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The macro-structural variability of the human neocortex

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ABSTRACT

The human neocortex shows a considerable individual structural variability. While primary gyri and sulci are found in all normally developed brains and bear clear-cut gross structural descriptions, secondary structures are highly variable and not present in all brains. The blend of common and individual structures poses challenges when comparing structural and functional results from quantitative neuroimaging studies across individuals, and sets limits on the precision of location information much above the spatial resolution of current neuroimaging methods. This work aimed at quantifying structural variability on the neocortex, and at assessing the spatial relationship between regions common to all brains and their individual structural variants. Based on structural MRI data provided as the "900 Subjects Release" of the Human Connectome Project, a data-driven analytic approach was employed here from which the definition of seven cortical "communities" emerged. Apparently, these communities comprise common regions of structural features, while the individual variability is confined within a community. Similarities between the community structure and the state of the brain development at gestation week 32 lead suggest that communities are segregated early. Subdividing the neocortex into communities is suggested as anatomically more meaningful than the traditional lobar structure.

Introduction

The current neuro-anatomical ontology (NeuroNames, 2010; Swanson, 2015) is based on the traditional abstraction from visual observation rather than quantitative, data-driven evidence. Considerable training is required for a human observer to recognize neocortical structures. Difficulties arise from the well-known fact that even primary macro-anatomical features show a remarkable structural variability, and secondary features may be prevalent in some individuals only. An abundance of neuro-anatomical literature describes detailed variation (e.g., of the operculum: Ayberk et al., 2012; Idowu et al., 2014; or sulcal patterns: Ono et al., 1990). However, a quantitative assessment of variation patterns is missing that may lead to a deeper understanding of the relationship between common and variable structures on the human neocortex.

This variability renders approaches for an automated quantification of neocortical structures as difficult. Digital brain atlases have been developed to aid the communication and registration of neuro-scientific information with increasing levels of sophistication (Brett et al., 2001; Evans et al., 2012; Shattuck et al., 2008; Talairach and Tournoux, 1988). These image-based approaches contain exemplary, generic information with (some) population-based but not individual variation. Manual outlining is still considered as the reference method for a precise segmentation of brain structures. Diligent procedures were developed that guide the delineation of macroscopic anatomy in individual brains (Klein and Tourville, 2012; Shattuck et al., 2008).

In contrast, several approaches were developed to represent anatomically meaningful, individual features of the neocortical surface in symbolic format. Most notably, Regis et al. (1995, 2005) introduced the concept of "sulcal roots" (or "pits") that correspond to locally deepest points of neocortical sulci. Lohmann and von Cramon (2000) developed a method for segmenting cortical patches as catchment basins centered at a sulcal roots. In a later publication, Lohmann et al. (2008) used gyral landmarks to define a common anatomical framework, into which sulcal pits were mapped. They describe 11 regional groups of major (deep) pits, and a larger set of minor (shallow) pits. Im et al. (2014) proposed a more refined approach to segment sulcal pits, and used a surface-based nonlinear atlas of sulcal patterns to map pits into a common space on a unit sphere. They selected deep pits manually, and segregated a map of 48 pit clusters that may serve as stable anatomical landmarks. We and others (Cachia et al., 2003; Yang and Kruggel, 2008) developed systems that use a derived network of neocortical patches to detect and label neocortical landmarks by symbolic pattern matching and learning processes. Auzias et al. (2013, 2015) picked up an idea already indicated by

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Lohmann et al. (2008) that sulcal pits are arranged in concentric chains along the anterior-posterior axis of the brain, folding into the temporal lobe. They propose a longitude/latitude scheme between an insular and a cingular pole for parameterizing the neocortical surface, and devise a nonlinear mapping to align sulcal bottom lines across individuals.

It has long been noted that deep primary convolutions of the neocortex develop first, and are less variable than more shallow, secondary folds that appear later (for a review, refer to Welker, 1990), suggesting that the development of primary structures is under tighter genetic control. While mathematical modeling (Toro and Burnod, 2005) demonstrated that the development of cortical convolutions is a consequence of cortical growth, the development of thalamo- and cortico-cortical connections determine the segregation of neocortical space (e.g., Rakic, 1988, 2004; Welker, 1990), and contribute to the definition of the folding pattern. Thus, it has been hypothesized that deep sulcal pits develop first and are more invariant than shallow ones across individuals. The early structural development of the human brain was recently studied by in utero MRI (Dubois et al., 2008; Habas et al., 2012). The study of cortical curvature maps derived from this imaging data confirm that major folds develop between gestation week 22 and 28. Meng et al. (2014), analyzed data acquired in a large-scale longitudinal study of the cortical development in infants from 0 to 2 years of age, and studied spatial distribution and temporal development of deep sulcal landmarks in a critical period of brain development. A recent study confirmed a genetic influence on the formation of sulcal pits (Le Guen et al., 2017), albeit with moderate heritability estimates between 0.2 and 0.5.

Several studies (Lohmann et al., 2008; Im et al., 2014; Meng et al., 2014; Nie et al., 2012; Auzias et al., 2015) used sulcal pits as landmarks on the cortical surface. All employed different nonlinear registration procedures to reduce the inter-individual variability for deriving clusters of sulcal pits. The analytic approach described here retained the individual variability, and avoided using arguable features or anatomical models underlying nonlinear registration procedures. To quantify structural patterns, we segmented the neocortical surface into disjoint patches centered around pits, termed basins (Yang and Kruggel, 2008). Basins capture local surface properties such as patch size, surface curvature, geodesic depth, and neighborhood relationships with adjacent basins, thus, provide a richer representation than just the location information of sulcal pits. We represented the neocortical surface as a graph of basins linked by their neighborhood relationships, and analyzed the local variation of corresponding basin labels across a large subject sample to characterize cortical regions in terms of their structural variability. Using a two-level clustering approach, we determined seven groups of "co-varying" basins, called communities here, that emerge from the data without injecting anatomical knowledge. We hypothesized that communities form a structural layer between a hemisphere and its basins, such that communities are similar in all normally developed brains, while the inter-individual variability is kept within a community.

Methods and materials

In the following, we describe the image data base of the population sample used in this study, the processing that led to the segmentation of white matter (WM)/grey matter (GM) interfaces, the basin segmentation process, and the clustering method from which the definition of basin communities emerged.

Subjects and imaging data

This work included imaging data of all 897 subjects in the "900 Subjects Release" of the Human Connectome Project released in December 2015. This sample consists of 503 females and 394 males in the age range of 20–40 years. Structural MR images were acquired on a customized Siemens 3T "Connectome Skyra" housed at Washington University in St. Louis, using a standard 32-channel Siemens receive head coil and a body transmission coil. T1-weighted data were acquired using a 3D MPRAGE protocol with parameters TR = 2400 ms, TE = 2.14 ms, TI = 1000 ms, flip angle 8°, FOV = 224 × 224 mm, 0.7 mm isotropic voxel size, 7 min 40 s acquisition time. T2-weighted data were acquired using a 3D T2-space protocol with parameters TR = 3200 ms, TE = 565 ms, FOV = 224 × 224 mm, 0.7 mm isotropic voxel size, 8 min 24 s acquisition time. For detailed information, refer to the release document (Human Connectome Project, 2017).

Image processing

Our processing started from triangulated meshes representing the WM/GM interface of the left or right cerebral hemisphere with a topological genus of zero. Such surfaces can be generated by several available software packages, and we described our processing chain below.

Unprocessed T1-and T2-weighted structural images were downloaded from the HCP database server. Imaging data were converted from NIFTI to BRIAN format (Kruggel, 2017). Each T1-weighted image was aligned with the stereotaxic coordinate systems and the corresponding T2-weighted image rigidly registered with the aligned data set. Both images were corrected for intensity inhomogeneities (Glasser et al., 2013). A mask for the intracranial compartment was generated based on the T1-weighted image using a registration approach (Hentschel and Kruggel, 2004) and applied to both images. The intracranial space was classified into four compartments based on a Gaussian mixture model (He et al., 2008), roughly corresponding to WM, GM, cerebro-spinal fluid (CSF) and connective tissue. The inner cavities of the WM segmentation (ventricles and basal ganglia) were filled via a patch-based approach using an atlas of 20 pre-segmented data sets (Coupe et al., 2011). From the resulting WM segmentation of the brain, the cerebellum and brain stem were clipped at a level of 15 mm below the plane of the anterior and posterior commissures, and split into hemispheres at the mid-sagittal plane. In each hemisphere, a multi-seeded region growing process (Segonne, 2008) was applied to reconstruct the object as a single c_{18}-connected component (Toriwaki and Yonekura, 2002). A triangulated surface was computed from this object (Nielson, 2003), and optimally adapted to the WM/GM interface as a deformable model using the intensity-corrected T1-weighted brain image. Meshes retained the individual dimensions in which images were acquired (≈ 1 mm vertex distance), and had a topological genus of zero. Each face represented an area of about 0.30 mm^2, each vertex a Voronoi area of about 0.60 mm^2 (Meyer et al., 2002).

Basin segmentation

The neocortical surface was segmented into patches using surface curvature and geodesic depth as local properties. Basins are regions grown from locally deepest points in convex regions at sulcal bottoms until they meet in concave regions at gyral crowns. We used a segmentation procedure that was revised from a previous publication (Yang and Kruggel, 2008).

Principal curvature components κ_1, κ_2 (Meyer et al., 2002) were computed at each vertex of the triangulated surface (see Fig. 1, top left) and converted into the shape index $s = \frac{2}{\pi} \arctan \frac{\kappa_1 + \kappa_2}{\kappa_1 - \kappa_2}$, that ranges between −1 (convex areas) and +1 (concave areas). For computing the geodesic depth, we used the hemispheric WM segmentation, filled sulci using a morphological closing operator, and computed a constrained distance transform on the difference image (Verbeek et al., 1986). The resulting depth values were interpolated in voxel space at vertex locations of the hemisphere mesh (see Fig. 1, top right).

The region growing process was seeded at locally deepest vertices, and each seed was addressed a unique label. In each iteration, all unlabeled vertices on the outer boundary of a region were examined, and the deepest vertex in a convex neighborhood was added to a region. The growing process ended when all vertices in a convex neighborhood were