Elastic Registration of Functional MRI Data to Sensorimotor Cortex

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Abstract — **Functional MRI (fMRI) studies often critically build on assignments of task related fMRI responses to brain anatomy that presuppose accurate registration of the functional data to anatomical space. Registration methods proposed in the literature for this purpose range from rigid body transformation which only allows for translation and rotation, over affine transformations additionally allowing for scale and shear, to high-dimensional non-linear methods such as elastic registration with hundreds of control parameters. There is only little data on the impact of transformation model complexity on fMRI localization accuracy. Here we have therefore compared the spatial accuracy of rigid body registration, affine registration, and elastic registration based on Bezier-spline transformations. To this aim, we have acquired fMRI data in subjects performing a hand movement task. When applying rigid body and affine registration, the response center of mass was erroneously assigned to the primary somatosensory instead to the primary motor cortex in 20% and 45% of cases, while such errors only occurred in 5% of elastically registered cases. Our findings demonstrate that sophisticated registration techniques can increase the assignments accuracy of fMRI responses to sensorimotor cortex. Furthermore we provide an outlook for methods based on high resolution fMRI circumventing the registration problem, that – compared to methods based on structural-functional co-registration – are suitable to achieve higher localization accuracy.**

Keywords — **Motor cortex, functional MRI, registration, spline transformation, high resolution**

I. Introduction

Function to anatomical structure assignment is fundamental to many current neuroimaging studies. To accurately assign functional maps to anatomical data, a co-registration problem has to be solved, if the anatomical information that can be derived from the functional images is not detailed enough and therefore additional high-resolution anatomical data sets are recorded. Then, the high resolution anatomical data set must be brought into spatial correspondence to the lower resolution functional data set. This is achieved by application of a registration algorithm finding a suitable spatial transformation from the source or 'moving' image to the reference or 'target' image.

Registration algorithms applied in fMRI brain imaging studies for the EPI-to-anatomy registration problem are mostly linear methods, but also non-linear approaches have been proposed (for a review see ref. [3]). Linear models in the general sense are those models retaining colinearity of image points, such as rigid body registration allowing translation and rotation in x, y and z (corresponding to 6 independent parameters). Within the linear framework, up to 9 additional parameters can allow for rescaling and/or perspective transformations. In contrast, non-linear registration is based on high-dimensional transformation maps allowing for elastic (hundreds of parameters) or fluid (thousands of parameters) deformations. In case of echo planar imaging (EPI) data, elastic registration may be useful for correction of geometric EPI distortions [4;8] that can be of magnitudes of several mm [2] potentially shifting functional responses into neighboring anatomical structures. There is however only little data on whether registration methods using high dimensional transformations have advantages for intra-individual registration of (distorted) EPI data to (relatively undistorted) anatomical MRI data. In the present study we have addressed this issue. Additionally we give a short outlook of how precise anatomical localization can also be achieved by circumventing the functional-structural registration problem.

II. Material and methods

In the present study we have therefore acquired hand movement related fMRI data from 2 subjects each taking

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part in 12 recording sessions. The motor task was a bimanual, rhythmic squeezing of a rubber ball enclosed in two plastic shells. BOLD contrast was measured using a 1.5 T MAGNETOM Vision imager (Siemens, Erlangen, Germany) employing a T2* sensitive multislice Echo Planar Imaging (EPI) pulse sequence with TR/TE/α = 3000 ms/84 ms/90^0. The field of view was 256x256 mm using a 128x128 matrix at a slice thickness of 4 mm. Each measurement acquired 8 slices with a 1mm interslice gap. Thus, a region of 39 mm was covered with a spatial resolution of 2x2x5 mm. The resulting functional maps were registered to the individual subjects' anatomical images using a 6 parameter rigid-body registration method, a 9 parameter affine method with additional rescaling in x, y, and z, and an elastic registration algorithm using approx. 500 parameters per data set (Fig. 1). The elastic algorithm used in our study is based on trilinear Bézier-splines and a 3-D voxel-based smoothness constrained optimization technique to determine the transformation that maps the functional data onto the coordinate system of the anatomical dataset, guaranteeing that the data are mapped one-to-one on each other and enabling subvoxel accuracy even for noisy low-resolution multislice datasets with local distortions up to several mm [5]. This algorithm was previously successfully used in fMRI studies (e.g. [1]). To compare spatial accuracy, we have determined the relative position of the SM1 response center of mass (CoM) to the central sulcus (CS) within the EP images, thus circumventing a registration step, and have compared this veridical position of the CoM, that is not affected by any registration errors, to the relative position of SM1 CoMs in respect to the CS in the anatomical images after application of the three different registration techniques.

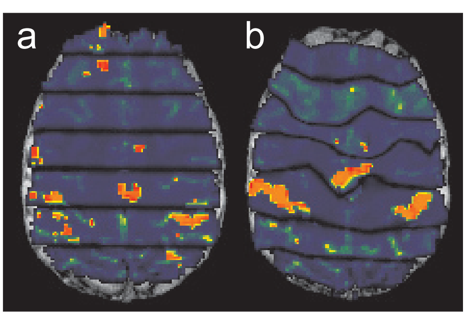

Fig. 1: Example of affine (a) and elastic (b) registration results of the same functional data set, shown for the identical anatomical slice. The statistically processed echo planar (EP) images are shown superimposed on the anatomical images, significant signal changes are displayed in orange.

III. Results

Each session of each of the two subjects yielded significant task related signal changes in multiple cortical areas. Activation was found in the left and the right central region in the vicinity of the precentral knob, a characteristic Ω-shape structure previously described as a landmark for the primary sensorimotor hand area [6]. There were, however, differences in the exact response locations in respect to the anatomical data when using the three registration techniques. The 3d co-ordinates of the center of mass (CoMs) of activation in the sensorimotor hand region were significantly different depending on the registration method used. The mean difference for the pair rigid vs. affine registration was significantly smaller that for the rigid vs. elastic and affine vs. elastic pair (t-test, $p<0.05$). The mean 3D-distances between CoMs with the different registration methods ranged from 1.9 mm for the rigid body registration vs. affine registration to 3.6 mm for affine vs. elastic matching. The maximum 3D-difference was also smallest for the pair rigid body/affine (3.1 mm).

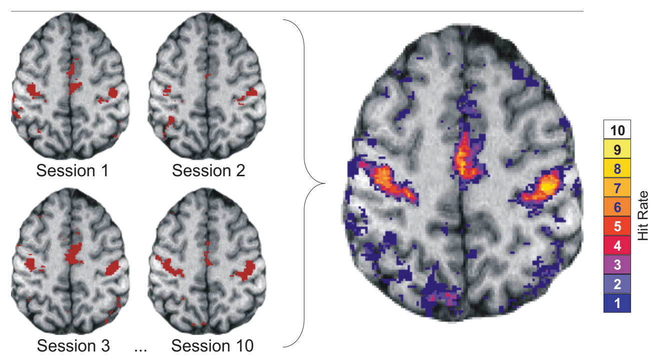

Fig. 2: Movement related fMRI responses and response probability ('hit rate') map. On the left, identical transversal anatomical slices of Subject 1 are shown with functional overlays from single recording sessions during bimanual hand squeezing movements (4 of the altogether 10 sessions shown). All 10 single activation maps were fused into a probabilistic activation map (right). For each voxel in the probabilistic map, it is color-coded in how many of the single sessions the voxel was classified as activated. The highest hit rates were found in the region of the right and left precentral knob, an anatomical landmark for the primary motor hand area, and within the interhemispheric fissure, corresponding to the region of the supplementary and cingulate motor areas.

In order to assess spatial accuracy of the different co-registration techniques, we first compared the hit rate histograms across the whole probabilistic maps of both subjects (Fig. 3). We grouped voxels into 'very high hit rate' voxels activated in 9 or 10 out of 10 recording sessions, 'high hit' rate voxels with 6 to 8, and 'low hit rate' voxels with 1 to 5 hits. Using elastic matching, there were more ‘high’ and ‘very high hit rate’ voxels and less ‘low hit rate’ voxels in the probabilistic functional map compared to the rigid body and affine matching. For instance, there were 84 high hit rate voxels using elastic matching, 42 using rigid body and 20 using affine matching. Within these responses, there were 6, 0 and 1 voxels which were activated in all 10 recording sessions, respectively. Most voxels with very high hit rates were found in the left and the right central region in the vicinity of the precentral knob (Fig. 2, 3). Form the 6 voxels with a 10/10 hitrate with elastic matching, 5 were in these areas (only one was found in the region of the medial wall frontal motor areas of subject 1). The hit rate of elastic matching was significantly higher than for affine and rigid body matching (sign test, $p<0.01$). There was no significant difference between the latter two methods.

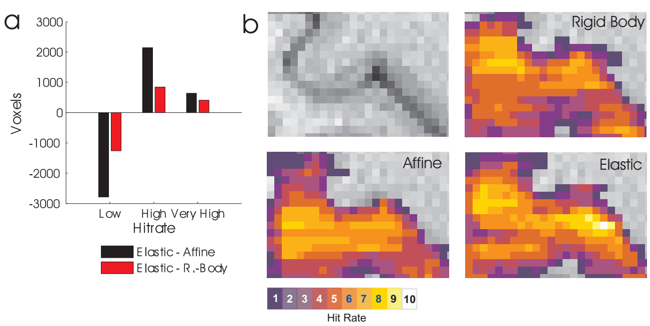

Fig. 3: Hit rate differences using the three different matching algorithms. (a) Voxels were grouped into three categories: voxels with very high hit rates (9 or 10 out of 10), with high hit rates (6-8 out of 10) and with low hit rates (1-5 out of 10). For each of these categories, differences between the results obtained with the three different matching algorithms are shown. Both very high and high hit rate voxels were more frequent in the maps obtained using elastic registration than in those based on rigid body or affine registration. Accordingly, low hit rate voxel were more frequent with the later two methods as compared to elastic registration. In (b) hit rate maps in an area around the left precentral knob of Subject 1 are shown. The T1 anatomical image of this region is shown in the upper left plot, hit rate maps are shown in the remaining three plots. Using elastic registration, but not using rigid body and affine registration, hit rates up to 10 were found in this region.

In order to further evaluate the accuracy of response assignment, we made use of the fact that the location of the CoM of the SM1 activation relative to the CS could be obtained from the EP images themselves (Fig. 4a). Thus, for each experiment and registration method the location of the CoMs relative to the CS (anterior, within and posterior) was determined, and in addition, the veridical location of the CoMs relative to the CS from the functional EP images. In most cases (40 out of 42), this veridical location was precentral, typically on the fringe of the Ω-shaped formation of the precentral knob (Fig. 4a). In three cases, the CoM was located within the CS, and in one case it was just posterior to the CS. With elastic registration, 31 CoMs (from 42) were accurate, in contrast to only 19 and 16 for linear and affine registration. ‘Completely wrong’ localizations (i.e. posterior to the CS while the veridical location was anterior, or anterior while the veridical location was posterior) occurred frequently with linear (8, or 20% of cases) and affine registration (18, or 45% of cases), in contrast to only 2 (or 5% of cases) such ‘completely wrong’ results for elastic registration.

IV. Discussion

In the present study we have investigated the impact of different registration techniques on the accuracy of fMRI in the human sensorimotor cortex. We show a significantly higher intra-subject reproducibility of movement related fMRI responses when using elastic as compared to rigid body and affine registration. In particular, voxel hit rates across 10 consecutive recording sessions were significantly higher when the elastic registration method was applied. A limitation of the present study however is that we have not used a distortion correction as part of image acquisition. Recently developed online distortion correction techniques can prevent/correct EPI distortions efficiently as part of the image acquisition process [7;9-11]. It therefore remains to be determined whether non-rigid registration can also improve spatial accuracy for EPI distortion corrected data as could be the case if the correction does not work perfectly but leaves some residual distortions. It also remains to be further investigated, why we found increased reproducibility using elastic registration as EPI distortions can be expected to be, to a large extend, reproducible for individual subjects. An important conclusion of the present study is that the choice of the registration technique alone can result in shifts of fMRI responses from one side of the central sulcus to the other, i.e. from the the precentral primary motor cortex (M1) to the postcentral primary somatosensory cortex (S1).

V. Outlook

As illustrated in Fig. 4a, anatomical information can to some extend also be derived from functional images. In an ongoing project we are developing an approach that is based on anatomical information available in functional MR images, optimizing this kind of information by using high resolution fMRI acquisition combined with recording protocols optimized for high anatomical contrast in the functional data. The resulting image quality was sufficient to determine the extent of motor cortex with a resolution close to 1mm in the functional data. In addition we use heat kernel smoothing [12] within the segmented motor cortex instead of 3D smoothing as commonly used. We propose than this approach – high resolution fMRI, direct segmentation of cortex, and heat kernel smoothing – by circumventing the co-registration problem is particularly well suited for high accuracy imaging of cortical function.

Accurate registration techniques as investigated in the present study will nevertheless remain vital in all situations where information from additional anatomical images is used to aid the interpretation of functional MRI data.

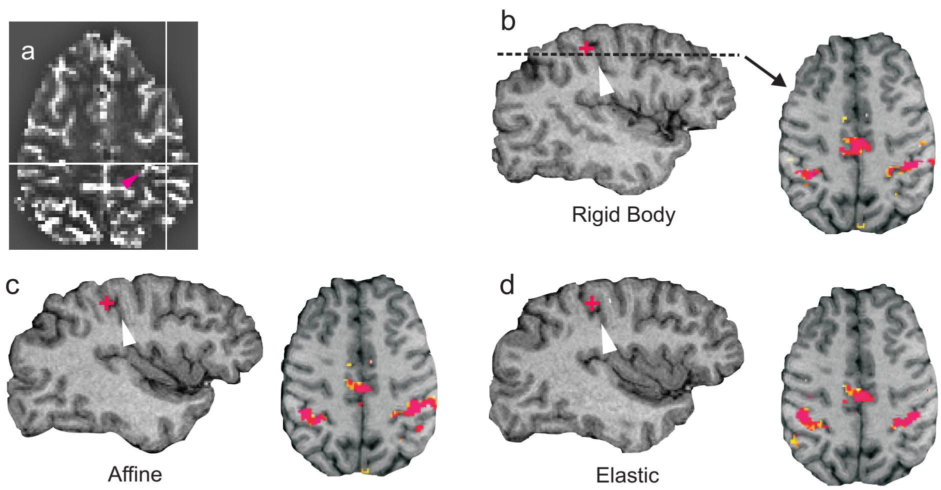

Fig. 4: Center of mass (CoM) of hand movement related responses relative to the central sulcus (CS). In (a), an EPI transversal slice is shown; the left CS with its typical shape is marked with a pink arrowhead. The CoM of the SM1 activation derived from the EP images of this recording session was located at the intersection of the white reference lines. In this case the CoM was clearly located anterior to the CS on the fringe of the precentral knob. Because the location the response is interpreted in respect to the EPI images underlying the functional analysis, in this case no registration is required and the relative CoM position can be assumed as veridical. In (b) the CoM location for the same recording session is indicated as a red cross on a sagittal anatomical slice as obtained using the rigid body registration. For the level indicated by the dashed line, a transversal anatomical slice with the rigid body registered activation map is depicted, showing responses both in the region of the right and left precentral knob as well as in the midline, corresponding to the supplementary motor area (SMA). The CS is marked with a white arrowhead. In (c) and (d), CoM location and functional responses in the same transversal slice are shown for the results obtained using affine and elastic registration. While with rigid bomdy registration the response CoM was located in the postcentral cortex, the CoM was found within the CS with the affine method. With the elastic registration the SM1 activation CoM was located precentrally, on the fringe of the precentral knob, as was the veridical CoM location determined directly in the EP image (a).

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