Separation of BOLD and non-BOLD drifts in multi-echo fMRI

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Introduction: fMRI time series are known to slowly drift and it has become standard to remove these drifts using linear regression; this filtering also removes slow neuronal changes that might be occurring. Assessment of very slow BOLD changes is nevertheless critical in studies of slow drug uptake effects, transcranial magnetic stimulation (TMS) induced changes or learning related cognitive changes. Thus far these studies have used arterial spin labeling (ASL) [1] to detect these changes, but unfortunately, this method has relatively low sensitivity and limited brain coverage per unit time. Conventional single echo fMRI has higher sensitivity than ASL, but cannot separate non-BOLD based signal drifts from neurally related changes in BOLD. In this study, we demonstrate that multi-echo independent components analysis (MEICA) [2] of multi-echo fMRI data can separate these two mixed low frequency signals and show very slow BOLD changes in the visual cortex from visual stimulation with slowly varying contrast.

Methods: 14 normal subjects (8 males, ages 22-36, median 23, mean 27) were scanned on a Siemens Skyra 3T scanner using a 32 channel coil with MPRAGE (res: 0.9mm) and multi-echo fMRI EPI scans (ipat2, res: 3.5mm, 28 slices, FA 90, TR 2 s, TEs: 14, 23,43 ms). A whole field flashing checkerboard at 7.5 Hz with a central fixation cross was used with varying contrast in the runs depicted in figure 1 on the right. It is expected that the BOLD response tracks the viewed contrast. The data was processed using MEICA (schematic in figure 2 on left), which decomposes the fMRI data using ICA and distinguishes BOLD and non-BOLD components based on a test of linear TE-dependence. Removing all non TE-dependent components specifically removed non-BOLD drifts while preserving BOLD baseline signal changes.

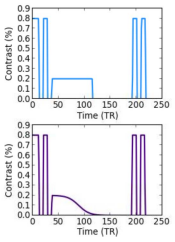


Figure 1. Task contrast amplitude as a function of time

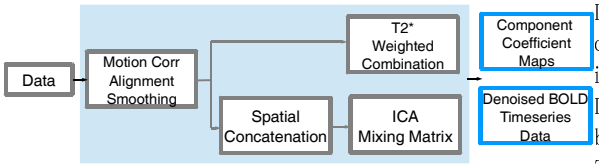


Figure 2. ME-ICA preprocessing steps

Results: Figure 3 to the left contains group average timeseries over voxels in V1 for the 20% block (left) and ramp (right) contrast tasks for denoised (dn) BOLD component, motion corrected conventional, and non-BOLD timeseries, the shading is the standard deviation about the mean (thick line). The V1 ROI was identified from a group map (thresholded at $p<0.01$ FWE) using a contrast localization task. The response to the task is clear for the block task in the dn-BOLD timeseries and there is a plausible negative trend for the ramp task. For the conventional timeseries the block task is visible but shows a positive trend, and in the ramp task the response looks somewhat flat. The non-BOLD component timeseries suggests that the positive trend found in the conventional timeseries is artifactual and obscures the ramp task.

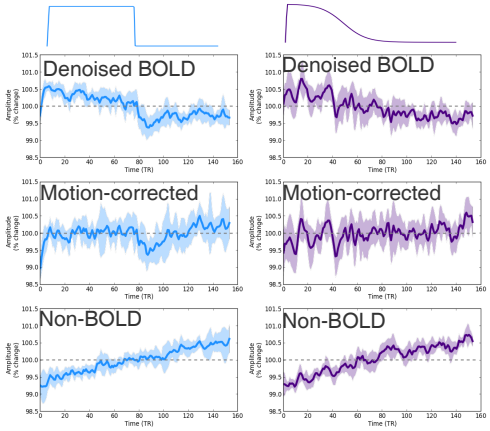
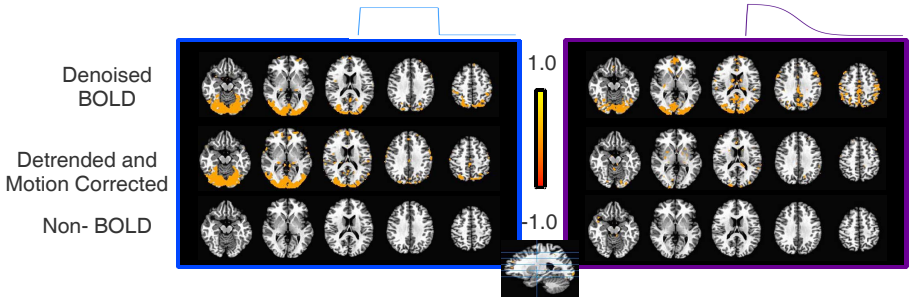


Figure 3. Group average timeseries for voxels in V1 in response to the block and ramp visual tasks.



Each row in figure 4 represents a group average of the individual correlation maps over all the subjects for the 20% block (left) and ramp (right) contrast tasks for the BOLD denoised components, detrended and motion corrected timeseries, and non-BOLD component timeseries. The maps are thresholded at $p<0.01$, FWE corrected. Only the task regressor was used in the model used to create the individual correlation maps. The BOLD component maps show clear localization to the visual cortex of the response in both tasks. The conventional timeseries shows a response in the visual cortex after detrending for the block task but not for the ramp task. The non-BOLD component timeseries shows no supra-threshold voxels, but does show non-specific response pattern at lower thresholds

Conclusion: MEICA denoising enables the clear delineation of slow task BOLD changes that occur over several minutes without additional pre-processing. This work opens the possibilities for new kinds of sustained fMRI paradigms as well as tracking the effects of TMS and the impact of cognitive drugs.

References: [1]Wang D. et al. (2011) Journal of Pharmaceuticals and Experimental Therapies, 337(2): 359-366 [2] Kundu, P. et al., (2012) Neuroimage 60(3):1759-1770