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Subject-Specific Structural Parcellations Based on Randomized AB-divergences

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Abstract

Brain parcellation provides a means to approach the brain in smaller regions. It also affords an appropriate dimensionality reduction in the creation of connectomes. Most approaches to creating connectomes start with registering individual scans to a template, which is then parcellated. Data processing usually ends with the projection of individual scans onto the parcellation for extracting individual biomarkers, such as connectivity signatures. During this process, registration errors can significantly alter the quality of biomarkers. In this paper, we propose to mitigate this issue with a hybrid approach for brain parcellation. We use diffusion MRI (dMRI) based structural connectivity measures to drive the refinement of an anatomical prior parcellation. Our method generates highly coherent structural parcels in native subject space while maintaining interpretability and correspondences across the population. This goal is achieved by registering a population-wide anatomical prior to individual dMRI scan and generating connectivity signatures for each voxel. The anatomical prior is then deformed by re-parcellating the brain according to the similarity between voxel connectivity signatures while constraining the number of parcels. We investigate a broad family of signature similarities known as AB-divergences and explain how a divergence adapted to our segmentation task can be selected. This divergence is used for parcellating a high-resolution dataset using two graph-based methods. The promising results obtained suggest that our approach produces coherent parcels and stronger connectomes than the original anatomical priors.

1 Introduction

Brain parcellations are extensively used to create structural connectomes from diffusion MRI (dMRI) scans [2]. While anatomical segmentations provide an adequate parcellation for a structural connectome, high-resolution connectomes cannot be generated. Additionally, parcellations specific to the structural connectivity will produce parcels that create a more effective structural connectome. For this reason, data-driven parcellation methods were proposed to generate study-specific [15] and subject-specific segmentations of the brain [14]. So far, however, most parcellation approaches have either been limited to small brain regions [14] or limited to groupwise segmentations [15]. Such strategies are well suited for describing healthy brain organization and for creating atlases, but the parcels extracted do not precisely correspond to individual brains, which may raise concern e.g. when studying populations where structural connectivity has been significantly altered by a brain disease.

To address this issue, several methods that simultaneously generate population and subject-specific structural parcellations have recently been proposed [4, 8, 15]. However, these methods rely exclusively on dMRI data without any anatomical prior. As a result, they require advanced tools for registering the diffusion scans to a common template, and suffer from the registration noise introduced by these methods.

In this work, we propose to mitigate these issues with a novel approach combining T1 anatomical priors with subject dMRI data. Our method generates highly coherent structural parcels in native subject space while maintaining interpretability and correspondences across the population. This goal is achieved by registering a population-wide anatomical prior to individual dMRI scans and generating connectivity signatures for each voxel. The anatomical prior is then deformed by re-parcellating the brain according to the similarity between voxel connectivity signatures while constraining the number of parcels. We investigate the use of a family of divergences known as AB-divergences, which generalize most signature similarities considered so far in the field [15]. We demonstrate how an AB-divergence adapted to our parcellation tasks can be selected, and we quantify the improvements of parcels coherence introduced by two graph-based parcellation methods when processing a high-resolution dataset. We finally measure the quality of the connectomes generated from our novel brain parcellations. The promising results obtained suggest that the second parcellation scheme tested improves parcel coherence and the ability of the probabilistic tractography algorithms to delineate long tracts. The remainder of the paper is organized as follows. In Sect. 2, we explain how connectivity signatures were extracted from DTI scans and used for parcellating individual brains. Experimental results are presented in Sect. 3. Discussions conclude the paper.

2 Methods

2.1 Connectivity Signatures

Our dataset consists of images of 9 healthy subjects between age 25 and 36 acquired at three timepoints separated by approximately two weeks. DTI images were acquired with a Siemens 3T VerioTM scanner, a monopolar Stejskal-Tanner diffusion weighted spin-echo, echo-planar imaging sequence (b-value = 1000 s/mm², TR/TE= 14.8s/111 ms, 2 mm isotropic voxels, 64 gradient directions). FreeSurfer [5] was used to parcellate the brain into 86 regions based on the Desikan atlas [6]. For each region, the probtrackx utility of FSL with its default parameters and 5000 seeds per voxel was used for probabilistic tractography [1] seeded from white matter to generate whole brain tractograms. The tractography was run separately in each participant's diffusion space, without registering images of all participants into a fixed template space. The 86 tract counts generated for each voxel were divided by their sum to create connectivities probabilities, which will be referred as connectivity signature in the sequel, as in [13, 16].

2.2 Parcellations and Tessellations

Our method exploits the connectivity signatures for parcellating each scan while fixing the center of the anatomical prior regions. This strategy maintains interpretability and correspondences across the scans while generating a parcellation adapted to each scan. The

center of a region was found by measuring a distance between all the pairs of region voxels and selecting the voxel with the smallest sum of distances to the others. In other words, we select the medioid of each region according to a distance, which was either the Euclidean distance between the voxels or a variant of Kullback-Leibler divergence between the connectivity signatures [3, 15].

We compared two segmentation methods for updating the anatomical priors: a recent graph-based parcellation method referred as sGraSP and based on a Markov Random Field (MRF) framework, and a Voronoi tessellation [11]. Both methods start with the computation of a similarity between the connectivity signatures of neighboring voxels, which is then used for computing a geodesic distance between all pairs of voxels by a fast variant of Dijkstra algorithm [7]. Tessellations are obtained by assigning each voxel to the closest center according to this geodesic distance. SGraSP parcellations are obtained by maximizing the similarity between the voxels signatures and their parcel center signature while constraining the shape of the generated parcels according to the geodesic distances [11]. Because sGraSP parcellations take two distances into account, they tend to be more coherent than tessellations [11]. As explained in the next section, we computed an AB-divergence for measuring the similarity between connectivity signatures.

Parcellations, tessellations and anatomical priors were compared by measuring adjusted Rand Indices [12] (aRI). The aRI of two parcellations $X = \{x_i\}$ and $Y = \{y_j\}$ is calculated by measuring the cardinal m_{ij} of the intersection between each parcel x_i and y_j and combining the m_{ij} as follows:

$$a_x = \sum_y m_{x,y}; \quad b_y = \sum_x m_{x,y} \quad (1)$$

$$aRI = \frac{\sum_{x,y} \binom{m_{x,y}}{2} - \left[\sum_x \binom{a_x}{2} \sum_y \binom{b_y}{2} \right] / \binom{N}{2}}{\frac{1}{2} \left[\sum_x \binom{a_x}{2} + \sum_y \binom{b_y}{2} \right] - \left[\sum_x \binom{a_x}{2} \sum_y \binom{b_y}{2} \right] / \binom{N}{2}} \quad (2)$$

2.3 Randomized AB-divergences

The family of AB-divergences introduced by Cichocki et al. generalizes several well-known divergences, including Alpha, Beta, and Kullback-Leibler divergences [3]. The AB divergence of two connectivity signatures p_i and q_i is calculated as follows when the sum of parameters α and β is not equal to zero:

$$D_{AB}^{(\alpha,\beta)}(p||q) = \frac{-1}{\alpha\beta} \sum_i \left(p_i^\alpha q_i^\beta - \frac{\alpha}{\alpha+\beta} p_i^{\alpha+\beta} - \frac{\beta}{\alpha+\beta} q_i^{\alpha+\beta} \right) \quad (3)$$

We considered only the symmetric AB-divergences, obtained by setting $\alpha = \beta$:

$$D_{AB}^{(\alpha,\alpha)}(p||q) = \frac{1}{2\alpha^2} \sum_i (p_i^{2\alpha} + q_i^{2\alpha} - 2p_i^\alpha q_i^\alpha) = \sum_i \left(\frac{p_i^\alpha}{\alpha\sqrt{2}} - \frac{q_i^\alpha}{\alpha\sqrt{2}} \right)^2 \quad (4)$$

This derivation demonstrates that these divergences can be measured by computing a squared Euclidean distance after projecting the connectivity signatures using the function ψ_α :

$$\psi_\alpha: (p_1, \dots, p_n) \mapsto (\overline{p}_1, \dots, \overline{p}_n) \quad \text{where} \quad \overline{p}_i = \frac{p_i^\alpha}{\alpha\sqrt{2}} \quad (5)$$

We exploited this property to propose an efficient strategy for the selection of the parameter α . Our approach relies on the idea that, when α is set correctly, the parcellation is driven more by the DTI data than by the brain geometry. At this point, the parcellations should be the most sensitive to the injection of noise. We used the random projection method presented in Fig. 1 [10] to simultaneously inject a limited amount of noise in our connectivity signatures and compress the connectivity signatures to accelerate the parcellations. The sensitivity of the results with respect to this noise injection was measured by parcellating the same data several times and measuring the aRI between these multiple repeats.

During these experiments, the mediods of the anatomical regions were selected according to the AB-divergence between the voxels. This choice yields a more dramatic aRI alteration with noise injection. By contrast, final parcellations and final tessellations were generated without randomization and for geometric mediods obtained by summing the Euclidean distance between the voxels of a region.

2.4 Parcellation Coherence

The quality of the parcellations was estimated by measuring the coherence of their parcels as follows. For each parcel pa the correlation matrix of the connectivity signatures Σ_{pa} was computed. The eigenvalues σ_{pa}^i of Σ_{pa} were computed and the parcel coherence $c(pa)$ was measured by the ratio between the largest eigenvalue and the Frobenius norm of Σ_{pa} :

$$c(pa) = \max_i \frac{|\sigma_{pa}^i|}{\|\Sigma_{pa}\|_2} \quad (6)$$

$c(pa)$ measures the concentration of the spectrum of Σ_{pa} in the largest eigenvalue. A coherence close to one indicates that the connectivity signatures of a parcel are almost collinear. This measure is commonly used for comparing functional brain parcellations [9]. We measured parcellation coherence $\mathcal{C}$ by averaging the coherence of the parcels according to their number of voxels $vol(pa)$:

$$\mathcal{C} = \sum_{pa} \text{vol}(pa) c(pa) / \sum_{pa} \text{vol}(pa) \quad (7)$$

2.5 Connectivity Matrices

Once the parcellations were generated, we updated the signatures by running the probabilistic tractography [1] again with the same settings and a hundred seeds per voxel, which represents several thousands of seeds per parcel. The signatures associated with the anatomical prior were recomputed with the same number of seeds for the sake of comparison. A connectivity matrix was generated for each scan and each segmentation method by averaging over each parcel the number of tracts reaching any other parcel. By counting separately short-range connections between adjacent parcels and long-range connections, we were able to estimate if a parcellation was helping probtrackx delineate the long connections which are the most important for creating full brain connectomes [1].

3 Results

3.1 AB-divergence Selection and Prior Adaptation

The AB-divergence parameter α was selected among the values (0.25, 0.5, 0.75, 1.0, 2.0, 4.0, 8.0), by parcellating each scan ten times, after reducing the projected signatures into (6, 8, 10, 12, 14, 16, 20, 25) dimensions via random projections. We report in Table 1 the average aRI for the different settings, and a comparison with parcellations based on the correlation between connectivity signatures. According to these results, we selected the AB-divergence with $\alpha = 0.75$ for generating our final parcellations and tessellations. For this parameter, our AB-divergence is much more sensitive than the standard correlations, and the results presented in Fig. 2 indicate that sGraSP modifies the anatomical prior more than the tessellations. As expected, both approaches generate parcellations closer to the prior than sGraSP segmentations from random centers. The large aRI measured suggest however that all the parcellations align quite well with the prior.

3.2 Parcels Coherences

Figure 3 presents the coherence measured for the anatomical parcels, for the tessellations and sGraSP parcellations. In addition, we measured for each scan the coherence of twenty parcellations generated using sGraSP for a random set of parcel centers. All the results demonstrate that the coherence was improved when re-parcellating the brain and that sGraSP outperforms the tessellations. sGraSP always generates coherent parcellations, even when the centers are selected at random. In general, the coherences measured were quite good. With more than 0.8, even the anatomical prior significantly and vastly outperformed the baseline coherences, close to 0.3, that we measured by randomly permuting the voxels of the anatomical prior (not shown). Our results indicate that sGraSP improved the overall coherence by shrinking large incoherent parcels and inflated small incoherent parcels, which improved parcels similarity.

3.3 Connectivity Matrices

Figure 4 indicates that probtrackx generates more long-range tracts when processing sGraSP parcellations, while short-range connections maintain at a level close to the anatomical prior. This result suggests that probtrackx is less often diverted by intra-parcel tracts when starting from a parcel generated by sGraSP. Tract counts obtained for the tessellations are weaker, more variable, and in lower agreement with anatomical tract counts. These results seem to indicate that the quality of the parcel boundaries, which is better for sGraSP and worse for the tessellations [11], has a significant impact on tractography results.

4 Discussions

In this paper, we propose a novel approach for deriving subject-specific structural brain parcellations. We start with an anatomical prior obtained through a standard T1 registration, which is used for computing voxelwise connectivity signatures. The prior is then refined according to the similarity between these signatures. We demonstrate how a similarity measure adapted to this parcellation task can be selected in a broad family of divergences and we compare a tessellation and an MRF parcellation frameworks. Our results demonstrate that the MRF framework better deforms the anatomical prior, generates more coherent parcels, and improves probabilistic tractography results. Future developments will offer the ability to adapt the number of parcels when fitting individual dMRI scans.

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input: data X of size $N \times T$, parameter t and number of power iteration q

1. form the $N \times t$ matrix Ω by sampling from Gaussian distribution $\mathcal{N}(0, 1)$
2. $U \leftarrow (X^T X)^q X^T \Omega$
3. get W by orthonormalizing the columns of U with Gram-Schmidt process
4. $Y \leftarrow XW$

output: projected data Y , of size $N \times t$

Fig. 1.

Random projection for data compression [10]. $q = 3$ yielded the best results.

Fig. 2.

(1) tessellations (2) corresponding parcellations (3) similarity with the anatomical prior, for tessellations (red), sGraSP parcellations (blue) and twenty sGraSP parcellation with centers selected from the anatomical prior at random (boxplots).

Fig. 3.

(1) parcellation coherence for the three methods compared and the median of twenty sGraSP parcellations generated with random centers (2) Average over the database of the 86 parcels coherences and standard error of these means (SEM). (3–5) average of parcels coherence and size (with SEM) (6) changes introduced by sGraSP.

Fig. 4.

After signatures update (1) number of tracts linking adjacent regions (“short range” connections) (2) long range connections. (3) total, sorted by sGraSP counts.

Table 1

Average pairwise aRI and associated standard error of the mean, for all AB-divergences and numbers of random projections n . These aRI were obtained by averaging over the 27 scans the 45 pairwise aRI measured for each scan.

n	$\alpha = 0.25$	$\alpha = 0.5$	$\alpha = 0.75$	$\alpha = 1.0$	$\alpha = 2.0$	$\alpha = 4.0$	$\alpha = 8.0$	Correlation
6	0.31 ± 0.008	0.34 ± 0.007	0.34 ± 0.011	0.38 ± 0.016	0.55 ± 0.023	0.75 ± 0.017	0.88 ± 0.009	0.73 ± 0.012
8	0.42 ± 0.010	0.43 ± 0.006	0.41 ± 0.011	0.43 ± 0.016	0.59 ± 0.022	0.78 ± 0.017	0.90 ± 0.008	0.77 ± 0.010
10	0.48 ± 0.011	0.48 ± 0.007	0.45 ± 0.011	0.47 ± 0.016	0.62 ± 0.021	0.80 ± 0.015	0.91 ± 0.007	0.80 ± 0.009
12	0.54 ± 0.010	0.52 ± 0.007	0.47 ± 0.011	0.50 ± 0.016	0.64 ± 0.020	0.81 ± 0.014	0.92 ± 0.007	0.82 ± 0.009
14	0.56 ± 0.011	0.56 ± 0.007	0.50 ± 0.011	0.52 ± 0.015	0.66 ± 0.021	0.82 ± 0.014	0.92 ± 0.007	0.84 ± 0.008
16	0.59 ± 0.010	0.58 ± 0.007	0.52 ± 0.011	0.53 ± 0.015	0.67 ± 0.02	0.83 ± 0.013	0.92 ± 0.007	0.85 ± 0.008
20	0.63 ± 0.010	0.61 ± 0.008	0.55 ± 0.010	0.56 ± 0.014	0.69 ± 0.019	0.84 ± 0.012	0.93 ± 0.006	0.87 ± 0.007
25	0.67 ± 0.009	0.64 ± 0.007	0.57 ± 0.010	0.58 ± 0.014	0.70 ± 0.018	0.84 ± 0.012	0.93 ± 0.006	0.89 ± 0.006
Av:	0.526	0.520	0.475	0.495	0.639	0.811	0.914	0.82