Surface-Based and Probabilistic Atlases of Primate Cerebral Cortex

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Brain atlases play an increasingly important role in neuroimaging, as they are invaluable for analysis, visualization, and comparison of results across studies. For both humans and macaque monkeys, digital brain atlases of many varieties are in widespread use, each having its own strengths and limitations. For studies of cerebral cortex there is particular utility in hybrid atlases that capitalize on the complementary nature of surface and volume representations, are based on a population average rather than an individual brain, and include measures of variation as well as averages. Linking different brain atlases to one another and to online databases containing a growing body of neuroimaging data will enable powerful forms of data mining that accelerate discovery and improve research efficiency.

Introduction

Staggering amounts of experimental data pertaining to brain structure and function have been obtained in recent years using a variety of neuroimaging methods. Structural MRI (sMRI) and functional MRI (fMRI) are especially widely used because they allow concurrent visualization of brain structure and function at high spatial resolution. Powerful ways to analyze, visualize, and access neuroimaging data are available and are rapidly evolving. Digital brain atlases are a key component of this growing arsenal, as they provide an objective and accessible spatial framework for representing complex experimental data sets. This review focuses on surface-based atlases of cerebral cortex in primates, especially humans. Cerebral cortex—the dominant structure of the human brain—poses special challenges because it is highly convoluted and because the pattern of folding varies greatly from one individual to the next. Surface-based methods of visualization and analysis (“cortical cartography”) are key to dealing with these cortical convolutions, but they are most useful when associated with complementary volumetric atlases.

In general, a brain atlas is a representation of anatomical structure and other reference information in a spatial framework that provides a useful repository of knowledge and facilitates the analysis of spatially localized experimental data of many types. Digital brain atlases have many advantages over conventional print atlases, primarily because they are interactive, searchable, and extensible. Interactive refers to the ability to navigate quickly and seamlessly through complex data sets, including options to view brain structure from many perspectives and to control what types of information are overlaid on the basic brain anatomy. Searchable refers to options for finding relevant data based on spatial coordinates, structural and functional labels, and a variety of other search criteria. Extensible refers to options for incorporating new information of diverse types into the atlas quickly and flexibly, without needing to await a new print edition.

The five main objectives of this review are (1) to discuss key structural and functional characteristics of human cerebral cortex that profoundly impact the analysis of neuroimaging data and dictate desirable features of a cortical atlas; (2) to characterize major brain atlases currently used in human and monkey neuroimaging; (3) to illustrate the utility of digital atlases for visualization, analysis, localization, and data mining; (4) to compare strategies used to compensate for individual variability and to relate these strategies to the biological basis of variability; and (5) to illustrate comparisons between human and macaque cortex using surface-based atlases. Other recent reviews cover a broader range of atlas-related issues (Devlin and Poldrack, 2007; Mazziotta et al., 2001; Toga and Thompson, 2001, 2002, 2003, 2005; Toga et al., 2006).

1. Individual Variability Is Large Relative to Cortical Area Dimensions

Deciphering the amazingly complex functional organization of cerebral cortex requires that experimental data be localized as accurately as possible within the convoluted cortical sheet. It is equally important to recognize the uncertainties and errors that inevitably occur when specifying cortical locations. To help frame these issues, it is instructive to consider the following questions about human cerebral cortex. What are the dimensions of the cortex and its functional subdivisions? What are the nature and magnitude of individual variability? What constraints are imposed by the spatial resolution and signal-to-noise routinely attainable in neuroimaging studies?

Human cerebral cortex is a thin sheet (3 mm thick on average) with a surface area of ~900 cm² per hemisphere—equivalent to a 13” (34 cm) pizza (Fischl and Dale, 2000; Henery and Mayhew, 1989; Jouandet et al., 1989; Makris...
subject mapping of many retinotopic visual areas (V1, V2, V3, etc.; DeYoe et al., 1996; Grill-Spector and Malach, 2004; Larsson and Heeger, 2006; Sereno et al., 1995; Swisher et al., 2007; Wandell et al., 2005, 2007; but see Jack et al., 2007). Extending this approach to obtain an accurate, fine-grained mapping of the entire human cortex is an extremely desirable objective, but an elusive one for several reasons. The signal-to-noise ratio obtained with fMRI is generally low, especially in regions outside early sensory and motor areas. Signal-to-noise can be enhanced by within-subject spatial smoothing and by intra-subject averaging, but each of these substantially degrades spatial resolution. Averaging across subjects entails registering the data to a common spatial framework, i.e., a brain atlas. The nature and magnitude of individual variability pose major challenges, making it critical to estimate the uncertainties and alignment errors associated with different atlases and registration strategies.

Four aspects of individual variability impact cortical registration. (1) Brain size and shape. Brains differ in total volume, linear dimensions, and overall shape within the cranial cavity. (2) Folding patterns. Humans and other highly gyrencephalic species show dramatic individual differences in the specific pattern of convolutions. This is illustrated with medial views of two example right hemisphere surfaces shown in their original 3D (“fiducial”) configuration and on inflated surfaces (Figures 2A and 2B). Three major sulci, the calcarine (CaS), parieto-occipital (POS), and cingulate (CiS) can be readily identified, but differences in shape and location are evident, particularly for the calcarine sulcus. Importantly, the assorted local features are the most variable. For example, the blue arrows in Figures 2A and 2B point to small folds in one hemisphere that are absent or different in orientation in the other. Each “cortical brainprint” represented by one of these sulcal depth maps is likely to be as unique as a human fingerprint pattern. (3) Areal size. Any given area differs in size by a factor of 2-fold or more across individuals. This has been documented most extensively for area V1 (Andrews et al., 1997; Stensaas et al., 1974) but has been demonstrated for other areas as well (Dougherty et al., 2005; Tramo et al., 1995; Van Essen, 2005a). Extensive convolutions allow this large cortical expanse to fit into a compact cerebral volume (about 18 cm long, 13 cm high, 14 cm total brain width). These relationships are illustrated for an exemplar brain (sMRI slice in Figure 1A) and the right hemisphere surface displayed in its original 3D (fiducial) configuration (Figure 1B). A map of “sulcal depth” (distance to the nearest gyrus) provides a useful measure of the original shape when viewing the inflated and flattened configurations (Figures 1C and 1D).

The cortical sheet contains a complex mosaic of cortical areas, each having distinct anatomical and functional characteristics. Accurate partitioning of the entire cortex has proven difficult, mainly because the differences between areas are often subtle. Competing partitioning schemes remain in use for most regions, leading to frequent debate and confusion, and the total number of cortical areas is not known for any species. Human cortex probably contains between 100 and 200 areas in each hemisphere (Van Essen, 2004b) arranged in a pattern that has strong bilateral symmetry but some important hemispheric asymmetries, especially in the temporal lobe (Toga and Thompson, 2003; Van Essen, 2005a). Assuming an intermediate value of 150 areas per hemisphere, each individual area would occupy ~6 cm² surface area on average, equivalent to a pepperoni-sized disk ~3 cm in diameter. A few areas are much larger (area V1 is ~20 cm² on average), while others are much smaller. Many areas are elongated and as little as 5-10 mm wide, such as the architectonic areas identified in orbitofrontal cortex (Öngür et al., 2003).

Spatial resolution in neuroimaging is limited by the size of the individual “voxels” (volume elements) acquired in each scan. Voxel dimensions are typically 1 mm³ for sMRI (as in Figure 1A) and 3 x 3 x 3 mm or larger for human fMRI. A typical cortical area with a volume of ~1800 mm³ (~600 mm² area x 3 mm thickness), would thus be equivalent to about 70 fMRI voxels in overall extent; small or narrow areas are only a few voxels wide.

It is possible to identify and map individual cortical areas using fMRI. The most notable successes involve single-
The variability of individual areas exceeds the estimates of variability in total cortical size and surface area (Andrews et al., 1997; Elston, 2006; Henery and Mayhew, 1989; A. Kline et al., 2005, Org. Hum. Brain Mapp., abstract). (4)

Area versus folding landmarks. Area V1 occupies most of the calcarine sulcus, but a variable portion of it extends into neighboring gyral and sulcal regions by up to several cm (Amunts et al., 2000; Rademacher et al., 1993). For most other cortical areas the correlation with cortical folding is even weaker (Amunts et al., 2007). In considering the impact of these different aspects of variability, it becomes important to clarify the concept of “corresponding” locations in different brains.

**Functional and Geographic Correspondences Are Conceptually and Empirically Distinct**

The overarching objective when registering individuals to an atlas is to align corresponding cortical locations as accurately as possible. Cortical locations in different individuals are in functional correspondence if they are part of the same cortical area and are matched in terms of whatever is mapped within that area. For example, each point in the visual field (e.g., the center of the foveal representation) can be used to define corresponding locations in area V1 of different individuals. In a similar vein, locations can be considered in geographic correspondence if they represent the same “geographic” feature (so named because gyri and sulci are akin to hills and valleys on the earth’s surface) or have a consistent relationship to other geographic features. For example, the posterior tip of the calcarine sulcus can be considered geographically corresponding in different individuals.

Three important caveats arise in applying these concepts to the realities of cortical structure and function. (1) Function-folding mismatches. Because areal boundaries vary relative to geographic landmarks, functional and geographic correspondences are inherently in conflict. The question is not whether they are mismatched, but by how much. The answers depend on the areas considered and on the particular individuals analyzed. For example, the center of the foveal representation might lie near the posterior tip of the calcarine sulcus in one individual and 3 cm lateral to it in another individual. When such mismatches occur, either the local visuotopic maps or the local folds can be aligned, but not both concurrently. (2) Ambiguous geographic correspondences. Variability in folding patterns can lead to ambiguity in the notion of geographic correspondence. For example, in Figures 2C and 2D (lateral views of inflated surfaces) the dorsal tip of the superior temporal sulcus (STS) is well-defined in Case C, but in Case D it has a distinct fork; the choice of which branch should be designated is the “real” dorsal tip is largely arbitrary. Similarly, the ventral-anterior tip of the STS is well defined in Case D but is ambiguous in Case C. (3) Folding mismatches. Given the observed degree of variability in cortical folding patterns, the challenges in registration go beyond just the problem of resolving ambiguous correspondences (e.g., which is the main dorsal STS branch in Case D). The deeper problem is that no registration that respects the topology of the cortical sheet can successfully match every major and minor fold in one individual with a corresponding fold in another individual. Instead, the registration process must tolerate folding mismatches, such as the crown of a gyrus in one individual corresponding to the fundus of a sulcus in another individual. Folding mismatches can occur at both a fine-grained scale, such as the irregular minor gyri and sulci in Figures 2A and 2B (blue arrows) and also at a more macroscopic scale, as with atypical “folding variants” in which a major sulcus or gyrus has a very different configuration in some
individuals compared to the most common pattern (Lyttleton et al., 2007; Mangin et al., 2004; Ono et al., 1990). These issues are very important when considering the strengths and limitations of various registration algorithms, a topic discussed in a later section.

Cortical organization has been studied extensively in many other primate species using anatomical, physiological, and/or neuroimaging approaches, but the macaque monkey is by far the most intensively studied nonhuman primate. The macaque is also particularly relevant to human neuroimaging, thanks to a growing number of macaque fMRI studies that facilitate interspecies comparisons (Brewer et al., 2002; Denys et al., 2004; Orban et al., 2004; Sereno and Tootell, 2005; Tsao et al., 2006; Vincent et al., 2007). There are many fundamental similarities across primate species, but also many obvious quantitative and qualitative differences. The surface area of macaque cerebral cortex is only 15% of that in humans (Van Essen et al., 2005), and it

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Figure 3. Shape Characteristics of Cerebral Cortex in an Individual Macaque

(A) A parasagittal section through the right hemisphere sMRI of macaque F99UA1 (a.k.a. the F9 atlas, Table 1). Red contour shows a slice through the fiducial cortical midthickness surface.

(B) The right hemisphere fiducial surface.

(C) The very inflated surface, with a map of sulcal depth.

(D) A flat map representation.

Data are accessible via http://sumsdb.wustl.edu/sums/directory.do?id=6650508.

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2. Probabilistic Brain Atlases Are Frameworks for the Future

Ideally, brain atlases for the 21st century should include many attributes and many types of data (cf. Toga et al., 2006). The following nine attributes are particularly important for digital atlases of cerebral cortex. Resolution. The atlas should represent brain structure at high spatial resolution. Areas. It should include maps of cortical areas based on as many as possible of the various partitioning schemes in current use. Probabilistic. Cortical areas, cortical folding patterns, and identified gyri and sulci should be represented probabilistically whenever possible, in a way that reflects variability in cortical convolutions and in the size, location, and internal (e.g., topographic) organization of cortical areas. Visualization. The atlas should be linked to powerful, flexible, and easy-to-use visualization tools, both surface-based and volume-based, to facilitate navigation and display of diverse data types. Coordinates. It should be associated with well-defined stereotaxic and surface-based coordinate systems to facilitate objective reporting of spatial location. Atlas-linked. It should be registered to other widely used cortical atlases and stereotaxic spaces, in order to facilitate comparisons across studies. Accessible. It should be readily accessible for visualization online and after downloading. Database-linked. It should be linked to searchable databases that allow a rapidly growing body of experimental data to be viewed, analyzed, and compared using the atlas framework. Extensible. It should be easy to update the atlas as new experimental data (e.g., newly charted cortical areas) become available.

No single atlas is fully satisfactory in meeting all of these criteria, but a number of useful digital atlases have emerged over the past decade. Unlike book atlases, digital brain atlas are not static entities with well-defined content. Instead, they have evolved into inherently complex and dynamic constructs in terms of their information content.
and how it is accessed. Portals to emerging atlases and associated neuroimaging tools are accessible via the Neuroscience Database Gateway (http://ndg.sfn.org/) and the Neuroimaging Informatics Tools and Resources Clearinghouse (NITRC) (http://www.nitrc.org/).

Table 1 provides a snapshot of major human and macaque digital cortical atlases that are currently accessible to the neuroimaging community for use in visualization and analysis. The first three columns indicate the primary visualization substrate for each atlas volume (column 1) and/or surface (columns 2 and 3). The primary anatomical “template,” which may be a volume and/or a surface, forms the core of an atlas, but the atlas itself may contain extensive additional reference data (columns 5 and 6; see below). Some atlases have multiple row entries, reflecting their availability in different stereotaxic spaces (column 4) or software platforms (column 8). We consider first the anatomical templates and visualization substrates for single-brain and population-average human atlases (columns 1–3).

The two single-subject atlases in widespread use differ in many respects. The classical Talairach atlas (Talairach and Tournoux, 1988 [“T88”]) defined a standard stereotaxic space that attained well-deserved prominence as a spatial framework for reporting coordinates of neuroimaging results (Fox et al., 1985, 2005). It is based on brain slice drawings from a single postmortem brain that are digitally accessible via the Sleuth (BrainMap) database.

The “Colin27” atlas is based on high-resolution imaging of a single subject initially generated in MNI space (Figure 4A) but also available after transformation to several other stereotaxic spaces. Available fiducial surfaces for the Colin27 atlas include representations of the gray-white (GW) boundary (Figure 4B), the pial surface (data not shown), and the cortical midthickness (CMT) representation (Figure 4C). The GW and pial surface representations can be used jointly to compute cortical thickness (Fischl and Dale, 2000). The CMT representation provides a more balanced representation of gyral and sulcal regions, which is important for analyses that involve measurements of cortical surface area (Van Essen et al., 2001).

Population-average atlases are increasingly widely used because they avoid the biases associated with the idiosyncratic cortical folding pattern of any particular brain, including T88 and Colin27. In a volume-averaged population atlas such as the ICBM 152 (a.k.a. MNI152, Figure 4D), residual variability is manifested by pronounced blurring between gray matter and white matter, especially in cortical regions.

Volume-averaged atlases have the advantage of complete coverage of the brain, regularity of spatial sampling (uniform voxel size), and the availability of many voxel-based visualization and analysis tools. Their major limitations relate to the difficulty of displaying complex, spatially distributed data and to the alignment errors associated with volume-based registration. Surface-averaged atlases have the advantage of flexible cortical visualization options and greater fidelity of surface-based registration. A major limitation is the exclusion of subcortical structures. Also, capitalizing fully on the alignment capabilities of surface-based registration requires high-quality surface reconstructions of each individual subject. Even with recent improvements in automated segmentation and error correction, insuring adequate quality control remains an important issue.

Given these inherent complementarities, a hybrid atlas that supports concurrent utilization of surfaces and volumes for visualization and analysis is naturally attractive. This is the objective of the PALS (Population-Average, Landmark, and Surface-based) atlas concept and the specific PALS-B12 atlas data set that is based on sMRI volumes from 12 normal young adults (Van Essen, 2005a). The PALS-B12 atlas volume was generated by averaging the individual sMRI volumes after registration to stereotaxic space (Figure 5A). The PALS-B12 atlas surfaces were generated by reconstructing the fiducial surface of each hemisphere, registering each surface to the atlas, and generating “average fiducial” surface representations for the left and right hemispheres (Figure 5B). In regions of low variability such as the central sulcus (CeS), major gyral and sulcal features are largely preserved, but in regions of high variability many features are averaged out and the average fiducial surface runs approximately midway along the depth of the major sulci, as evidenced in the surface contours visible in Figure 5A. The PALS atlas provides flexible visualization options that include inflated, very inflated, flat map, and spherical configurations (Figures 5C–5F; Table 1). In each surface configuration, a map of average sulcal depth provides an objective measure of cortical shape that has well-defined features in regions of low variability and is blurred in regions of high variability.

A key aspect of surface-based registration involves representing each individual hemisphere’s surface by a “standard mesh” (Saad et al., 2004) that contains a fixed number of surface nodes. A standard mesh can implicitly define what constitutes geographic correspondence, based on the atlas and registration algorithm used. For example, the more posterior of the highlighted nodes (black) in Figure 5 is consistently on the postcentral gyrus of the PALS atlas surfaces (Figures 5A–5F) and in the two individual hemispheres (Figure 5G). The more anterior node, in a region of higher variability, lies on the precentral gyrus in one individual but in the precentral sulcus in another.

Another important aspect of correspondence involves comparisons between the left and right hemispheres. In the PALS atlas, both the left and right hemispheres were registered to an unbiased target (based on landmarks derived from both hemispheres). This implicitly defines geographically corresponding locations in the two hemispheres (see highlighted nodes in Figure 5) and facilitates analyses of hemispheric symmetries and asymmetries (Van Essen, 2005a; Van Essen et al., 2006).

Study-Specific Averages and Age-Specific Atlases
An alternative population-average strategy is to generate study-specific population-average surfaces that are based on a group of subjects within a given study but not linked to
## Table 1. Digital Atlases of Human and Macaque Cerebral Cortex

<table>
<thead>
<tr>
<th>Volume (Template)</th>
<th>Fiducial Surface</th>
<th>Other Configurations</th>
<th>Stereotaxic Space</th>
<th>Source</th>
<th>Content</th>
<th>Software</th>
<th>Citation</th>
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<td><strong>Single-Brain Atlases: Human</strong></td>
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<tr>
<td>1. Talairach</td>
<td>T88</td>
<td>TD&lt;sup&gt;a&lt;/sup&gt;</td>
<td>gyr; Brod</td>
<td>Sleuth,&lt;sup&gt;b&lt;/sup&gt; AFNI&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Talairach and Tournoux, 1988; Lancaster et al., 2000</td>
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<td>2. Colin27 sMRI&lt;sup&gt;g&lt;/sup&gt;</td>
<td>MNI</td>
<td>TD,&lt;sup&gt;a&lt;/sup&gt; WPA&lt;sup&gt;d&lt;/sup&gt;</td>
<td>gyr; Brod</td>
<td>FSL,&lt;sup&gt;e&lt;/sup&gt; SPM&lt;sup&gt;f&lt;/sup&gt;</td>
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<td>Caret&lt;sup&gt;i&lt;/sup&gt;</td>
<td>CMT</td>
<td>inflated, flat, sphere</td>
<td>MNI, T88, 711-2B</td>
<td>—</td>
<td>sulci; Brod, Vis, OrbFront</td>
<td>Caret&lt;sup&gt;i&lt;/sup&gt;/SumsDB&lt;sup&gt;th&lt;/sup&gt;</td>
<td>Van Essen, 2002, 2004a</td>
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<td>FreeSurfer&lt;sup&gt;o&lt;/sup&gt;</td>
<td>GW, pial</td>
<td>sphere</td>
<td>MNI</td>
<td>—</td>
<td>gyr; subcortical</td>
<td>FreeSurfer&lt;sup&gt;o&lt;/sup&gt;</td>
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<td>GW, pial</td>
<td>inflated</td>
<td>MNI</td>
<td>JAM&lt;sup&gt;i&lt;/sup&gt;</td>
<td>areas</td>
<td>SUMA&lt;sup&gt;p&lt;/sup&gt;</td>
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<td>3. MNI 305&lt;sup&gt;a&lt;/sup&gt;</td>
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<td>4. ICBM 152&lt;sup&gt;s&lt;/sup&gt;</td>
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<td>JAM&lt;sup&gt;i&lt;/sup&gt;, TA&lt;sup&gt;j&lt;/sup&gt;, HOA&lt;sup&gt;i&lt;/sup&gt;</td>
<td>gyr; areas</td>
<td>BIC,&lt;sup&gt;j&lt;/sup&gt; AIR,&lt;sup&gt;i&lt;/sup&gt; SPM,&lt;sup&gt;f&lt;/sup&gt; FSL,&lt;sup&gt;e&lt;/sup&gt; AFNI&lt;sup&gt;c&lt;/sup&gt;</td>
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<td>6. LONI (LPBA40)&lt;sup&gt;s&lt;/sup&gt;</td>
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<td>PubBrain&lt;sup&gt;s&lt;/sup&gt;</td>
<td>GM, WM (P)</td>
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<td>sulci; areas</td>
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*Population-Average Atlas: Macaque*


<sup>a</sup>http://ric.uthscsa.edu/new/resources/talairachdaemon/talairachdaemon.html
<sup>b</sup>http://brainmap.org/
<sup>c</sup>http://afni.nimh.nih.gov/afni/
<sup>d</sup>http://www.fmri.wfubmc.edu/cms/software
<sup>e</sup>http://www.fmrib.ox.ac.uk/fsl/
<sup>f</sup>http://www.fil.ion.ucl.ac.uk/spm/
<sup>g</sup>http://www.bic.mni.mcgill.ca/brainweb/
<sup>h</sup>http://www.talairach.fr/
<sup>i</sup>http://www.sph.sc.edu/comd/rorden/mricro.html
<sup>j</sup>http://brainmap.wustl.edu/caret/
<sup>k</sup>http://sumsdb.wustl.edu/sums/directory.do?id=6363287&dir_name=COLIN_CEREBRAL
<sup>l</sup>http://sumsdb.wustl.edu/sums/
<sup>m</sup>http://sourceforge.net/project/shownotes.php?release_id=325132
<sup>n</sup>http://surfer.nmr.mgh.harvard.edu/surfer/DownloadAndInstall
<sup>o</sup>http://afni.nimh.nih.gov/afni/suma
<sup>p</sup>http://www.bic.mni.mcgill.ca/software/mni_autoreg/
<sup>q</sup>http://www.bic.mni.mcgill.ca/software/
<sup>r</sup>http://www.bic.mni.mcgill.ca/cgi/icbm_view/
<sup>s</sup>http://www.fmrib.ox.ac.uk/fs/atlases-atlas-descriptions.html
<sup>t</sup>http://bishopw.loni.ucla.edu/AFR5/index.html
<sup>u</sup>http://www.loni.ucla.edu/ICBM/Downloads/Download_Atlases.shtml
<sup>v</sup>http://www.loni.ucla.edu/Atlases/Atlas_Detail.jsp?atlas_id=12
<sup>w</sup>http://www.pubbrain.org/
<sup>x</sup>http://www.loni.ucla.edu/ad/AD_ASPVA.html
<sup>y</sup>http://sumsdb.wustl.edu/sums/directory.do?id=6585200&dir_name=CARET_TUTORIAL_SEPT-06
<sup>z</sup>http://surfer.nmr.mgh.harvard.edu/
<sup>aa</sup>http://www.nil.wustl.edu/labs/kevin/nf2k/p1.htm
<sup>ab</sup>http://www.loni.ucla.edu/Atlases/Atlas_Detail.jsp?atlas_id=2
<sup>ac</sup>http://www.loni.ucla.edu/Research/Atlases/Data/monkey/MonkeyAtlasViewer.shtml
<sup>ad</sup>http://brainmaps.org/
<sup>ae</sup>http://sumsdb.wustl.edu/sums/directory.do?id=6653275
any particular atlas (Argall et al., 2006; Goebel et al., 2006; Lyttelton et al., 2007). This successfully reduces intersubject variability and can facilitate a variety of within-group analyses (Figure 6A; see also below). However, it is less amenable to quantitative comparisons of results across studies unless and until the data are subsequently registered to a common surface-based atlas. A related concept involves age-specific template atlases that represent shape characteristics within defined age groups, ranging from infants (J. Hill et al., 2007, Soc. Neurosci., abstract) to elderly adults (Thompson et al., 2001). Mappings between different age-specific atlases, when available, allow quantitative comparisons across ages.

Another class of study-specific population-average atlas involves surface representations of just the exposed (gyral) portions of cerebral cortex (Shi et al., 2007; Thompson et al., 2000; Toga and Thompson, 2002; Toga et al., 2001). Because these “gyral maps” (Figures 6B and 5C) do not explicitly represent buried cortex (which constitute about two-thirds of total cortical surface area), they differ from full-hemisphere atlases (e.g., PAS-B12 and FreeSurfer Average-40) in terms of topology and completeness of the cortical representation. Nonetheless, it should be feasible to generate mappings between gyral map atlases and the corresponding gyral portions of full-hemisphere atlases, thereby facilitating migration of data between these two widely used classes of surface-based atlas.

**Location, Location, Location!**

The realtors’ mantra about the paramount importance of location has a parallel in neuroimaging, where many different options are used to specify location within the brain. Cartographers describe locations on the earth’s surface using spatial coordinates, geographic labels, and political labels. Analogous strategies are used within the brain; the main distinction is between coordinate-based and region-based descriptions of location.

**Coordinate-Based Localization**

Spatial coordinates provide a concise, precise, and objective way to express location in a brain atlas relative to an anatomically defined origin (the anterior commissure in the Talairach and other human atlases). A “template” or atlas represents the underlying structure, and a registration process uses a particular algorithm to match any individual brain to the atlas. Available volumetric atlases differ in the dimensions and shape of the template, in the registration process by which the template was generated.
A growing collection of probabilistic architectonic maps have been generated from architectonic analyses of post-mortem brains by the Zilles laboratory in Juelich. This process involves objective charting of areal boundaries, registration of individual hemispheres to the Colin27 brain template, and summation across individual cases to generate population-average architectonic maps (Amunts et al., 2005).

Region-Based Localization

Atlases gain in usefulness when locations can be expressed in relation to identified geographic and/or functional regions. Sources of geographical information derived from single subjects and available in one or more atlases include cortical gyri and classical Brodmann areas derived from the original Talairach atlas, Talairach Daemon (Table 1, “TD” in column 5); anatomically defined subregions of the Colin27 brain in the Automated Anatomical Labeling (AAL) tool; and Brodmann, visuotopic, and orbitofrontal areas on the Colin27 surface (Caret).

Probabilistic maps that represent the range of variability in a standard population provide an increasingly important way to cope with individual variability. Available probabilistic representations of cortical geography include cortical and subcortical probability maps in the FSL Harvard/Oxford Atlas (HOA), the LONI Sub-Volume Probabilistic Atlas (SVPA), and maps of identified sulci in the PALS atlas.

A powerful alternative strategy for geographic localization involves automated sulcal/gyral identification algorithms that can be applied to individual subjects registered to atlas space. BrainVisa (http://brainvisa.info/) and FreeSurfer software currently provide such options. Efforts to improve automated identification of cortical and subcortical structures are ongoing in many laboratories (Cachia et al., 2003; Desikan et al., 2006; Fischl et al., 2004; Klein et al., 2005; Mega et al., 2005). While these processes are not perfect, given the complexity and variability of convolutions (Ono et al., 1990; see above), they are likely to provide better estimates for any given individual than those derived from probabilistic maps of a standard population.
et al., 2007; Eickhoff et al., 2005, 2007). These “Juelich architectonic maps” (‘‘JAM’’ in Table 1, column 5) are associated with several atlases and are accessible via several software platforms. Though extremely valuable, the available probabilistic architectonic maps currently cover only a minority of the cortical expanse. Registration to the Colin27 brain has been carried out using both linear and nonlinear algorithms. The high-dimensional nonlinear registration achieves tighter clustering of each area in the single-subject target atlas, but there is a potential disadvantage in using a registration strategy that differs from the linear (e.g., FSL’s FLIRT) or low-dimensional nonlinear (e.g., SPM2) algorithms typically used in fMRI studies (Poldrack and Devlin, 2007; Van Essen and Dierker, 2007). When using probabilistic architectonic maps to infer the cortical area(s) associated with any given fMRI activation pattern, the choice of which registration method provides greatest accuracy is an empirical question that warrants further investigation.

3. Atlases Are Key to Data Mapping and Data Mining

Digital brain atlases are invaluable for the analysis and visualization of vast amounts of structural and functional neuroimaging data obtained in ongoing experimental studies. The specific analysis options available are too numerous, diverse, and platform dependent to be covered systematically here, but it is useful to draw attention to two general ways in which atlas utility can be enhanced. These involve data migration across platforms and data mining across studies.

Migration across Platforms

No single software platform is comprehensive in its data analysis and visualization capabilities, and many studies can benefit from analyses that make use of multiple platforms. Cross-platform data migration can occur at many analysis stages, such as intensity normalization on one platform (FSL), segmentation on another (FreeSurfer), and surface-based registration on a third (Caret/PALS). One increasingly common two-stage approach is to ‘‘analyze volumes, visualize surfaces.’’ More specifically, this entails carrying out primary analyses of fMRI data in the volume domain, thereby capitalizing on sophisticated volumetric analysis tools (SPM, AFNI, etc.). Results are then mapped onto a surface-based atlas (e.g., PALS) to aid in visualization and further analysis. For example, Figure 7 shows fMRI activation patterns from three studies initially analyzed in distinct stereotaxic spaces (T88, MNI, and 711-2B). Volume-averaged results were mapped to the appropriate space-specific PALS atlas by an easily executed process of ‘‘multi-fiducial mapping’’ that minimizes biases arising from folding variability (Van Essen, 2005a). Each set of fMRI activations is displayed in relation to the boundaries of visuotopic areas (colored contours) that were themselves mapped to the PALS atlas by surface-based registration. This facilitates objective assessment of the degree of overlap between motion-selective (Figure 7A; Lewis et al., 2000) and object-selective (Figure 7B; Denys et al., 2004) activations to one another, to area MT (red contours) and other cortical areas, and to the vibrotactile activation pattern, in early blind individuals (Figure 7C; Burton et al., 2004).

Cross-platform data migration and analysis can be facilitated by increased use of common data formats. For volume data, NIfTI (Neuroimaging Informatics Technology Initiative, http://nifti.nimh.nih.gov/) is an emerging standard that is supported by a growing number of neuroimaging software platforms. An analogous effort for surface representations (GIFTI) began more recently but will hopefully become widely adopted as well.

Data Mining

Investigators interested in relating their current neuroimaging results to what is already known must extract relevant findings from a neuroimaging literature that has mushroomed to thousands of studies in dozens of major neuroscience journals, with specific results displayed in many formats. It is increasingly difficult to carry out thorough, careful, objective comparisons of results residing in this expanding cacophony of neuroimaging studies. To address this problem, progress is needed on multiple fronts, but especially in the enhancement of neuroimaging databases and data mining tools.

One domain that is ripe for enhanced data mining involves the stereotaxic coordinates frequently used to report the centers of activation foci and other regions of interest. An estimated 3000 neuroimaging studies had reported about 10^5 stereotaxic coordinates as of 2004 (Fox et al., 2005), and the number of new studies reporting coordinate data is now growing by perhaps 1000 per year. Because tables of stereotaxic coordinates scattered in
various journal articles are not readily searchable, stereotaxic coordinates need to be deposited in a searchable database to allow effective data mining. Currently, two complementary databases each house a substantial and growing portion of the relevant literature. The BrainMap database (http://brainmap.org/) currently contains ~43,000 coordinates from ~1200 studies, searchable using the downloadable Sleuth application. The SumsDB database currently contains ~13,000 searchable coordinates from ~450 studies; search results can be viewed online on the PALS atlas (via WebCaret) or downloaded for offline analysis using Caret.

The complementary nature of these two databases can be illustrated by searching each for studies related to a particular functional task such as mental rotation. Using Sleuth, this identifies hundreds of coordinates from 29 studies, displayed on slice views relative to the Talairach atlas outline (Figure 8A). Extensive metadata relating to each study are available within the BrainMap database. Flexible meta-analysis options, including Activation Likelihood Estimation (Turkeltaub et al., 2002; Laird et al., 2005) facilitate meta-analysis studies (Fox et al., 2005). In SumsDB a meta-analysis of mental rotation studies (Zacks, 2007) identified 319 coordinates from 32 studies that can be displayed on the PALS atlas surface online using WebCaret or offline in Caret (Figure 8B).

Cross-study comparisons and meta-analyses like those illustrated in Figures 7 and 8 must of course be carried out with careful attention to potential confounds. These include differences in task design or other methodological details, spatial biases in the primary data, and a variety of other differences across studies. On the other hand, there are obvious downsides to failing to make adequate comparisons with previously published results. Data mining tools that facilitate access to key data and to the associated primary literature will improve research efficiency and allow investigators to concentrate on data analysis and interpretation rather than finding and formatting the relevant published data.

Stereotaxic coordinates provide only a sparse representation of the complex fMRI activation patterns reported in any given study, and there is a growing need for databases that can handle complex volumetric and surface-based neuroimaging data, such as the examples shown in Figure 7. SumsDB and WebCaret are customized for combined surface and volume storage and visualization. A major emphasis is on specific data sets associated with published figures that include WebCaret “scenes” exactly replicating figure contents. The figure legends in the present review include links to SumsDB/WebCaret that demonstrate this feature.

The precision with which stereotaxic coordinate points (“foci”) are displayed in Figure 8 belies the fact that the underlying experimental fMRI activations are associated with major spatial uncertainties and biases. These uncertainties depend on many factors, but a particularly important one is the fidelity of registration from individuals to the atlas. This motivates further discussion of different approaches used to improve intersubject alignment.

4. Surface-Based Registration Outperforms Volume-Based Registration

Currently, most fMRI studies are analyzed largely or entirely in the volume domain using well-established software platforms (SPM, AFNI, etc.). However, surface-based analyses of individual subjects, accompanied by surface-based registration (SBR) to improve intersubject alignment, are increasingly common. In theory, SBR has an intrinsic advantage over volume-based registration (VBR) because it respects the topology of the cortical sheet. A key issue is whether in practice the gains in intersubject alignment are sufficient to warrant more
widespread adoption of the SBR approach. Empirically, many studies have now demonstrated that SBR indeed can achieve substantially better alignment than VBR for several types of experimental data, including fMRI activation patterns (A. Anticevic et al., 2007, Cogn. Neurosci. Soc., abstract; Argall et al., 2006; Desai et al., 2005; Fischl et al., 1999, 2004; Goebel et al., 2006; van Atteveldt et al., 2007), simulated fMRI data (Jo et al., 2007), identified cortical sulci (A. Anticevic et al., 2007, Cogn. Neurosci. 2004), and architectonic areas (Yeo et al., 2007).

Figure 9 illustrates why SBR outperforms VBR and sets the stage for comparing SBR algorithms. Using the same example hemispheres as in Figure 2, the very different trajectories of the calcarine sulcus (CaS) in Cases A and B are evident in medial surface views (Figures 9A and 9B), in parasagittal sMRI slices (Figures 9C and 9D), and in segmented maps of its dorsal bank (CaSd, Figure 9E). In the volume-averaged population map for all 12 contributing subjects (Figure 9F), the CaSd showed considerable dispersion, signifying only moderately consistent alignment. In contrast, surface-based registration to the PALS atlas (using the “PALS-SBR” process) yielded much better alignment of the CaSd for the two individuals (Figure 9G) and for the population average (Figure 9H). By a quantitative measure, the alignment was 2.5-fold better for SBR than for VBR for the calcarine sulcus and on average 1.7-fold better for the 18 sulci tested (Van Essen, 2005a).

In general, the aim of SBR should be to align sulci that are relatively consistent in shape but not to force large local deformations in regions where variability is high and folding mismatches are to be expected. In practice, various SBR methods differ markedly in the degree of local deformation tolerated in the registration process. At one end of the spectrum, the SUMA-SBR method (Argall et al., 2006) introduces no local deformations to improve alignment and is therefore unlikely to be optimal in aligning major landmarks like the central sulcus and calcarine sulcus. In contrast, the global energy-minimization approach of FreeSurfer-SBR (Fischl et al., 1999) achieves good alignment of major sulci, but it results in pronounced local distortions when matching local features in regions where folding mismatches are to be expected (Figure 2 in Wisco et al., 2007; D.C.V.E., unpublished data). PALS-SBR is intermediate between these two and may be closer to optimal, insofar as it uses a small number of explicit landmarks to align major sulci and aims to minimize areal distortions in the intervening regions. Careful testing using common data sets is needed to better characterize the strengths and limitations of these and several other available SBR methods (Chung et al., 2003, 2005; Clouchoux et al., 2005; Goebel et al., 2006; Lyttelton et al., 2007) and to help guide algorithmic refinements that further improve intersubject alignment. Also, in order to fully capitalize on the advantages of intersubject SBR analyses, it is important to have surface-based statistical analysis methods that allow significance to be evaluated quantitatively. Such methods are under active development, but many are already available for both morphometric and fMRI studies using major software packages, including FreeSurfer, SUMA, Caret, Brain Voyager (see Table 1), and SURFTRACC (Lyttelton et al., 2007; Robbins et al., 2004).

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5. Surface-Based Analyses Facilitate Monkey-Human Comparisons

Like their human counterparts, macaque brain atlases come in several varieties (Table 1, rows 11–17). Digital sMRI-based atlases include several single-subject volumetric atlases, plus the F99 hybrid surface-volume atlas (Van Essen, 2002, 2004a). The population-average surface-volume F6 atlas serves as a useful target for fMRI studies (Vincent et al., 2007) and has been registered to the F99 atlas so that data can migrate from one to the other. The F99 and F6 atlases also contain a large repertoire of associated reference data available in the SumsDB database (see Figure 10 legend), including 12 areal partitioning schemes (one of which is a probabilistic architectural map), and connectivity data plus links to the CoCoMac connectivity database (http://www.cocomac.org/). The Saleem and Logothetis (2006) printed macaque atlas includes MRI images, histological sections, and areal partitioning schemes, and the associated “D99” MRI volume is accessible online (Table 1, row 16). Another useful resource is the labeled histological sections of macaque, human, and other species that are available at http://brainmaps.org/.

A substantial minority of macaque cortical areas have convincing or strongly suspected homologs in humans, based on similarities in architecture and/or functional organization (Öngür et al., 2003; Orban et al., 2004; Petrides, 2005; Sereno and Tootell, 2005; Tootell et al., 2003; Van Essen, 2005b). Surface-based atlases can play a pivotal role in evaluating candidate homologies and facilitating objective quantitative comparisons of cortical organization in monkeys and humans. This is because the profound species differences in folding and in area-folding relationships make geographic (shape) features generally unsatisfactory as a constraint on registration and instead require landmarks based on known or suspected homologies. Using landmark-constrained interspecies registration involving 23 presumed homologies, Figure 10 shows a map of architectonically delineated cortical areas in the macaque (Figure 10A), the same macaque areas registered to human cortex (Figure 10B), and a map of human.
architectonic areas for comparison (Figure 10C). A map of cortical expansion in humans versus macaque based on this registration shows several hotspots of particularly high expansion (Figure 10D). Future studies capitalizing on additional experimental information brought into this atlas framework and analyzed using interspecies surface-based registration may help resolve the key evolutionary issue of whether local cortical expansion has occurred mainly by the emergence of entirely new areas or mainly by differential expansion of existing areas in a common ancestor.

Concluding Remark
The roles played by brain atlases in the study of the cerebral cortex will continue to expand and evolve rapidly. These infrastructural advances will greatly improve our ability to tackle questions that get at the core of what makes us uniquely human, what characterizes our individuality to tackle questions that get at the core of what makes us uniquely human, what characterizes our individual personalities and capabilities, and what goes wrong in countless brain diseases and disorders.

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REFERENCES


