

## Effect of Distortion Correction on Group Level Statistics in fMRI of Medial Temporal Lobe

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### Introduction

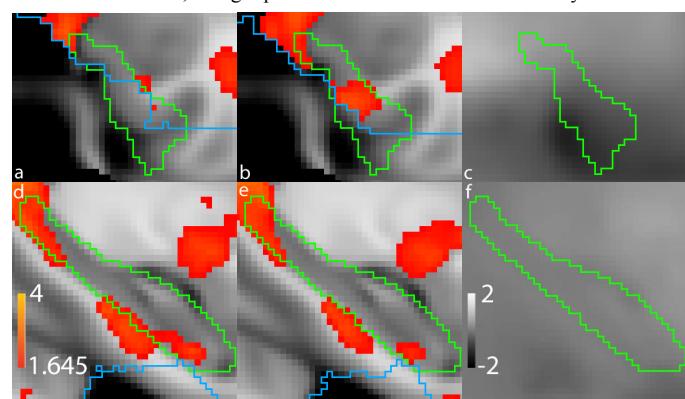
Spatially varying magnetic susceptibility gives rise to geometric distortions in single shot EPI images. In fMRI this causes local misregistration between functional and anatomical images. Different approaches have been proposed to alleviate this problem [1-4], all of which require additional scans and/or postprocessing steps. Hence one would want to perform these additional steps only if they give a real benefit to the fMRI results in terms of improved registration accuracy and power of the functional analysis in the region of interest. The purpose of this study was to evaluate the effect of applying distortion correction by the reverse gradient method [4] in a large group study in which very weak activation effects in the entorhinal cortex and hippocampus were analyzed.

### Material and Methods

**Functional scans:** 25 healthy male subjects were scanned during a spatial encoding paradigm in which they learned 35 different environments distributed over 7 runs. The paradigm comprised for each of the 35 environments; a 30 second learning period in the virtual environment, 15 second post stimulus encoding and a 15 second odd even task. Scanning was performed at 3T (Siemens TIM TRIO) using the vendor provided 32 channel head coil. Single shot 2D GRE-EPI, optimized for high PE pixel BW was used with the following parameters; TE/TR = 28/2110.8 ms, 40 slices with 116x116 matrix size, 1.9 mm isotropic resolution, GRAPPA acceleration factor 4, BW per pixel in the PE direction = 49.26 Hz. Correction scans were acquired between functional runs, as well as one anatomical MP-RAGE. The correction scans were SE-EPI scans with TE/TR = 90/4600 ms, nrep=10, otherwise identical to GRE-EPI scans. Two sets of correction scans were acquired with opposing phase encoding direction, and each set was averaged and used to calculate a distortion map [4]. **Processing:** The functional scans were corrected according to the distortion map after they were motion corrected and registered to the appropriate correction scan. Two functional analyses were performed using FSL, one using the distortion corrected functional scans and one using the original non-corrected data. The functional scans were registered (affine transform) to the MNI152\_1mm standard via the T1W anatomical scan (rigid body transform) using FLIRT with normalized mutual information as cost function. Group level statistics were then calculated. To evaluate the registration accuracy the cost function values for the registration of the functional scans to the anatomical T1W scans were calculated and a paired t-test was performed on the difference between the corrected and the non-corrected functional scans. To investigate the effect of the distortion correction on the group level statistics, as well as the level of distortion, four ROIs were selected using the FSL atlas tool; left/right entorhinal cortex EC (Juelich), left/right hippocampus HC (Harvard-Oxford). Volume of activation in these ROIs using z-value threshold of 1.645 were extracted as well as peak z-values. All distortion maps were registered to standard space using the transformation matrices from the registration of the functional analyses and a population average distortion map  $\langle d \rangle$  was calculated. The mean value of  $\langle d \rangle$  within the ROI, as well as the spatial variation in  $\langle d \rangle$  within each ROI was calculated. In addition the total volume of the intensity based mask generated in FSL was calculated.

### Results and discussion

The difference in the final value of the cost function was  $-0.0032 \pm 1.7 \cdot 10^{-5}$  (mean  $\pm$  SEM),  $p < 0.001$ , between corrected and non-corrected data, confirming that the registration to the anatomical scan improved. Results from the ROI analysis are summarized in table 1. In EC, both the number of activated voxels and peak z value increase after distortion correction. Mean  $\langle d \rangle$  and std  $\langle d \rangle$  values indicate that there is both a general shift in position and local warp-field in this ROI. These observations are confirmed in figure 1a-c, where an activated cluster centered in EC appears after distortion correction. The border of the FSL mask shows that after distortion correction, a larger portion of EC has sufficient intensity across all runs to be included in the functional analysis. In HC the number of activated voxels within the ROI is reduced, while the peak z-value increases on the left side and decreases on the right side. The mean  $\langle d \rangle$  and std  $\langle d \rangle$  indicates that the distortion is mostly a position shift while the degree of warp is low. In figure 1d-f we see that the position of the activated cluster is shifted away from the ROI after distortion correction, thus explaining a part of the observed reduction in volume of activation within the ROI. The total volume of the FSL mask generated for the group level analysis in FEAT increased by 7 % after distortion correction. This means more voxels survived through the FSL analysis, in particular in regions with large distortions, as illustrated in EC in figure 1a-b. The details of why the FSL-mask was larger for the distortion corrected data should be further investigated. Also there is a systematic difference in mean  $\langle d \rangle$  between the hemispheres.



**Figure 1.** Left entorhinal cortex EC (a-c), left hippocampus HC (d-f). Orange voxels have z-value above 1.645 (encoding period / learning period) using non-corrected functional scans (a, d) and using distortion corrected functional scans (b, e). Corresponding map of the mean distortion in the voxel across all runs (c, f). The green lines mark the ROIs and blue lines mark the edge of the FSL-generated mask.

**Table 1.** Entorhinal cortex left/right (ECL/ECR), hippocampus left/right (HCL/HCR), non-distortion corrected (NC) and corrected (C) functional data,  $d$  is the distortion and  $\langle d \rangle$  is the mean distortion in a voxel across all functional scans,  $V_{roi}$  is the volume of the ROI while  $V_{roi \cap mask}$  is the volume of the intersection of the ROI and the FSL mask.

	Unit	ECL	ECR	HCL	HCR
NC, $z > 1.645$	$\text{mm}^3$	90	377	799	782
C, $z > 1.645$	$\text{mm}^3$	266	472	669	666
NC, $z_{\text{peak}}$		2.71	3.49	4.57	3.26
C, $z_{\text{peak}}$		2.89	3.62	4.81	3.17
Mean $\langle d \rangle$	pxl (Hz)	-0.48 (-20)	-0.75 (-32)	0.01 (0.4)	-0.32 (-14)
Std $\langle d \rangle$	pxl (Hz)	0.41 (20)	0.40 (20)	0.11 (5.3)	0.10 (4.7)
$V_{roi}$	$\text{mm}^3$	3537	3994	4167	4471
NC, $V_{roi \cap mask}$	$\text{mm}^3$	1086	1701	4163	4470
C, $V_{roi \cap mask}$	$\text{mm}^3$	1665	1786	4164	4467

In conclusion, we found that there was a clear positive effect of distortion correction in the entorhinal cortex, even for this optimized EPI-protocol with bandwidth along PE direction of 49 Hz/pixel.

### References

- [1] P. Jezzard et al. *Magn Reson Med*, 34(1):65-73, 1995. [2] P. J. Reber et al. *Magn Reson Med*, 39(2):328-30, 1998. [3] M. Zaitsev et al. *Magn Reson Med*, 52(5):1156-66, 2004. [4] D. Holland et al. *NeuroImage*, 50(1):175-83, 2010.