data Collection

GE 3T MR 750 MRI scanner, GE 32 channel head coil.
GRE EPI, TR=2s, TE=15.4, 29.7, & 44.0ms, FA=75^{o}
33 oblique slices, 3.5mm^3 voxels, 0mm gap, 64x64 grid, ASSET=2.
1mm^3 MPRAGE T1 weighted and proton density weighted scans were collected during each session to use for tissue segmentation and registration.

Data are from two healthy adults (1M, 1F) collected over 9 days. Each day included 10-13 340 sec runs of the same task. Each volunteer had 103 total runs of the task.



The task involved 5 cycles of a 20s flickering checkerboard followed by 40s of fixation. A letter or number appeared for 0.4s 4 times in each stimulus block. The volunteer would press a button indicating if a letter or number appeared (Gonzalez-Castillo 2012).

Preprocessing

Data were processed using AFNI and Python (for the ME-ICA denoising code) in each volunteer's native space. The anatomical scans from the 9 sessions were registered to the scan from the first session. The data were despiked, slice time corrected and motion corrected. The first scan of every session was aligned to the anatomical scan from the same day and then the first day's anatomical scan. Alignment and motion correction parameters were calculated on the middle echo time series and applied to all 3 echoes as a single transformation matrix.

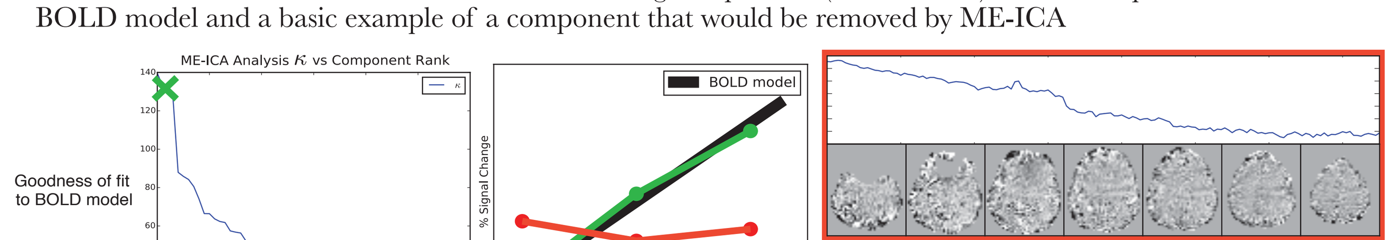
ME-ICA denoising was then performed using code from https://bitbucket.org/prantikk/me-ica . The optimally combined time series are a weighted average of the three echoes. The denoising process involved running a spatial ICA on the optimally combined time series, removing components that were deemed unlikely to be BOLD weighted, and recombined the remaining components into a denoised data set. The decision criteria were slightly adjusted from the released code to more conservatively keep components. The changes include removing one rejection criterion which occasionally would reject high kappa components because they had high variance, making the rho elbow 95% of its original value, and adjusting one line of code to increase the chance high kappa components are classified as BOLD related.
The middle echo time series (Echo 2) with TE=29.7ms was considered a standard single-echo fMRI run for comparison analyses.

Contrast-to-noise

A finite impulse General Linear Model (GLM) for reach run was performed on the data. Using the results from the GLM, significance maps (FDR < 0.05), and contrast to noise (CNR: magnitude of the hemodynamic response function divided by the standard deviation of the residuals) were created for two regions of interest, the Calcarine Sulcus and the Lateral Genticulate Nucleus.

ME-ICA Denoising

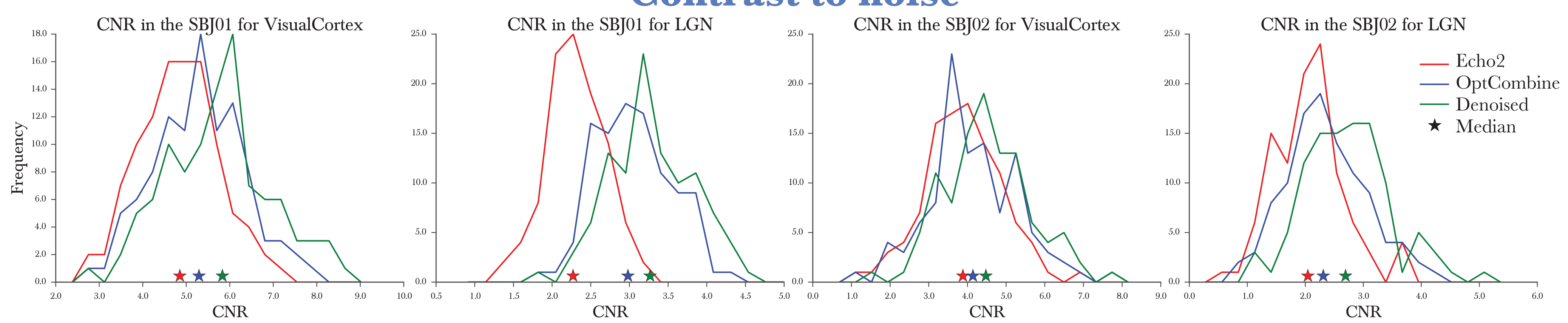
In multi-echo fMRI, the same slice is rapidly acquired at several echo times after each excitation. Multi-echo denoising is based on the idea that the magnitude of a BOLD weighted signal will scale with echo time, but artifacts that aren't BOLD weighted will be constant (Kruger 2001 & Peltier 2002). ME-ICA denoising splits multi-echo data into ICA components, removes the components that are unlikely to represent BOLD fluctuations, and then reconstructs a denoised time series with the remaining components (Kundu 2011). Below is a plot of the theoretical BOLD model and a basic example of a component that would be removed by ME-ICA



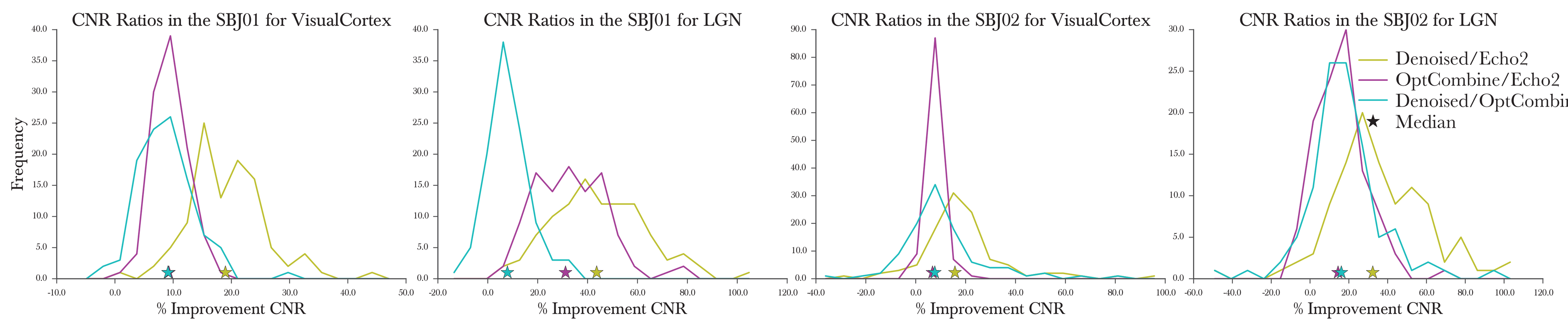
This component was rejected by ME-ICA. Based on the time series, it is possible that this component is associated with scanner drift.

Results

Contrast to noise

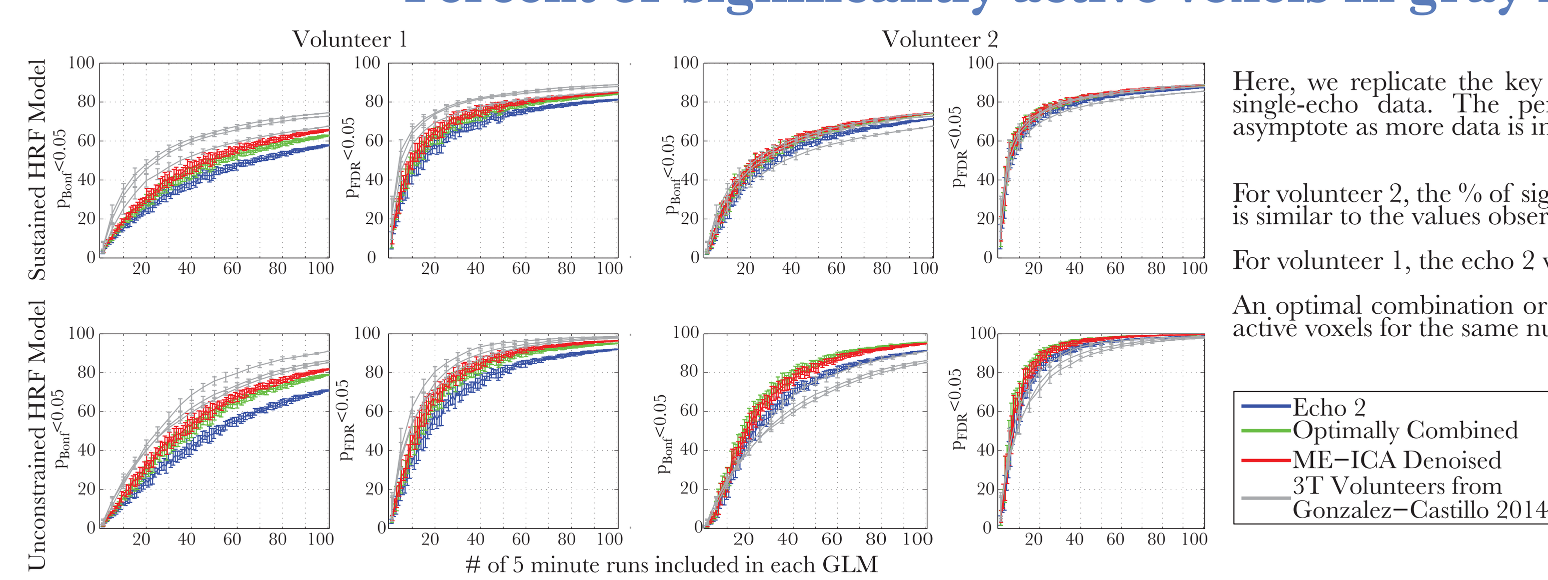


Both multi-echo denoising techniques show raw CNR improvement compared to single echo imaging. The level of improvement varies across subjects and regions but is consistent.



These plots show the percent improvement for the ratio in a single run of each of the denoising techniques. Both multi-echo techniques show clear improvement over single echo denoising. There is also a reliable improvement of ME-ICA denoising over the Optimally combined data. It is important to note that the improvement is not as good as hoped though and this is discussed in the conclusions.

Percent of significantly active voxels in gray matter



Here, we replicate the key finding in Gonzalez-Castillo 2014, which used single-echo data. The percent of significantly active voxels does not asymptote as more data is included in the analysis.

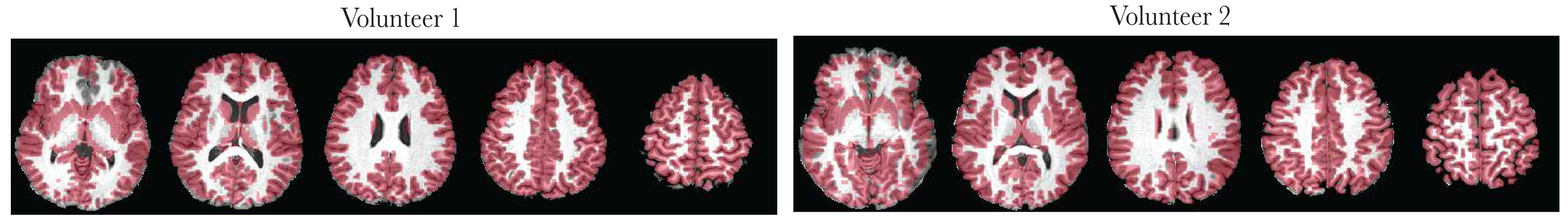
For volunteer 2, the % of significantly active voxels as more runs are included is similar to the values observed in the previous study.

For volunteer 1, the echo 2 values are lower than previously observed.

An optimal combination or ME-ICA denoising results in more significantly active voxels for the same number of runs

Gray Matter Masks

Volunteer 1 Volunteer 2

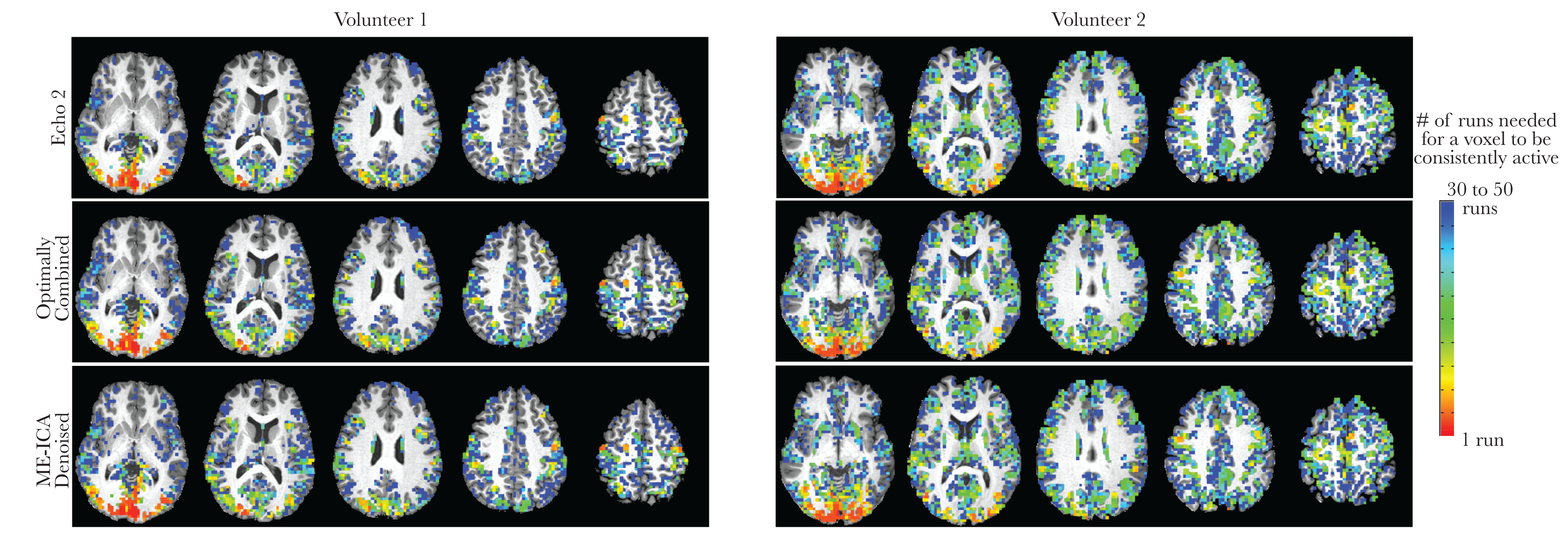


The model was fit with 1 to 100 runs (The "Number of Averages"). For every number of averages, 10 combinations of the 103 runs were randomly selected. The percent of significantly active voxels for each permutation of runs and each number of averages were calculated for each volunteer. To estimate how consistent the activation maps are, averages of 1-50 runs were calculated with 100 permutations each.

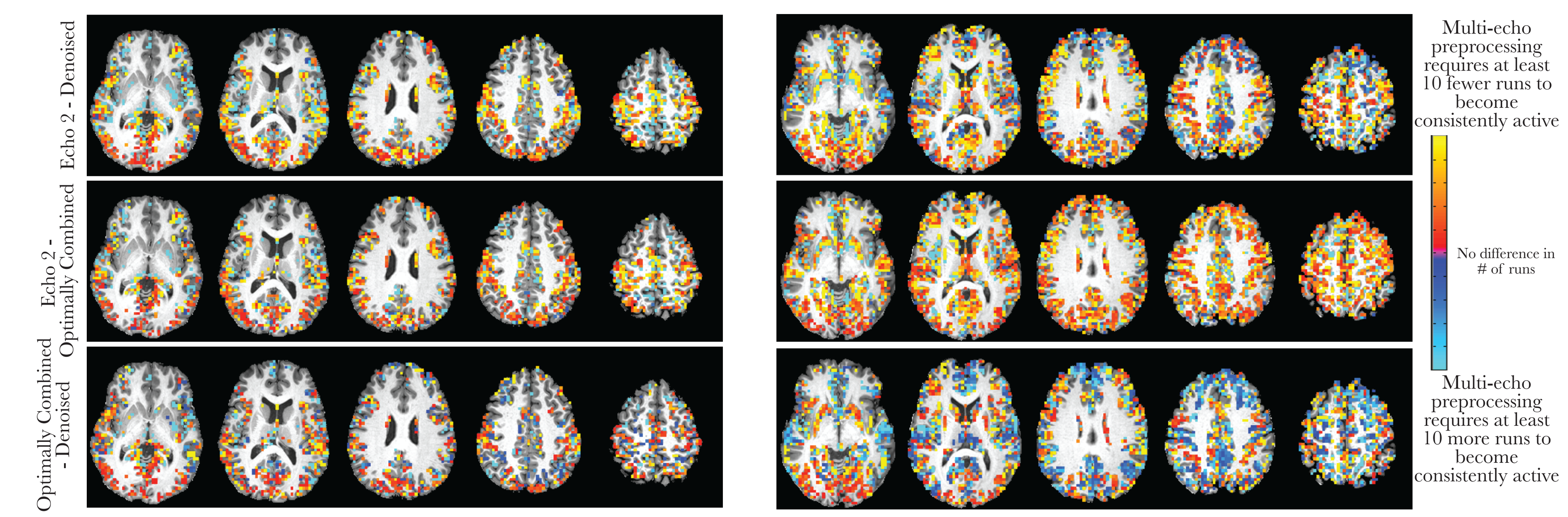
Creating Significant Activation Maps

We paralleled the steps used in Gonzalez-Castillo 2014 as closely as possible. The 5 minutes of task each run starting from the first stimulation period were used in all General Linear Model (GLM) analyses. The GLM included either a Sustained model with the task response being modeled by a fixed hemodynamic response shape or an Unconstrained model with the task modeled by 30 impulse functions so that any task-correlated response shape could be considered significant.
The GLM was fit using the AFNI program 3dREMLfit. Data were thresholded using a very conservative Bonferroni threshold (for the total number of gray matter voxels) or a False Discovery Rate (FDR) threshold.
Calculations for the percent of active voxels were done within a gray matter mask. Voxels were classified as gray matter with the AFNI function 3dSeg applied to the registered average of the anatomical images. This mask was downsampled to the EPI resolution and voxels that were at least 33% gray were used. Voxels were included in the mask only if they contained fMRI data in all 103 runs.

Number of runs needed to for a voxel to be consistently active



GLMs for 100 permutations of runs were calculated for 1-50 runs. Significance was a Bonferroni corrected threshold of p<0.05. If a voxel was significant in 95% of the permutations of runs, then it was considered consistently active. The above maps show the number of runs needed for each voxel to be consistently active. A red voxel means that the voxel was consistently active with only 1 run included in the GLM. A blue voxel means that it did become consistently significant, but the GLM required 30-50 runs to reach that point.



These maps are the subtraction of pairs of the previous maps. This shows how many more runs are needed to reach the same level of consistent activity
For both volunteers, fewer runs are needed to reach consistency for most voxels when comparing echo 2 to the Optimally Combined or Denoised time series.
Volunteer 1 shows the same level of consistency with fewer runs for Denosied vs Optimally Combined, but this contrast is less clear in volunteer 2

Conclusion

We present additional evidence that the number of voxels that cross a significance threshold is very sensitive to the amount of data included in the analysis.

We show that multi-echo fMRI provides more CNR than single-echo fMRI and can be used to increase the number and consistency of significant voxels with less data

We also see evidence that ME-ICA denoising improves results for individual runs in almost all cases in regions with reliable activation and in most cases in areas with less robust responses. Future work will examine volunteer 1 to better understand why the echo 2 activity maps were less widespread and what aspects of the denoising process improved these results.

Our results suggest a promising future for ME-ICA denoising, but the variability in CNR improvement after denoising shows the method can be improved. Future work will focus on finding better ways to use the multi-echo information to empirically identify and keep relevant signal and remove noise.

Acknowledgments

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