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A Comparative MRI Study of the Relationship Between Neuroanatomical Asymmetry and Interhemispheric Connectivity in Primates: Implication for the Evolution of Functional Asymmetries

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Abstract

The authors tested the theory that hemispheric specialization evolved as a consequence of reduced interhemispheric connectivity by examining whether neuroanatomical asymmetries were associated with variation in the ratio of corpus callosum size to brain volume (CC:VOL) and to neocortical surface area (CC:NEO) in human and nonhuman primates. Magnetic resonance images were collected in a sample of 45 primates including 8 New World monkeys, 10 Old World monkeys, 4 lesser apes, 17 great apes, and 6 humans. CC:VOL and CC:NEO were determined and correlated with measures of brain asymmetry. The results indicate that brain asymmetry significantly predicted CC:VOL and CC:NEO. Subsequent analyses revealed that species variation in functional asymmetries in the form of handedness are also inversely related to CC:NEO. Taken together, these results support the hypothesis that leftward brain asymmetries may have evolved as a consequence of reduced interhemispheric connectivity.

The corpus callosum (CC) is the major neural pathway connecting the two cerebral hemispheres in placental mammals. The primary function of the CC is to connect homologous cortical areas between the two hemispheres along an anterior–posterior continuum. Histological studies in nonhuman primate brains suggest that the anterior portion (e.g., genu) of the CC connects the anterior–frontal areas whereas the posterior areas (e.g., splenium) connect the occipital and the temporal cortex (Pandya & Seltzer, 1986). Recently, individual differences in CC size among humans have been correlated with brain size, sex, age, and functional asymmetries in humans (see Driesen & Raz, 1995, for review). The most intriguing findings have been the reports of gender and handedness differences in CC morphology. For example, females have been reported to have larger CC areas after statistically controlling for differences in brain size (Driesen & Raz, 1995). Additionally, it has been reported that non–right-handed individuals have larger CC areas compared with right-handed individuals (e.g., Witelson, 1985). The reported gender and handedness differences in CC morphology have both been linked to differences in cerebral lateralization. For both females and left-handed individuals, it is argued that they are less lateralized than their counterparts because of increased interhemispheric connectivity between hemispheres (Witelson, 1989).

To the extent that biological factors have been proposed to explain differences in CC morphology in humans, it is somewhat surprising that little research has been conducted on examining factors that influence CC morphology in nonhumans, particularly closely related nonhuman primates (Holloway & Heilbronner, 1993). In nonhuman primates, data from cadaver specimens (LaCoste & Woodward, 1988), and more recently from magnetic resonance imaging (MRI) scans (Rilling & Insel, 1999), indicate significant differences in CC size in relation to brain volume between species. With respect to the ratio of CC size to brain volume, the findings indicate that the ratio is significantly lower in humans compared with nonhuman primate species including apes and monkeys (see Figure 1). One explanation of this difference is that as the brain enlarged in primate evolution, interhemispheric connections became longer and slower and it became more efficient to process information in small local networks with shorter axons. Therefore, long-distance axonal projections, including interhemispheric projections via the CC, were pruned in larger brains. This had the effect of confining certain functions to a single hemisphere that had previously been bilaterally distributed. In other words, increased laterality of function may have been an emergent property accompanying brain enlargement in primate evolution (Rilling & Insel, 1999; Ringo, Doty, Demeter, & Simard, 1994). If functional and neuroanatomical asymmetries are correlated, then this theoretical model predicts that more asymmetric brains should have less interhemispheric connectivity, as evidenced by a smaller ratio of CC size to brain volume.

In contrast, it could be argued that more lateralized brains require greater interhemispheric connectivity for the organism to possess a unified consciousness (Sperry, 1984). If this explanation is correct, then more-asymmetric brains should have larger ratios of CC size to brain volume. Unfortunately, there is not a single study examining the relation between brain asymmetry, brain volume, and CC morphology in nonhuman primates. This observation is particularly relevant in light of the recent evidence of taxonomic differences in functional asymmetries in nonhuman primates (see Corballis, 1992; Hopkins, 1996; Ward & Hopkins, 1993). For example, with specific reference to variations in hand preference, population-level right-handedness has been reported for coordinated bimanual actions in apes but not in New World monkeys (Colell, Segarra, & Sabater-Pi, 1995; Hopkins, 1995; Westergaard & Suomi, 1996); hand-preference data for coordinated actions in Old World monkeys have produced mixed results (Fagot & Vaclair, 1988; Westergaard, Champoux, & Suomi, 1997; Westergaard & Suomi, 1996). Regarding neuroanatomical asymmetries, great apes exhibit larger and more consistent left-occipital, right-frontal petalia asymmetries (LeMay, 1985) and have been reported to have a left-hemisphere asymmetry in sylvian fissure length, whereas monkeys do not (Yeni-Komshian & Benson, 1976; but see Heilbronner & Holloway, 1988). More recently, left-hemisphere asymmetries in the planum temporale have been reported in great apes, and these morphological asymmetries were not readily observed in lesser apes and monkeys (Gannon, Holloway, Broadfield, & Braun, 1998; Hopkins, Marino, Rilling, & MacGregor, 1998). Taken together, these data suggest that changes in CC morphology may be linked to phylogenetic changes in the manifestation of functional and neuroanatomical asymmetries in nonhuman primates.

The purpose of this study was to examine the relationship between brain asymmetry and interhemispheric connectivity in anthropoid primates. Specifically, we sought to examine how and whether brain asymmetry was associated with the ratio of CC size to brain volume in different primate species. In addition to the ratio of CC size to brain volume, we were also interested in the relationship between brain asymmetry and the ratio of CC size to neocortical surface area. Our specific interest in neocortical surface area rather than total brain volume was due to the fact that callosal neurons link cortical neurons and that the number of neocortical neurons underneath a given area of cerebral cortex is quite similar across primates (Haug, 1987; Rockel, Hiorns, & Powell, 1980). Therefore, the ratio of CC area to neocortical surface area may provide a better estimate of interhemispheric connectivity between cortical neurons

than overall brain volume. In evaluating brain asymmetry, both direction and magnitude of bias were considered in the analyses. Our rationale for considering both aspects of asymmetry was that none of the theories relating the evolution of brain asymmetry to CC morphology explicitly state which of these dimensions is critical. For example, Witelson (1985) suggested that non-right-handed individuals are less lateralized, as reflected in a larger CC, compared with right-handed individuals. In this case, *less lateralized* means that they deviate from the typical right-sided bias, but it does not mean that the individuals differ in the strength of their hand preferences. It is quite conceivable that left- and right-handed individuals can differ in their direction of bias but be equally lateralized in terms of the strength of their preferred hand use. In terms of CC morphology in relation to brain asymmetry, it is possible that different individuals or species can be equally lateralized (after accounting for brain size difference) but differ in the direction of their asymmetries (e.g., see Cowell, Kertesz, & Denenberg, 1993, for discussion). Therefore, we sought to assess how each of these dimensions of laterality influences CC morphology in relation to brain volume and neocortical surface area.

Method

Subjects

MRI scans of the brain were collected in a sample of 45 primates including 6 humans, 18 monkeys, 4 lesser apes, and 17 great apes. Within the monkey sample there were two anthropoid families represented, Cebidae and Cercopithecidae. In the ape sample, the anthropoid families included Hylobatidae and Pongidae. The number of individuals and genus representation for each taxonomic group can be seen in Table 1. There were 3 men and 3 women in the human sample, 7 females and 10 males in the Pongidae family, 5 males and 5 females in the Cercopithecidae family, and 4 males and 4 females in the Cebidae sample.

Procedure

This project involved using two MRI scanners (Phillips, Model 51 [Best, the Netherlands], each with 1.5-T superconducting magnets) housed at Emory University Hospital. Prior to transportation for scanning, the non-human subjects were first immobilized with a ketamine injection (10 mg/kg) and subsequently anesthetized with propofol (40–60 mg/kg/hr) following standard Yerkes Regional Primate Research Center (YRPRC) veterinary procedures. The subjects remained anesthetized for the duration of the scans as well as during the time needed to travel between YRPRC and Emory University Hospital, after which they were temporarily housed in a single cage for 6 to 12 hr to allow the effects of the anesthesia to wear off before returning them to their home cage. Human participants were scanned without the aid of anesthesia. For all subjects, T1-weighted images were collected for the entire brain using a gradient echo protocol (pulse repetition = 19.0 ms, echo time = 8.5 ms, field of view = 180 mm, slice thickness = 1.2 mm, slice overlap = 0.6 mm, number of signals averaged = 8, 256 × 256 matrix). The archived data were stored on optical diskettes and transported to a Sun Sparcstation- 1 workstation for postimage processing. The monkeys were scanned in the prone position using a human knee coil, whereas the apes and humans were scanned using a human head coil. Scan duration was a function of brain size but ranged from 40 to 80 min for the monkeys and the apes and humans, respectively. Measurements of the brain were done using EasyVision software that allowed for multiplanar reformatting of the scans in various planes of interest.

CC Measurement

To obtain a true midsagittal slice for CC measurements, all scans were reformatted into a plane perpendicular to the midline of both the coronal and the axial planes. The midsagittal slice could be easily identified in the sagittal stack by checking its position on the coronal and axial reference views. Midsagittal CC area was traced manually using EasyVision's area tool. Mean

coefficients of variation for repeated CC area measures were 2% (intrarater, $n = 10$) and 4% (interrater, $n = 7$). To compare differences in callosal regions (i.e., the splenium or the genu), the CC was divided into five equal parts by the following method: A straight line was drawn from the rostral to the caudal tip of the CC. A second line was drawn perpendicular to the first at one fifth the distance from the rostral to the caudal tip. The area of the CC in front of this line was measured with the area tool and roughly corresponds to the genu. A second perpendicular line was drawn two fifths of the way to the caudal tip. The area between this line and the first perpendicular line represents the *rostral-midbody*. The same procedure was used to measure areas in the other three fifths. Moving caudally, these are referred to as the *central-midbody*, *caudal-midbody*, and *splenium*.

Brain Asymmetry Measurement

The brain asymmetry measure was derived from previous studies that have assessed petalia patterns in different primate species. Petalia asymmetries refer to frontal and occipital lobe protrusions that leave a demarcation on the skulls and can be determined using endocasts. Previous studies have reported that humans, apes, and monkeys exhibit a left-occipital, right-frontal petalia asymmetry (Falk, 1987; Falk et al., 1990; LeMay, 1985), and recently researchers have developed a methodology that allows for measurement of cerebral width (which presumably reflects petalia asymmetries) using MRI scans (Hopkins & Marino, 2000). From the MRI scans and using multiplanar reformatting software, measures of brain asymmetry were assessed following the procedures used by Kertesz, Black, Polk, and Howell (1986) in humans. Briefly, the scans were reformatted in the horizontal plane in 1-mm slices along the anterior-posterior commissure line. The first horizontal slice above the third ventricle was identified, and the length of each hemisphere was determined by measuring from the frontal to the occipital pole, 5 mm lateral to the midline. Four width measurements were taken, corresponding to 10% and 30% of the length from the frontal and occipital pole. These were collectively referred to as the *anterior-frontal* (AF; 10% from the frontal pole), the *posterior-frontal* (PF; 30% from the frontal pole), the *parietal lobe* (PAR; 30% from the occipital pole), and the *occipital lobe* (OCCP; 10% from the occipital pole). Widths were measured from the midline to the lateral surface of the brain (in tenths of a millimeter).

Brain Volume and Neocortical Area

In each two-dimensional axial slice, brain tissue was identified and separated from surrounding tissues (cerebrospinal fluid, meninges, blood vessels, muscle, fat, and bone) through a combination of computerized thresholding based on pixel signal intensities and manual editing. In each slice, the area of the selected tissue was calculated, and these areas were integrated across all slices to arrive at a volume estimate for the entire brain. For the neocortical area, brains were oriented in the plane of the anterior and posterior commissures and sliced into 10 evenly spaced coronal sections. The most anterior slice was 1/11th of the way from the rostral to the caudal tip of the brain. The second slice was 2/11th of the way, the third slice 3/11th, and so on. In the left hemisphere of each slice, the length of the neocortical surface area was traced manually, and after measuring all slices we summed the surface lengths and multiplied them by the distance between slices to derive an estimate of the area. The neocortical area for the left hemisphere was doubled to yield an estimate of total neocortical surface area.

Data Analysis

Log-transformed data were used in all analyses to meet the assumption of linearity necessary in multiple regression analyses. For the CC, brain volume, and neocortical surface area measures, this simply required that the log values be determined for each raw value. For the brain asymmetry measure, the log value of the raw left- (L) and right-hemisphere (R) value for each region was derived and used for determining the asymmetry quotient in each region.

The asymmetry quotient (AQ) was derived using the formula $AQ = [(R - L)/(R + L) \times 0.5]$.

¹ This formula accounted for individual and species variations in brain volume. Negative values reflected a left-hemisphere bias, and positive values reflected a right-hemisphere bias. The absolute value of the AQ (ABS) reflected the magnitude of asymmetry (herein referred to as ABS-AF, ABS-PF, etc.). AQ and ABS values were derived for each of the cerebral width measures. Alpha was set to $p < .05$ for all analyses.

Results

Intercorrelations in Cerebral Width Measures

In multiple regression analysis, it is important that the predictor variables be uncorrelated, and therefore a Pearson product-moment correlation was performed between the measures of cerebral width to determine whether there was any redundancy in the measures. This was done for both the directional and absolute degrees of asymmetry. The results can be seen in Tables 2 and 3. For both the direction and strength of asymmetry, the AQ-AF and AQ-PF measures significantly correlated, as did the AQ-PAR and AQ-OCCP. AQ-PAR and AQ-PF did not correlate with each other, nor did AQ-AF and AQ-OCCP. For the magnitude in asymmetry values similar results were found, with ABS-AF and ABS-PF significantly correlating with each other, as did the ABS-PAR and ABS-OCCP measures. No other correlations were significant. On the basis of these results, only the AF and OCCP measures of direction and magnitude of asymmetry were used as independent predictor variables in the regression analyses.

Total CC Analyses

The initial analysis focused on determining the relationship between brain asymmetry and either the ratio of CC size to brain volume or the ratio of CC size to neocortical surface area. For this analysis, the total CC size was divided by brain volume to derive a ratio of CC size to brain volume (CC:VOL). Similarly, the total CC size was divided by the neocortical surface area to derive a ratio of these two attributes of the brain (CC:NEO). Subsequently, we regressed the AQ-AF and AQ-OCCP values on each of the ratio measures. For both CC:VOL, $F(2, 42) = 9.09, p < .001$, and CC:NEO, $F(2, 42) = 9.37, p < .001$, the measures of brain asymmetry accounted for a significant proportion of variance. The multiple R values for each regression were .55 and .56, respectively. Of the two cerebral width measures, the AQ-OCCP was the only significant predictor of CC:VOL ($\beta = .521, p < .001$) and CC:NEO ($\beta = .532, p < .001$). The positive beta values indicate that subjects with larger left-hemisphere biases (as indicated by a negative value) had smaller ratio scores (see Figures 2 and 3). To determine whether strength of lateral bias was a significant predictor of the ratio measures, the same regression analyses were performed but using the ABS scores for the two cerebral areas rather than the AQ scores. For the CC:VOL ($R = .366$) and CC:NEO ($R = .420$) ratio scores, the ABS values did not account for a significant amount of variance, although the results were borderline significant, CC:VOL, $F(2, 42) = 2.95, p < .08$; CC: NEO, $F(2, 42) = 2.66, p < .10$.

Analyses of Regional Variation in CC Morphology

To assess whether there was differential expansion of specific regions of the CC in relation to brain asymmetry, we performed subsequent regression analyses using ratio scores derived for each CC region rather than the entire CC area. For this analysis, the area measures of each CC region (genu, rostral-midbody, central-midbody, caudal-midbody, splenium) were divided by

¹We recognize that the range in AQ scores derived from log values would differ from AQ derived from the raw width data. To be consistent with the other measures, we opted to use the AQ values derived from log values. To assure that this decision did not skew our results, we performed the same regression analyses using AQ values derived from the raw values instead of AQ values from the log values. The results were virtually identical to those reported in the Results section.

the total neocortical surface area. In order to reduce the probability of Type I error due to an increased number of analyses, we derived ratio scores only for the neocortical surface area measure. For each regional ratio measure, we regressed the AQ-AF and AQ-OCCP scores. The multiple R values for the genu, rostral-midbody, central-midbody, caudal-midbody, and splenium were .364, .379, .312, .314, and .161, respectively. The R values were significant only for the genu, $F(2, 42) = 3.21, p < .05$, and rostral-midbody, $F(2, 42) = 3.52, p < .05$. For each area, the AQ-OCCP measure was the sole variable accounting for a unique portion of variance (genu, $\beta = .359, p < .02$; rostral-midbody, $\beta = .380, p < .02$).

Potential Correlates With Species Differences in Hand Preference

The previous analyses focused on the relation between neuroanatomical asymmetries and the ratio in CC size to total neocortical surface area and total brain volume. To the extent that these ratio measures explain phylogenetic variation in neuroanatomical asymmetries, they should similarly explain variation in functional asymmetries. Of course, this hypothesis assumes that structural and functional asymmetries are correlated and develop from similar neurobiological mechanisms. In the past 10 years, there has been a plethora of behavioral research on the distribution of hand preference in nonhuman primates (reviewed above). Recently, Westergaard, Kuhn, and Suomi (1998) have compared the distribution of hand preference in 13 species of nonhuman primates when required to reach from either a quadrupedal or bipedal posture. Of the 13 species compared, there was a wide range of phylogenetic representation within the order primates including prosimians, Old World monkeys, New World monkeys, great apes, and humans. Westergaard et al. (1998) reported that there is a gradual shift as one ascends the primate order from population-level left-hand preference to population-level right-handedness for both quadrupedal and bipedal reaching (see Figure 4). Given that these data have been collected using similar if not identical procedures in each species, they provide a useful comparative data set for analysis in relation to the MRI data collected in this study.

Of the 13 species compared on hand preference by Westergaard et al. (1998), we had MRI data on at least 2 individuals in 9 of these species: squirrel monkeys, capuchin monkeys, rhesus monkeys, gibbons, orangutans, gorillas, bonobos, chimpanzees, and humans. In an attempt to test whether our various measures of neuroanatomical structure could explain some species variation in hand preference, a number of regression analyses were performed. For the species hand-preference values, we used the mean handedness index (HI) scores provided in the article by Westergaard et al. (1998). The mean HI scores for each species were derived by calculating the individual HI score for each individual and averaging them for the sample. Individual HI values were determined by subtracting the number of left-hand reaches from the number of right-hand reaches and dividing by the total number of reaches: $HI = (R - L)/(R + L)$. Negative HI values reflect left-sided biases in hand preferences, whereas positive values reflect right-sided biases.

In our analyses, we regressed the mean HI scores on the mean CC:NEO ratio score for each species. We also regressed the mean HI scores on the mean AQ-AF and AQ-OCCP values for each species to determine whether the hand-preference data correlated with the measures of neuroanatomical asymmetry. Finally, we regressed the mean AQ-OCCP values on the mean CC:NEO ratio score for each species to assess whether the previously reported findings using the individual data points could be replicated using the mean data points for each species. The regressions were performed on the HI scores for both the bipedal and quadrupedal reaching data reported by Westergaard et al. (1998).

Depicted in Table 4 are the summaries of the regression analyses for each CC region and measure of hand preference (bipedal and quadrupedal reaching). For bipedal reaching, significant negative associations were found for the genu, rostral-midbody, and splenium, indicating that species with higher HI values (reflecting right-handedness) had smaller ratio

values (reflecting reduced interhemispheric connectivity; see Figure 5A). There was a borderline significant association between the HI values and the total CC area. For quadrupedal reaching, significant negative associations were found between the HI values and ratio scores of the genu and splenium. There was no significant association between the mean AQ-AF ($r = .24, ns$) and AQ-OCCP ($r = -.48, ns$) measures and the bipedal reaching HI scores, indicating that the raw measures of neuroanatomical asymmetry did not correlate with the measures of functional asymmetry. Finally, the regression between the mean CC:NEO score and the mean AQ-OCCP for each species revealed a significant association ($r = .771, p < .02$; see Figure 5B), indicating that species with lower AQ values (reflecting left-hemisphere asymmetries) had smaller ratio measures. The slope of this regression was 4.77, which was similar to that reported for the regression analysis using the individual data points (slope = 3.85). This result, in essence, replicated the previous neuroanatomical findings but by using a different level of analysis (mean per species compared with individual data).

Discussion

Several significant findings emerged from this study. First, brain asymmetry accounts for a significant proportion of variance in the ratio of CC size to overall brain volume and neocortical surface area in primates. Subjects with larger left-hemisphere asymmetries in occipital-lobe width had smaller ratio scores. Second, analysis of specific regions of the CC indicated that occipital-lobe asymmetry significantly correlated with ratio scores of the genu and rostral-midbody (see Table 3). Finally, directional biases in hand-preference data in nine nonhuman primate species significantly correlated with the CC:NEO ratio scores. Species with greater preferential use of the right hand had smaller CC:NEO ratio scores.

The general results from this study support the hypothesis that directional asymmetries and interhemispheric connectivity are related. Although this theory has been proposed to explain individual differences in functional and neuroanatomical asymmetries, on the basis of our findings, this theory appears to also account for phylogenetic variation in neuroanatomical and functional asymmetries. The principal evidence in support of this conclusion was the significant correlations found between the brain asymmetry measures and the CC:VOL and CC:NEO ratio scores. Species with larger left-hemisphere cerebral-width asymmetries had smaller CC:NEO ratios. Similarly, species that show greater population-level right-handedness had smaller CC:NEO ratios. As far as we know, this is the first evidence that measures of neuroanatomical and functional asymmetry account for a significant proportion of variability in CC morphology in nonhuman primates. Previous studies have focused solely on the relation between phylogenetic changes in brain volume and CC morphology (see above) without consideration of asymmetry, and some authors have noted that other factors may contribute to the variability observed in different species. Clearly, our results support this conclusion and, at a minimum, suggest that the directional biases of neuroanatomical or functional asymmetry may be one of these important contributing factors.

The directional biases rather than magnitude of neuroanatomical asymmetry were critical for predicting the ratio scores. This was evident by the fact that ABS asymmetry values did not account for a significant proportion of variability in the CC:VOL or CC:NEO ratio scores. It is not clear why this is the case as there is no *a priori* reason to assume that one directional bias (e.g., the left hemisphere) would lead to smaller ratios in CC size to brain volume or neocortical surface area over another (e.g., Rosen, Sherman, & Galaburda, 1989). Nonetheless, this is an important distinction, particularly for comparative studies of the relationship between CC morphology and either functional or neuroanatomical asymmetries because different investigators use different terms and criteria when defining the word *asymmetry* (see Cowell et al., 1993, for discussion). With the increasing evidence of functional and neuroanatomical

asymmetries in nonhuman species, more attention will need to be drawn to this distinction when making within- and between-species comparisons.

When considering specific regions of the CC, the AQ-OCCP accounted for a significant proportion of variance in the genu and rostral-midbody. It is not clear why the AQ-OCCP asymmetry predicts the anterior regions of the CC, because primarily homotopic pathways in the posterior regions of the CC connect cortical regions in the occipital lobe. One possibility may be that the occipital lobe asymmetries are a consequence of expansion in the frontal lobe that creates a left-to-right torquing action in the organization of the two hemispheres (Best, 1988). In this scenario, the occipital-lobe asymmetries are a consequence of functional asymmetry in the frontal regions, but they do not manifest themselves on the MRI scans or in the shape of the skull, except in humans (see LeMay, 1985). Species variation in hand preferences were also associated with specific regions of the CC, specifically the genu, rostral-midbody, and splenium. Species that show a greater propensity for population-level right-handedness had smaller ratio values. As with the neuroanatomical data, it is not exactly clear why these regions are implicated, but it is of note that these are the two regions of the CC for which most of the individual variation in human hand preferences are observed (see Driesen & Raz, 1995). Further analyses with a wider range of species with varying degrees of hand preference should help to clarify this matter.

There are several limitations to this study that warrant further consideration in future studies. First, we used heterogeneous samples of primate species within each taxonomic family with the exception of Hylobatidae. We also had relatively small sample sizes for each species within a family. Although we do not believe that this negates the findings of our study, it will be important in future research to either expand the sample sizes and species representation in each family or restrict the species variation and dramatically increase sample size for each species. Second, we used only one measure of brain asymmetry, and clearly there are other lateralized structures in the brain that could be used in future research, such as the sylvian fissure (Aboitiz, Scheibel, & Zaidel, 1992). Third, attempts need to be made to correlate the structural aspects of asymmetry and CC morphology with individual functional asymmetries in different primate species. Most importantly, neuroanatomical and functional asymmetry data must come from the same subjects. Finally, it is important to recognize that our findings are restricted to CC morphology, and it is possible that differences in other aspects of interhemispheric connectivity could offset the observed differences. For example, the relative function of the anterior and posterior commissures in different primate species is virtually unknown (Rilling & Insel, 1999). Further work is clearly needed on species variation in interhemispheric connectivity.

In conclusion, the results of this study represent the first quantitative evidence of species differences in lateralization related to aspects of brain volume, neocortical surface area, brain asymmetry, and CC morphology. On the basis of our findings, we would argue that of fundamental importance in explaining individual functional lateralization is interhemispheric connectivity in relation to neuroanatomical asymmetry. Rather than focusing solely on measures of brain asymmetry in relation to functional asymmetry, we advocate that one must consider the additional relationship between the volume of the brain and how each hemisphere is connected to each other. Adopting this perspective in assessing neuroanatomical asymmetries will hopefully contribute to understanding of individual as well as species differences in functional asymmetries.

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References

- Aboitiz F, Scheibel AB, Zaidel E. Morphometry of the sylvian fissure and corpus callosum, with emphasis on sex differences. *Brain* 1992;115:1521–1541. [PubMed: 1422802]
- Best, CT. The emergence of cerebral asymmetries in early human development: A literature review and a neuroembryological model. In: Molfese, DL.; Segalowitz, SJ., editors. *Brain lateralization in children: Developmental implications*. Guilford Press; New York: 1988. p. 5-34.
- Colell M, Segarra MD, Sabater-Pi J. Manual laterality in chimpanzees (*Pan troglodytes*) in complex tasks. *Journal of Comparative Psychology* 1995;109:298–307. [PubMed: 7554826]
- Corballis, MC. *The lopsided brain: Evolution of the generative mind*. Oxford University Press; New York: 1992.
- Cowell PE, Kertesz A, Denenberg VH. Multiple dimensions of handedness and the human corpus callosum. *Neurology* 1993;43:2353–2357. [PubMed: 8232955]
- Driesen NR, Raz N. The influence of sex, age, and handedness on corpus callosum morphology: A meta-analysis. *Psychobiology* 1995;23:240–247.
- Fagot J, Vauclair J. Handedness and manual specialization in the baboon. *Neuropsychologia* 1988;26:795–804. [PubMed: 3194046]
- Falk D. Brain lateralization in primates and its evolution in hominids. *Yearbook of Physical Anthropology* 1987;30:107–125.
- Falk D, Hildebolt C, Cheverud J, Vannier M, Helmkamp RC, Konigsberg L. Cortical asymmetries in the frontal lobe of rhesus monkeys (*Macaca mulatta*). *Brain Research* 1990;512:40–45. [PubMed: 2337807]
- Gannon PJ, Holloway RL, Broadfield DC, Braun AR. Asymmetry of chimpanzee planum temporale: Humanlike pattern of Wernicke's brain language area homolog. *Science* January 9;1998 279:220–222. [PubMed: 9422693]
- Haug H. Brain sizes, surfaces, and neuronal sizes of the cortex cerebri: A stereological investigation of man and his variability and a comparison with some mammals (primates, whales, marsupials, insectivores, and one elephant). *American Journal of Anatomy* 1987;180:126–142. [PubMed: 3673918]
- Heilbronner PL, Holloway RL. Anatomical brain asymmetries in New World and Old World monkeys: Stages of temporal lobe development in primate evolution. *American Journal of Physical Anthropology* 1988;76:39–48. [PubMed: 3136655]
- Holloway RL, Heilbronner P. Corpus callosum in sexually dimorphic and nondimorphic primates. *American Journal of Physical Anthropology* 1993;87:349–357. [PubMed: 1562061]
- Hopkins WD. Hand preferences for a coordinated bimanual task in 110 chimpanzees: Cross-sectional analysis. *Journal of Comparative Psychology* 1995;109:291–297. [PubMed: 7554825]
- Hopkins WD. Chimpanzee handedness revisited: 54 years since Finch (1941). *Psychonomic Bulletin & Review* 1996;3:449–457.
- Hopkins WD, Marino L. Asymmetries in cerebral width in nonhuman primate brains as revealed by magnetic resonance imaging (MRI). *Neuropsychologia* 2000;38:493–499. [PubMed: 10683399]
- Hopkins WD, Marino L, Rilling JK, MacGregor LA. Planum temporale asymmetries in great apes as revealed by magnetic resonance imaging (MRI). *NeuroReport* 1998;9:2913–2918. [PubMed: 9760145]
- Kertesz A, Black SE, Polk M, Howell J. Cerebral asymmetries on magnetic resonance imaging. *Cortex* 1986;22:117–127. [PubMed: 3709188]
- Lacoste, M.-C.d.; Woodward, DJ. The corpus callosum in nonhuman primates: Determinants of size. *Brain, Behavior and Evolution* 1988;33:261–267.
- LeMay, M. Asymmetries of the brains and skulls of nonhuman primates. In: Glick, SD., editor. *Cerebral lateralization in nonhuman species*. Academic Press; New York: 1985. p. 223-245.

- Pandya, DN.; Seltzer, B. The topography of the commissural fibers. In: Lepore, F.; Ptito, M.; Jasper, HH., editors. Two hemispheres-one brain: Functions of the corpus callosum. Alan R. Liss.; New York: 1986. p. 47-73.
- Rilling JK, Insel TR. Differential expansion of neural projection systems in primate brain evolution. *NeuroReport* 1999;10:1453–1459. [PubMed: 10380962]
- Ringo JL, Doty RW, Demeter S, Simard PY. Time is of essence: A conjecture that hemispheric specialization arises from inter-hemispheric conduction delay. *Cerebral Cortex* 1994;4:331–343. [PubMed: 7950307]
- Rockel AJ, Hiorns RW, Powell TPS. The basic uniformity in structure of the neocortex. *Brain* 1980;103:221–244. [PubMed: 6772266]
- Rosen GD, Sherman GF, Galaburda AM. Interhemispheric connections differ between symmetrical and asymmetrical brain regions. *Neuroscience* 1989;33:525–533. [PubMed: 2636706]
- Sperry RW. Consciousness, personal identity, and the divided brain. *Neuropsychologia* 1984;22:661–673. [PubMed: 6084824]
- Westergaard GC, Champoux M, Suomi SJ. Hand preference in infant rhesus macaques. *Child Development* 1997;68:387–393. [PubMed: 9249955]
- Ward, JP.; Hopkins, WD. Primate laterality: Current behavioral evidence of primate asymmetries. Springer-Verlag; New York: 1993.
- Westergaard GC, Kuhn HE, Suomi SJ. Bipedal posture and hand preference in humans and other primates. *Journal of Comparative Psychology* 1998;112:56–63.
- Westergaard GC, Suomi SJ. Hand preference for a bimanual task in tufted capuchins (*Cebus apella*) and rhesus macaques (*Macaca mulatta*). *Journal of Comparative Psychology* 1996;110:406–411. [PubMed: 8956511]
- Witelson SF. The brain connection: The corpus callosum is larger in left-handers. *Science* August 16;1985 299:665–668. [PubMed: 4023705]
- Witelson SF. Hand and sex differences in the isthmus and genu of the human corpus callosum: A postmortem morphological study. *Brain* 1989;112:799–835. [PubMed: 2731030]
- Yeni-Komshian G, Benson D. Anatomical study of cerebral asymmetry in the temporal lobe of humans, chimpanzees and monkeys. *Science* April 23;1976 192:387–389. [PubMed: 816005]

Figure 1. Mean ($\pm SE$) ratio of corpus callosum size to brain volume (CC:VOL) and to neocortical surface area (CC:NEO) in five primate taxonomic families (data from Rilling & Insel, 1999).

Figure 2. Scatter plots of individual ratio measures of corpus callosum to brain volume (CC:VOL) and log occipital lobe asymmetries for the entire sample of primates. F = female, M = male.

Figure 3. Scatter plots of individual ratio measures of corpus callosum to neocortical surface area (CC:NEO) and log occipital lobe asymmetries for the entire sample of primates. F = female, M = male.

Figure 4. Mean handedness index (HI) values for each of 13 primate species for quadrupedal (quad) and bipedal (biped) reaching (data from Westergaard et al., 1998).

Figure 5.

A: Regression analyses of mean log occipital lobe asymmetry and mean ratio measures of corpus callosum to neocortex surface area (CC:NEO) for nine primate species. B: Regression analyses of mean handedness index (HI) values for bipedal reaching and mean CC:NEO ratio measures for nine primate species.

Table 1

Nonhuman Primate Subjects Used in the Study

Family and common name	Genus	Species	N
Pongidae			
Chimpanzee	<i>Pan</i>	<i>Troglodytes</i>	7
Bonobo	<i>Pan</i>	<i>Paniscus</i>	4
Orangutan	<i>Pongo</i>	<i>Pygmaeus</i>	4
Gorilla	<i>Gorilla</i>	<i>Gorilla</i>	2
Hylobatidae			
Gibbon	<i>Hylobates</i>	<i>Lar</i>	4
Cercopithecidae			
Rhesus	<i>Macaca</i>	<i>Mulatta</i>	4
Mangabey	<i>Cercocebus</i>	<i>Torquatus</i>	4
Baboon	<i>Papio</i>	<i>Papio</i>	2
Cebidae			
Capuchin	<i>Cebus</i>	<i>Apella</i>	4
Squirrel	<i>Samiri</i>	<i>Sciureus</i>	4

Table 2
Intercorrelations Between Different Measures of Directional Asymmetries in Cerebral Width

Measure	AQ-AF	AQ-PF	AQ-PAR
AQ-PF	.472 ^{**}		
AQ-PAR	.063	.297 [†]	
AQ-OCCP	-.126	.091	.676 ^{**}

Note. AQ-AF = asymmetry quotient (AQ) of anterior-frontal; AQ-PF = AQ of posterior-frontal; AQ-PAR = AQ of parietal lobe; AQ-OCCP = AQ of occipital lobe.

[†]
 $p < .10$ (marginally significant).

^{**}
 $p < .01$.

Table 3

Intercorrelations Between Different Measures of Magnitude of Asymmetries in Cerebral Width

Measure	ABS-AF	ABS-PF	ABS-PAR
ABS-PF	.363 [*]		
ABS-PAR	.129	.200	
ABS-OCCP	.163	.190	.483 [*]

Note. ABS-AF = absolute value of the asymmetry quotient (ABS) of anterior-frontal; ABS-PF = ABS of posterior-frontal; ABS-PAR = ABS of parietal lobe; ABS-OCCP = ABS of occipital lobe.

^{*}
 $p < .05$.

Table 4
Correlation Coefficients, Slopes, and t Values for Each Measure of Hand Preference and Corpus Callosum (CC) Region

Hand preference	CC Region					Total
	Genu	Rostral-midbody	Central-midbody	Caudal-midbody	Splenium	
Bipedal reaching						
R	-.956	-.716	-.497	.107	-.798	-.604
Slope	-0.292**	-0.073*	-0.043	0.009	-0.071**	-0.277†
t	-8.69	-2.72	-1.51	0.28	-3.50**	2.00†
Quadrupedal reaching						
R	-.720	-.591	-.392	-.139	-.789	-.478
Slope	-0.293	-0.081	-0.045	-0.016	-0.095**	-0.294
t	-2.75*	-1.94†	-1.13	-0.37	-3.40**	-1.44

† $p < .10$ (marginally significant).

* $p < .05$.

** $p < .01$.