EVENT-RELATED WHOLE-BRAIN FMRI: EPI WITH SLICE DEPENDENT ECHO TIMES VERSUS STANDARD EPI

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Introduction:
EPI is commonly utilized for whole-brain fMRI due to its high temporal resolution (spatial coverage). Drawbacks for fMRI are compromised BOLD sensitivity (BS) and signal loss due to susceptibility gradients occurring near air-tissue interfaces like in subcortical and prefrontal areas of the human brain [1]. Reducing the echo time (TE) from the standard value of 40-50ms used at 3.0 T weakens signal attenuation and enhances BS in crucial areas. Stöcker et al. proposed an EPI with slice dependent TE to meet optimal BS in different regions [2]. At 3.0T, robust amygdalae activation has been detected at TE of 27ms [3]. At that field strength, we present an event-related whole-brain fMRI study testing an EPI with slice dependent TE (modified EPI) against an EPI with TE of 27ms (standard EPI).

Methods:
Scanning was performed on a 3.0 T scanner (Tim Trio; Siemens Medical Solutions, Erlangen, Germany). BS simulation requires local gradient strengths and T_2^* values. For this, phase data and T_2^* weighted images were acquired from six healthy subjects using a spoiled multigradient-echo FLASH sequence measuring 40 slices with 220mm field-of-view (FOV), 64x64 matrix size and 2.5mm slice thickness. Each phase dataset was collected at five different TEs, 2.45, 5.12, 7.79, 10.46, 13.13ms. Linear least-squares fits were applied to estimate local through- and in-plane gradients G_{sz} and G_{sp}, i.e. along the z- and the phase-encode direction, respectively. Intensity images were collected at twelve different TEs, ranging from 5 to 140ms. A sinc-modulated exponential function was fitted to the data to estimate local T_2^* values [4]. In order to inter-subject average gradient and T_2* maps, normalization to the common MNI EPI-template brain was performed. BS simulations indicated optimal TE-values to maximize BS for several regions like the amygdalae or the prefrontal cortex (PFC). T_2* and gradient strength values with an error of more than 20 percent at 95% confidence bounds were discarded for BS calculations. Twelve subjects performed twice a probabilistic reversal learning task [5], which predominantly involved limbic and frontal brain regions. The modified and the standard EPI sequences were counterbalanced to avoid ordering effects. Each standard EPI dataset comprising 40 axial slices aligned to AC-PC was acquired with the following parameters: TE=27ms, matrix: 96x96, TR=2.7s, FOV=220mm, bandwidth: 1270 Hz, slice thickness: 2.3mm. The TEs of the modified EPI matched approximately but not perfectly the previously calculated optimal values for two reasons. First, different regions may share the same slice and secondly, image registration may suffer from unnatural intensity changes [2]. Therefore a smooth transition zone of slice dependent TE is implemented. TEs increased linearly from slice 1 with TE of 22ms to slice 27 with TE of 47ms and then remained constant until slice 40. Bandwidth was increased to 1578Hz to account for shorter echo trains. The remaining imaging parameters were consistent in both EPIs. Statistical analysis was performed using SPM2 [The MathWorks, Inc: Stastistical Parameter Mapping, 2002].

Results:
Single subject BS curves are plotted against different TE values, ranging from 0 to 100ms in fig. 1. Before BS was calculated, T_2* values and gradient field strengths G_{sz} and G_{sp} were averaged over all voxels within a specific area. BS peaks at TE^{opt}=23ms in the amygdalae (T_2*=39±7ms), at TE^{opt}=29ms in the olfactory cortex (T_2*=37±7ms) and at TE^{opt}=37ms in the PFC (T_2*=51±5ms). Group analysis results (p<0.001 unc., clustersize 5) of the whole-brain fMRI study (fig. 2, fig. 3) using the modified EPI (fig. 2b, fig. 3b) and the standard EPI (fig. 2a, fig. 3a), respectively. The reward-punishment contrast shows activation in limbic and prefrontal brain areas. The number of supra-threshold voxels found in putamen, thalamus, parahippocampal gyrus, hippocampus, and superior frontal cortex is more than twice as high in the modified EPI as in the standard EPI (tab. 1). More activation is found in the middle frontal gyrus and the olfactory cortex using the standard EPI. Maximal Z-scores are slightly higher in most regions when using the modified EPI (Tab 1).

Discussion:
BS simulation for different brain areas demonstrated the importance of adapting TE to achieve maximal BS. In addition, we showed in an event-related whole-brain fMRI study that statistical inference can be considerably enhanced by using slice dependent TEs at 3.0T. Adjusting TE for different regions becomes even more important at higher field strength since susceptibility gradients increase with B_0. In future work we will investigate the benefits of this technique at 7.0T.

References:
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[3] Morawetz et al. [2007] Magn. Reson. Imag. 26: 45-53
[4] Peters et al. [2007] Magn. Reson. Imag. 25: 748-753
[5] Linke et al. [2009] Neuroimage [Epub ahead of print]

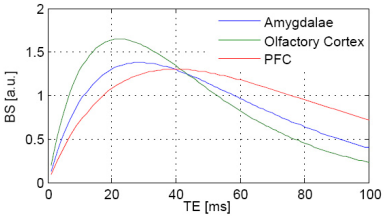

***Figure 1**. BS simulated for amygdalae, olfactory cortex and prefrontal cortex of a single subject. Each brain region must be imaged at different TE to achieve maximal BS.*

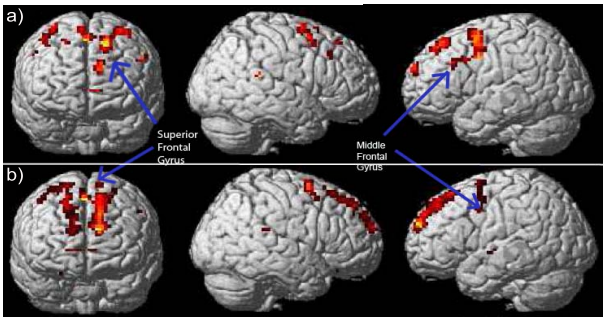

***Figure 2.** One sample t-test results (random effects) of the whole-brain fMRI study, using the standard EPI **(a)** and the modified EPI sequence **(b)** (p<0.001 unc., clustersize 5). The reward-punishment contrast shows activation in the PFC.*

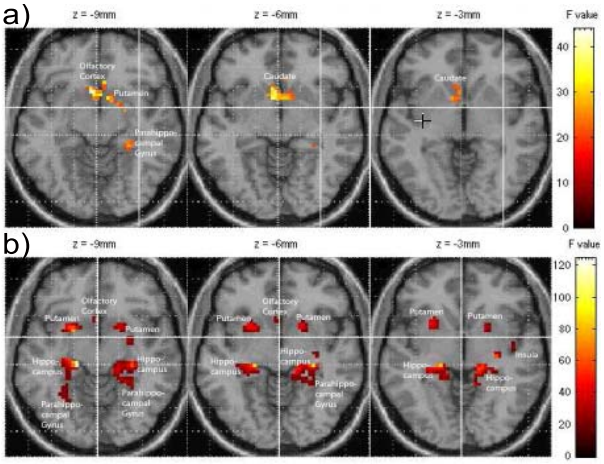

***Figure 3**. One sample t-test results (random effects) of the whole-brain fMRI study using the standard EPI (a) and the modified EPI (b) (p<0.001 unc., clustersize 5). The reward-punishment contrast shows activation in caudate, putamen, olfactory cortex, parahippocampal gyrus, insula and hippocampus.*

ROI →	1	2	3	4	5	6	7	8	9	10
N_{std}	43	44	15	6	13	429	129	261	245	57
Z_{std}^{max}	4.0	4.2	4.1	3.9	3.9	4.6	4.3	4.4	4.6	4.2
N_{mod}	65	61	219	89	0	943	262	563	104	18
Z_{mod}^{max}	4.0	4.0	4.5	4.6	x	5.1	5.0	5.5	4.3	3.9

***Table 1.** $N_{std/mod}$ is the sum of supra-threshold voxels (p<0.001 unc., clustersize 5) for different ROIs (see legend below) found in the standard and the modified EPI datasets for the contrasts reward-punishment, reward-baseline and punishment-baseline. $Z_{std/mod}^{max}$ specifies the maximal Z-score. ROI 1: Insula, ROI 2: Amygdalae, ROI 3: Putamen, ROI 4: Thalamus, ROI 5: Caudate, ROI 6: Parahippocampal Gyrus, ROI 7: Hippocampus, ROI 8: Superior Frontal Gyrus, ROI 9: Middle Frontal Gyrus, ROI 10: Olfactory Cortex.*