DTI-driven segmentation of human cortex - methods, validation and reproducibility

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Introduction

Delineation of functionally distinct areas of the brain plays an important role in neuroscience and is also of clinical relevance. Traditionally, functional imaging methods such as fMRI and H2O-PET are employed while a task is performed that is designed to activate a particular part of an individual's functional anatomy. Such tasks, however, are unavailable for many structures and rely on the scanned person's ability to cooperate, which can be limited in children and the diseased. Diffusion tensor imaging (DTI) offers an alternative way to explore functional anatomy based on differences in connectivity rather than task-related activation. To this end, we exploit the fact that even when functionally disparate regions are close in location, their connectivity patterns to other regions of the brain differ. Here, we present and validate a fully automated approach utilising k-means segmentation of connectivity profiles to differentiate between a) SMA and pre-SMA and b) Brodmann's areas 44 and 45. We investigate the validity and reproducibility of these parcellations in comparison to functional MRI data and to population maps of cytoarchitecture.

Methods

Diffusion data were recorded in 2x2x2 mm^3 voxels using three repetitions of 60 isotropically distributed diffusion directions and a b-factor of 1000 s mm^{-2} on a Siemens Sonata 1.5T scanner. To establish reproducibility, eight volunteers were scanned repeatedly on three different dates for the Brodmann area study, while nine volunteers were scanned once for SMA vs. pre-SMA. In the latter group, BOLD fMRI data were recorded in 2x2x5 mm voxels using EPI (TR 2.5 s, 30s per block, 6 repetitions) while the subjects performed a finger-tapping and a serial subtraction task in a block design. fMRI data were analysed using FMRIB's software library and probability distributions on fibre direction were calculated from diffusion data at each voxel using described methods. One subject in the SMA group was excluded due to poor functional imaging results. A medial cortical mask was created in standard space including pre-SMA and SMA regions[1]. For area 44 and 45, a sagittal slice of cytoarchitectonic data as part of FZ Julich's SPM anatomy toolbox[2] was thresholded at 20% probability and transformed to MNI 152 standard space. For each subject, connectivity profiles for every voxel in either mask were generated, then a) reordered using a spectral reordering algorithm and then manually divided into two clusters, and b) automatically segmented using k-means clustering[3]. For SMA vs. pre-SMA, only voxels that had been activated in the fMRI experiment were evaluated. Agreement between connectivity-based and fMRI segmentation was quantified using the fMRI results as reference. For area 44 vs. 45, validation was performed against cytoarchitectonic probability maps. Fig. 1 shows that DTI-driven segmentation relies neither on sulcal anatomy nor the mask's gap.

Results

Voxels identified as pre-SMA using fMRI were 82% (SD 0.167) likely to be classified as such by k-means segmentation, and 74% (SD 0.183) likely to be classified as such using manual segmentation of the spectrally reordered CC matrix. For SMA voxels, the probabilities are 79% (SD 0.143) and 87% (SD 0.133) respectively. Due to the probabilistic nature of the cytoarchitectonic masks used, an ideal segmentation of Brodmann's areas 44 and 45 in the mask used would result in probabilities of 40.9% for area 44 and 52.4% for area 45. Classification using k-means clustering recovered 95% of the maximum possible value (area 44, 0.389±0.0207) and 90% (area 45, 0.471±0.0542), whereas manual segmentation of the spectrally reordered CC matrix achieved 96% (0.392±0.0160) and 94% (0.495±0.0285). Areal agreement between the two approaches averaged 87.0% (SD 0.1362) and 86.7% (SD 0.1629). Standard deviation of areal recovery between sessions was 0.020 for k-means clustering and 0.014 for segmentation after spectral reordering, indicating high reproducibility. Fig. 2 shows a typical result.

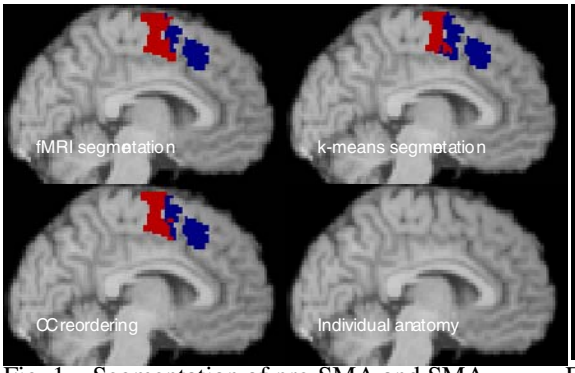

Fig. 1 – Segmentation of pre-SMA and SMA

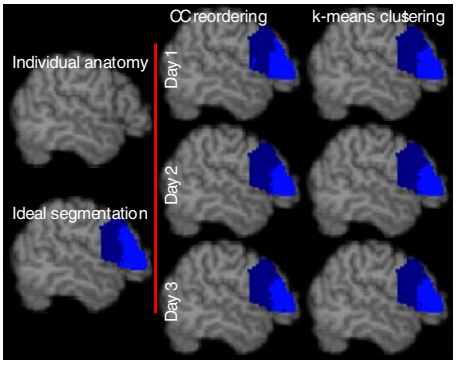

Fig. 2 – Segmentation of Areas 44/45

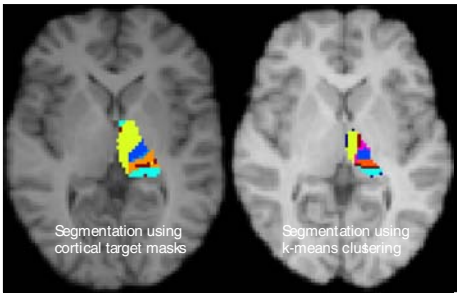

Fig. 3 – Thalamic segmentation

Discussion

We have demonstrated the feasibility, accuracy and reproducibility of fully automated segmentation of cortical functional areas by their connectivity profiles and validated this method against functional imaging, cytoarchitectonic maps and a recently published semi-automatic approach of connectivity-based classification. It will be useful in exploring the layout of functional systems in individual subjects, also, preliminary results suggest that it is capable of segmenting structures of the deep gray matter into functionally disparate regions (Fig. 3) without using a-priori target masks.

References 1. Johansen-Berg H, Behrens TE et al. Changes in connectivity profiles define functionally distinct regions in human medial frontal cortex. Proc Natl Acad Sci U S A 2004; 101(36):13335-13340. 2.Amunts K, Schleicher A, Burgel U, Mohlberg H, Uylings HBM, Zilles K. Broca's region revisited: Cytoarchitecture and intersubject variability. Journal of Comparative Neurology 1999; 412(2):319-341.3. DTI-Tractography Based Parcellation of Human Precentral Gyrus. HBM'05; Toronto, Canada: 2005.