Model-based and data-driven analysis of whole brain EVI demonstrates increased statistical power compared to EPI at 3 T

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Objective. Whole brain multiple-slab echo-volumar-imaging (EVI) is a novel methodology that provides up to an order of magnitude higher temporal resolution compared to multi-slice echo-planar imaging (EPI). However, fMRI sensitivity of EVI and EPI has not yet been systematically compared using statistical parametric mapping (SPM) [1]. In this study, we assess extent and maximum *T*-score of activation in an auditory-gated visual-motor task for both modalities. Furthermore, the finer time course information available in EVI lends itself to data-driven analysis to identify physiological noise sources and spurious activation.

Methods. Multiple-slab EVI [2] and multi-slice EPI data were acquired in 2 right-handed healthy subjects using a clinical 3 T scanner equipped with 12-channel head array coil. EVI in AC/PC orientation was run with TR=280 ms, TEeff=28 ms, no. slabs: 4, slab thickness: 24 mm, FOV=256x256x96 mm, image matrix per slab: 64x64x8, α=10°, voxel size (mm) 4x4x4, 600 volumes, acquisition time: 2 min 40 s. In-plane reconstruction of complex images was carried out online, whereas the reconstruction in the 3rd dimension was performed online using TurboFIRE software [3]. EPI in the same slice orientation using identical scan time was run with TR=2 s, TE=28 ms, FOV (mm): 256x256, image matrix: 64x64, 32 slices, slice thickness: 4 mm, no inter-slice-gap, voxel size (mm): 4x4x4, 84 volumes. The experimental paradigm consisted of 5 epochs of 4 s of visual stimulation (eyes open) and sequentially finger tapping versus rest and eyes closed. Hypothesis-driven statistical inference on whole brain imaging data, both EPI and EVI, was carried out using SPM8. Spatial preprocessing comprised realignment and coregistration, spatial normalization and reslicing, and spatial Gaussian filtering with an isotropic kernel FWHM (mm): 8x8x8. EPI data were slice timing corrected before motion correction. Model specification included global scale correction, high-pass filtering with cut-off period 48 s > 2x2s (on) + 14x2s (off) =32 s. The model hemodynamic response function (HRF) included the first derivative in both modalities that allowed discrimination of events with higher temporal resolution. In a second step, data-driven model-free analysis was carried out by independent component analysis (ICA) implemented in batch-type fixed-point FastICA algorithm [4]. Spatial coordinates were converted from MNI to stereotaxic space by GingerALE software package [5]. Anatomically hierarchical labeling and Brodmann areas (BA) assignment for gray matter was performed by interrogating online Talairach Client [6] for +/- 4 mm volumes centered on voxels with the highest *T*-score in the most extended clusters.

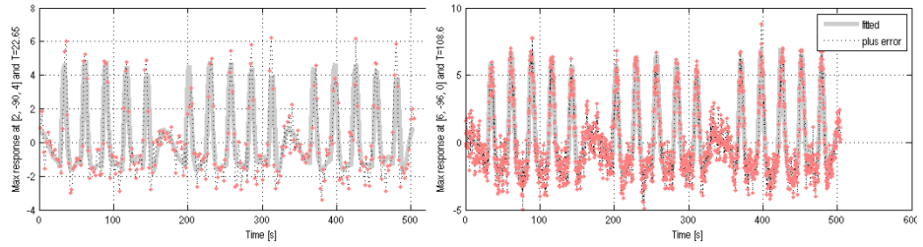

Fig. 1 - Auditory-gated visual-motor activation disclosed by EPI (left) and EVI (right) fMRI data analysis.

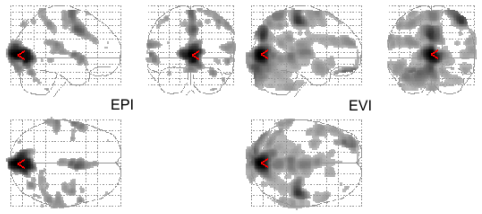

Fig. 2 – Orthogonal view of activations in data: EPI (left) and EVI (right).

Results. Both EVI and EPI magnitude MR images (Figs. 1&2), statistical inference revealed significant task-related signal changes in primary (V1) and secondary (V2) visual cortex (BA 17&18), primary somatosensory cortex (BA 3,1&2), and primary and auditory association cortex BA 41&42). Maximum *T*-values and percent BOLD signal changes were significantly higher with EVI than EPI. Both cluster- and set-level inferences revealed more extended areas of cortical activation for EVI at $p<0.001$ corrected, FWE control, similar thresholds (5.75 and 5.77), and corrected for serial correlation. SNR was computed between the main cluster and off the brain considering a ROI cube centered on max *T* and containing 125 voxels for computing the mean signal, and a similar cube positioned off the brain for evaluating the standard deviation of background noise. In ICA analysis, minimum description length was used to estimate concatenated data model for each modality indicating a lower dimensionality (16) for EVI compared with EPI (23). Activations running in parallel were easily discriminated in distinct components yet having the time courses of activations in quasi-similar correlation with the TC model used in SPM. A clearly delineated periodic signal (Fig.3) was detected by spatial ICA in all EVI data sets.

Table – Comparative statistical values of EVI versus EPI data analysis.

Imaging modality	Voxel-level inference (*T* max)	Cluster-level* inference	Set-level inference	Temporal CNR	Spatial SNR	Degrees of freedom
EPI	22.65	4,204	26	4.1	102	213
threshold = 5.77	23.63	13,263	19	4.3	128	213
p-value < 0.001	**23.14**	**8,733**	**22**	**4.2**	**115**	**213**
EVI	108.66	17,296	31	5.8	134	1761
threshold = 5.75	61.37	22,374	20	6.2	146	1761
p-value < 0.001	**85.02**	**19,835**	**25**	**6.0**	**140**	**1761**

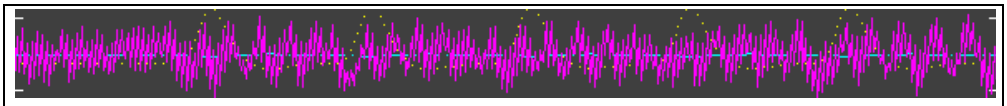

Fig. 3 - Periodically modulated time course of activation for one session disclosed by spatial ICA of EVI data

Discussion. The higher fMRI sensitivity of EVI compared to EPI (Table) is primarily due to the larger number of volumes per unit time compared to EPI. EVI suffers only moderate reduction of spatial SNR, thus maintaining statistical power. Furthermore, EVI provides maximum BOLD sensitivity per unit time, comparable to multi-echo EPI [2]. EVI is sensitive to steady-state effects that introduce signal fluctuations (Fig. 3). To investigate periodic signal changes further experiments in phantoms revealed that fluctuations were present in pure water, but absent in Agarose, suggesting T1 dependent steady-state effects. The EVI statistical data presented in the table above appear inflated compared with the EPI counterparts due to temporal correlation that exist for very short TR in SPM, which is not fully unaccounted for in SPM8.

Conclusion. The high temporal resolution of EVI provides much larger degrees of freedom to model the hemodynamic response than EPI, which improves statistical significance. Data driven analysis in EVI is complementary to model-based analysis to identify sources of variability that can be modeled as confounds in model-based analysis to further increase statistical power. This study demonstrates that EVI is a novel fMRI modality, which provides higher temporal resolution and fMRI sensitivity compared to EPI.

References. 1. Friston K.J., *et al*., Academic Press, 2007; **2.** Posse S., *et al.*, ISMRM *Abstracts*, 3590 (2010); **3.** Posse S., *et al*., *Hum Brain Mapp,* 12:1 (2001) 25-41; **4.** Hyvärinen A, *et al*., Wiley, 2001; **5.** Eickhoff S., *et al*., *Hum Brain Mapp*, 30:9 (2009) 2907-26; **6.** Lancaster J.L., *et al*., *Hum Brain Mapp*, 10 (2000) 120-31.

Acknowledgments: R.M. has been supported by the Fulbright Scholar Program Advanced Research in the Unites States, Grant #495/2010-2011.