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CORRECTING INHOMOGENEITY-INDUCED DISTORTION IN FMRI USING NON-RIGID REGISTRATION

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Abstract

Magnetic field inhomogeneities in echo planar images (EPI) can cause large distortion in the phase encoding dimension. In functional MRI (fMRI), this distortion can shift activation loci, increase inter subject variability, and reduce statistical power during group analysis. Distortion correction methods that make use of acquired magnetic field maps have been developed, however, field maps are not always acquired or may not be available to researchers. An alternative approach, which we pursue in this paper, is to estimate the distortion retrospectively by spatially registering the EPI to a structural MRI. We describe a constrained non-linear registration method for correcting fMRI distortion that uses T_1 -weighted images and does not require field maps. We compared resting state results from uncorrected fMRI, fMRI data corrected with field maps, and fMRI data corrected with our proposed method in data from 20 subjects. The results show that the estimated field maps were similar to the acquired field maps and that the proposed method reduces the overall error in independent component location.

1. INTRODUCTION

Most functional MRI (fMRI) experiments are based on images that demonstrate blood oxygen level dependent (BOLD) signal contrast. To track changes in blood oxygenation with high temporal resolution, these images are typically acquired with a fast echo-planar imaging (EPI) readout. EPI enables measurement of BOLD signal from the whole-brain with a temporal resolution on the order of seconds. However, the use of a long EPI readout also makes the data sensitive to inhomogeneities in the main (B_0) magnetic field. Specifically, B_0 inhomogeneity results in geometric distortion of reconstructed EPI images. This problem is especially severe in brain regions where B_0 inhomogeneity is consistently large. For example, the distortion can exceed 20 mm near tissue-air interfaces such as frontal sinuses and the ear canals (where magnetic susceptibility varies rapidly, leading to unavoidable variations in the B_0 field).

B_0 inhomogeneity depends on the geometry of the imaging subject's anatomy, the orientation of that anatomy with respect to the B_0 field, and several other factors such as the scan-dependent magnetic shim settings. This generally means that B_0 inhomogeneity is not known in advance, and should be measured ("field mapping") for each scan session in order

to construct an accurate forward model of the distortion process. Several field map based methods have been developed for correcting EPI distortion, e.g. [1, 2]; however, field maps may not be available during data analysis, e.g., if they were not collected during scanning or were not included in a data repository. An alternative to acquiring field maps is to estimate the distortion using nonlinear image registration to map the distorted EPI data to an anatomical reference image.

Several registration based methods have been developed previously for distortion correction in EPI. Kybic et al. introduced a method that estimated the distortion by registering the EPI data to a T_2 -weighted MRI using spline-based registration and a least squares cost function [3]. Studholme et al. developed a method to correct EPI distortion using nonlinear registration to a T_1 -weighted MRI by maximizing normalized mutual information [4]. More recently, Bhushan et al. developed a method for correcting EPI distortion in diffusion weighted MRI by applying a similar method and including a Parzen window to smooth the probability distribution functions [5]. Similar to [4, 5], we employ mutual information for our registration metric, which enables us to register the distorted fMRI to a T_1 -weighted image. T_1 -weighted images have high tissue contrast, making them useful for both analysis of brain morphometry and registration based distortion correction. We parameterize distortion using a thin plate B-spline and maximize an information metric between the fMRI and T_1 -weighted images, as was done in [4,5], using analytical derivatives based on a Parzen window, as in [5]. We have further added Jacobian regularization to the registration process to reduce over-fitting. This can be a significant problem when registering fMRI to T_1 images due to poor contrast between grey matter (GM) and white matter (WM). We applied our method to fMRI and T_1 data from 20 subjects for which field maps were also collected. We compared the results of resting state analysis produced from uncorrected fMRI, fMRI data corrected with field maps, and fMRI data corrected with the proposed method.

2. METHODS

We model the measured echo planar image, I_m , as a distorted version of the true image, I_t , at each position, $\vec{p}$:

$$I_m(\vec{p}) = I_t(\vec{p} + \vec{\Phi}_t(\vec{p})) S(\vec{p}) \quad (1)$$

where $\vec{\Phi}_t$ is the change in spatial position, i.e., the offset due to distortion, and S is a local intensity scale factor due to signal pile up or stretching. S is characterized by the Jacobian determinant of coordinate mapping. $\vec{\Phi}_t$ is a function of gradient strength, local inhomogeneity, and, in the case of phase encoding, time (see [1–4]). Distortion is largest along the phase-encode axis. Therefore, we model distortion as unidirectional along that axis (assumed x) and ignore the effects in other dimensions. We thus estimate the true image as a function of the measured EPI image and the estimated distortion:

$$\hat{I}_t(\vec{p}) = I_m(\vec{p} - [\psi(\vec{p}), 0, 0]^T) \left(1 + \frac{\partial \psi(\vec{p})}{\partial x}\right)^{-1} \quad (2)$$

where ψ is the estimated inverse (unidirectional) field map, and $(1 + \partial\psi(\vec{p})/\partial x)$ is the simplified Jacobian determinant of the coordinate mapping under the assumption of unidirectional distortion. We parameterize $\hat{\psi}$ as a cubic B-spline:

$$\hat{\psi}(x, y, z) = \sum_{i,j,k} \Psi_{ijk} B(i-x) B(j-y) B(k-z) \quad (3)$$

where $[x, y, z]^T$ and $[i, j, k]^T$ are continuous and discrete coordinates in the field of view, respectively, and Ψ_{ijk} is the B-spline parameter at $[i, j, k]^T$.

We estimate the inverse distortion field by maximizing the mutual information between the estimated true image, $\hat{I}_t$, and a T_1 -weighted anatomical image, I_A , while minimizing change in intensity and thin plate spline bending energy. We thus find $\hat{\psi}$ that satisfies:

$$\hat{\psi} = \underset{\psi}{\operatorname{argmin}} \left(-MI(I_A, \hat{I}_t) + \alpha E_{tps}(\psi) + \beta E_j(\psi) \right) \quad (4)$$

where MI is the mutual information between the two images, E_{tps} is the thin plate spline bending energy of $\hat{\psi}$, E_j is the integral of the squared Jacobian determinant of $\hat{\psi}$, and α and β are regularization weights [6]. Both E_j and E_{tps} have closed form solutions for B-splines. We solve the objective function (eq. 4) using the limited memory BFGS algorithm. We compute an analytical gradient by estimating the empirical joint density function of image intensities by applying a cubic B-spline Parzen window of radius 4.

We tested our algorithm on fMRI data of 20 healthy male 26-to-30 year old subjects from the Human Connectome Project (HCP) database [7]. Each subject underwent MRI in a Siemens Skyra 3T scanner with a customized SC72 gradient insert. Data included a T_1 -weighted structural (3D MPRAGE TR=2400 ms, TE=2.14 ms, TI=1000 ms, flip angle=8°, 0.7 mm isotropic voxels), a resting state fMRI (Gradient-Echo EPI, TR=720 ms, TE=33.1 ms, flip angle=52°, Matrix: $208 \times 180 \times 72$, FE $\times$ PE $\times$ SS, 2 mm isotropic voxels, Multiband factor: 8, Echo spacing= 0.58 ms, 1400 volumes), a 32-Channel bias field estimation (BIAS, 2 mm isotropic voxels, TR=250 ms, TE=1.01 ms) and a Spin-Echo field map (L/R Reversed Gradients, TR=7060 ms, TE=58 ms, flip angle=90°, 2 mm isotropic voxels, Echo spacing=0.58 ms).

Each subject's fMRI was processed three different ways: once with no EPI distortion correction (NDC), once with field map distortion correction (FDC) using FSL TOPUP [8], and once with the registration-based distortion correction method (RDC). We used the HCP pipeline to construct MNI-aligned fMRI data from the NDC, RDC and FDC fMRI [9].

To create a suitable fMRI volume for nonlinear registration, we applied motion correction, bias field correction and time-averaging to each fMRI to produce I_m . We estimated the bias field from the 32-channel BIAS image and then applied the estimate to the time-averaged fMRI. We then registered the T_1 -weighted image to I_m using rigid registration based on mutual information, to produce I_A – the fMRI-aligned anatomical image. Finally, we estimated the $\hat{\psi}$ that maximizes mutual information between $\hat{I}_t$ and I_A .

We used the estimated field map to correct distortion at each time point in the fMRI. First, we applied the motion transform computed at the time point to move the inverse distortion, $\hat{\psi}$, into the native space of each fMRI volume. We then applied the transform inverse distortion as an x -directed deformation in the volume. Finally, we applied the same inverse motion transform to the distortion-corrected volume, to bring it into the space of the first fMRI volume.

3. RESULTS

We compared NDC, RDC and FDC results for 20 HCP subjects. An example of the improvement due to each method is shown for one subject in Fig. 1. Note the improved alignment of the temporal lobes and reduction in overall distortion throughout the brain. For all 20 subjects, we performed a voxelwise comparison of the RDC estimated field map and the TOPUP field map. To do so, we concatenated all offsets within the brain from both FDC and RDC methods, then computed the correlation. We found that that two were correlated ($r = 0.58$, $R^2 = 0.33$), although regions of large distortion remained as seen in the field map comparison (Fig. 2).

To determine the impact of RDC on resting state fMRI, we performed group-wise independent components analysis using MELODIC (FSL v5.0.7, no smoothing) by spatially concatenating the NDC, RDC, and FDC versions of each fMRI and then temporally concatenating subjects. The resulting components should therefore be temporally identical within subjects (across methods) and spatially identical within methods (across subjects). We manually identified components that were confined to grey matter and compared the results across methods. We found no significant difference due to correction method in the average activation level among the analyzed components. Visual inspection showed that the activation maps computed when no distortion correction was applied were misaligned relative to the field map corrected results; the registration-based correction showed greater agreement with the field map-based method (see Fig.3). To quantify the IC shift and the degree to which the registration based method improved this, we thresholded the significance maps ($p > 0.9$) to produce regions of interest (ROI) for each component, then compared NDC and RDC ROIs with those from the FDC group (Fig. 3). We then compared the overlap of each component, and found the components produced from uncorrected fMRI mismatched the FDC components in 27,484 (219 cm³) voxels. In the RDC group, there were 34% fewer mismatches (14,142 mismatched voxels; 113 cm³). Testing the set of differences among all GM components there was a significant reduction in mask differences ($p < 1.5 \times 10^{-8}$).

4. DISCUSSION

In this work, we have described a method for estimating distortion in fMRI by using constrained registration to a T1-weighted anatomical reference image. We have validated the method by comparing the estimated field maps with collected field maps. We then compared the results of ICA with and without the registration-based correction to the results of ICA after correcting distortion using acquired field maps. While in this work we have

only compared the results to field mapping methods, future work would benefit from comparison with other EPI correction methods, e.g., those developed in [4,5].

The main limitation of this method is caused by limited contrast in fMRI; though matching CSF boundaries will usually be possible, over-fitting can occur if regularization weights are not set sufficiently high. This limits the amount of distortion that can be matched, because the algorithm may not be able to distinguish between stretched GM and GM that is less bright due to a combination of bias fields and low GM/WM contrast. This is one possible reason why regions with larger distortion was not correctly estimated (see Fig. 2). While reducing regularization weighting might improve the fit in such locations, it would permit over fitting elsewhere. A further limitation is that signal compressed into a single voxel cannot be uniquely recovered, even if geometry is properly estimated; this is also the case when using correction based on field maps.

In our validation studies, we found that the registration based distortion correction method estimated a distortion field that was correlated with the distortion measured using a magnetic field map, although it was not able to match larger distortions. We also found that our method improved the alignment of ICs versus uncorrected fMRI. While not as powerful as field map methods, this method provides utility in cases where field maps may not be available.

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Fig. 1.

Coronal image slices from an HCP subject. EPI images are shown in grey scale; the tissue boundary from the T_1 -weighted image is shown as a green outline. There is notable geometric distortion in the temporal lobes (indicated by red arrows). **a)** Original uncorrected EPI. **b)** Registration based distortion corrected EPI. **c)** Field-map corrected EPI.

Fig. 2.

Scatter histogram of offsets from the collected field map versus offsets from registration (in mm). Dashed line with slope of 1 shown for reference. Overall, the estimated distortion is correlated with the true distortion ($r = 0.58$, $R^2 = 0.33$). Histogram was computed using all 20 subjects.

Fig. 3. Selected GM independent components in MNI space. Components are shown as regions of voxels where $p > 0.9$. Blue regions indicate location of ICs in the field map corrected fMRI. **Left:** Red regions indicate components from uncorrected fMRI. **Right:** Red regions indicate components from RDC fMRI. Overlap of red and blue is shown in magenta, indicating concordance between the methods. Note the shifted activation patterns in the uncorrected (left) images, due to Left/Right distortion. After registration based distortion correction (right, red), there is better alignment of the activation pattern with the activation pattern from field map corrected fMRI (blue).