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## NeuroImage

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#### Technical Note

# Local landmark-based registration for fMRI group studies of nonprimary auditory cortex

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#### ARTICLE INFO

#### Article history: Received 21 May 2008 Revised 12 July 2008 Accepted 23 July 2008 Available online 8 August 2008

Keywords:
Auditory cortex
Averaging
fMRI
Registration
Sound recognition
Sound localization

#### ABSTRACT

Interindividual functional and structural brain variability is a major problem in group studies, in which very focal activations are expected. Architectonic studies have shown that the human primary auditory area, which is located with a great constancy on Heschl's gyrus, is surrounded by several nonprimary auditory areas with surface areas of 40–310 mm². The small size of the latter makes them only partially accessible to fMRI group studies, because of imprecision in realignment when using currently available registration procedures. We describe here a new method for sulcal realignment using a non-rigid local landmark-based registration and show its application to the registration of fMRI acquisitions on the supratemporal plane. After an affine global voxel-based registration, which transforms all brains into the same standard space, we propose a non-rigid local landmark-based registration method based on thin-plate splines for matching the two sulci delimiting Heschl's gyrus of a given brain to the corresponding sulci of a reference brain. We show here that, in comparison with global affine and non-rigid approaches, our method leads in group studies to i) a much more precise alignment of Heschl's gyrus; and ii) a putatively optimal superposition of functionally corresponding areas on and around Heschl's gyrus.

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#### Introduction

Similar to fingerprints, the adult human brain exhibits significant interindividual variability in its global structure, such as in overall size and shape, and also in its local structures, such as in the configuration, length, number and location of gyri and sulci (Amunts et al., 2000, 1999; Geyer et al., 1999; Penhune et al., 1996; Rademacher et al., 1993). The major advances in functional imaging are due to the establishment of statistical methods that allow comparison of individually brains (Mazziotta et al., 2001, 1995; Roland and Zilles, 1994; Van Essen, 2005). The need to locate precisely the site of functional activation within an anatomic framework contributed to the considerable expansion of registration methods. The purpose of interindividual registration is to minimize or remove structural variability to achieve better correspondence of the functionally homologous brain regions across individuals. The most commonly adopted techniques for registering images into the same standard space have two principal characteristics: they are global, considering the entire three-dimensional (3D) brain volume,

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and they employ voxel-based registration (VBR), using gray level intensities to evaluate a similarity measure with a template (Collins et al., 1994; Friston et al., 1995; Woods et al., 1992). The drawback of VBR methods is that they are not adapted to match highly variable sulcal patterns.

The human auditory cortex is particularly sensitive to precise registration since it contains, in the vicinity of the primary auditory area, at least six other nonprimary areas that are relatively small, with surface areas between 40 mm<sup>2</sup> and 310 mm<sup>2</sup> (Rivier and Clarke, 1997; Wallace et al., 2002). A shift of 4 mm or more in the cortical alignment between corresponding functional areas in individual brains may yield false negative results in group activation studies.

Separate analysis of individual subjects has been recommended to avoid false negative results due to the imprecise realignment of auditory structures (Hashimoto et al., 2000; Schonwiesner et al., 2002; Viceic et al., 2006). However, this approach is time consuming, subjective as to the definition of homologous activation patterns, and lacks the statistical power of group studies.

The need for precise sulcal alignment led to the fast development of the non-rigid local landmark-based registration (LBR) methods (Argall et al., 2006; Desai et al., 2005; Kang et al., 2004). When comparing LBR with global VBR, several authors agree with two facts: i) the local methods are more accurate in precise sulcal superposition than the global methods and ii) non-rigid transformations, such as

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thin-plate splines (TPS) (Kang et al., 2004), fluid deformation (Desai et al., 2005; Van Essen, 2005), and morphing (Desai et al., 2005; Fischl et al., 1999b) provide better interindividual matching than rigid-body or affine transformations. The aforementioned studies have employed two-dimensional (2D) representation of the cortical surface either by cortical inflation to a sphere (Van Essen, 2005) or by flattening to a 2D sheet-surface based atlas (Dale et al., 1999; Fischl et al., 1999a). The cortical inflation and flattening present several drawbacks related to unavoidable distortions of distances and area measurements that they introduce (Fischl et al., 1999a).

The use of local landmark-based registration is most powerful when functional areas have a fixed relationship with distinct anatomical landmarks. This is the case for the primary auditory area, which lies on Heschl's gyrus in most subjects (Rademacher et al., 2001; Zilles et al., 1988).

We present here a new method for a non-rigid local landmark-based registration (LBR), which allows a more precise interindividual matching of local anatomical structures, such as sulci. In contrast to other methods applying a local registration on the cortical surface, our method is performed in the 3D brain volume. In order to avoid inaccuracy due to the manual selection of landmarks (Kang et al., 2004), we propose a semi-automatic landmark extraction algorithm, where only the identification of the beginning and the end of the sulci of interest is necessary. We did not resort to automatic recognition of sulci as proposed by previous studies (Caunce and Taylor, 2001; Lohmann and von Cramon, 2000; Mangin et al., 1995; Rettmann et al., 2002; Riviere et al., 2002; Royackkers et al., 1999; Vaillant and Davatzikos, 1997). The sulcal pattern of the supratemporal plane is highly variable and the automatic detection fails to identify unequivocally sulci delimiting Heschl's gyrus.

A previous study that performed LBR on the supratemporal region used five anatomical landmarks and observed that in comparison to global VBR, LBR yielded functional maps with improved resolution (Kang et al., 2004). However, to our knowledge no study has examined the effect on functional group studies of sulcal realignment on the supratemporal plane. To assess the performance of our sulcal LBR, we compared it with two other registration methods: a) the single affine global VBR (aVBR) and b) the combination of the affine global VBR and a non-rigid global VBR (VBR), both implemented in Statistical Parametric Mapping (SPM2) software (Wellcome Department of Cognitive Neurology, London, UK; www.fil.ion.ucl.ac.uk/spm; Friston et al., 1994). To illustrate the differences between the three aforementioned methods, we applied them on anatomical and functional datasets of auditory processing on the supratemporal plane involved in sound recognition, "what," and sound localization, "where" pathways (Maeder et al., 2001).

#### Methods

A sagittal conventional T1-weighted 3D gradient-echo sequence was acquired for 15 normal volunteers on a 3 Tesla MRI system (Philips Intera, Philips Medical Systems, Best, The Netherlands). Each volume of anatomical MR images consisted of 128 sagittal sections that covered the whole-head volume and that were acquired with following parameters: repetition time (TR)=9.9 ms, echo time (TE)=4.6 ms, flip angle=8°, matrix size=256×256, field of view (FOV)=256 and slice thickness=1 mm, yielding isotropic voxels of 1 mm<sup>3</sup>.

Fifteen normal volunteers participated in this study, aged between 22 and 32 years; eight were female (mean age 24.5 years; SD=3.2 years) and seven were male (mean age 25.6 years; SD=1.8 years). All study participants had normal audition, were right-handed except one, and did not have a history of neurological or psychiatric disorders. A written informed consent was obtained from each participant prior to participation in the study. This study was approved by the Ethical Committee of the Faculty of Biology and Medicine of the University of Lausanne.

Normalization of structural images to the standard space

The image preprocessing (Fig. 1) was conducted with SPM2 software. To improve the normalization, the anatomical data were first corrected for the intensity inhomogeneity using the bias correction as implemented in SPM2 software. For the normalization to the SPM2 Montreal Neurological Institute (MNI) T1 2×2×2 mm template (Friston et al., 1995), registration parameters were estimated and applied on the structural images using a 12-parameter affine transformation as implemented in SPM2 software. At this stage all structural images were transformed into the same standard space. We will refer to this preprocessing as global affine voxel-based registration (aVBR). For the global non-rigid voxel-based registration (VBR), the affine transformation was followed by a non-rigid registration with a transformation modeled by discrete cosine transform basis functions (7×9×7 DCT basis).

#### Local landmark-based registration

The images that underwent the aVBR were further processed through several steps. First, a smooth pial mesh of each hemisphere representing the boundary of the gray matter-cerebrospinal fluid interface was created with Freesurfer software (http://surfer.nmr. mgh.harvard.edu/) (Fischl et al., 1999b; Talavage et al., 2004).

Second, the sulci of interest were identified and further used as landmarks for the local registration. The anterior limit of the first

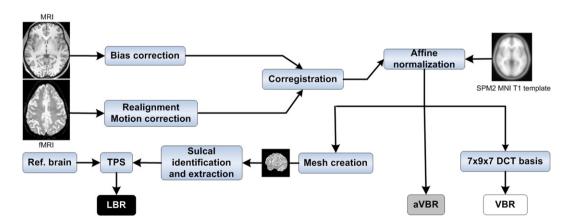


Fig. 1. Processing steps involved in this study. First, the brains were transformed into the same standard space defined by the SPM2 MNI T1 template. Subsequent transformations were performed by three different registration methods: global affine voxel-based registration (aVBR), global non-rigid voxel-based registration (VBR), and our local landmark-based registration (LBR).

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