EFFECT OF MULTI-ECHO DENOISING ON THE AMOUNT OF DATA REQUIRED TO SEE WIDE-SPREAD ACTIVITY

Daniel A Handwerker[1], Benjamin E Gutierrez[1], Javier Gonzalez-Castillo[1], Vinai Roopchansingh[2], Laura C 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

Given sufficient data, nearly the entire brain will show significant activation in response to a simple block design task (Gonzalez-Castillo 2012). This observation highlights the arbitrary nature of significance thresholds and points to a future of fMRI where other aspects of hemodynamic response shapes are used to understand function. Unfortunately, these whole brain activity maps required approximately 9 hours of the same block design task per volunteer (Gonzalez-Castillo 2012 & 2014). Such information has limited utility until fMRI data improves so that similar quality data can be obtained in a more practical amount of time.

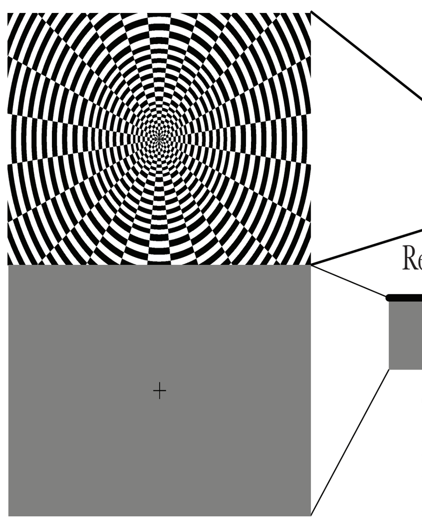
We collected 9 hours of multi-echo fMRI data from two volunteers and calculated the percent and consistency of signifcantly active voxels. We compared results using just the middle echo, an optimal combination of 3 echoes (Posse 1999), and after the ME-ICA denoising procedure (Kundu 2012 & 2013).

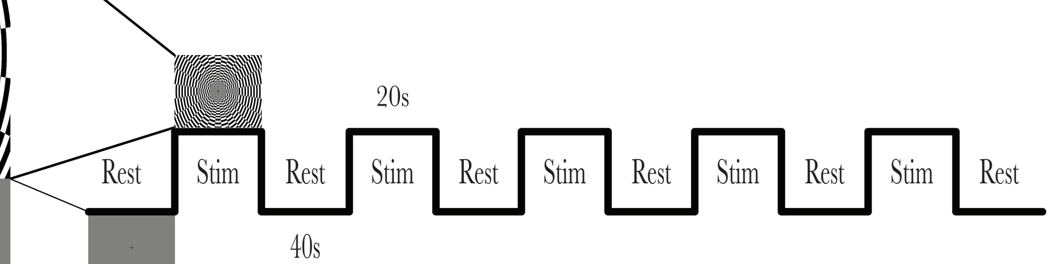
METHODS

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°
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

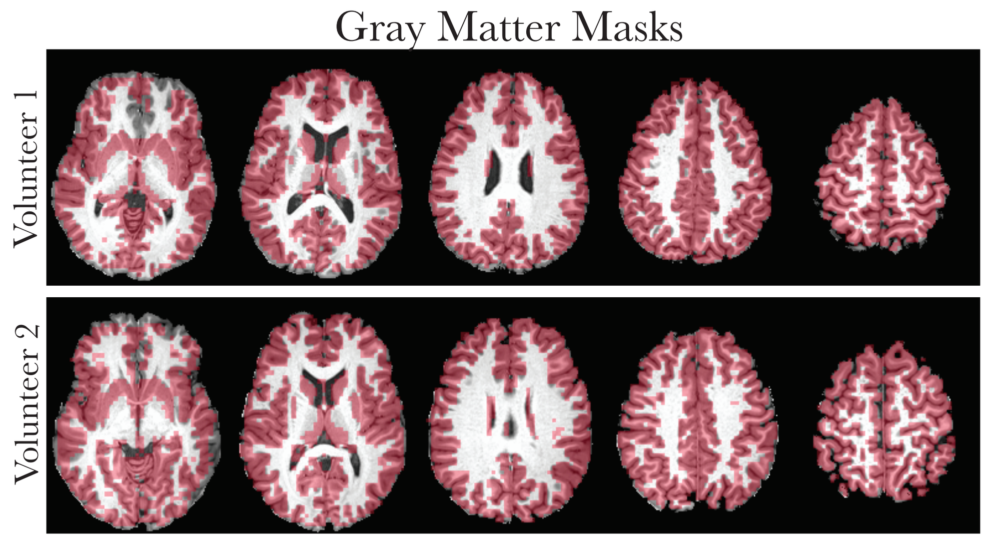
Data were processed using AFNI and Python (for the ME-ICA denoising code) in each volunteer's native space. The anatomical scans from the 9 sessions were registered to the scan from the first session. The data were despiked, slice time corrected and motion corrected. The first scan of every session was 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 transform 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.

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.

Gray Matter Masks



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 was calculated for each volunteer. To estimate how consistent the activation maps are, averages of 1-50 runs were calculated with 100 permutations each.

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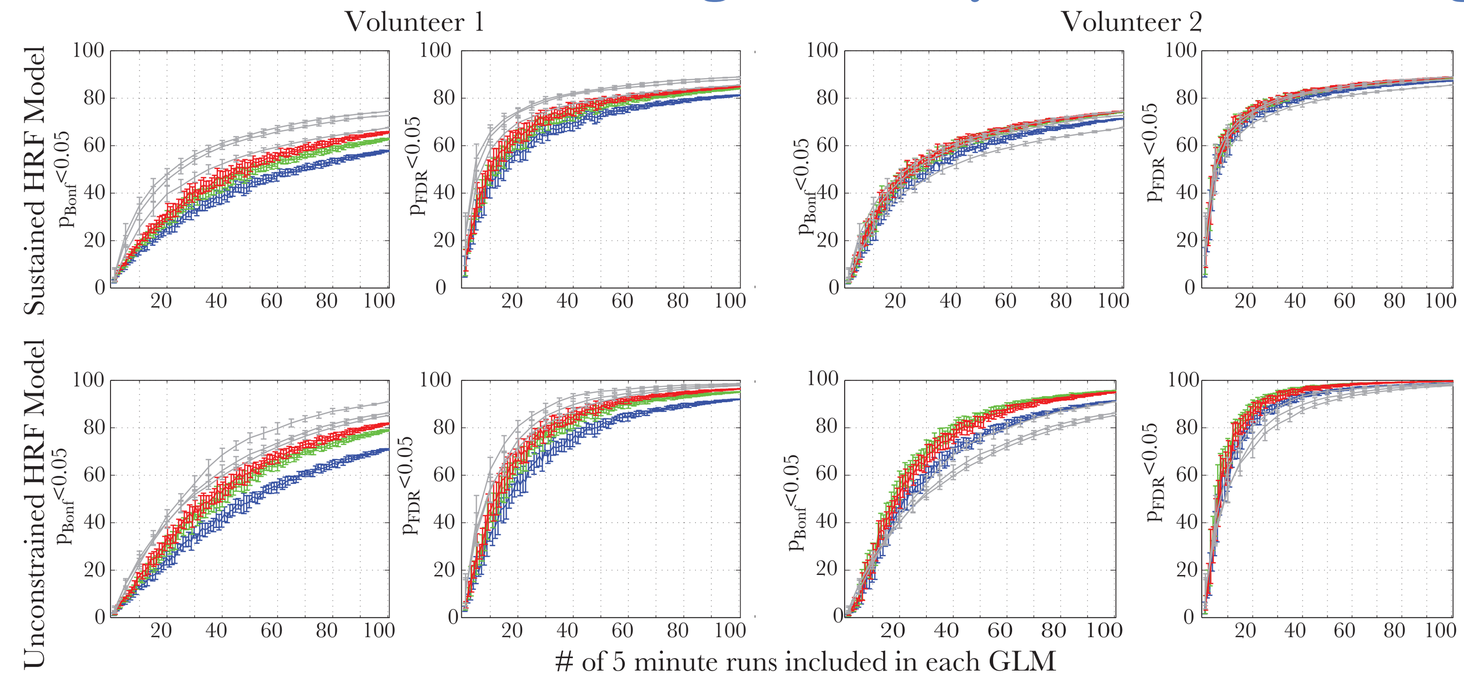
RESULTS

Percent of significantly active voxels in gray matter



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.

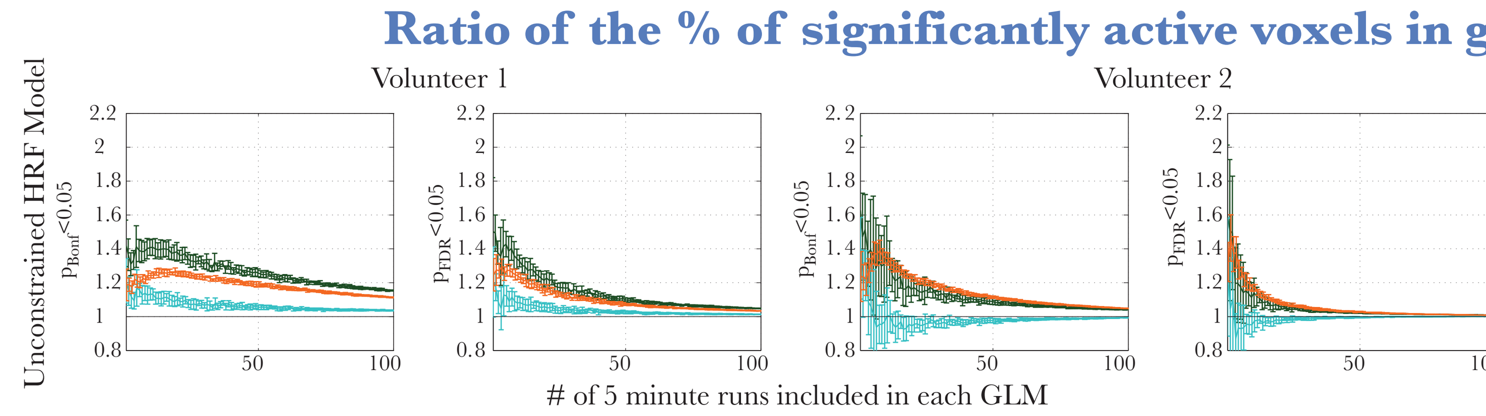
For volunteer 2, the % of significantly active voxels as more runs are included is similar to the values observed in the previous study.

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

Echo 2
Optimally Combined
ME−ICA Denoised
3T Volunteers from Gonzalez−Castillo 2014

Ratio of the % of significantly active voxels in gray matter



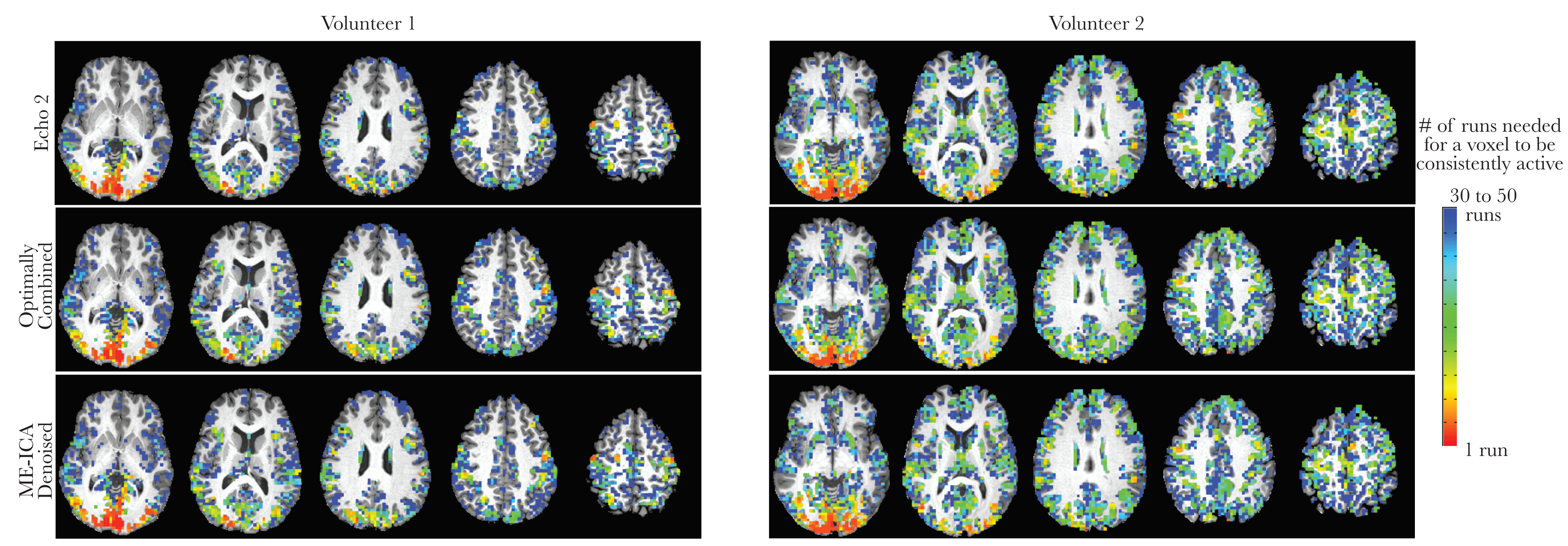
For every permutation of runs, the plot show the ratio of the % of significantly active voxels between two preprocessing options.

Both volunteers show a 20-40% increase in the number of significantly active voxels for the optimally combined or denoised time series vs echo 2 for the amount of runs collected in most other fMRI studies.

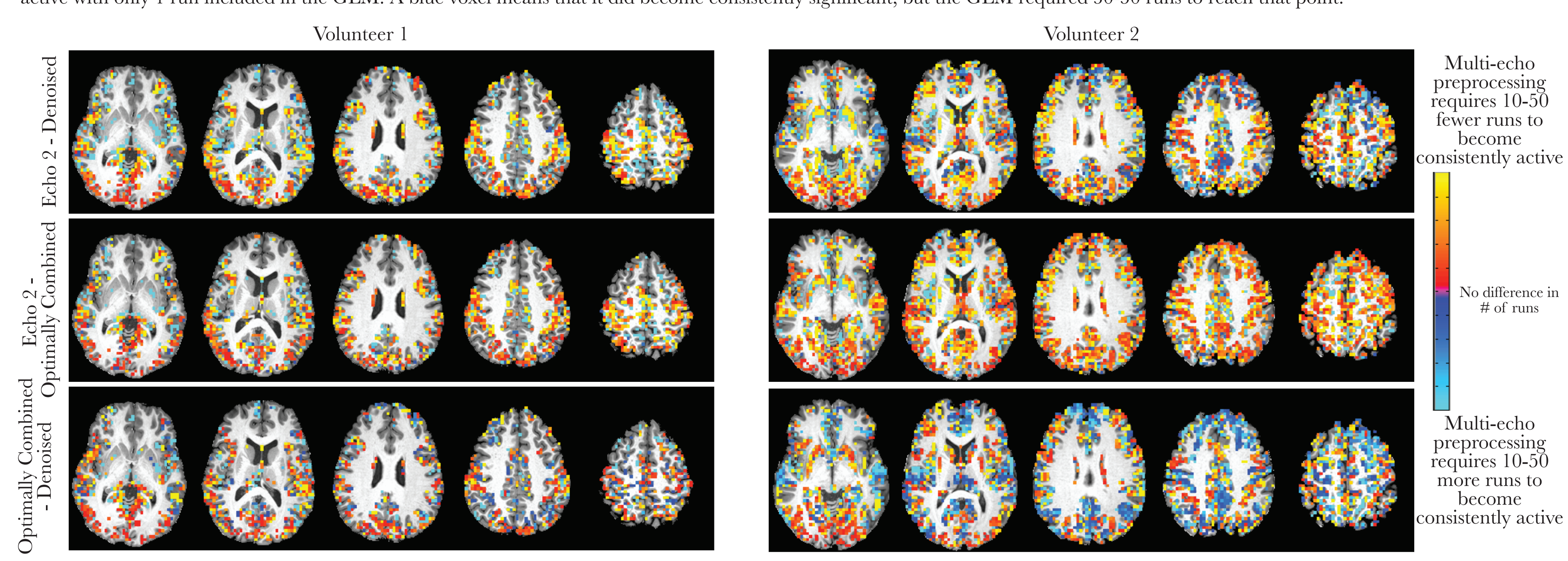
Volunteer 1, but not 2 shows an increase for Denoising vs the Optimally Combined time series.

Denoised/Echo 2
Optimally Combined/Echo 2
Denoised/Optimally Combined

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

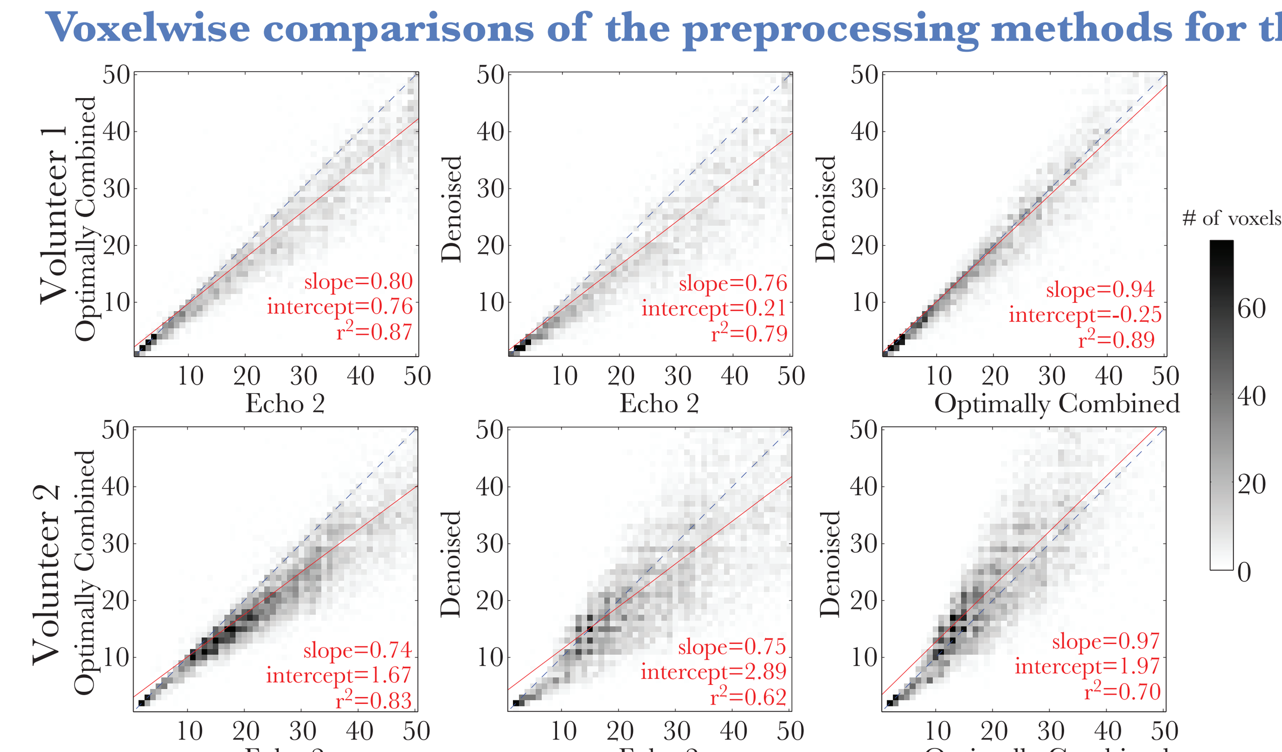


GLMs for 100 permutations of runs were calculated for 1-50 runs. Significance was a Bonferroni corrected threshold of $p<0.05$. If a voxel was significant in 95% of the permutations of runs, then it was considered consistently active. The above maps show the number of runs needed for each voxel to be 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 maps above. 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

Voxelwise comparisons of the preprocessing methods for the # of runs needed for consistent activity



The voxels in the above maps are plotted here as joint histograms. Values that fall on the dashed blue line mean that the two preprocessing methods require the same number of runs in a GLM to show significant activity. Values below the dashed blue line mean the y-axis preprocessing method shows the same consistency in fewer runs. The red lines are the linear fit to these data.

Both volunteers show increased consistency with fewer runs when multi-echo processing is used. There is no clear improvement in consistency between the Optimally Combined and Denoised preprocessing methods.

CONCLUSIONS

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.

Multi-echo fMRI provides more SNR than single-echo fMRI and can be used to increase the number and consistency of significant voxels with less data.

We see some evidence that ME-ICA denoising improves results for inidvidual runs (poster 3931) and sometimes across multiple runs, but the improvement is inconsistent. Some of this inconsistency might be because highly experienced volunteers with minimal head motion had fewer sources of noise that Denoising can identify and remove.

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.

We also plan to examine other ways to use multi-echo data with the goal of more consistently removing non-BOLD noise.

Contact: dan.handwerker@nih.gov http://fim.nimh.nih.gov