

# MULTI-ECHO FMRI ENHANCES RELIABILITY OF BRAIN-WIDE BOLD RESPONSES TO A NATURALISTIC MOVIE

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# INTRODUCTION

As fMRI researchers increasingly tackle naturalistic, complex experimental paradigms, response reliability is often used in place of response amplitudes as a metric of each voxel's responsiveness to a stimulus. A voxel's response from one run is used as a model for the same voxel's response in the other runs, a process that is repeated for each possible pairing of runs. Voxels with "reliable" responses are those that consistently show positive correlations across pairings (Hasson, 2004). This approach is especially useful in cases where the mapping from stimulus to response is not well characterized, such as the free viewing of a naturalistic movie. But the relatively unconstrained nature of these paradigms translates to a low contrast-to-noise ratio, so response reliability measures have much to gain from denoising techniques. To this end, we apply multi-echo independent component analysis (MEICA), a recently developed technique that has shown great promise in resting-state and task-based analyses (Kundu, 2012; Kundu, 2013), to data from the free viewing of a naturalistic movie.

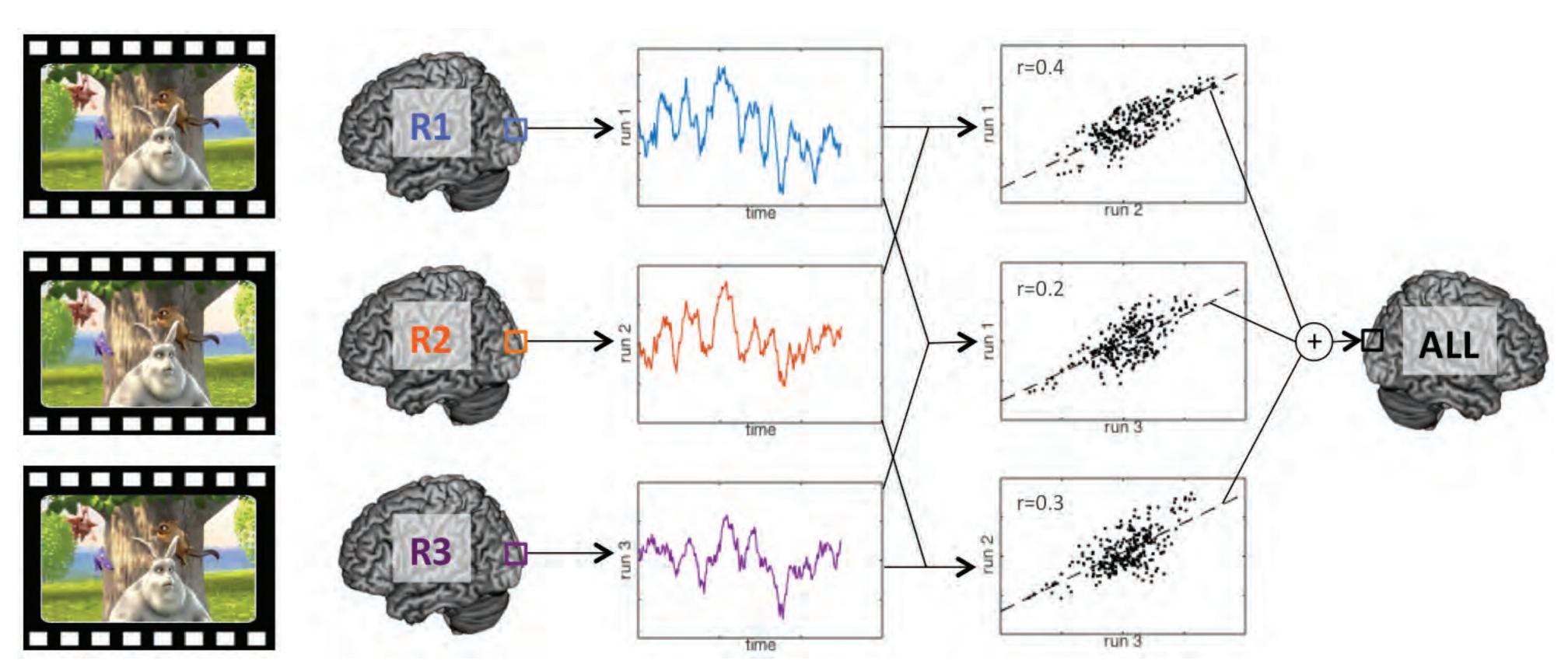


Figure 1: Demonstration (with simulated data) of the intra-subject correlation (ISC) analysis used to assess response reliability in this study. The subject views the same video on N different runs (N=3 above). For each voxel, the time-course on each run is correlated with the time-course on each other run to get a correlation coefficient. The (N-1)\*N/2 resulting correlation coefficients are averaged, and the result is mapped back on to the voxel's position. To assess significance, the correlation coefficients are compared to zero using a one-tailed t-test with FDR correction (q<0.05) for multiple comparisons.

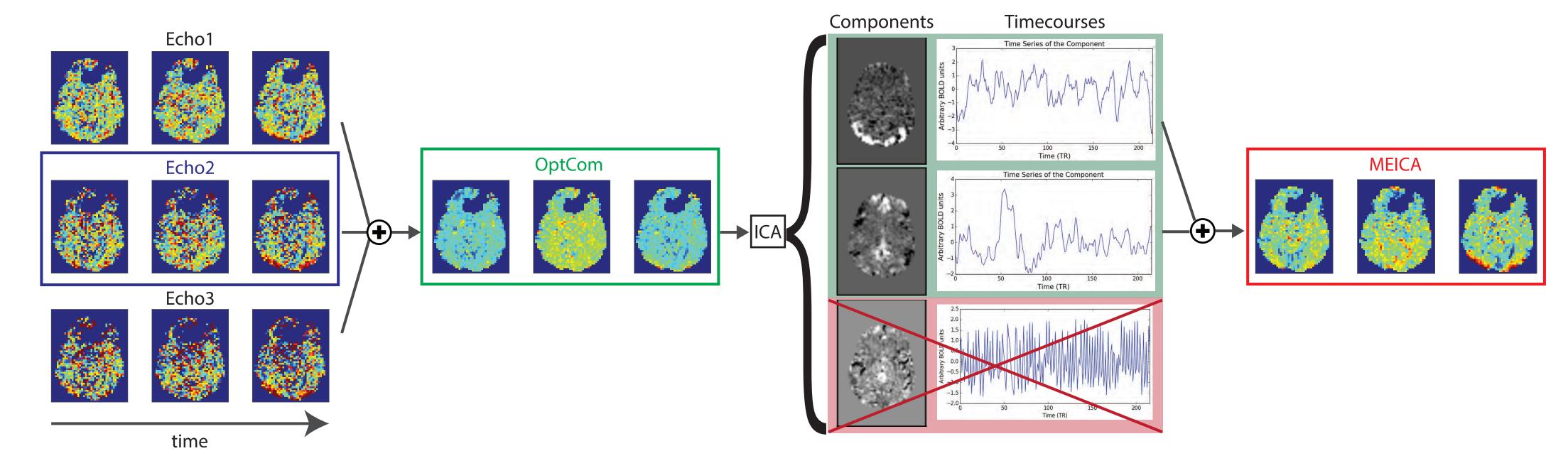
## METHODS

#### **Data Collection**

GE 3T MR 750 MRI scanner, GE 32 channel head coil. GRE EPI, TR = 2 s, TE = 15.4, 29.7, & 44.0 ms,  $FA = 75^{\circ}$ 33 oblique slices, 3.5mm<sup>3</sup> voxels, 0mm gap, 64x64 grid, ASSET=2. Despiking, slice time correction, motion correction, registration 1mm<sup>3</sup> MPRAGE T1-weighted and PD-weighted scans were collected during each session for tissue segmentation & registration.

#### **Preprocessing**

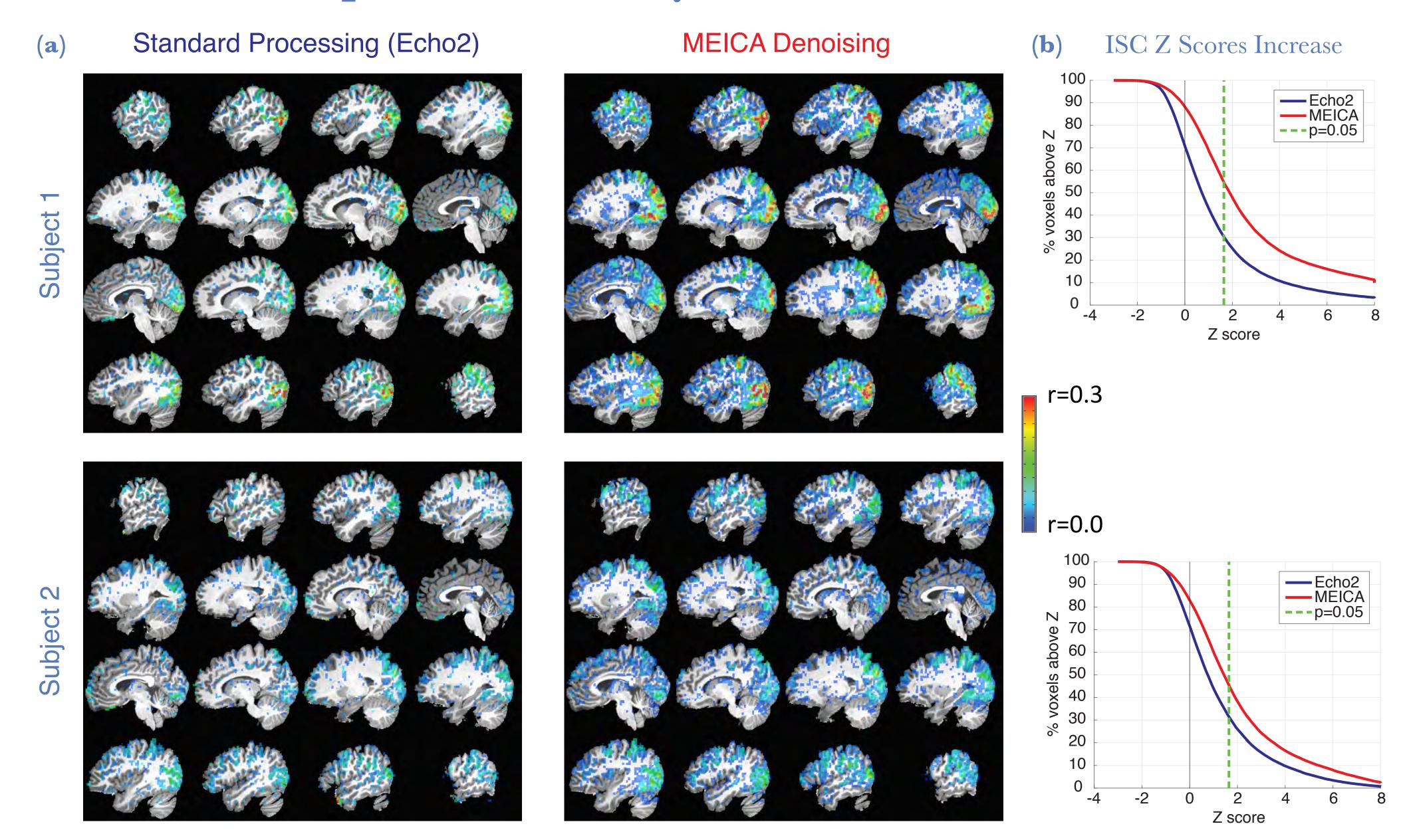
Data are from two healthy adults (1M, 1F) collected over 9 days. Each day included 1-2 viewings (16 and 17 total) of a 420s video. were applied. Alignment and motion correction parameters were calculated on Echo2 and applied to all three echoes.



**Figure 2:** Preprocessing methods. The Optimally Combined ("OptCom") time series is 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 recombining the remaining components into a denoised data set. This "MEICA" denoising was performed using code from https://bitbucket.org/prantikk/me-ica. The three time series in boxes above will be used as input to ISC.

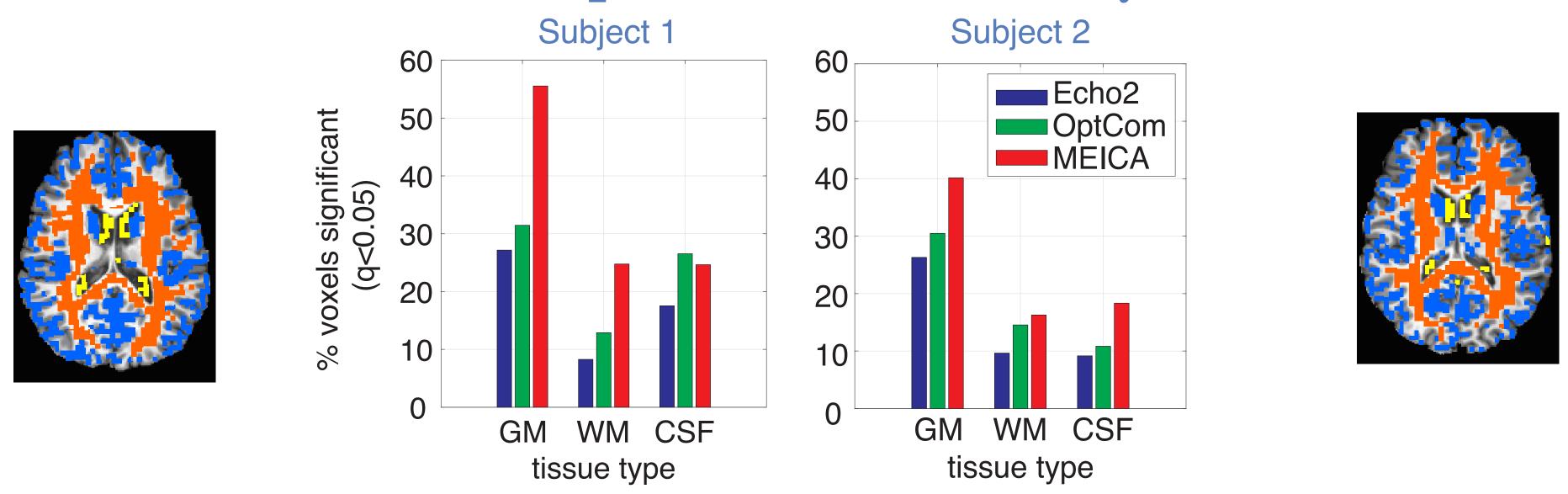
### RESULTS

### Response Reliability is Greater with MEICA



**Figure 3:** (a) Average correlation coefficient r across ISC pairings, thresholded at FDR-corrected q<0.05, for Subject 1 (top) and 2 (bottom), using Echo2 (left) or MEICA denoised (right) timeseries as input. (b) Reverse cumulative histogram of voxel-by-voxel Z scores across the whole brain for Subject 1 (top) and 2 (bottom), with uncorrected p=0.05 marked in green.

### Greatest Improvement is in Gray Matter



**Figure 4:** Percentage of voxels in each tissue type found to have significantly reliable activation (q<0.05) using each preprocessing method. GM = gray matter, WM = white matter, CSF = cerebrospinal fluid. Tissue type masks (seen on outside plots for slice z=15) are based on AFNI's 3dSeg segmentation transformed into EPI space and thresholded at  $p_{CM} > 0.75$ ,  $p_{WM} > 0.9$ , and  $p_{CSE} > 0.9$ .

#### Newly Reliable Voxels are Mainly in Gray Matter

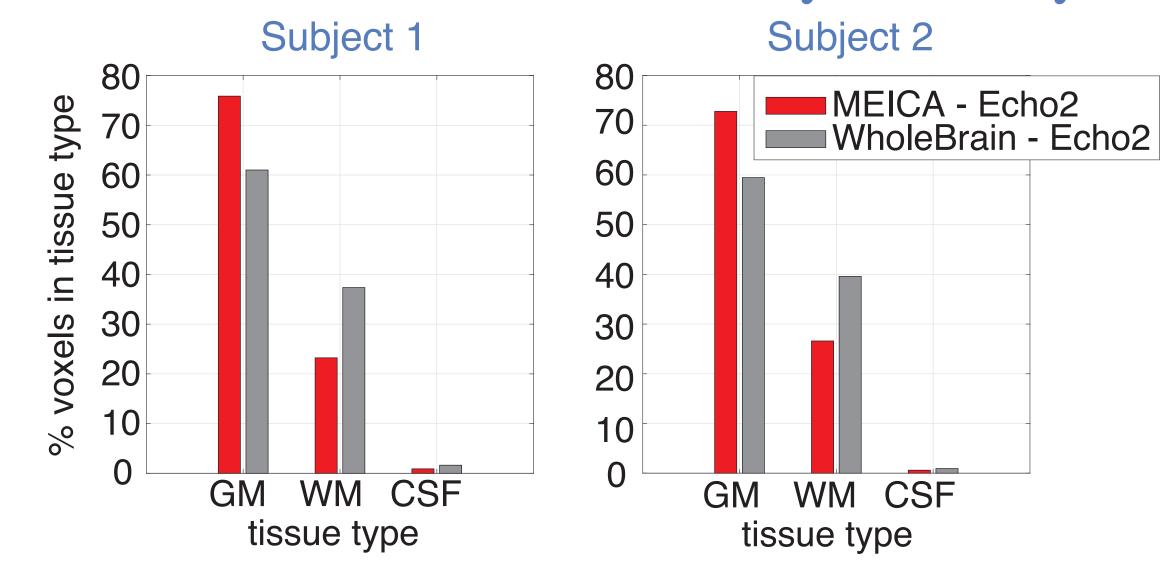


Figure 5: Breakdown of voxels found to have significantly reliable activation with MEICA but not Echo2 preprocessing. These voxels are significantly more likely to be in GM than would be expected by chance (gray bars), based on a binomial test, p<1e-16. Outer plots show voxels in one slice (z=15) that are significantly reliable in MEICA but not Echo2 preprocessing.

#### Results are not Explained by Blurring or IC Removal

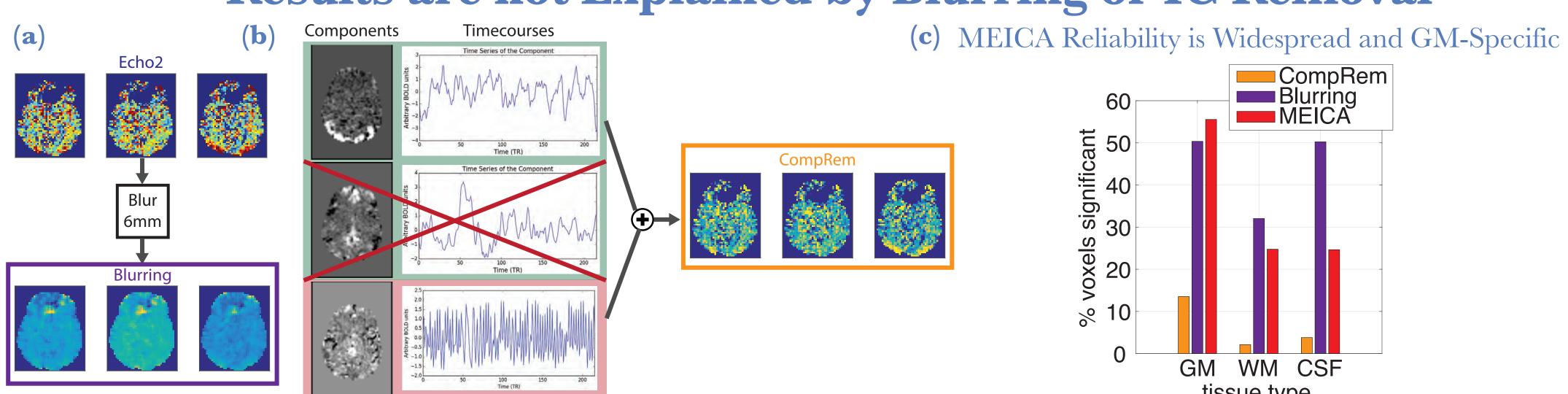
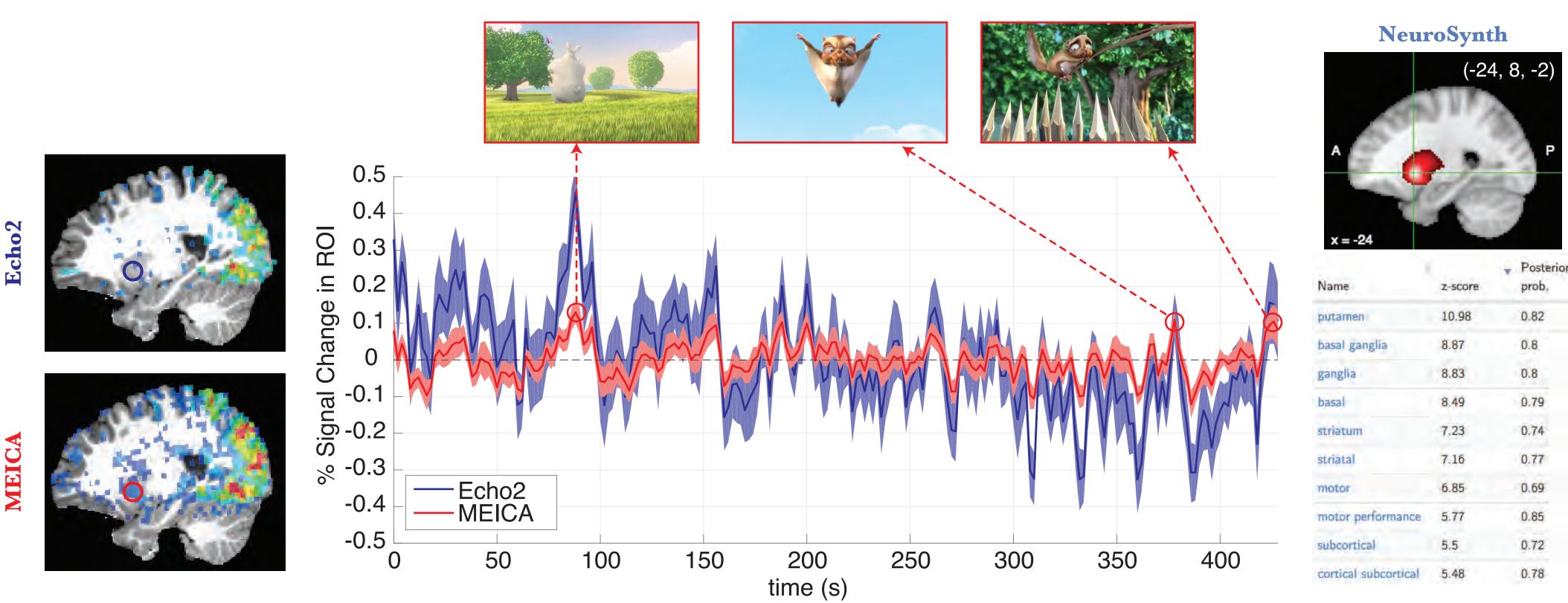


Figure 6: (a) Echo2 data were spatially blurred with a 6mm Gaussian and used for the "Blurring" control analysis. (b) Components were removed at random until the same amount of variance as MEICA was removed. The result is used in the "CompRem" control analysis. (c) CompRem produces much less response reliability than MEICA. Blurring's newly significant voxels are not as specific to GM.

#### Linking Newly Reliable Regions to Stimulus



**Figure 7:** A 5mm-radius spherical ROI whose response was significantly reliable with MEICA but not Echo2 processing (for Subject 1) was examined for its link to the stimulus using the "reverse correlation" technique (Hasson, 2004). The mean +/- standard error (across sessions) time-course of activity in the ROI is displayed in the main plot. The three times evoking the greatest activity in this area were mapped back onto the video frames that were most likely to have coincided with them (assuming an HRF delay of 5 s). These video frames are shown above the main plot. At right, the ROI center's connectivity and term associations from the NeuroSynth database.

### CONCLUSIONS

The addition of Multi-Echo ICA denoising to intra-subject correlation analysis in a naturalistic paradigm results in a much greater spatial extent of reliable activation. This suggests that many areas of the brain are involved in processing naturalistic stimuli but are too obscured by noise to appear in standard ISC analyses. This result serves as a naturalistic-stimulus extension of recent findings that the low CNR of task-based fMRI studies generates numerous false negatives (Gonzalez-Castillo, 2012). These new observations may inspire new, more targeted studies: using reverse correlation analysis (Hasson, 2004), we may generate testable hypotheses about the roles of these regions in the processing of dynamic visual stimuli.

#### REFERENCES

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