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Normal Neuroanatomical Variation in the Human Brain: An MRI-Volumetric Study

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ABSTRACT Normative data on the in vivo size of the human brain and its major anatomically defined subdivisions are not readily available. In this study, high-resolution magnetic resonance imaging was used to measure regional brain volumes in 46 normal, right-handed adults (23 men, 23 women) between the ages of 22–49 years. Parcellation of the brain was based on neuroanatomical landmarks. The following brain regions were measured: the cerebral hemispheres, frontal lobe, temporal lobe, parietal lobe, occipital lobe, cingulate gyrus, insula, cerebellum, corpus callosum, and lateral ventricles. Males tend to be significantly larger than females, for the whole brain and for nearly all of its major subdivisions, including the corpus callosum. However, the proportional sizes of regions relative to total volume of the hemisphere are remarkably similar in males and females. Variation in size of region is always greater than variation in proportional representation. Asymmetries in brain regions are not profound, with the exception of the cingulate gyrus, which is larger in the left hemisphere. Brain regions are highly correlated in size, with the exception of the lateral ventricles. After controlling for hemisphere size, the volumes of the frontal and parietal lobes are significantly negatively correlated. The occipital lobe tends to be less sexually dimorphic than other major lobes, and less correlated with other brain regions for volume. These results have implications for understanding whether or not certain sectors of the brain have shown relative expansion over the course of hominid and hominoid evolution. Am J Phys Anthropol 118:341–358, 2002.

Normative data on the in vivo size of the human brain and its major anatomically defined subdivisions are not readily available. The widespread use of high-resolution neuroimaging techniques began in the early 1990s, and since then, numerous studies have been undertaken that apply these techniques to the volume measurement of various brain structures. Unfortunately, the vast majority of these studies contribute little to the understanding of normal variation in the human brain. There are several reasons for this: heterogeneous subject groups, focus on anatomically circumscribed areas, "geographical" rather than anatomical parcellations of the brain (e.g., dividing the brain into a forebrain and a hindbrain), parcellation schemes that are not explicit and are difficult for others to reproduce, low-resolution sampling, and so on. For example, an extensive and still-growing literature on regional brain sizes and schizophrenia has developed over the past 10 years (reviewed by Lawrie and Abukmeil, 1998; McCarley et al., 1999; Wright et al., 2000). In general, for the reasons cited above, these studies do not provide a useful baseline source of data for the volumetric study of the normal brain (for an exception, see Goldstein et al., 1999), although they offer valuable insights into the neuroanatomy of patients with schizophrenia.

Magnetic resonance imaging (MRI) has become the method of choice for the volumetric study of the brain (Peters et al., 1998), supplanting postmortem surveys and measures of brain size based on the external size of the skull. Estimates of brain size from external cranial measures are unreliable, since head shape is at least partially determined by factors other than brain size. Simmons (1942) provided examples demonstrating that skulls with very similar external measurements can have extremely different internal capacities, and vice versa. In a more recent study, Wickett et al. (1994) found that head perimeter was not significantly correlated ($r = 0.228$) with total brain volume as determined by MRI. Furthermore, in a study of archaic and modern

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Homo frontal cranial profiles, Bookstein et al. (1999) found that external and internal morphologies of the frontal bone are determined by "entirely independent factors." Their results indicate that the internal morphology of the frontal region (and thus the anterior brain morphology) has been remarkably conservative over the past 500,000 years of hominid evolution, although the external morphology is highly variable across taxa.

Autopsy studies have traditionally been the most important source of direct measures of brain volume (e.g., Pakkenburg and Voigt, 1964, and references therein; Ho et al., 1980a, b). Problems associated with autopsy studies include variable treatment of the specimens after death, shrinkage or expansion during preservation (Skullerud, 1985), and lack of control in the selection of study populations (e.g., a bias towards older and/or unhealthy subjects). Some of these problems can be overcome with very large sample sizes (>1,000 individuals), which can be obtained from official autopsy records. Although data from postmortem studies are still useful, magnetic resonance imaging is now the most commonly used method to study brain size and macrostructure. The main advantages of in vivo MRI over postmortem studies include much greater control over subject selection and the ability to digitally manipulate brain images, allowing parcellation and measurement of a variety of brain subregions and structures.

Volumetric MRI studies have addressed several issues of anthropological relevance over the past several years. While several studies demonstrate a modest (approximately $r = 0.4$), statistically significant relationship between total brain volume and IQ test score performance (e.g., Willerman et al., 1991; Andreasen et al., 1993; Schoenemann et al., 2000), brain volumes do not correlate strongly with other and more specific cognitive measures (Egan et al., 1994; Schoenemann et al., 2000). MRI studies of twins indicate that while overall brain volume appears to be under genetic control, sulcal and gyral anatomy and asymmetries associated with handedness are not (Bartley et al., 1997; Steinmetz et al., 1995; Baaré et al., 2001). Studies of neonates, children, and adolescents have refined our understanding of the course of normal brain development (e.g., Pfefferbaum et al., 1994; Hüppi et al., 1998). Comparative neuroanatomical studies of primates are providing greater understanding of phylogenetically important patterns of brain volume and organization (Semendeferi et al., 1997; Rilling and Insel, 1999; Semendeferi and Damasio, 2000; Hopkins and Marino, 2000). In suggesting a theoretical foundation for MRI volumetric research, Caviness et al. (1999) argued that "volume is an evolutionarily and developmentally regulated fundamental property of tissue volumetric regularities are systematic manifestations of the rules of histogenetic processes and serve systematically the requirements of neural systems operation." Volumetric regularities (or irregularities) can be examined by determining coefficients of variation for specific structures or by assessing correlations in volume between different regions.

This study examines variation in regional brain volumes in a group of 46 normal, right-handed adult individuals (23 men and 23 women), determined using high-resolution magnetic resonance imaging. Regions assessed include: the cerebral hemispheres, frontal lobe, temporal lobe, parietal lobe, occipital lobe, cingulate gyrus, insula, cerebellum, corpus callosum, and lateral ventricles. Parcellation criteria are based as much as possible on anatomical landmarks. Gender differences, asymmetries, size correlations among brain regions, and proportional sizes of regions are determined. Raw data are presented in the Appendices as a resource for other investigators.

MATERIALS AND METHODS

Subjects

Subjects were 23 men (mean age = 32.1 years, standard deviation (s.d.) = 8.8, range 22–49 years) and 23 women (mean age = 32.6 years, s.d. = 7.5, range 23–47 years) of European descent recruited primarily by advertisement from the general Iowa City community. All were right-handed (scores on the Oldfield-Geschwind Handedness Inventory: men, mean = +92, s.d. = 12.9; women, mean = +94, s.d. = 6.6) with no left-handedness in first-degree relatives, healthy, and with no history of neurological or psychiatric illness. Since these subjects were originally selected to serve as controls for the study of patients with brain lesions, data on stature, body weight, and occupational status were not collected. All subjects gave informed consent in accordance with institutional and federal rules.

Image acquisition

Thin-cut magnetic resonance (MR) images were obtained in a General Electric Signa scanner operating at 1.5 Tesla, using the following protocol: SPGR/50, TR 24, TE 7, NEX 1 matrix 256×192, FOV 24 cm. We obtained 124 contiguous coronal slices, 1.5 or 1.6 mm thick, and with an interpixel distance of 0.94 mm. Three data sets were obtained for each brain during each imaging session. These were coregistered and averaged post hoc using Automated Image Registration (AIR 3.03, UCLA, Woods et al., 1992; Holmes et al., 1998). The final data volumes had anisotropic voxels with an interpixel spacing of 0.7 mm and interslice spacing of 1.5–1.6mm.

All brains were reconstructed in three dimensions (3-D) on a Silicon Graphics workstation using Brainvox (Damasio and Frank, 1992; Frank et al., 1997), an interactive family of programs designed to reconstruct, segment, and measure brains from MR-acquired images. An automated program, extensively validated against human experts (Grabowski et al., 2000), was used to segment images into three primary tissue types (white, gray, and CSF). Before tracing regions of interest (ROIs), brains were re-

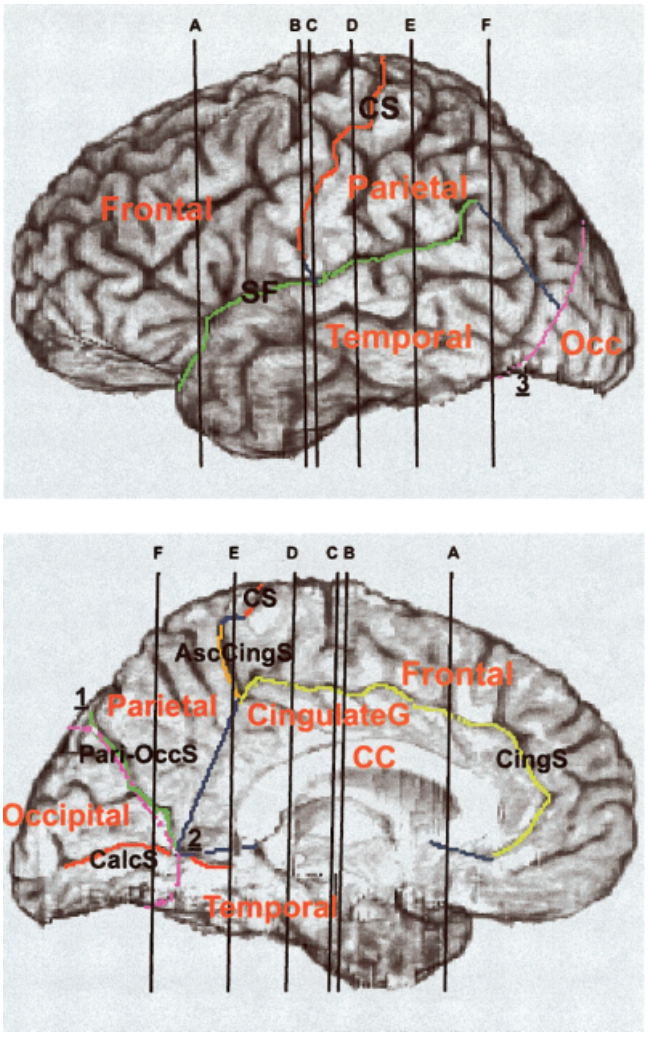

Fig. 1. Parcellated left cerebral hemisphere: lateral and mesial views. Lobes and other structures are printed in red; sulci and limiting points are printed in black. Cuts A–F correspond to coronal slices in Figure 2. Nonsulcal boundaries are blue, except for the occipital cut which is in magenta. Points labeled 1, 2, and 3 were used to define the plane of the occipital cut (see text and Fig. 3). Occ, occipital; CS, central sulcus; SF, Sylvian fissure; Pari-OccS, parieto-occipital sulcus; CingS, cingulate sulcus; AscCingS, ascending branch of the cingulate sulcus; CC, corpus callosum, CalcS, calcarine sulcus.

aligned along a plane running through the anterior and posterior commissures (i.e., the AC-PC line); this ensured that coronal slices in all subjects were perpendicular to a uniformly and anatomically defined axis of the brain.

Regions of interest

ROIs were traced by hand on contiguous coronal slices of the brain. Anatomical landmarks were identified and marked on the surface of 3-D reconstructions of the left and right hemispheres, which had been extracted from the skull and other overlying tissues (Fig. 1). ROIs were traced separately in each hemisphere. Volumes reported are the sum of the gray and white matter segmentations and do not include CSF (with the obvious exception of the lateral ventricles). The parcellation scheme described below was based on four primary references: Rademacher et al. (1992), Ono et al. (1990), Damasio (1995), and Duvernoy (1991).

The parcellation of the brain is illustrated in Figures 1 and 2. In Figure 1, the major regions and surface landmarks are marked and labeled. The positions of six coronal cuts (A–F) are also marked; the corresponding coronal images are presented in Figure 2. Examination of Figures 1 and 2 should be sufficient for most readers to gain a basic understanding of the parcellation scheme. For those interested in the precise rules of parcellation and tracing ROIs, our method is presented in greater detail below.

Hemispheres, cerebellum, lateral ventricles, and basal ganglia and thalamus. These structures do not require surface anatomical landmarks for tracing, and can be easily identified on coronal slices (Fig. 2). The volume of the lateral ventricle is derived from the CSF segmentation only. This will result in a very slight underestimation of the volume due to the presence of the choroid plexus, which is not interpreted by the segmentation program as CSF. The hemisphere volume is the sum of all other volumes of the cerebrum; it does not include the cerebellum, unless noted. The basal ganglia (including the claustrum) and thalamus were traced in a single ROI, and the gray matter volumes of the ROIs were calculated. These values were subtracted from the frontal or parietal lobe volumes as appropriate. The gray matter of the basal ganglia and thalamus comprises less than 5% of the total volumes of the parietal and frontal lobes (data not shown). The hypothalamus and brain stem are excluded from all tracings. Posteriorly, the brain stem can be identified easily (Fig. 2D). Anteriorly, in the slices immediately posterior to the anterior commissure, the inferior boundary of the frontal (or parietal) lobe is formed by a line linking the depth of the parahippocampal fissure to the top of the third ventricle, thus excluding the hypothalamus. When the thalamus appears, the line is drawn from the parahippocampal fissure to the bottom of the third ventricle (Fig. 2B,C).

Frontal lobe. The major sulcal boundaries of the frontal lobe are the Sylvian fissure, the central sulcus, and the cingulate sulcus (Fig. 1). On the lateral surface, the central sulcus often does not reach the Sylvian fissure; when this happens, a short line is drawn extending the central sulcus to the Sylvian fissure. The superoposterior boundary on the mesial surface is formed by the ascending branch of the cingulate sulcus and the mesial extension of the central sulcus. Since these sulci do not join, an arbitrary line linking the two is drawn along the surface of the brain in the parasagittal cut in which the end of the central sulcus is seen. The cingulate gyrus and insula are excluded from the frontal lobe (Fig.

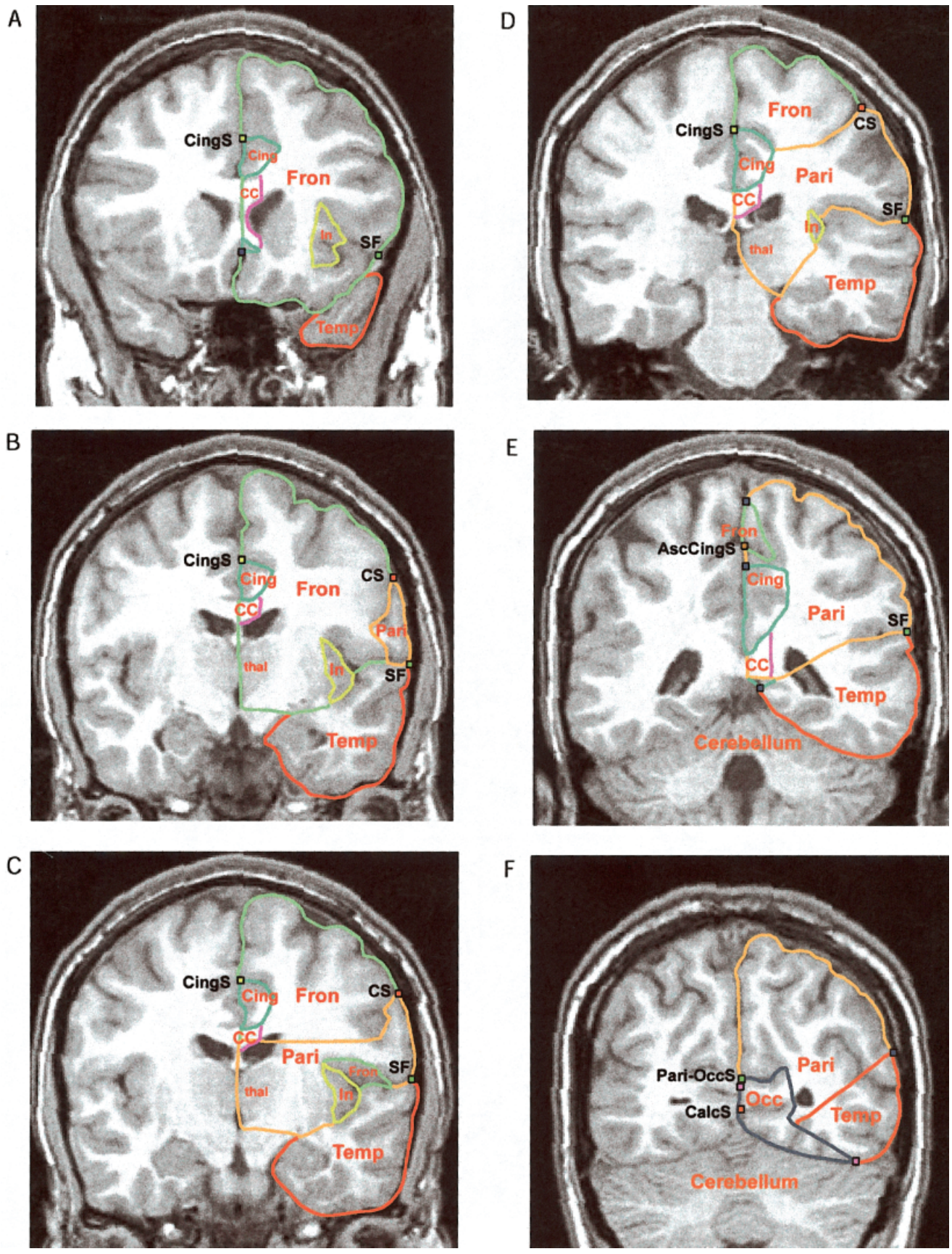

Fig. 2. A–F: Regions of interest traced in coronal cuts A–F, as indicated in Figure 1. Surface parcellation landmarks are represented by colored squares. Blue squares correspond to nonsulcal linking lines. Magenta squares in F indicate intersection of the occipital cut with this slice. See text for rules and conventions for tracing ROIs. Cing, cingulate gyrus; CingS, cingulate sulcus; Fron, frontal; SF, Sylvian fissure; CC, corpus callosum; In, insula; Temp, temporal; thal, thalamus; Pari, parietal; CS, central sulcus; AscCingS, ascending branch of the cingulate sulcus; Pari-OccS, parieto-occipital sulcus; CalcS, calcarine sulcus; Occ, occipital.

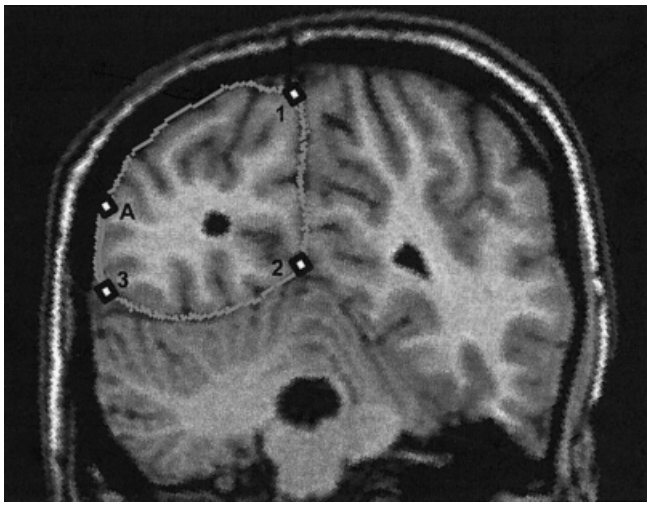

Fig. 3. Oblique slice corresponding to occipital cut in right hemisphere. Point 1 is the superior extent of the parieto-occipital sulcus, point 2 is the intersection of the calcarine and parieto-occipital sulci, and point 3 corresponds to the preoccipital notch. Shortline indicates one-fourth of the distance between the preoccipital notch and the superior extent of the parieto-occipital sulcus (point 1). Point A is linked to the end of the Sylvian fissure on the lateral surface of the hemisphere, to form part of the posterior boundary of the temporal lobe (see Fig. 1).

2A,B). The gray matter of the basal ganglia and the thalamus are also excluded.

Occipital cut. The occipital cut forms the anterior boundary of the occipital lobe and the posterior boundaries of the parietal and temporal lobes (Fig. 1). It is a plane defined by the following three points: the superior end of the parieto-occipital sulcus (point 1, Figs. 1, 3) and the junction of the parieto-occipital and calcarine sulci (point 2) on the mesial surface, and the preoccipital notch on the lateral surface (point 3). This plane is automatically rendered as a slice by the Brainvox image analysis program (Fig. 3). On this slice, the appropriate hemisphere is outlined, generating the limiting line on the surface of the brain that corresponds to the "cut." In coronal slices, this line appears as two points on the surface of the brain.

Temporal lobe. The temporal lobe is bounded by the Sylvian fissure superiorly and the parahippocampal fissure mesially (Fig. 1). The Sylvian fissure is traced to its most posterior extension, regardless of whether the terminal branch is ascending or descending. On the mesial surface, the posterior boundaries are formed by the occipital cut and an arbitrary line drawn from the junction of the parieto-occipital and calcarine sulci to the most inferior point of the splenium of the corpus callosum. On the lateral surface, the boundary between the temporal and occipital lobes is formed by the occipital cut. An additional limiting line is drawn from the end of the Sylvian fissure to a point (A in Fig. 3) along the lateral portion of the occipital cut. This point is one-quarter of the distance from the preoccipital notch (point 3) to the parieto-occipital sulcus (point 1), as measured along the surface of the brain in the coronal slice containing the occipital cut (Fig. 3). This line forms the boundary between the temporal and parietal lobes.

Occipital lobe. The occipital lobe is bounded by the occipital cut, with the exception of the superomesial boundary, where instead the parieto-occipital sulcus is used to separate the occipital from the parietal lobe (Fig. 1).

Parietal lobe. The boundaries are the central sulcus, Sylvian fissure, ascending branch of the cingulate sulcus, occipital cut, and the arbitrary line separating it from the temporal lobe as described above (Fig. 1). The parietal lobe is separated from the posterior cingulate by a line drawn from the origin of the ascending branch of the cingulate sulcus to the junction of the parieto-occipital and calcarine sulci. Basal ganglia and thalamic gray matter are excluded from the parietal volume.

Cingulate gyrus. The cingulate gyrus is bounded by the cingulate sulcus and the callosal sulcus (Fig. 1). The inferior boundary of the anterior cingulate gyrus is formed by a line drawn from the antero-inferior end of the sulcus to the posterior point of the rostrum of the corpus callosum (this corresponds to the antero-inferior end of the callosal sulcus). The posterior cingulate is separated from the parietal and temporal lobes by the two arbitrary lines described above. In cases of double cingulate sulci, the "outside" sulcus was chosen as the boundary for the gyrus.

Insula. The insula is defined by the circular sulcus clearly seen in coronal cuts (Fig. 2A–D). Anteriorly, the insula may appear as a small amount of gray matter embedded in the surrounding tissue of the frontal lobe. The insula is separated from the rest of the hemisphere by a line linking the deepest extent of both ends of the circular sulcus. When the claustrum becomes visible, the line is edited to exclude it.

Corpus callosum. The corpus callosum was defined in coronal cuts as the white matter bounded superiorly by the callosal sulcus and inferiorly by the lateral ventricles or the third ventricle (Fig. 2A–E). The lateral boundaries of the callosum were formed by dropping lines straight down (perpendicular to the AC-PC line) from the depth of the callosal sulci to the ventricles. The corpus callosum is included in the volumes of the frontal and parietal lobes (actually, half in each hemisphere). Surface area on the mesial surface has traditionally been used to quantify callosal size. The corpus callosum was also traced on the mesial surfaces of 3-D reconstructions of both hemispheres (Fig. 1) in order to obtain two independent measures of the same structure. The average value of the two measures (one from each hemisphere) was taken as the surface area of the corpus callosum. Two schemes were used

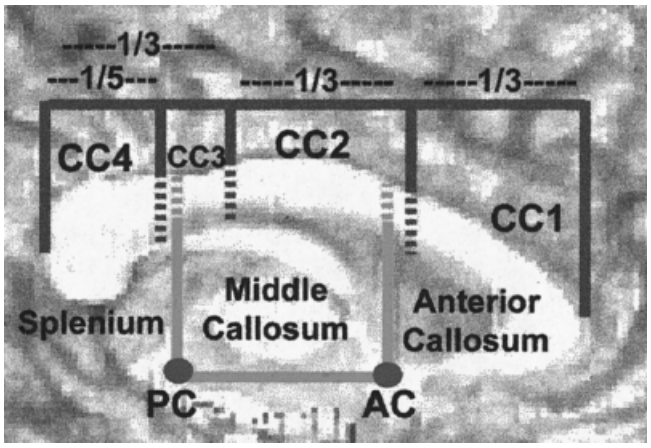

Fig. 4. Two methods were used to parcellate the corpus callosum. Top lines indicate conventional method of dividing the structure, based on overall length of the corpus callosum. Bottom lines indicate divisions based on positions of the anterior and posterior commissures. AC, anterior commissure; PC, posterior commissure.

to volumetrically parcellate the corpus callosum (Fig. 4). The first followed the conventional divisions of the corpus callosum based on the length of the callosum in midsagittal view, as described in Witelson (1989). Four areas were measured: CC1, the anterior third, incorporating the rostrum, genu, and rostral body; CC2, the middle third, which includes the anterior and posterior midbody; CC3, the isthmus, which is the region between the points indicating the posterior third and the posterior fifth; and CC4, the posterior fifth, corresponding to the splenium. The second scheme was developed by us as a method of parcellating the corpus callosum that is independent of the length of the structure, which is itself dependent on its highly variable shape. The corpus callosum was divided into three parts: anterior callosum, middle callosum, and splenium. This was done by drawing lines on the mesial surface of the hemisphere from the posterior and anterior commissures to the superior boundary of the corpus callosum, perpendicular to the AC-PC line (Fig. 4).

Tracing conventions. In addition to the basic landmarks, several other rules were used to ensure consistency in the tracing of ROIs in coronal slices.

1. Brains were traced on coronal slices from anterior to posterior separately by hemisphere.
2. All ROIs on each slice were traced concurrently as much as possible.
3. When making a connection between two sulci, a line was drawn through the CSF of the first sulcus, and then through the gray matter at the base of the sulcus perpendicular to the gray-white junction. A straight line was then drawn to the gray-white junction of the second sulcus, at the point perpendicular to the depth of that sulcus. The line joining the two sulci may be edited to include or exclude intervening structures as appropriate.
4. After the temporal stem appears (the connection between the temporal and frontal lobes), the separation between the two lobes is a line drawn through the Sylvian fissure to the depth of the inferior branch of the circular sulcus and then linked to the depth of the parahippocampal fissure (Fig. 2 B–D). The connecting line was edited to include the amygdala into the temporal lobe when necessary.
5. When the central sulcus first appears anteriorly, it is typically pointing downwards (Fig. 2B). At this point, the parietal lobe is seen as a lateral gyrus (the postcentral) surrounded by the frontal lobe. When the depth of the central sulcus was superior to the top of the insula, the connecting line separating the parietal from the frontal was taken across as a horizontal line to the mesial segment of the hemisphere ROI or to the lateral boundary of the cingulate gyrus, whichever it intersects first (Fig. 2C). When the central sulcus was higher than the cingulate sulcus, the parietal and frontal lobes were separated by a line linking the depths of these sulci (Fig. 2D).
6. In general, the occipital cut was treated as though it is a knife cut. No effort was made to include sulci that may be intersected by this plane. An exception was made when tracing the most anterior part of the occipital lobe. In coronal slices, the occipital lobe first appears infero-mesial to the temporal lobe. On these slices, the occipital ROI was defined by the extent of the occipital cut, which appears as two points intersecting the coronal slice. These points are treated as de facto sulci, and they are linked according to the rule 3, above. On the coronal slice where the parieto-occipital and calcarine sulci intersect, the parieto-occipital sulcus becomes the boundary for the occipital lobe, as described above. The parieto-occipital sulcus was traced through to its depth and then around the gray matter of the calcarine sulcus. From here, a perpendicular line was drawn to a line formed by the occipital cut, and then extended to the inferior point of the cut (Fig. 2F). On these slices, the temporal lobe was bounded inferiorly by the occipital lobe and superiorly by a line drawn from the lateral landmark to a point halfway between the two points of intersection of the occipital cut through the slice. The temporal lobe will typically form a "wedge" on these slices, decreasing in size as it moves posteriorly through the brain.

Reliability

The vast majority of ROIs were traced by one of the authors (J.S.A.), with review and consultation with one of the other authors (H.D.). A reliability study was undertaken comparing the tracing of J.S.A. with an expert tracer who was not otherwise involved with this project. The left frontal and occipital lobes (chosen as the least and most arbitrary of the ROIs) were traced in a random sample of 10 study subjects, starting with the identification of

TABLE 1. Volumes in cubic centimeters of major regions of the human brain and sex difference statistics (t-*test* P-*value and female/male ratio)*[1]

Region	Side	Males			Females			F vs. M	
		Mean (range)	s.d.	CV	Mean (range)	s.d.	CV	*P*-value	F/M
Hemisphere	Left	618.9 (512.2–722.9)	54.7	8.8	547.0 (472.6–674.3)	47.8	8.7	0.000	0.88
(including cerebellum)	Right	621.7 (513.5–733.9)	58.3	9.4	552.7 (475.8–688.3)	49.5	9.0	0.000	0.89
Frontal	Left	205.2 (163.4–286.9)	25.8	12.6	182.8 (157.0–228.0)	17.0	9.3	0.001	0.89
	Right	208.3 (170.0–263.8)	24.0	11.5	186.2 (162.4–228.5)	17.2	9.2	0.001	0.89
Temporal	Left	120.0 (96.4–153.3)	14.9	12.4	104.6 (88.9–127.0)	9.5	9.1	0.000	0.87
	Right	122.8 (94.3–158.0)	16.2	13.2	103.6 (91.3–132.5)	9.4	9.1	0.000	0.84
Parietal	Left	136.5 (116.0–159.8)	12.6	9.2	118.2 (90.4–146.7)	13.6	11.5	0.000	0.87
	Right	136.7 (110.9–173.0)	15.3	11.2	122.8 (91.7–160.4)	16.3	13.3	0.005	0.90
Occipital	Left	48.5 (35.9–57.8)	6.6	13.6	44.9 (32.9–63.5)	8.8	19.6	ns	0.93
	Right	48.5 (38.4–59.6)	6.7	13.8	43.9 (31.0–59.4)	8.3	18.9	0.043	0.91
Cingulate	Left	23.4 (18.0–35.3)	4.2	17.9	19.9 (13.7–28.1)	3.6	18.1	0.005	0.85
	Right	19.7 (12.2–28.4)	3.4	17.3	19.0 (14.2–28.9)	3.2	16.8	ns	0.96
Insula	Left	9.0 (6.5–12.5)	1.3	14.4	8.0 (6.5–10.0)	0.8	10.0	0.002	0.89
	Right	9.8 (7.6–13.7)	1.4	14.3	8.4 (7.1–10.2)	0.8	9.5	0.000	0.86
Cerebellum	Left	76.3 (62.2–93.6)	7.5	9.8	68.6 (56.6–78.2)	5.7	8.3	0.000	0.90
	Right	76.0 (61.9–91.3)	7.3	9.6	68.8 (56.4–78.9)	5.8	8.4	0.001	0.91
Lateral ventricles	Left	7.1 (2.3–25.3)	4.7	66.2	4.5 (1.1–11.1)	2.6	57.8	0.030	0.64
	Right	6.8 (2.2–22.3)	4.7	69.1	4.8 (2.1–9.1)	2.1	43.8	ns	0.71

[1] s.d. standard deviation; CV, coefficient of variation; F, female; M, male; ns, not significant.

surface landmarks. The nonstudy tracer was also allowed to consult with H.D., who did no tracing herself. Nonparametric correlations (Spearman's rho) between the volumes obtained by the two tracers were r = 0.988 ($P < 0.001$) for the frontal lobe, and r = 0.952 ($P < 0.001$) for the occipital lobe.

Statistical analysis

All statistical analyses were performed using SPSS for Windows, version 9.0.0 (SPSS, Inc., Chicago, IL, 1999). Independent-samples *t*-tests were used to compare means. Correlation coefficients (Pearson's), partial correlations, and principal components analysis were used to look at the interactions among variables. Hemispheric asymmetries were examined with pairwise *t*-tests and a conventional asymmetry index ([L − R]/[L + R/2]). Volume determinations from ROIs were made using tal-programs, a family of image analysis programs developed in our laboratory (Frank et al., 1997).

RESULTS

Total brain volumes (including all lobes of the cerebrum, the basal ganglia and thalamus, and cerebellum, and excluding the ventricles) were 1,273.6 cc (s.d. = 115.0; range, 1,052.9–1,498.5) for men and 1,131.1 cc (s.d. = 99.5; range, 974.9–1,398.1) for women. Male brains were significantly larger than female brains ($P < 0.001$). Volumes for the major lobes and sectors of the brain are presented in Table 1. For most sectors, males were significantly larger than females, with female volumes being about 85–90% of the male volume. Exceptions to this pattern include the left occipital, right cingulate, and lateral ventricles. Note that women have the largest and smallest left occipital lobe measures. Although the lateral ventricles were substantially larger in men than in women, the difference is only weakly statistically significant, reflecting the presence of a few large outliers in the male sample.

Coefficients of variation (CV) are similar in men and women for overall hemisphere volume. For the various regions, CVs tend to be similar between the right and left hemispheres. Males have higher CVs in the frontal and temporal lobes and the insula. Female CVs are higher for the parietal and occipital lobes. There is no clear relationship between the size of a region and its CV, although it is clear that the occipital lobe and cingulate gyrus are more variable than the other major neural structures. The lateral ventricles are far more variable than any other region in the brain.

Corpus callosum volume measures are presented in Table 2. Absolute volumes of all regions are larger in men than in women, although the difference reaches significance only for the total corpus callosum volume and the CC4 region. The CVs indicate that it is somewhat more variable in men, and the largest and smallest callosa measured belong to men. The midbody region is more variable in women, however (see CV for the middle callosum and CC2). The midline surface measure of callosal size did not show a significant difference ($P = 0.083$) between the sexes (men, 598 mm^2, s.d. = 87.2; women, 556.9 mm^2, s.d. = 69.3). Callosal surface area was significantly correlated with total callosal volume (in women, r = 0.884, $P < 0.001$; in men, r = 0.931, $P < 0.001$). In both men and women, the callosal volume is about 1% of the total hemisphere volume. Proportional breakdowns within the callosum are presented in Table 3. The proportional sizes of the various subregions, as defined by either parcellation scheme, are very similar in men and women.

The callosal subregions (examined separately in the two parcellation schemes) tend to be highly correlated for volume ($P < 0.01$); however, there are some exceptions (i.e., $P > 0.05$). Splenium and middle callosum volumes were positively but not significantly correlated (men, r = 0.408; women, r =

TABLE 2. Volumes in cubic centimeters of corpus callosum and its major divisions, and sex differences statistics (t-test P-value and female/male ratio)[1]

Region	Males			Females			F vs. M	
	Mean (range)	s.d.	CV	Mean (range)	s.d.	CV	*P*-value	F/M
Total callosum	10.6 (7.2–13.7)	1.6	15.1	9.7 (8.0–12.4)	1.3	13.4	0.045	0.91
Anterior callosum	4.4 (2.8–6.2)	0.8	18.2	4.1 (3.1–5.4)	0.6	14.6	ns	0.93
Middle callosum	2.3 (1.6–3.2)	0.4	17.4	2.1 (1.4–2.8)	0.4	19.0	ns	0.91
Splenium	3.9 (2.3–5.0)	0.7	17.9	3.5 (2.5–4.6)	0.5	14.3	ns	0.90
CC1	4.0 (2.6–5.6)	0.7	17.5	3.6 (2.8–4.8)	0.6	16.7	ns	0.90
CC2	2.1 (1.5–2.8)	0.3	14.3	2.0 (1.6–2.5)	0.3	15.0	ns	0.95
CC3	1.1 (0.7–1.6)	0.3	27.2	1.0 (0.7–1.5)	0.2	20.0	ns	0.91
CC4	3.4 (2.1–4.3)	0.6	17.6	3.1 (2.2–4.2)	0.5	16.1	0.048	0.91

[1] s.d., standard deviation; CV, coefficient of variation; F, female; M, male; ns, not significant.

TABLE 3. Corpus callosum sectors as a proportion of total callosum volume

Sector	Males			Females		
	Mean	s.d.	CV	Mean	s.d.	CV
Anterior callosum	0.417	0.033	7.9	0.420	0.030	7.1
Middle callosum	0.215	0.027	12.6	0.213	0.028	13.1
Splenium	0.368	0.041	11.1	0.366	0.034	9.3
CC1	0.375	0.026	6.9	0.374	0.028	7.5
CC2	0.200	0.019	9.5	0.205	0.015	7.3
CC3	0.101	0.019	18.8	0.103	0.021	20.4
CC4	0.323	0.029	9.0	0.318	0.027	8.5

TABLE 4. Partial correlations among corpus callosum subregion volumes, controlling for total volume of the corpus callosum (females on left, males in italics)[1]

	Anterior CC	Middle CC	Splenium
Anterior CC		*−0.167*	*−0.714***
Middle CC	−.330		*−0.571***
Splenium	−0.597**	−0.561**	

	CC1	CC2	CC3	CC4
CC1		*−0.220*	*−0.327*	*−0.598***
CC2	−0.153		*0.115*	*−0.421*
CC3	−0.473*	−.023		*−0.268*
CC4	−0.544**	−0.397	−0.294	

[1] CC, corpus callosum.
* $P < 0.05$.
** $P < 0.01$.

0.323). CC3 and CC4 were also not significantly correlated (men, r = 0.383; women, r = 0.201); in women, CC3 was also not significantly correlated with CC1 (r = 0.149) or CC2 (r = 0.312). Partial correlations controlling for total callosum volume indicate an inverse relationship between the splenial region and other callosal subregions (Table 4). After controlling for callosal size, splenium volume was significantly negatively correlated with the volumes of the anterior callosum and middle callosum. Similarly, CC4 volume was negatively correlated with CC1 in both men and women.

Measures of hemispheric asymmetry are presented in Table 5. The asymmetry index, which takes into account absolute differences in volume between the hemispheres, indicates that the cingulate in men is substantially larger (by approximately 20%) in the left vs. the right hemisphere. In women, the right lateral ventricle is significantly larger than the left. Weaker asymmetries are present for the cingulate in women and the insula in both men and women. Pairwise *t*-tests, which measure the tendency for one side to be larger than the other irrespective of the absolute differences between them, confirm the asymmetry of the cingulate in males and the insula asymmetries. Some other significant results indicate a mild tendency for right hemisphere structures to be larger than left.

The proportional volume representation of the brain regions in the hemispheres is presented in Table 6. For all regions, there is very little variation according to sex or hemisphere. The frontal lobes comprise 38% of the volume of the cerebrum, the temporal lobes 22%, the parietal lobes 25%, the occipital lobes 9%, the cingulate gyri 4%, and the insula 1.7%. The cerebellum is about 12% of the cerebrum and cerebellum combined. Note that for most regions, the CV for proportion are substantially lower than the CV for volume, with the exception of the cerebellum, corpus callosum, and occipital lobe in men.

Volume correlations among the various structures are presented for men and women, right and left hemispheres, in Tables 7 and 8. In general, correla-

TABLE 5. Lateralization statistics[1]

Region	Sex	Asymmetry Index (s.d.)[2]	Pairwise *t*-test *P*-value
Hemisphere	M	−0.005 (0.009)	0.007 (r > l)
	F	−0.011 (0.007)	0.000 (r > l)
Frontal	M	−0.016 (0.033)	ns
	F	−0.019 (0.023)	0.001 (r > l)
Temporal	M	−0.023 (0.091)	ns
	F	0.010 (0.081)	ns
Parietal	M	0.000 (0.085)	ns
	F	−0.036 (0.061)	0.009 (r > l)
Occipital	M	0.000 (0.152)	ns
	F	0.022 (0.118)	ns
Cingulate	M	0.169 (0.158)	0.000 (l > r)
	F	0.045 (0.181)	ns
Insula	M	−0.077 (0.061)	0.000 (r > l)
	F	−0.050 (0.046)	0.000 (r > l)
Cerebellum	M	0.004 (0.030)	ns
	F	−0.003 (0.021)	ns
Lateral ventricles	M	0.064 (0.369)	ns
	F	−0.119 (0.297)	ns

[1] ns, not significant; l, left; r, right.
[2] Asymmetry index = (L − R)/[(L + R)/2].

TABLE 6. Brain regions as proportion of hemisphere volume (not including the cerebellum)[1]

		Males			Females		
Region	Side	Mean	s.d.	CV	Mean	s.d.	CV
Frontal	Left	0.381	0.019	5.0	0.382	0.011	2.9
	Right	0.379	0.010	2.6	0.385	0.011	2.6
Temporal	Left	0.221	0.014	6.3	0.219	0.013	5.9
	Right	0.225	0.018	8.0	0.215	0.015	7.0
Parietal	Left	0.252	0.019	7.5	0.247	0.015	6.1
	Right	0.251	0.017	6.8	0.253	0.019	7.5
Occipital	Left	0.090	0.011	12.2	0.093	0.013	14.0
	Right	0.089	0.013	14.6	0.090	0.012	13.3
Cingulate	Left	0.043	0.005	11.6	0.042	0.006	14.3
	Right	0.036	0.004	11.1	0.039	0.005	12.8
Insula	Left	0.017	0.0020	11.8	0.017	0.0012	7.1
	Right	0.018	0.0020	11.1	0.017	0.0012	7.1
Cerebellum	Left	0.124	0.011	8.9	0.126	0.009	7.1
	Right	0.123	0.010	8.1	0.125	0.009	7.2
Lateral ventricles	Left	0.013	0.0089	68.5	0.010	0.0057	57.0
	Right	0.012	0.0082	68.3	0.010	0.0049	49.0
Corpus callosum	*Total*	0.010	0.0013	13.0	0.010	0.0011	11.0

[1] Cerebellum proportion is (cerebellum/[hemisphere + cerebellum]).

TABLE 7. Pearson correlations among left hemisphere regional volumes (females on left, males in italics)

	Hemisphere	Frontal	Temporal	Parietal	Occipital	Cingulate	Insula	Cerebellum	Lateral ventricles
Hemisphere		*0.901***	*0.877***	*0.602***	*0.464**	*0.696***	*0.503**	*0.576***	*0.165*
Frontal	0.955***		*0.784***	*0.238*	*0.475**	*0.479**	*0.582***	*0.392*	*0.140*
Temporal	0.813***	0.774***		*0.476**	*0.077*	*0.614***	*0.355*	*0.437**	*0.181*
Parietal	0.835***	0.717***	0.488*		*0.201*	*0.599***	*0.015*	*0.431**	*0.070*
Occipital	0.731***	0.690***	0.376	0.628***		*0.251*	*0.490**	*0.163*	*−0.033*
Cingulate	0.584***	0.533***	0.537***	0.405	0.305		*0.354*	*0.185*	*0.046*
Insula	0.743***	0.739***	0.586***	0.529***	0.671***	0.235		*0.137*	*0.033*
Cerebellum	0.611***	0.544***	0.700***	0.378	0.127	0.322	0.480*		*0.241*
Lateral ventricles	−0.117	−0.006	0.025	−0.265	−0.270	0.012	0.022	0.034	

* $P < 0.05$.
** $P < 0.01$.

tions among regions are not only significant but high. The cingulate gyrus is somewhat less highly correlated than other brain regions. The least highly correlated region is the occipital lobe in men, where the highest correlations to other regions are less than r = 0.50. The lateral ventricles are only weakly correlated, if at all, to the overall sizes of other brain regions.

Partial correlations controlling for hemisphere volume are presented in Tables 9 and 10. In both hemispheres and in both sexes, a significant inverse relationship between frontal and parietal lobe volume is present. Similarly, a consistent (with the exception of the left hemisphere in males) inverse relationship is also seen between the parietal and temporal lobes, and between the occipital and tem-

TABLE 8. Pearson correlations among right hemisphere regional volumes (females on left, males in italics)

	Hemisphere	Frontal	Temporal	Parietal	Occipital	Cingulate	Insula	Cerebellum	Lateral ventricles
Hemisphere		*0.961***	*0.795***	*0.787***	*0.336*	*0.709***	*0.579***	*0.650***	*0.461**
Frontal	0.940***		*0.681***	*0.681***	*0.271*	*0.660***	*0.632***	*0.482**	*0.496**
Temporal	0.722***	0.658***		*0.351*	*0.134*	*0.564***	*0.644***	*0.468**	*0.464**
Parietal	0.850***	0.728***	0.414*		*0.365*	*0.545***	*0.173*	*0.541***	*0.240*
Occipital	0.769***	0.699***	0.569***	0.500*		*0.234*	*0.197*	*0.252*	*−0.017*
Cingulate	0.579***	0.557***	0.097	0.519*	0.494*		*0.375*	*0.336*	*0.177*
Insula	0.723***	0.660***	0.703***	0.460*	0.678***	0.377		*0.199*	*0.417**
Cerebellum	0.667***	0.544***	0.455*	0.552***	0.363	0.371	0.461*		*0.362*
Lateral ventricles	−0.239	−0.106	−0.006	−0.372	−0.244	−0.301	−0.020	−0.156	

* $P < 0.05$.
** $P < 0.01$.

TABLE 9. Partial correlations among left hemisphere brain regional volumes, controlling for volume of left hemisphere (excluding cerebellum; females on left, males in italics)

	Frontal	Temporal	Parietal	Occipital	Cingulate	Insula
Frontal		*−0.101*	*−0.896***	*0.112*	*−0.537***	*0.304*
Temporal	0.137		*−0.100*	*−0.820***	*0.003*	*−0.259*
Parietal	−0.594***	−0.532*		*−0.109*	*0.330*	*−0.420*
Occipital	−0.230	−0.566***	−0.066		*−0.128*	*0.322*
Cingulate	−0.110	0.155	−0.211	−0.278		*−0.015*
Insula	0.178	0.023	−0.261	0.244	−0.356	

* $P < 0.05$.
** $P < 0.01$.

TABLE 10. Vartial correlations among right hemisphere brain regional volumes, controlling for volume of right hemisphere (excluding cerebellum; females on left, males in italics)

	Frontal	Temporal	Parietal	Occipital	Cingulate	Insula
Frontal		*0.220*	*−0.573***	*−0.243*	*−0.294*	*0.265*
Temporal	−0.113		*−0.712***	*−0.697***	*−0.028*	*0.343*
Parietal	−0.437*	−0.542***		*0.183*	*−0.041*	*−0.587**
Occipital	−0.214	0.006	−0.504*		*−0.007*	*−0.000*
Cingulate	0.036	−0.568***	0.065	0.080		*−0.105*
Insula	−0.105	0.379	−0.415	0.261	−0.071	

* $P < .05$.
** $P < .01$.

TABLE 11. Principal components analysis: factor loadings for components with eigenvalues >1

	Men, left hemisphere components			Men, right hemisphere components		Women, left hemisphere components			Women, right hemisphere components	
Region	1	2	3	1	2	1	2	3	1	2
Cerebellum	0.556	0.332	0.263	0.635	0.242	0.667	0.420	0.091	0.702	−0.026
Occipital	0.479	−0.608	−0.017	0.289	0.761	0.700	−0.562	0.096	0.810	0.089
Frontal	0.860	−0.241	0.183	0.949	−0.009	0.938	−0.023	0.113	0.895	0.130
Parietal	0.611	0.438	−0.437	0.701	0.489	0.791	−0.283	−0.211	0.820	−0.291
Temporal	0.852	0.214	0.009	0.815	−0.411	0.821	0.241	0.182	0.687	0.550
Cingulate	0.731	0.053	−0.411	0.711	0.193	0.623	0.271	−0.389	0.612	−0.385
Insula	0.562	−0.664	0.167	0.640	−0.302	0.773	−0.173	0.474	0.770	0.415
Corpus callosum	0.486	0.255	0.018	0.654	−0.098	0.510	0.375	−0.585	0.722	−0.242
Lateral ventricles	0.213	0.349	0.757	0.610	−0.415	−0.093	0.707	0.454	−0.298	0.734

poral lobes (with the exception of the right hemisphere in males).

Results of a principal components analysis are presented in Table 11. For both hemispheres in women and for the left hemisphere in men, factor loadings clearly indicate high correlations in volume among all or most brain regions, with the exception of the lateral ventricles. For the right hemisphere in men, the occipital lobe loads on a factor separate from all other brain regions. Principal component 2 for the left hemisphere in men and component 3 for the left hemisphere in women defy simple classification.

DISCUSSION

This study establishes regional brain volumes derived from high-resolution MR imaging for a series of 46 normal, healthy, right-handed individuals (23 men, 23 women) between ages 22–49 years. Parcellation of the brain into major lobes and regions was

based on neuroanatomical landmarks as much as possible. Although this study was fundamentally inductive in design, the data presented are relevant to a variety of theoretical issues, some of which will be discussed below. The raw data are presented in Appendices A–D.

Total brain volume

The mean total brain volumes found here (1,273.6 cc for men, and 1,131.1 cc for women) are very comparable to the results from other high-resolution MRI-volumetric studies. Peters et al. (1998), in their primary sample of 69 men and 48 women, reported mean brain sizes of 1,243 cc (s.d. = 110) and 1,130 cc (s.d. = 112), respectively. Our results are also very similar to those of Courchesne et al. (2000) for a group of individuals ranging in age from 19 months to 80 years (mean 21.4 years, s.d. = 20). They reported a male brain size of 1,286.4 cc (s.d. = 133) and a female size of 1,137.8 cc (s.d. = 109). The individuals in our study and in the other two studies were predominantly of European descent, and brain volumes excluded CSF, meninges, and other nonbrain tissues.

Other MRI studies reported larger brain volumes, but CSF was often included in calculations of total brain volume (e.g., Giedd et al., 1996), which would typically add about 140–150 cc to the volume (Peters et al., 1998). Even with CSF excluded, higher mean brain volume values were found, such as in "Sample S" of Peters et al. (1998), where the mean volume for women was 1,282 cc, and for men, 1,427 cc.

Nonetheless, the convergence of our results with those of Peters et al. (1998, primary sample) and Courchesne et al. (2000) indicates that the average brain size in a well-nourished population of predominantly European ancestry is about 1,260 cc for men and 1,130 cc for women. Peters et al. (1998) argued that the "canonical" textbook brain size of 1,450 g for men, based on postmortem measures, may have to be revised downwards, given a specific weight of 1.031 g/cc of brain matter (Zilles, 1972, in Peters et al., 1998). Actually, the canonical 1,450 g may be a bit high, even based on autopsy studies. Although Pakkenberg and Voigt (1964) reported a mean of 1,440 g for men and 1,282 g for women (in a Danish population), these values are relatively high compared to earlier studies (see references in Pakkenberg and Voigt, 1964). Ho et al. (1980a) found that the white male mean was 1,392 g and the white female mean was 1,252 g, in a sample from Cleveland, Ohio. However, Skullerud (1985) reported a male mean of 1,527 g and a female mean of 1,292 g in a Norwegian autopsy sample.

The discrepancy between MRI and autopsy results may be due to basic differences in what is being measured. Autopsy brain weights typically include some portion of the dura mater and meninges, the filled lateral ventricles (as taken directly from the cadaver (Pakkenberg and Voight, 1964) or refilled with liquid for measurement (Skullerud, 1985)), and the brain stem and perhaps a small portion of the spinal cord. All of these are typically excluded in MRI studies. If we multiply our male mean of 1,273.6 cc by 1.03 g/cc (= 1,311 g) and add 35 g (estimate for the brain stem/spinal cord portion derived from Skullerud (1985) and our cerebellum volume) plus an additional 14 g (for fluid in the lateral ventricles), we can estimate an "autopsy-equivalent" brain weight for our male sample of 1,360 g. This approaches some of the autopsy results, even without an estimate for the outer coverings of the brain that are typically included in reported brain weights.

Sex differences

As seen in Table 1, we found significant sex differences in volume for several of the brain regions examined. However, the large number of statistical comparisons of possibly interrelated variables necessitates a Bonferroni correction (Bland, 2000) for the alpha-level of statistical significance (0.05/20 = 0.0025, which is probably very conservative in this context). At this alpha-level, male volumes are significantly larger for the hemispheres, frontal lobes, temporal lobes, left parietal lobe, insula, and cerebellum, and the right parietal and left cingulate approach this significance level. The occipital lobes, corpus callosum, and right cingulate are less sexually dimorphic, although in all cases the male mean is greater than the female.

The percent volume sex differences for the lateral ventricles are substantially greater than the approximately 10% seen in other brain structures, yet the differences are not statistically significant. The individual results in the Appendices show that there are some men with very large ventricles and some women with very small ventricles. It is interesting to note that a meta-analysis of regional brain volumes in schizophrenia found that the most robust neuroanatomical difference was that people with schizophrenia had lateral ventricles 116% the size of the comparison subject groups (Wright et al., 2000). Although this is a highly replicable finding, our CVs for lateral ventricular volume indicate that it is not a very profound difference in the context of normal variation. Indeed, we had one male subject whose lateral ventricular volume was approximately 350% of the male mean, and a female subject whose volume was only 25% of the female mean.

The sex differences we observed for the major lobes (frontal, temporal, parietal, and occipital) are reasonably congruent with the results from other studies, despite different parcellation schemes. In a study of cortical (gray matter only) volumes in 10 men and 10 women, Kennedy et al. (1998) reported a significant difference in size for the parietal lobe only. Frontal and temporal lobes were also clearly larger in males, although not significantly so in this relatively small subject group. Other studies indicate that women have a higher percentage of gray matter than men (Gur et al., 1999); thus, measures focusing on the cortex may attenuate sex differences in volume. We agree with Kennedy et al. (1998) that

the occipital lobe is the least dimorphic of the major lobes, despite the fact that our parcellation of the occipital is somewhat different from theirs (our occipital volumes are about 25% smaller). In both studies, CVs indicate that the occipital lobe is substantially more variable in women than in men, whereas the temporal lobe and insula are substantially more variable in men than women.

Our results for the major lobes can also be contrasted to those reported by Nopoulos et al. (2000). They used an automated parcellation and volume-determination technique (Andreasen et al., 1996), which is not comparable to our method, although they found that for large brain structures, it correlates reasonably well to hand-tracing based on anatomical landmarks. Nopoulos et al. (2000) reported that the "raw means" for all four major lobes were substantially larger in males than in females, although their "adjusted means" (for total cerebral tissue) showed no significant difference. Similarly, there was no significant difference in cerebellum size. They did not find differences between men and women in variability in the temporal and occipital lobes, as we and Kennedy et al. (1998) did. Since their automated method involves resizing the brain in Tailarach space (Tailarach and Tournoux, 1998), it may be expected that indices of variability in their measures will differ from those based on a nonresized brain.

We did not measure height or body size in our subjects. Other studies have shown that total brain size differences between the sexes remain significant after controlling for height (Holloway, 1980; Nopoulos et al., 2000). However, Peters et al. (1998) found that the variance ascribable to sex drops to about one-third of its original value if height is a covariable, although sex remains a significant factor. Peters et al. (1998) argued that the relationship between height (which is not as straightforward to measure as often assumed) and brain size itself is by no means clear at this point. Nopoulos et al. (2000) found a significant correlation between height and cerebral tissue volume only in women.

Our study and others consistently demonstrate that men have larger brains than women. However, studies of sexual dimorphism in brain size in nonhuman primates indicate that this pattern is not unique to humans and therefore is unlikely to be the result of encephalization or enhanced cognition in the hominid lineage (Holloway, 1980; Falk et al., 1999). These data suggest that human sex differences in cognitive performance (Kimura, 1999) are unlikely to be traced to gross differences in the size or shape of the major lobes.

Corpus callosum

We used a volumetric measure of callosal size, which correlated highly to more traditional surface measures. It is important to keep in mind that the "surface" of the corpus callosum is an artifact of splitting the brain, either with a knife or with a computer mouse. Our definition of the callosum as the white matter fiber bundle inferior to the cingulate gyrus in coronal slices may be a more anatomically rigorous way of measuring the structure if high-resolution, 3-D MRI scans are available. The anterior and posterior commissures can be easily identified in coronal slices, and they provide consistent landmarks for dividing the callosum into an anterior, a middle, and a posterior section, the latter corresponding to the splenium.

We found that the corpus callosum was significantly larger in men than in women, although this was barely statistically significant for the total volume. The CC4 (posterior fifth) was also significantly larger in men. Men were larger than women for each of the subdivisions in the two schemes used to parcellate the callosum, although with the exception of CC4, these differences were not significant. Overall, the female callosum is about 91–92% of the male in size, and this ratio is reflected in the subdivisions. The callosum was substantially more variable in men than women.

Sexual dimorphism in the corpus callosum has been extensively studied, especially since the report of de Lacoste-Utamsing and Holloway (1982) that the splenium was larger and more bulbous in females rather than in males (see also Holloway et al., 1993). Numerous follow-up studies failed to confirm this finding (e.g., Kertesz et al., 1987; Oppenheim et al., 1987; Witelson, 1989; Clarke et al., 1989; Pozzilli et al., 1994; Constant and Ruther, 1996). Other studies found sex differences in the callosum, although not necessarily in the splenial region. For example, Steinmentz et al. (1992) found that the proportional representation of the isthmus (CC3 in this study) was greater in men than in women (although the statistical significance of this finding was very low, given the number of comparisons they made), and Burke and Yeo (1994) found that women had a proportionally larger anterior callosum than men. Jäncke et al. (1997) suggested that individuals with smaller brains have a relatively larger corpus callosum size, which may account for the gender differences observed in some studies. In their review and meta-analysis, Bishop and Wahlsten (1997) concluded that there is no consistent evidence supporting the claim that the splenium is larger in women, and that the callosum is slightly larger in men, corresponding to overall brain size. Our results are consistent with these conclusions, especially regarding the splenium (and contra, e.g., Davatzikos and Resnick, 1998). The relative difference between men and women in mean callosal size is similar to that seen in other parts of the brain. The relatively high degree of variability in the structure may require a larger sample size than we have measured to make this gender difference statistically significant.

The partial correlations for the corpus callosum presented in Table 4 indicate one pattern seen in both males and females: there is an inverse volume relationship between the splenium and other parts of the callosum. In other words, individuals with larger splenia will tend to have relatively small mid-

dle and anterior callosa. This is also seen using the more traditional parcellation scheme with the inverse relationship between CC4 and CC1. This finding has implications for interpreting the possible functional significance of increased splenial size in the callosum. If increased size in the splenium is due to increased interhemispheric communication in the occipital region, as many investigators have suggested, then this occurs at the expense of interhemispheric communication in the anterior part of the brain. Of course, it remains to be seen if there really is any systematic variation in the sizes of the subdivisions of the corpus callosum.

Hemispheric asymmetries

We find no particularly strong patterns of volume asymmetries in either sex (Table 5). The major exception is the cingulate in men, which is significantly larger in the left hemisphere. This is consistent with Paus et al. (1996), who found that a paracingulate sulcus (leading to a "double cingulate") is significantly more likely to be found in the left as opposed to the right hemisphere. The cingulate in women also shows a leftward asymmetry, although not as pronounced as in men. However, it is the most leftward asymmetric structure in women.

Pairwise *t*-tests indicate a slight intraindividual bias towards the right hemisphere being larger than the left, which is reflected more strongly in lobe asymmetries in women rather than men. In women only, both the frontal and parietal lobes tended to be larger on the right than on the left.

Lobes as a proportion of hemisphere volume

The proportional values display a remarkable consistency across sexes for all brain structures (Table 6). This is even reflected in the subdivisions of the corpus callosum. A similar proportional consistency between sexes was found by other researchers. Peters et al. (1998), following the postmortem study by Skullerud (1985), divided the brain into forebrain and hindbrain regions along a coronal plane that included the mamillary bodies and the posterior commissure. They calculated a hindbrain volume/forebrain volume ratio of 0.146 in both sexes, which was virtually identical to the results of Skullerud (1985). Despite size differences, male and female brains are certainly configured according to a similar plan.

In addition, for both sexes and all structures, CV for proportion are always less than CV for volume. This would allow one to predict that over the course of evolution, volume changes in the whole brain should be more prominent than regional changes in proportion, given the relative amounts of variability available for natural selection to work with. Semendeferi et al. (1997) and Semendeferi and Damasio (2000) found that the proportional representation of the major lobes in the brains of humans and great apes is remarkably similar. Their results are consistent with the analyses of Finlay and Darlington (1995; see also Finlay et al., 2001; Jerison, 1991), who looked at covariation in size of brain structures across 131 mammalian species. Finlay and Darlington (1995) argued that the conserved order of neurogenesis during development imposes a constraint on the relative scaling of one structure compared to another. These data are not consistent with the claim of great relative frontal lobe expansion during the course of human evolution (Deacon, 1997), which as Holloway (1968) pointed out, is not nearly so "obvious" as some earlier anatomists claimed it was.

The partial correlations (Tables 9 and 10) shed further light on whether or not differential expansion of a single lobe is likely to have occurred in hominid evolution. After controlling for hemisphere size, we found a strong negative correlation between frontal and parietal lobe volumes. In other words, individuals with relatively larger frontal lobes tended to have relatively small parietal lobes. The relative sizes of the frontal and parietal lobes are largely determined by the position of the central sulcus, which is one of the earliest sulci to appear in fetal development (at 6–7 months; Ono et al., 1990). The inverse relationship between frontal and parietal lobe size indicates that selective enlargement of the frontal lobe in evolution would have a specific cost: a decrease in size of the parietal lobe. Since the parietal lobe is also primarily composed of association cortex, and thus as critical to the "higher functions" as the frontal lobe, this seems an unlikely tradeoff. Rather, as discussed above, concerted expansion of the major structures of the hominid brain seems a more likely mechanism. Inverse volume relationships between the parietal and temporal lobes and the temporal and occipital lobes appear to be mediated by the Sylvian fissure, another fundamental feature of the human brain that appears relatively early in development.

It is important to keep in mind that statistical consistency is not neuroanatomical destiny. After all, the size of the human brain relative to body size is much larger than expected, based on regression analyses of other mammalian species (Jerison, 1973; Martin, 1983). And while structures such as the human hippocampus are about the size expected for a mammal with a brain our size, the human olfactory lobes are smaller than would be expected (Jerison, 1991). Still, the striking uniformity across sexes in the proportional division of the brain is consistent with the view that the human brain reflects its mammalian heritage at this level of organization.

Correlations and factor analysis

In light of the discussion above, it comes as no surprise that the various regions of the brain are highly correlated for size, as the results in Tables 7 and 8 demonstrate. The lateral ventricles, however, are not at all strongly correlated with regional or total brain volume. This is apparent from the principal components analysis; of the 36 correlations

reported for the lateral ventricles, only one reaches a significance level of $P < 0.01$.

The occipital lobe is the only major brain region that fails to show a uniformly strong correlation in volume with other brain regions. In men, right occipital volume does not correlate significantly with any other brain region volumes, and the significant correlations for the left hemisphere are all at a relatively low level (i.e., $r < 0.50$, $P < 0.05$). This is somewhat surprising, considering that the occipital lobe in women is substantially more variable than in men.

In several respects, the occipital lobe emerges in this study as the major brain region that deviates most from volume patterns seen in other regions: 1) in men, occipital volume does not correlate strongly, if at all, to volumes of other brain regions; 2) in women, the variation in occipital volume is greater than that seen for any other brain region; 3) occipital volume is not significantly different in men and women; and 4) the occipital lobe is much more variable in terms of its proportional volume, compared to other major lobes, with CV very similar to that of the much smaller cingulate gyrus.

There are several factors that may be relevant to explaining these occipital lobe patterns. First, the occipital lobe does not include much of the white matter core of the hemisphere. Since men have a greater proportion of white matter than do women (Gur et al., 1999), the absence of the white matter core may attenuate the total volume sex differences. This would lead one to predict that the frontal and temporal poles are also unlikely to show sex differences in volume, since they are structures that contain little of the white matter core. Second, the parcellation of the lobe is based on relatively, but certainly not totally, arbitrary anatomical criteria. Our occipital "cut" is based on three anatomical points, two of which (supero-mesial end of the parieto-occipital sulcus, and the intersection of the calcarine and parieto-occipital sulci) are reasonably clear. The third point, the preoccipital notch as seen in a lateral view of the hemisphere, may not be considered an intrinsic brain landmark, since its position and form may be influenced by the structure of the tentorium cerebelli. The position of the preoccipital notch is variable, although we found no systematic difference between men and women in its structure (data not shown). This indicates that preoccipital notch form is not responsible for the increased variability in occipital lobe volume seen in women.

The absence of a good landmark for delineating the occipital lobe on the lateral surface of the hemisphere may, of course, be a reflection of the intrinsic qualities of the cortex in that region of the brain. Parcellation of the cortex requires taking into account cytoarchitectonic factors (Brodmann, 1999 [reprint of 1909]), gyral and sulcal anatomy (Welker, 1990), and functional fields of activation (Roland and Zilles, 1998). The occipital lobe in humans has undergone a major reorganization compared to other anthropoid primates. The tempo and mode of this reorganization have been the subject of intense debate (starting with Falk, 1980; see Holloway, 1985, 1991; Falk, 1991, and references therein). The lunate sulcus, which forms an approximate lateral boundary between the parietal and occipital lobes in most primates, is either missing in humans or present as an insignificant, posteriorly placed sulcus (Ono et al., 1990). Area 17, the primary visual cortex, is present almost entirely mesially in humans, compared to its expansive presence on the lateral occipital surfaces of most primate brains (Brodmann, 1999 [reprint of 1909]; von Bonin and Bailey, 1947). Although it was often thought that the shift and reduction of area 17 in humans were a direct result of expansion of parietal association regions, recent studies have shown that a reduced lateral primary visual cortex is also seen in chimpanzees (Holloway et al., 2000), indicating that expansion was not a prerequisite for occipital reorganization. Note that our partial correlation results did not indicate an inverse volumetric relationship between the parietal and occipital lobes. The point we are trying to make here is that the occipital lobe or region in primates may be relatively less constrained compared to other brain regions in terms of its functional and cytoarchitectonic organization and sulcal anatomy. Our results indicate that it may also be less volumetrically constrained than other regions. Further research on the occipital lobe of human and nonhuman primates will be necessary to test the validity of these hypotheses.

CONCLUSIONS

Using high-resolution imaging, a sex-balanced and homogenous subject group, and a brain parcellation scheme based on explicit neuroanatomical criteria, this study demonstrates several volumetric patterns reflecting the organization of the normal human brain. Males tend to be significantly larger than females, for the whole brain and for nearly all of its major subdivisions. In males and females, the proportional sizes of regions relative to total volume of the hemisphere are remarkably similar. The coefficients of variation in size were greater than the coefficients of variation for proportion for all regions. This is consistent with the hypothesis that over the course of evolution, change in brain size is less constrained than changes in the relative sizes of different brain regions. Asymmetries in brain regions are not profound, with the exception of the cingulate gyrus, which is larger in the left hemisphere. The leftward asymmetry in the cingulate gyrus is counter to a trend for right hemisphere structures to be larger than left, especially in women. Brain regions are highly correlated in size, with the exception of the lateral ventricles. The lateral ventricles themselves are extremely variable in size, which may have implications for using them as nonpathognomonic markers for diseases such as schizophrenia. When controlling for hemisphere size, a consistent negative correlation for volume between the frontal and parietal lobes is observed. This indicates

APPENDIX A. Volumes in cubic centimeters of major regions of the human brain: male subjects[1]

Subject (age)	Hemisphere		Frontal		Temporal		Parietal		Occipital		Cingulate		Insula		Cerebellum		Lateral ventricles	
	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R
1M (46)	588.9	592.6	226.9	232.6	137.9	143.0	138.7	137.6	53.4	49.5	23.6	20.4	8.3	9.6	76.7	75.6	8.4	8.6
2M (45)	572.3	577.4	222.9	229.3	132.0	120.6	142.1	146.0	44.3	52.9	22.7	19.4	8.2	9.3	81.6	78.1	4.8	5.2
3M (43)	553.3	553.4	208.9	208.6	121.9	113.8	139.4	141.6	49.5	59.5	24.3	18.9	9.2	11.0	70.6	71.5	10.7	7.0
4M (38)	521.7	519.1	197.5	197.1	103.2	119.5	138.0	129.0	55.2	49.1	18.6	14.9	9.3	9.6	74.3	71.0	5.0	5.1
5M (28)	490.5	489.5	181.5	186.3	118.1	113.1	129.1	124.3	35.9	38.4	18.5	18.9	7.5	8.4	76.8	71.3	3.9	4.0
6M (28)	556.6	557.9	203.5	210.8	130.0	130.2	147.8	140.7	45.2	46.0	21.1	21.1	9.0	9.3	74.1	73.6	2.3	2.4
7M (42)	548.6	548.2	206.9	209.2	120.9	132.2	133.6	140.2	53.7	38.6	23.0	17.2	10.4	10.9	71.4	73.4	11.5	6.5
8M (32)	610.1	617.7	220.8	233.8	130.7	127.7	159.8	165.2	53.4	55.8	35.3	24.4	10.0	10.7	74.7	78.8	3.7	6.2
9M (49)	471.8	467.3	175.3	174.3	97.2	94.3	121.6	117.5	50.5	55.3	18.3	17.6	8.9	8.3	78.3	77.2	4.5	3.9
10M (42)	513.3	508.1	192.6	197.7	121.7	107.6	124.6	115.0	41.0	59.6	23.8	17.0	9.6	11.0	72.7	71.6	7.1	8.4
11M (23)	448.1	451.3	163.3	170.0	96.4	104.6	116.2	113.9	43.6	42.7	21.7	12.2	6.9	7.9	64.1	62.1	2.7	3.8
12M (23)	542.1	544.9	201.4	205.0	107.5	126.7	146.5	140.9	55.0	45.9	22.9	17.3	8.9	9.0	93.6	91.3	7.9	7.4
13M (38)	575.7	589.5	223.0	235.0	122.3	136.3	141.5	132.8	51.1	49.3	27.8	24.9	10.0	11.2	69.7	70.0	10.5	12.8
14M (26)	493.7	496.7	186.7	187.1	101.4	108.2	129.8	128.2	45.3	42.8	21.7	20.8	8.8	9.7	64.4	67.0	3.6	2.2
15M (32)	580.4	578.5	214.3	213.2	127.0	104.4	156.1	173.0	50.4	58.4	26.3	21.8	6.5	7.6	83.5	83.2	6.0	3.4
16M (29)	486.5	487.4	186.1	182.6	100.3	102.4	120.2	131.4	52.6	43.1	19.4	19.6	8.1	8.4	62.2	61.9	7.4	3.1
17M (33)	482.5	483.4	173.4	176.8	107.0	127.0	134.1	110.9	37.8	39.2	20.8	19.4	9.4	10.0	74.1	76.6	3.4	2.6
18M (22)	639.8	650.3	286.9	263.8	142.1	154.2	116.0	151.2	57.1	46.5	25.2	21.0	12.5	13.7	83.1	83.5	7.6	15.4
19M (23)	630.9	640.8	237.5	249.1	153.3	158.0	155.5	147.2	45.9	47.7	29.1	28.4	9.7	10.2	83.3	83.2	8.4	10.6
20M (25)	577.3	586.6	201.8	214.3	128.2	137.1	149.1	144.1	57.8	57.1	29.6	22.6	10.9	11.4	82.8	85.7	4.7	6.4
21M (24)	522.1	532.6	190.8	200.4	121.7	120.6	140.0	142.9	39.6	42.3	22.4	17.6	8.0	8.8	84.5	82.7	25.3	22.3
22M (24)	547.3	549.6	213.3	206.9	113.5	119.9	136.4	141.1	56.5	51.4	18.0	20.9	9.6	9.6	79.5	80.2	7.5	5.1
23M (24)	526.4	529.1	204.5	206.0	125.6	123.1	123.3	129.2	41.5	45.2	23.1	17.0	8.4	8.6	78.1	77.9	5.8	4.3

[1] L, left; R, right.

APPENDIX B. Volumes in cubic centimeters of major regions of the human brain: female subjects[1]

Subject (age)	Hemisphere		Frontal		Temporal		Parietal		Occipital		Cingulate		Insula		Cerebellum		Lateral ventricles	
	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R
1F (39)	487.1	494.8	179.8	188.5	118.8	112.6	118.5	120.5	39.4	47.0	22.9	17.4	7.7	8.8	76.7	76.7	4.7	4.8
2F (36)	469.6	474.7	177.0	180.0	108.3	91.3	121.1	134.2	40.1	40.7	15.9	21.1	7.1	7.4	63.7	63.3	2.0	2.1
3F (32)	462.6	461.7	171.9	179.2	98.5	91.7	122.8	126.2	37.3	39.0	25.0	17.7	7.2	7.9	65.3	63.9	3.7	5.5
4F (26)	536.2	543.9	204.8	215.3	117.1	100.2	128.7	136.0	49.3	55.2	28.1	28.9	8.2	8.3	73.8	74.2	1.8	2.1
5F (41)	419.4	424.8	157.0	165.0	94.3	93.8	111.3	105.9	34.7	38.8	15.6	14.2	6.5	7.1	61.9	63.8	3.1	3.1
6F (28)	456.2	462.5	176.2	175.8	109.5	100.9	111.0	120.7	33.7	35.1	17.6	21.6	8.3	8.5	73.1	75.6	11.1	8.6
7F (47)	475.4	477.4	175.1	184.8	92.5	106.1	130.8	120.3	50.4	41.0	18.2	17.1	8.4	8.2	63.8	65.5	6.7	5.4
8F (32)	443.9	449.9	164.1	164.9	102.2	99.9	113.8	124.5	38.8	34.2	17.3	18.8	7.8	7.5	70.4	69.4	1.1	2.2
9F (23)	512.8	514.7	205.4	207.9	113.9	97.9	121.3	139.8	43.0	40.9	20.7	19.7	8.5	8.4	72.5	73.8	7.3	6.7
10F (37)	416.0	419.4	161.7	162.4	88.9	96.1	98.9	101.7	39.6	36.3	20.1	15.1	6.8	7.7	56.6	56.4	7.0	8.2
11F (28)	484.7	490.2	190.1	193.6	110.5	105.5	112.6	127.3	39.5	37.2	23.7	18.2	8.3	8.4	69.3	69.1	10.8	7.6
12F (24)	535.0	537.0	202.5	200.5	100.5	103.0	146.7	152.2	58.3	51.6	18.6	20.8	8.4	8.9	71.3	68.5	3.5	3.1
13F (26)	464.5	471.4	176.0	180.9	103.6	94.1	113.9	110.6	43.7	53.2	18.5	23.2	8.8	9.4	69.6	68.6	2.9	4.2
14F (28)	426.8	428.9	165.8	170.5	95.5	99.8	90.4	91.7	48.5	41.5	19.6	17.9	7.2	7.5	64.2	62.0	4.4	9.1
15F (43)	471.8	477.7	175.3	182.0	104.4	102.4	116.5	123.9	45.9	46.1	22.0	15.6	7.8	7.7	72.1	72.5	4.7	4.7
16F (24)	493.8	502.9	190.7	189.8	105.1	106.5	123.7	134.2	46.3	45.6	20.0	18.5	8.0	8.4	78.2	78.9	4.1	3.8
17F (41)	470.5	473.2	184.1	184.2	99.8	107.5	114.8	113.0	47.8	42.3	15.9	17.8	8.1	8.3	62.5	61.7	4.1	4.5
18F (27)	429.9	432.9	168.2	166.0	92.0	97.2	104.1	111.8	39.5	31.0	17.9	18.4	8.2	8.5	62.9	63.2	2.1	2.7
19F (26)	517.3	528.3	195.8	203.4	113.0	116.2	118.1	121.9	63.5	59.4	17.6	17.5	9.3	10.0	67.0	68.8	4.6	6.2
20F (42)	474.1	479.3	189.4	198.3	104.8	110.9	111.2	105.0	40.5	39.2	20.9	17.7	7.3	8.2	67.2	67.0	6.3	5.1
21F (41)	529.8	533.4	193.5	193.0	107.7	115.1	140.5	135.7	56.4	59.1	23.5	21.7	8.2	8.9	65.3	68.5	1.5	2.9
22F (35)	428.3	439.8	171.3	169.3	98.2	100.8	104.4	107.7	32.9	37.7	13.7	16.0	7.7	8.4	73.3	73.0	3.9	3.6
23F (23)	597.9	610.7	228.0	228.5	127.0	132.5	143.9	160.4	63.2	57.2	25.7	21.9	10.0	10.2	76.4	77.6	2.8	4.0

[1] L, left; R, right.

APPENDIX C. Corpus callosum measures: male subjects[1]

Subject (age)	Surface area	Total volume	Anterior callosum	Middle callosum	Splenium	CC1	CC2	CC3	CC4
1M (46)	714.6	12.4	5.5	2.3	4.6	4.9	2.3	1.2	4.0
2M (45)	602.8	11.2	4.6	2.7	3.9	4.2	2.1	1.3	3.6
3M (43)	569.1	10.6	4.6	2.0	4.0	4.0	1.9	0.9	3.8
4M (38)	756.7	13.2	5.3	3.0	4.9	4.8	2.6	1.6	4.3
5M (28)	676.5	12.4	4.8	2.6	5.0	4.5	2.7	1.2	4.0
6M (28)	540.5	9.7	3.8	2.3	3.6	3.5	2.5	0.9	2.9
7M (42)	563.0	9.5	4.0	1.7	3.7	3.4	1.8	0.9	3.4
8M (32)	676.6	10.7	4.6	2.0	4.1	4.2	2.0	1.3	3.2
9M (49)	614.0	10.6	4.3	2.4	3.9	4.0	2.0	1.4	3.2
10M (42)	485.6	9.5	3.5	1.9	4.1	3.2	1.9	0.8	3.6
11M (23)	513.1	8.1	3.9	1.8	2.3	3.3	1.8	0.9	2.1
12M (23)	591.4	10.7	4.4	2.2	4.1	4.1	2.0	1.1	3.5
13M (38)	630.1	11.1	4.5	2.0	4.6	4.0	1.9	0.7	3.9
14M (26)	549.7	9.1	3.5	1.9	3.7	3.1	1.9	0.9	3.3
15M (32)	624.6	11.3	4.4	2.9	4.0	3.8	2.4	1.4	3.7
16M (29)	611.6	10.2	3.9	2.2	4.1	3.8	1.8	1.3	3.4
17M (33)	416.8	7.2	2.8	1.6	2.8	2.6	1.5	0.7	2.5
18M (22)	670.0	12.7	6.1	2.4	4.3	5.6	2.5	0.8	3.7
19M (23)	777.6	13.7	6.2	3.2	4.3	5.5	2.8	1.3	4.1
20M (25)	577.9	9.9	4.1	2.9	3.0	3.5	2.3	1.2	3.0
21M (24)	551.2	11.0	4.6	2.2	4.2	4.2	2.2	0.9	3.7
22M (24)	490.2	8.4	4.1	2.0	2.3	3.6	1.7	0.9	2.3
23M (24)	552.2	9.8	4.0	1.9	4.0	3.8	1.8	0.8	3.3

[1] Midline surface area in square millimeters. Volumes in cubic centimeters.

that selective expansion of the frontal lobe in hominid evolution could only have come at the cost of parietal lobe volume. The occipital lobe tends to be less sexually dimorphic than other major lobes, and less correlated with other brain regions for volume. This could indicate that over the course of hominid brain evolution, the occipital region may be less volumetrically constrained compared to other regions in terms of its relative size.

We believe that this study, the largest of its kind to date, demonstrates the importance of volumetric analyses of the anatomically parcellated human brain. In order to understand the variation in regional brain size along various dimensions (e.g., sex, age, handedness), we need to better understand the volumetric relationships among the various regions and between the whole brain and its components.

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APPENDIX D. Corpus callosum measures: female subjects[1]

Subject (age)	Surface area	Total volume	Anterior callosum	Middle callosum	Splenium	CC1	CC2	CC3	CC4
1F (39)	447.3	9.1	3.8	1.8	3.5	3.3	1.8	0.8	3.2
2F (36)	459.1	8.6	3.4	2.0	3.3	2.9	2.1	1.0	2.7
3F (32)	608.1	10.5	4.7	2.0	3.8	4.2	2.1	1.2	2.9
4F (26)	584.0	10.5	4.7	2.0	3.7	4.2	2.2	0.8	3.3
5F (41)	533.9	9.3	4.2	2.6	2.5	3.5	1.9	1.1	2.8
6F (28)	550.4	8.9	3.6	1.6	3.8	3.2	1.8	0.9	3.0
7F (47)	505.0	9.2	3.7	2.1	3.5	3.2	1.9	1.1	3.1
8F (32)	564.0	8.6	3.4	1.8	3.4	3.3	1.7	1.1	2.5
9F (23)	678.0	11.9	4.7	2.8	4.4	4.5	2.4	1.1	4.0
10F (37)	493.2	8.0	3.3	1.5	3.2	2.8	1.8	0.7	2.7
11F (28)	519.5	9.7	4.5	1.9	3.3	3.8	2.4	0.8	2.7
12F (24)	607.6	11.2	4.7	2.0	4.6	4.1	2.0	1.2	3.9
13F (26)	593.9	10.4	4.6	1.9	3.8	3.9	2.2	0.9	3.3
14F (28)	480.8	8.0	3.8	1.4	2.8	3.5	1.6	0.7	2.2
15F (43)	704.8	12.4	5.4	2.4	4.6	4.8	2.3	1.0	4.2
16F (24)	631.9	11.7	4.8	2.7	4.1	4.4	2.5	0.9	3.9
17F (41)	482.9	8.9	3.6	1.8	3.5	3.3	1.6	0.7	3.3
18F (27)	502.8	8.6	3.4	2.0	3.2	3.1	1.9	1.0	2.6
19F (26)	562.1	9.2	4.0	1.9	3.3	3.5	1.9	0.8	3.1
20F (42)	578.0	9.6	4.6	2.2	2.8	4.1	1.9	0.9	2.6
21F (41)	592.4	10.1	3.8	2.7	3.6	3.2	2.1	1.5	3.3
22F (35)	494.5	8.0	3.1	1.8	3.1	2.8	1.6	0.9	2.6
23F (23)	634.7	10.3	4.0	2.5	3.7	3.8	2.2	1.4	3.0

[1] Midline surface area in square millimeters. Volumes in cubic centimeters.

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