

A DEFORMABLE BRODMANN AREA ATLAS

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ABSTRACT

Functional MRI studies commonly refer to activation patterns as being localized in specific Brodmann areas, referring to Brodmann's divisions of the human cortex based on cytoarchitectonic boundaries [3]. Typically, Brodmann areas that match regions in the group averaged functional maps are estimated by eye, leading to inaccurate parcellations and significant error. To avoid this limitation, we developed a method using high-dimensional nonlinear registration to project the Brodmann areas onto individual 3D co-registered structural and functional MRI datasets, using an elastic deformation vector field in the cortical parameter space. Based on a sulcal pattern matching approach [11], an N=27 scan single subject atlas (the Colin Holmes atlas [15]) with associated Brodmann areas labeled on its surface, was deformed to match 3D cortical surface models generated from individual subjects' structural MRIs (sMRIs). The deformed Brodmann areas were used to quantify and localize functional MRI (fMRI) BOLD activation during the performance of the Tower of London task [7].

1. INTRODUCTION

fMRI BOLD activation is generally transformed to a standardized space and reported in terms of the Talairach and Tournoux atlas coordinates [10] and associated Brodmann areas [2,7]. These transformations however, are highly insensitive to an individual's cortical pattern, and may lead to an inaccurate representation of the probable locations of Brodmann areas. At the same time, computational brain atlases [11] and computational anatomic techniques are increasingly used in fMRI studies [6]. For example, individual fMRI BOLD activation data can be deformed, using high-dimensional nonlinear registration, to a geometrical average group model of the cerebral cortex, to allow intersubject averaging and empower statistical analysis. In this rapidly developing field, methods to report the functional loci relative to individual and group models of the cortex have not yet become standardized. Visual inspection [12] and histograms of single points representing cortical regions [9] have been used. However, these methods are difficult to replicate and extend to group fMRI studies, due to large inter-subject differences in cortical anatomy. In this paper we describe a method (based on cortical pattern matching [11]) to deform a digital map of the Brodmann areas to an individual subject's cortical surface model. Similarly, this method can also be applied to diagnostic

group models where cortical pattern matching approaches are used for inter-subject data alignment. This allows fMRI BOLD activation for an individual subject, or a group, to be described and quantified in relation to the deformed Brodmann areas.

2. METHOD

2.1 Definition of Brodmann Areas on the Cortex

The right brain hemisphere of the Montreal Neurological Institute intensity-averaged single-subject MRI atlas (MNI colin27; [15]) was used to generate a sMRI which was symmetric across the central sagittal plane, giving an sMRI with two identical hemispheres (called colinRR). This was performed so that the mapping of the Brodmann areas described on one hemisphere could be reflected onto the other. (The Brodmann areas are thought to have a consistent relation to the gyral anatomy of each hemisphere, so the classical maps are plotted on one hemisphere only). From the colinRR sMRI, a 3D model of the cerebral cortex was extracted [11].

Using the description of the Brodmann areas on the colin27 cerebral cortex given by the Caret package [13], the Brodmann area boundaries were described by 3D surface curves on the right hemisphere cortical surface model. Each curve was digitized at high spatial frequency, so that the 3D distance between each point was not greater than a voxel. Each point of each line describing a Brodmann area border was then

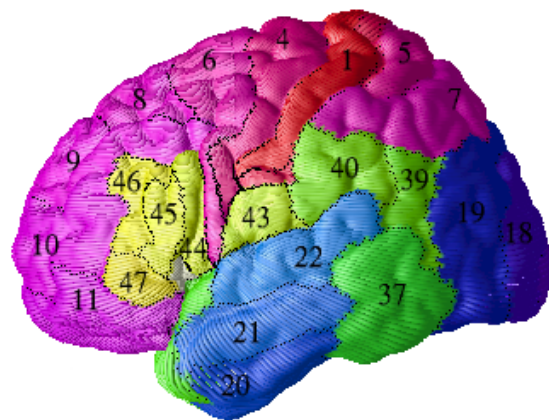


Figure 1: Brodmann areas and Brodmann area boundaries displayed on the colinRR cerebral cortex 3D surface model.

mapped to the nearest point on the cortical surface.

The cortical surface model, which was labeled with Brodmann area boundaries, was converted to a file format compatible with the cortical pattern matching method [11] where each hemisphere is represented by 256 x 256 vertices. Each surface vertex was then labeled with a number defined by the Brodmann area that contained it (i.e., a vertex within Brodmann area 22 was given the label 22). Vertices in locations where the Brodmann areas had not been described were labeled as undefined. This included small sections of the inferior surface and medial wall not visible in the models of cortex used here. Because the gyral patterns of the left and right hemispheres of the colinRR cortex are the same, by definition, the resulting right hemisphere vertices with Brodmann area labels were mapped to the left hemisphere to provide a parcellated left hemisphere model. Figure 1 shows the lateral left view of the colinRR cerebral cortex model visualizing the Brodmann areas and Brodmann area boundaries.

2.2 Individual Subject's sMRI and fMRI Acquisition

To apply the deformable Brodmann area model to an individual subject, sMRI and fMRI BOLD activation data were acquired using a Magnetom Vision 1.5 T MRI scanner (John Hunter Hospital, Newcastle, Australia). The subject's sMRI was collected with approximate dimensions of 164 x 256 x 256 with each voxel being approximately 1.0 x 1.0 x 1.0 mm³. fMRI BOLD activation volumes were collected with the echoplanar imaging technique (EPI). T2-weighted sequences were acquired using a 64 x 64 matrix and 16 axial slices (TR = 2.7 s, 6.25 x 6.25 x 8 mm³ resolution).

While lying in the MR scanner, the subject was presented with 7 Tower of London tasks [7] of difficulty varying from 0 (zero-move) to 7 (active). Briefly, this task has been used to examine executive function/dysfunction in the frontal lobe [7]. During each task, 10 fMRI volumes were acquired resulting in 70 volumes per run (covering the total brain volume). This sequence was repeated 3 times.

2.3 Preprocessing of sMRI and fMRI

The fMRI BOLD data were motion corrected across all three sequences using SPM99 [5]. A two-step intensity normalization procedure was adopted. Within each sequence, images were intensity normalized to give a mean volume intensity of 1000. A mean image for each sequence was generated, and subtracted from every individual volume within its associated acquisition sequence. This resulted in (for each sequence) a mean baseline signal of zero at every voxel, with individual volume acquisitions representing variation around that mean. Volumes across all sequences were then concatenated to produce a single series. Data were subsequently co-registered to the sMRI and spatially smoothed using a Gaussian filter with a full width at half maximum (FWHM) of 15 x 15 x 9 mm³. Student's *t*-tests were performed at each voxel comparing the zero-move versus active tasks, with the results represented as maps of *z*-scores.

The subject's sMRI was then aligned to an ICBM [4] template followed by digital filtering to reduce intensity inhomogeneity due to radio-frequency bias [8]. A 3D parametric surface model of the cerebral cortex was then extracted from the subject's aligned sMRI [11]. The *z*-scores

were then mapped to the subject's cortical surface model and clustered based on $|z| > 3.88$ ($P < 0.05$ corrected for multiple comparisons).

2.4 Sulcal Tracing and Warping

For both the colinRR and the subject's cerebral cortex model, at least 15 sulci were identified on each hemisphere and traced (depending on existence). Six control lines mapping the midline hemisphere boundaries at the interhemispheric margin were also identified and traced onto the cortical surface models [14]. These surface curves were used as landmarks in the geometric averaging and warping of subjects to create average models of cerebral cortex [6,9].

Using the covariant version of the Navier-Cauchy partial differential equations [11], the colinRR model of cerebral cortex was elastically deformed to the individual subject's cortical surface model. This process sets up a computed correspondence between the two surfaces by projecting corresponding sulcal landmarks into the cortical parameter space, and computing a flow field that matches them exactly. The vertices of the deformed colinRR cortex were then used to poll the undeformed colinRR cortex with Brodmann area labeled vertices for the nearest vertex, in terms of Euclidean distance. The Brodmann area label associated with this undeformed vertex location was then allocated to the deformed vertex to form the deformed and labeled colinRR cerebral cortex model. Finally, as the individual subject's cortical surface model and the deformed and labeled colinRR cerebral cortex model are in the same space, the Brodmann area labels were assigned to the individual subject's cortical surface, giving the Brodmann areas on the subject's cerebral cortex model.

3. RESULTS

For the purposes of this paper just the left hemisphere has been used to present the analysis. Figure 2 shows a 2D representation of the left hemisphere Brodmann areas before and after the elastic deformation. Figure 3 shows the deformed Brodmann area labels over the subject's cortical surface model. The color coding indicates the Brodmann Area. From Figure 3, the adaptation of the Brodmann areas to the sulci, via the flow in the cortical parameter space, can be seen. In particular, the boundaries of Brodmann areas 20, 21 and 22 align correctly with the inferior and superior temporal sulci. Using the functional information described in Section 2.3, Figure 4 shows

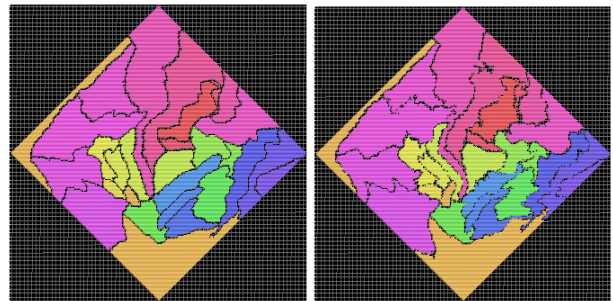


Figure 2: 2D representation of the left hemisphere Brodmann areas before deformation (*left*) and after deformation (*right*).

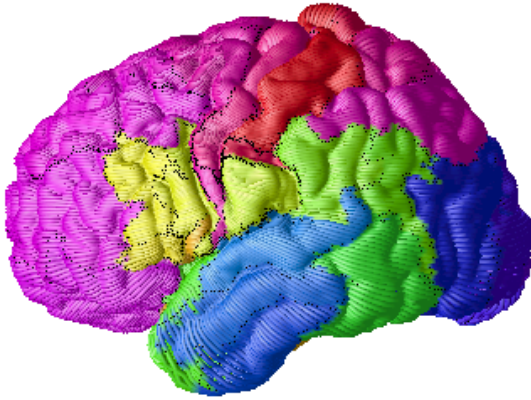


Figure 3: Left lateral view of color-coded deformed Brodmann areas elastically adapted to the individual cortical surface.

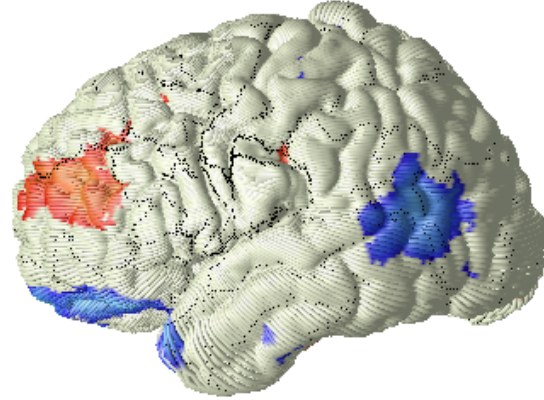


Figure 4: Left lateral view of the deformed Brodmann area partition mapped onto an individual surface that is also texture-mapped with the individual cortical surface z -scores ($p < 0.05$ thresholded).

Table 1: Left hemisphere clusters ($N > 20$ surface voxels critically thresholded at $P < 0.05$ and corrected for multiple comparisons). These clusters describe regions with significant BOLD response (block design) when performing the Tower of London Task (ud denotes undefined Brodmann area).

Anatomical Region	Brodmann Area [% of cluster]	Unit count of cluster	Maximum z of cluster	Mean z of cluster	Standard deviation of cluster
Superior and middle frontal gyri	9[16%], 10[81%], 46[3%]	770	5.424	4.511	0.410
Superior frontal gyrus (medial)	6[100%]	335	5.030	4.224	0.217
Post central gyrus	1[10%], 2[71%], 40[19%]	31	4.571	4.194	0.182
Parietal lobe, pre-cuneus	7[100%]	26	4.440	4.107	0.146
Orbital gyri	10[9%], 11[78%], ud[14%]	1414	-9.468	-5.716	1.556
Lateral temporal parietal region	19[32%], 22[7%], 37[29%], 39[32%]	457	-6.778	-5.029	0.774
Temporal pole	21[14%], 38[86%]	49	-6.647	-4.909	0.738
Lateral occipitotemporal gyrus	20[93%], 37[7%]	58	-6.385	-4.81	0.686

the deformed Brodmann areas on the individual cortical surface z -scores ($p < 0.05$ thresholded for multiple comparisons).

Clusters of BOLD functional information were then classified and quantified based on the percentage of the cluster lying within a Brodmann area. Table 1 shows the anatomical region, Brodmann area and percentage of the cluster lying in the Brodmann area, with the number of vertices in the cluster, and the maximum, mean and standard deviation of the z -scores of the cluster.

4. CONCLUSIONS AND FUTURE WORK

We have described a deformable Brodmann area atlas method that allows visual and tabular quantification of individual and group structural and functional data. The deformation was based on matching the sulcal pattern of the labeled atlas with that of the subject. This set of deformed Brodmann areas was applied to the sMRI and fMRI BOLD activation of a subject

performing the Tower of London Task, providing a standardized measure of activation on the cortical surface.

While this description of the Brodmann areas represents the most accurate available to the authors at the time, it would be desirable to obtain detailed Brodmann cytoarchitectonic areas from post-mortem brains, perhaps including probabilistic maps [1]. With this, and application of the same methods as described in this paper, investigations into the sulcal and gyral features that best align the deformable Brodmann areas to an individual and the relationship between the Brodmann areas and function could be rigorously established.

5. ACKNOWLEDGMENTS

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