Direct comparison of BOLD measurements acquired using functional spectroscopy versus EPI

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Introduction: Functional spectroscopy (FS) measures changes in T2* associated with changes in blood oxygenation within a single volume of interest (VOI) [1]. FS uses a double spin-echo PRESS pulse sequence that gives a water-dominated free induction decay (FID) reflecting changes in VOI neural activation through a blood oxygenation level-dependent (BOLD) signal. While several groups have demonstrated that BOLD can be measured using FS, no study has directly compared FS BOLD measurements with echo-planar imaging (EPI), which is by far the most widely used pulse sequence for functional neuroimaging. To address this question we developed a pulse sequence that allows the simultaneous acquisition of FS and EPI data. We used this pulse sequence to test whether FS is more sensitive to BOLD changes than EPI by measuring the same BOLD signal with both sequences.

Methods: A combined FS/EPI pulse sequence was developed to measure BOLD using both techniques simultaneously (Figure 1). Within a single TR, first a standard EPI slice acquisition is performed, followed by the FS sequence for single VOI without water suppression. Although only one EPI slice and FS VOI are shown here, many of either can be collected each TR. The sequence was implemented using the IDEA system provided by Siemens for pulse sequence development. To compare FS and EPI BOLD measurements, four subjects were scanned using a 1.5 T Avanto system and a 32-channel head coil (Siemens Healthcare, Erlangen, Germany). During all functional scans subjects viewed flashing checkerboard stimuli designed to produce strong visual cortex activation in a block design (16s blocks with an initial baseline of 46s). A VOI in visual cortex was identified in each subject by performing an initial functional localizer scan, during which whole-brain EPI volumes were collected while the subject viewed the visual stimulus (TR=2s, TE=40ms, BW=2298Hz/px, 64x64 matrix size, FOV=208mm^2, 32 slices, 3mm slice thickness, 106 measurements). Just after imaging, the resulting volumes were analyzed using FSL to reveal voxels that responded strongly to the visual stimulus. This activation map was used to place the center of a VOI in primary visual cortex (Figure 2).

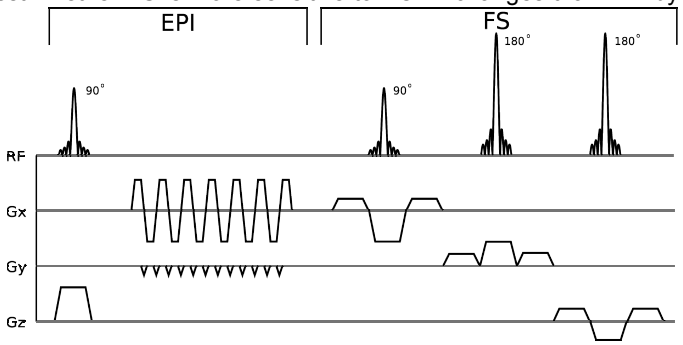

Figure 1: Combined FS/EPI pulse sequence for simultaneous BOLD.

After locating a VOI, each subject performed 3 scans to measure VOI BOLD: 1) a simultaneous FS/EPI scan, 2) an individual FS scan, and 3) an individual EPI scan. Imaging parameters for FS were: TR=2s, TE=40ms, VOI size=9x9x9mm^3, vector size=1024, BW=2300Hz. The EPI parameters were identical to the functional localizer scan except only a single 9mm thick slice was acquired. The position and orientation of the FS VOI and the EPI slice were matched so that the 3x3 square of voxels in the center of the EPI slice exactly matched the FS VOI. The simultaneous FS/EPI run was always performed second, and the order of the individual FS and individual EPI scans were alternated (first or third) between subjects.

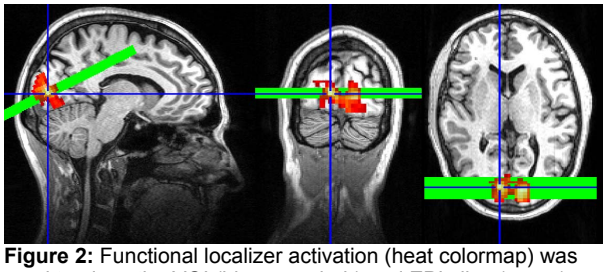

Figure 2: Functional localizer activation (heat colormap) was used to place the VOI (blue crosshair) and EPI slice (green).

FS FIDs were combined across coils using an SVD-based method that aims to eliminate common-mode white noise. Each coil-combined FID was fit to an exponential in the time domain (using *fminsearch* in Matlab) to estimate the amplitude (signal strength) and T2* (decay rate) at that TR. The T2* estimate over time was taken as the FS BOLD time series. The individual coil EPI measurements were reconstructed from raw data using custom image reconstruction software in Matlab, and the resulting coil images were combined using the standard sum-of-squares method. To compute an EPI BOLD time series in the VOI, the mean intensity of the central 9 voxels of the slice was computed.

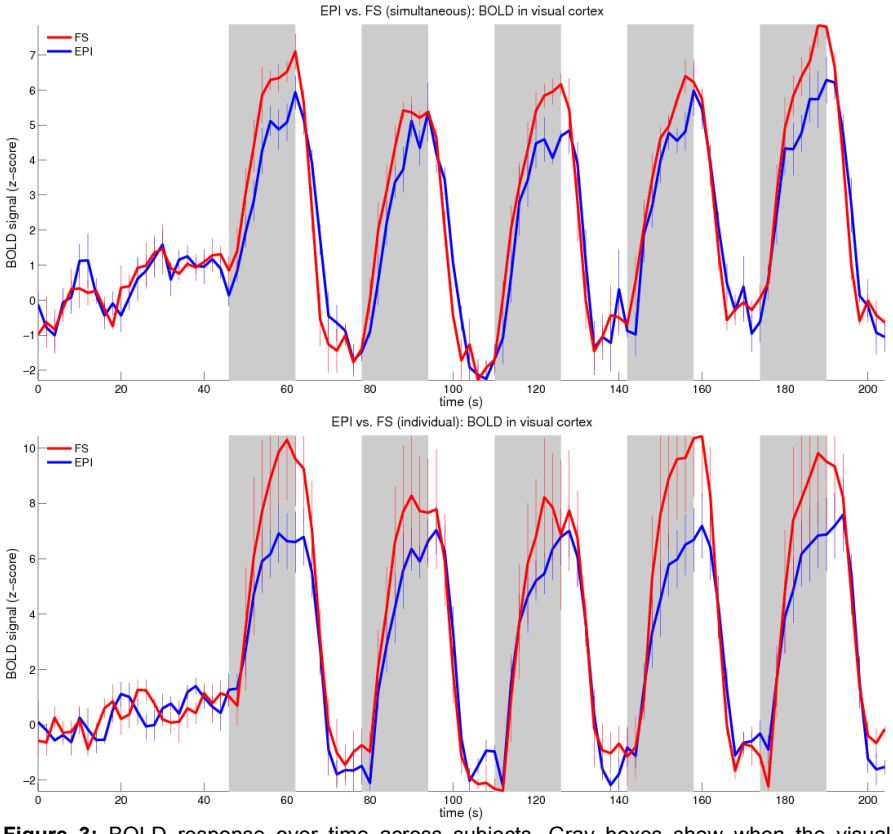

Figure 3: BOLD response over time across subjects. Gray boxes show when the visual stimulus was presented. Error bars represent standard error across subjects.

All time series were converted to percent signal change and fit to a general linear model with bases accounting for trends and stimulus related neural activation. The residual error of the fit over the first 46 measurements was used to estimate the variance of each run, which allowed conversion of each time series to BOLD signal in units of *z*-score over time.

Results and Discussion: FS BOLD measurements were consistently higher than EPI by a modest amount (Figure 3). A second level analysis comparing BOLD activation between these two methods across subjects showed that FS BOLD is (only barely) significantly higher than EPI BOLD ($t(3)=2.4$; $p=0.049$, one-tailed paired *t*-test for FS > EPI) when the two types of data are acquired simultaneously (Figure 3, top panel). Figure 3 (bottom panel) shows the increased variance present in the group FS and EPI time series when acquired individually (perhaps due to alternating acquisition order). This variance dictated that no significant difference was found for individual scans, although a larger mean difference between mean FS and EPI BOLD is apparent compared to simultaneous acquisition. These results suggest a small but systematic advantage to using FS over EPI. Future work will test the ability of these methods to measure BOLD at high temporal rates.

Reference: [1] Hennig, et al., 1994. MRM 31, 85-90

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