Anatomical–behavioral relationships: corpus callosum morphometry and hemispheric specialization

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Abstract

We obtained midsagittal measures of the corpus callosum in 60 healthy young adults (right-handed and left-handed males and females), and examined whether individual differences in anatomical measures of callosal connectivity are related to behavioral laterality measures in the same subjects. In an attempt to tap functionally-distinct callosal “channels”, four behavioral laterality tasks were used that differed in sensory modality (visual, auditory, tactile) and/or level of cognitive processing (sensory versus semantic). In addition, the tasks had both intrahemispheric and interhemispheric conditions. Sex differences were found for measures of the posterior body (i.e. isthmus) of the corpus callosum, which, in turn, interacted with handedness. In contrast, only handedness effects were found for the behavioral laterality measures. Anatomical–behavioral correlations did not disclose relationships between callosal size and performance on task conditions requiring sensory interhemispheric integration or transfer. Instead, the correlational findings are consistent with the view that the corpus callosum participates in such higher order “control” functions as the support of bilateral representation of language, functional interhemispheric inhibition, and the maintenance of hemispheric differences in arousal. This is consistent with the finding that regional callosal size is related to the number of small diameter fibers, which are presumed to interconnect homologous association cortices in the two hemispheres.

Key words: Corpus callosum; Hemispheric specialization; Interhemispheric functions; Cerebral asymmetry

1. Introduction

Some 150 years of clinical research with hemisphere-damaged patients, 30 years of research with commissurotomy patients and 40 years of experiments with normal subjects converge on the finding of complementary hemispheric specialization for higher functions in the normal brain. The interpretation of laterality effects in normal subjects is more complicated than that of commissurotomized patients since one must consider the role of the corpus callosum in addition to functional cerebral hemispheric differences (cf. [70]). In particular, we have a limited understanding of the functions of the corpus callosum in higher cognitive processing. For instance, models of laterality effects that assume the corpus callosum serves primarily excitatory functions (e.g. [6,61]) vs. primarily inhibitory functions (e.g. [13,17]) lead to different predictions concerning the relationship between degrees of callosal connectivity and of behavioral laterality effects. The basic excitatory model posits that the corpus callosum serves to share information between the cerebral hemispheres. In this view, laterality effects should decrease with greater callosal connectivity since interhemispheric sharing of information would tend to mask underlying hemispheric differences in tasks that require interhemispheric exchange. Other laterality models argue for a role of the corpus callosum in maintaining independent processing in the two hemispheres (e.g. [13,37,72]), such as the act of “shielding” the influences of one hemisphere from the other [42]. This latter view is compatible with an interhemispheric inhibitory role of the corpus callosum. Here, laterality effects may be heightened by the presence of greater callosal connectivity, since interhemispheric inhibition would highlight the differences between the hemispheres. Physiologically, most, if not all, callosal fibers are excitatory in nature [32]. However, inhibitory influences could be produced by post-callosal inhibitory interneurons. In sum, the inhibitory model predicts that laterality
effects should be positively related to degree of callosal connectivity, while the excitatory model predicts a negative relationship in lateralized tasks that involve callosal transfer. To explore these two competing hypotheses, we obtained morphometric measures of the midsagittal view of the corpus callosum in normal healthy subjects, and determined whether these gross anatomical measures of callosal connectivity were related to individual differences in behavioral measures of hemispheric specialization and interhemispheric communication. Recent histological findings of post-mortem human brains support the assumption that midsagittal corpus callosum area is a reflection of the degree of anatomical connectivity between the cerebral hemispheres. Aboitiz et al. [1] examined 20 human brains and found a significant positive relationship between corpus callosum area and number of small diameter callosal fibers (less than 3 μm in diameter, which constitute about 99.9% of all callosal fibers, and are believed to interconnect homologous association cortices [1]).

There is already compelling evidence that functional differences between the cerebral hemispheres, such as left hemispheric specialization for most language functions, can have measurable anatomical correlates, such as longer Sylvian fissure lengths and larger planum temporale areas on the left than on the right side in most normal subjects [20,24]. Recent findings demonstrate that callosal measures can also vary with anatomical hemispheric differences, and therefore, may similarly be related to functional hemispheric asymmetries. In the rat, the volume of visual area 17 is asymmetric across the hemispheres, and this asymmetry is in turn negatively correlated with the density of callosal terminations in this area [57]. This finding suggests that greater anatomical hemispheric asymmetry is associated with decreased callosal connectivity. Analogous findings have been obtained in human brains. Aboitiz et al. [2] found that in males, but not in females, hemispheric asymmetries in post-mortem measurements of Sylvian fissure length and planum temporale area were both significantly and negatively correlated with the midsagittal area of the isthmus of the corpus callosum. The isthmus lies in the posterior body of the corpus callosum (see Fig. 1a) and contains fibers from the peri-Sylvian region [16,50]. Aboitiz et al.’s [2] finding indicates that as hemispheric differences in anatomical measures from posterior language areas increase, the size of the corresponding callosal region tends to decrease. This finding is also consistent with the view that there may be a need for greater callosal connectivity in less lateralized brains [68].

An inverse relationship between hemispheric asymmetries and callosal measures is consistent with Witelson [67,68] and Habib et al. [26] who found larger corpus callosums in subjects demonstrating left hand preferences than in consistent-right-handers. Left-handed subjects on average exhibit smaller behavioral laterality effects than right-handers, suggesting that their cerebral hemispheres are functionally more similar than those of right-handers [8]. In turn, left-handers have greater anatomical hemispheric symmetry than right-handers, at least for measures of the peri-Sylvian area [40,63]. Both the behavioral and the anatomical evidence are thus consistent with the view that left-handers are more likely to have bilateral representation of language functions. Witelson [68] proposed that left-handers may require greater callosal connectivity in order to support their bihemispheric language functions. Other studies, however, have failed to find differences in corpus callosum size between left- and right-handed groups [28,35,46,47,55,62]. This matter has been clouded by differences across studies in (i) the method used for classifying handedness groups, (ii) the material used (post-mortem vs. MRI), and (iii) subject demographics (e.g. cancer patients vs. healthy volunteers). One issue examined in the present study is whether different handedness classifications (i.e. consistency vs. direction of hand preferences) affect group differences in callosal morphometry.

Kertesz et al. [35] were the first to measure total midsagittal corpus callosum area and behavioral laterality effects in the same individuals, and they failed to find any anatomical–behavioral relationships. Subsequent investigations have considered subdivisions of the corpus callosum, which presumably reflect functionally distinct “channels”. To date, these latter studies have used verbal dichotic listening tests for investigating behavioral laterality effects [30,47]. Contrary to the findings of Kertesz.
et al. [35], O'Kusky et al. [47] demonstrated significant negative correlations between a behavioral laterality index and both total midsagittal callosal area and the areas of anterior subdivisions of the corpus callosum. The conflicting results could be a function of the stimuli used since Kertesz et al. [35] used consonant–vowel (CV) syllables while O'Kusky et al. [47] used dichotic words. Hines et al. [30], using nonsense CV syllables, also did not find any significant correlations between a laterality measure and the areas of any of the four callosal regions examined. However, they did obtain a marginally significant negative correlation between the behaviorally lateralized measure and the combined areas of the splenium (i.e. the posterior fifth of the corpus callosum) and the isthmus. Could it be that the finding of Hines et al. [30] with nonsense syllables is related to the sensory functions ascribed to the posterior corpus callosum (cf. [25,56]), while the result of O'Kusky et al. [47] with words is related to the putative semantic functions of the anterior corpus callosum (cf. [59])? We will show that this is not so.

In order to more thoroughly investigate the possibility that behavioral laterality effects may vary with callosal size, we examined the relationships between corpus callosum morphometry and behavioral measures from four lateralized tasks: (i) lateralized visual nonsense-shape discrimination, (ii) lateralized texture discrimination, (iii) dichotic listening to CV syllables, and (iv) lateralized lexical decision with associative priming. These tasks were systematically chosen to vary by sensory modality (visual, tactile, or auditory) and type of processing (decisions based on perceptual vs. semantic features), in order to tap different functions of the corpus callosum that are presumably topographically-distinct. There is considerable anatomical (e.g. [16,27,31,38,43,50]) and clinical data suggesting that the corpus callosum is by-and-large topographically organized with respect to functionally-distinct cortical areas. Patients with lesions of discrete callosal regions exhibit isolable disconnection syndromes. Visual disconnection is produced by lesions to the posterior splenium [14,56]. Auditory disconnection is associated with lesions of the isthmus area [3,65], although other evidence suggests a more anterior location [15,22,56]. Tactile disconnection for non-verbalizable stimuli is evident with lesions to the body of the corpus callosum [33], particularly the mid-body [5]. Finally, an interesting case study by Sidtis et al. [59] suggests a relationship between the anterior corpus callosum and verbal-semantic processing.

All of the tasks except dichotic listening were designed to have both unilateral/intrahemispheric conditions (i.e. trials where stimuli were restricted to a single visual field or hand) and bilateral/interhemispheric conditions (i.e. trials where stimuli were presented across the visual fields or hands). In this manner, laterality effects were obtained from the intrahemispheric conditions, while the interhemispheric conditions enabled us to directly test the hypothesis that individual differences in performances on tasks requiring cross-callosal comparisons or integration may be related to individual differences in callosal size (e.g. [52]).

To summarize, a callosal excitation or transfer hypothesis would predict positive correlations between the sizes of specific callosal regions and performances for corresponding interhemispheric conditions of a specific modality and/or level of processing. In the case of the intrahemispheric conditions, we need to distinguish tasks that exhibit exclusive hemispheric specialization (“callosal relay” in Zaidel [70]), as in the dichotic listening task, from tasks that allow independent hemispheric processing of contralateral stimuli (“direct access” in Zaidel [70]), as we expect in visual shape discrimination, tactile comparison, and primed lexical decision. For the dichotic listening task, the transfer hypothesis predicts a negative correlation between corpus callosum morphometry (particularly the “posterior body” where auditory fibers cross) and the right ear advantage. This is because the laterality effect reflects transfer of the left ear signal from the right hemisphere to the left hemisphere (e.g. [70]), and presumably, the more effective the interhemispheric auditory transfer, the smaller the right ear advantage. For direct access tasks, the excitation/transfer hypothesis predicts no correlation between hemispheric scores and callosal morphometry. By contrast, a callosal inhibition hypothesis would predict a negative correlation between the scores of one hemisphere or the laterality effect and the size of the inhibitory callosal “channel”. Of course, if the callosal channel serves to “shield” the separate hemispheres, then a larger channel should correlate positively with the performance in one or both hemispheres. This in turn could result in a positive (or negative) correlation of channel size with the laterality effect. Thus, the theory is strongly underdetermined by possible empirical outcomes.

2. Materials and methods

2.1. Subjects

Sixty graduate students from varied fields of specialization at the University of California, Los Angeles were the subjects for both the magnetic resonance imaging and the behavioral testing. Half of the subjects were right handed and half were left handed for writing, and both sexes were equally represented, resulting in 15 subjects per sex x handedness group. Ages ranged from 21 to 43 years (Mean = 28.2 years), and there were no significant group differences in age. All of the subjects were born and educated in North America, 90% were Caucasian and the others were either Asian-American or African-American. A questionnaire
was used to screen subjects for past or present neurological disorders, visual or auditory impairments, and dyslexia.

2.2. Measure of handedness

Handedness was assessed using a modified version of the Edinburgh Handedness Inventory [48]. It included nine items which assessed hand preference for writing, drawing, throwing a ball, striking a match, slicing bread with a knife, using a spoon, comb, toothbrush, and scissors.

All 30 of the self-reported right-handed subjects were found to be consistent-right-handers, demonstrating no left hand preference for any of the nine handedness items. Furthermore, none had immediate family members (parents or siblings) that were left handed. The 30 self-reported left-handed subjects consisted of 14 consistent-left-handers (i.e. no right hand preference for any of the tasks) and 16 mixed-handers (i.e. right hand preference for at least one task). There were equal numbers of males and females in these two left-handed groups. Unless specified otherwise, the consistent-left-handers and the mixed-handers were treated as one group and will hereafter be referred to as left-handers.

2.3. Magnetic resonance imaging

Midsagittal brain images were obtained from a 0.3 tesla FONAR Beta 3000 magnetic resonance imager, using the following parameters: TR = 500 ms, TE = 28 ms, FOV = 19.2 cm. Slice thickness was between 5 and 7 mm and images were magnified to approximately 1.5 x life size to obtain accurate measures of the corpus callosum. Midsagittal cerebral area was also determined at 1 x magnification.

2.4. Anatomical measurements of the corpus callosum

Tracings were made of the midsagittal views of the corpus callosum and the cerebral cortex. Each structure was traced twice, by two different experimenters, and the measures were averaged across the experimenters as the correlation coefficients between them were large (e.g. r = 0.95 for total corpus callosum area). The tracings were digitized using a Hewlett Packard Scanjet Scanner, and computerized algorithms were used to partition the corpus callosums and to acquire the morphometric measurements.

2.5. Corpus callosum partitions

We examined two different methods for partitioning the corpus callosum into subregions. The first method, adapted from Witelson [68], derives subdivisions based on fractions of the maximum anterior-posterior corpus callosum length (Fig. 1a). The second method, adapted from S. Clarke et al. [12], uses a curved reference line that takes the curvature of the corpus callosum into account (Fig. 1b). In both cases, corpus callosums were subdivided into halves, thirds, and the posterior fifth. This resulted in the following five subdivisions listed in an anterior-to-posterior direction: (1) anterior third (rostrum, genu, and anterior body), (2) anterior midbody, (3) posterior midbody, (4) isthmus and (5) splenium.

In addition to the callosal area measurements, two linear measures of the corpus callosum were determined as shown in Fig. 1c: (1) maximum splenial width and (2) minimum body width (from the region between the anterior-third and the splenium). These widths were obtained from measures made perpendicular to the curved reference line.

2.6. Normalization procedures

Midsagittal corpus callosum area did not significantly correlate with midsagittal cerebral area (r = 0.23, P > 0.05). Since corpus callosum size was not dependent on cerebral size, callosal measures were not normalized for cerebral area.

Corpus callosum subdivision measures were highly correlated with overall corpus callosum area. Therefore, in addition to non-normalized or actual measures, we also examined regional corpus callosum measures normalized for total corpus callosum area (i.e. measured as percent of total corpus callosum area). This normalization procedure may reveal group differences in the representation or "importance" of specific corpus callosum subregions when overall corpus callosum size has been controlled. Normalized linear measures were also examined using the square root of total corpus callosum area (to provide a unit-less measure).

2.7. Behavioral laterality tasks

2.7.1. Lateralized shape discrimination—visual modality

For this first task, subjects decided whether pairs of visually-presented geometric figures were the same or different. The stimuli were 20 different Vanderplas 12- to 16-point geometric figures [66], presented as identical or different pairs to either the left visual hemifield (LVF), the right visual hemifield (RVF), or bilaterally (i.e. one figure appeared in each visual hemifield). Fig. 2 shows a LVF "different" and a bilateral "same" presentation. Forty unique stimulus pairs were constructed—20 "same" pairs and 20 "different" pairs—such that all 20 of the original figures were equally represented. All 40 pairs were
presented in all three visual field conditions (LVF, RVF, and bilateral), resulting in 120 test trials. The figures subtended from 1.6° to 2.3° in visual angles, with the innermost edge presented 2° from the vertical meridian. For unilateral conditions, the figures were positioned one above another, separated by 2.4° of visual angle, while in bilateral conditions the figures were positioned along the horizontal meridian (Fig. 2). Twelve practice trials were provided, using figures different from those used in the test set.

The experiment took place in a dimly lit room, and a chin rest was used to minimize head movements and to maintain a fixed eye-to-screen distance. Each trial began with an auditory "Ready!" prompt, as a reminder to fixate on a central fixation dot (1° in diameter). The stimulus was then presented for 50 ms onto a back-projection screen. Same and different responses were made by means of a toggle switch positioned at the midline. The direction that the toggle key was pushed (i.e. forward or backward) to indicate a “same” or a “different” response was counterbalanced across the subjects as was whether a subject started with the left or right hand. The response hand was switched half-way through the session.

2.7.2. Lateralized texture discrimination—somatosensory modality

For each trial of this task, subjects felt two pieces of sandpaper and indicated whether or not they were of identical roughness. Subjects used two fingers (index and middle) from either the right hand, left hand, or one finger from each hand (dichhaptic). The following nine grades of 3 M brand sandpaper were used, where each value represents the number of grains per linear inch: 50, 60, 80, 100, 120, 150, 180, 220, and 240 grit. Non-identical pairs were formed by combining each grade of sandpaper with one that differs by either one, two, or three steps. Six such pairings (50–60, 150–180, 150–220, 180–220, 180–240, and 220–24) were excluded from the analyses since accuracies for these pairs were at chance across subjects. Consequently, 15 unique “different” pairs were considered. Nine identical pairs were formed using the nine grades of sandpaper. A greater number of non-identical than identical pairs were used to allow for a wide range of differences in roughness. This was done to accommodate individual differences in tactile sensitivity, therefore reducing the possibility of obtaining floor and ceiling effects. Subjects were not told about this manipulation. All 26 stimulus pairs were presented in each stimulation condition (i.e. right hand, left hand, and dichhaptic). The test was run in blocks of five trials, with all trials in a block performed with the left hand, right hand, or dichhaptically. The sandpaper stimuli were frequently replaced with new material.

The 5 cm x 6 cm pieces of sandpaper were affixed to blocks of wood, which were placed sandpaper-side down on top of a wooden, toplevel box-like structure that contained a front opening for the fingers. A divider between the two pieces of sandpaper ensured that a single finger only felt its corresponding piece of sandpaper. Prior to receiving the test stimuli, the subject felt the entire sandpaper spectrum with each hand. For the actual test, the subject was blind-folded, the hands were positioned palms-up, the two designated fingers were inserted into the box, and when cued, the pieces of sandpaper were felt by lifting and then pulling the fingers across the sandpaper in a single motion. The subject indicated whether the stimuli were the “same” or “different” by motioning with a thumbs-up or thumbs-down response, respectively, using the hand(s) which was (were) stimulated.

2.7.3. Dichotic listening to consonant-vowel syllables—auditory modality

The dichotic stimuli were pairs of the six CV syllables Bee, Dee, Gee, Pee, Tee, Kee produced from natural tokens, aligned and matched using the PCM system at Haskins Laboratories with the help of Dr. Terry Halwes. All possible pairings, except identical pairings, were made and equally represented in blocks of 60 trials. For each dichotic trial, one CV syllable was presented to the right ear while at the same time a different syllable was presented to the left ear. The inter-trial interval was 7 s. The stimuli were played at 68 dB (HTL) on an Akai Pro1000 2-track stereo reel-to-reel tape deck. Calibrated telephonic TDH-49P headphones were used, and the channels were reversed half-way through the session. A practice set of 30 binaural trials (i.e. both ears received the same stimulus) were given to familiarize the subject with the six CV syllables. Subjects responded by pointing to the corresponding consonant (i.e. B, D, G, P, T, or K) that was printed on a response sheet. For the 120 dichotic test trials, the subject was instructed to try to identify both the left and right ear stimulus on each trial. The response hand was alternated half-way through the experiment, and the initial hand used for responding was counterbalanced across subjects. The percentage of left ear and right ear stimuli that were identified was determined.
2.7.4. Laterized lexical decision with associative priming—semantic facilitation

The lexical decision task consisted of laterized primes, all concrete nouns, and laterized targets, half of which were common concrete nouns and half of which were orthographically regular non-words. Of the targets that were words, half were associatively related to the respective prime word and half were unrelated. The associated prime-target pairs (e.g. NEST-BIRD) were chosen from free association norms (using a criterion probability of 0.40 or greater of responding with the target word when given the prime word [51, 58]). Unrelated (or unassociated) word pairs (e.g. COAL-WEED) were matched to associated pairs, controlling for word length, familiarity, and concreteness [64]. In addition to the 32 associated pairs and 32 unassociated pairs there were 64 prime–non-word pairs (e.g. SOAP-DERN). These orthographically regular non-words were formed by taking real words and either rearranging or replacing one or two letters. Prime and target word length varied from three to seven letters. The 128 stimuli were arranged into 8 blocks, each block containing a randomized ordering of 4 associated pairs, 4 unassociated pairs, and 8 non-word pairs. Within each block, the four possible prime–target visual field combinations [i.e. LVF prime–RVF target (LR), RL, LL, and RR] were equally represented, and occurred equally often for each of the three pair types. All subjects received the same order of stimulus pairs, but the visual field assignments for each stimulus pair was pseudorandomly determined for each subject. Thirty-two additional pairs were derived for practice trials.

The stimuli subtend a visual angle of 2° to 3°, and were presented at an eccentricity of 2° (between the fixation marker and the inner edge of the stimulus) on a monochrome monitor controlled by an IBM-PC compatible computer. The experiment took place in a dimly lit room and the subject sat with his/her head resting on a chin rest. Each trial consisted of the following sequence: 100 ms laterized prime, 500 ms interstimulus-interval, 60 ms laterized target, and a 3-s period to respond if the target was a word (i.e. Go/No go response), before commencement of the next trial. Subjects were told to ignore the prime as it would always be a real word. Subjects were not informed about the manipulation of prime–target association. The response hand was alternated halfway through a session, and the initial response hand was counterbalanced across subjects.

3. Results

3.1. Corpus callosum morphometry

3.1.1. Comparison of the two partitioning methods

For each of the five regional corpus callosum areas, correlations determined between the corresponding regions from the straight-line and curved-line partitioning methods were all large and significant ($r = 0.96$ for the anterior-third, $r = 0.92$ for the anterior midbody, $r = 0.93$ for the posterior midbody, $r = 0.87$ for the isthmus, and $r = 0.88$ for the splenium; $P < 0.001$ in all cases). Sex and handedness effects were similar for the two methods.

### Table 1

Means and standard deviations (S.D.) for midsagittal measures of the corpus callosum (CC) and for midsagittal cerebral area for right-handers (RHdrs) and left-handers (LHdrs) of both sexes.

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
<th>Univariate ANOVAs</th>
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<tr>
<td></td>
<td>RHdrs ($n = 15$)</td>
<td>LHdrs ($n = 15$)</td>
<td>RHdrs ($n = 15$)</td>
</tr>
<tr>
<td>Mean S.D.</td>
<td>Mean S.D. S.D.</td>
<td>Mean S.D. S.D.</td>
<td>Mean S.D. S.D.</td>
</tr>
<tr>
<td>Midsagittal cerebral</td>
<td>10274 739</td>
<td>10257 903</td>
<td>9194 760</td>
</tr>
<tr>
<td>Total CC</td>
<td>668.8 81.8</td>
<td>706.2 94.0</td>
<td>659.3 78.4</td>
</tr>
<tr>
<td>Anterior third</td>
<td>260.8 38.6</td>
<td>285.5 46.4</td>
<td>256.9 40.1</td>
</tr>
<tr>
<td>Anterior midbody</td>
<td>81.6 15.1</td>
<td>84.3 15.1</td>
<td>79.0 12.7</td>
</tr>
<tr>
<td>Posterior midbody</td>
<td>71.4 15.0</td>
<td>69.8 10.6</td>
<td>71.0 9.3</td>
</tr>
<tr>
<td>Isthmus</td>
<td>52.2 11.7</td>
<td>57.9 11.1</td>
<td>59.3 13.2</td>
</tr>
<tr>
<td>Splenium</td>
<td>202.4 21.2</td>
<td>208.4 30.7</td>
<td>192.6 24.4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Linear measures (mm)</th>
<th>Min. body width</th>
<th>Max. splenial width</th>
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</thead>
<tbody>
<tr>
<td>Mean S.D.</td>
<td>Mean S.D.</td>
<td>Mean S.D.</td>
</tr>
<tr>
<td>Midsagittal cerebral</td>
<td>3.8 0.9</td>
<td>12.3 1.0</td>
</tr>
<tr>
<td>Total CC</td>
<td>4.2 1.0</td>
<td>12.2 1.1</td>
</tr>
<tr>
<td>Anterior third</td>
<td>4.6 1.0</td>
<td>12.5 1.7</td>
</tr>
<tr>
<td>Anterior midbody</td>
<td>4.6 0.8</td>
<td>12.5 1.8</td>
</tr>
<tr>
<td>Posterior midbody</td>
<td>0.38*</td>
<td>0.21</td>
</tr>
<tr>
<td>Isthmus</td>
<td>1.15</td>
<td>0.02</td>
</tr>
<tr>
<td>Splenium</td>
<td>0.80</td>
<td>0.05</td>
</tr>
</tbody>
</table>

The test statistic ($F$) for each univariate analysis of variance test is also given (df = 1, 56).

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

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consistent with previous findings [4]. Consequently, only the results from the straight-line partitioning method will be presented since this has been the more common method used by researchers.

### 3.1.2. Sex and handedness effects

Table 1 contains the means for midsagittal cross-sectional cerebral area and for the non-normalized corpus callosum measures from each sex by handedness group. For each anatomical measure, effects of sex and handedness were tested using univariate two-way analyses of variance (ANOVA).

#### 3.1.3. Midsagittal cerebral area

The mean midsagittal cerebral area was 11% larger for males than for females ($F_{1.56} = 22.62, P < 0.001; M = 102.7 \text{ cm}^2$ and $M = 92.5 \text{ cm}^2$, respectively). There were no significant effects of handedness.

#### 3.1.4. Corpus callosum measures

1) **Non-normalized corpus callosum measures.**

The total corpus callosum area, the areas of the five subdivisions, and the two callosal width measures were examined. While there were no significant effects involving handedness, a significant sex difference for minimum body width was evident ($F_{1.56} = 6.38, P < 0.025$), being larger in females ($M = 4.6 \text{ mm}$) than in males ($M = 4.0 \text{ mm}$).

2) **Corpus callosum measures normalized for total callosal area.**

The normalized minimum body width measure was also significantly larger in females than in males ($F_{1.56} = 9.11, P < 0.01; M = 17.7\%$ and $15.2\%$, respectively). In addition, normalized isthmus area was larger in females than in males ($F_{1.56} = 4.81, P < 0.05; M = 8.70\%$ and $7.98\%$, respectively). Again, there were no significant effects involving handedness.

#### 3.1.5. Handedness inventory scores—other classifications

There were no handedness differences in callosal measures when subjects were categorized as right handed or as left handed by whether all hand preference items were performed with the right hand or not, respectively. Since the left-handed group is actually comprised of both mixed-handed and consistent-left-handed individuals, all of the subjects were reclassified as consistent-right-handed (CRH), mixed-handed (MH), or consistent-left-handed (CLH). There were still no significant effects of handedness nor any significant interactions of sex and handedness. Witelson [67,68] and Habib et al. [26] found significant handedness effects in callosal measures, but unlike the present study, their “non-consistent-right-handed” groups contained either very few CLH cases (Habib et al.) or no CLH cases (Witelson). For comparison purposes, analyses of our data were repeated excluding the CLH subjects. Again, no significant main effects of handedness were found. However, the sex by handedness interaction was significant for the normalized isthmus measure ($F_{1,42} = 4.24, P < 0.05$) and approached significance for non-normalized isthmus area ($F_{1,42} = 4.06, P = 0.0504$). As can be seen in Fig. 3, the isthmus constitutes a greater proportion of the corpus callosum in CRH females than in CRH males, while no sex difference is apparent for the MH group. More importantly, CRH females and MH females exhibit similar normalized isthmus sizes, while the greater isthmus ratios for MH males than for CRH males approached significance ($P = 0.07$; Fig. 3). As discussed below, this sex by handedness interaction for the isthmus is identical to that found by Witelson [68], and partially replicates findings of Habib et al. [26] and of Denenberg et al. [18].

### 3.2. Behavioral laterality tasks

Since the texture discrimination and dichotic listening tasks only provided accuracy data, for consistency we chose to statistically examine accuracies, rather than reaction times, for each of the four behavioral tasks.

#### 3.2.1. Lateralized shape discrimination—visual modality

Both between-subject (sex, handedness) and within-subject [spatial position (LVF, RVF, bilateral)] effects were tested using an ANOVA. There were no significant effects that included sex or handedness. The main effect of spatial position was significant ($F_{2,112} = 6.02, P < 0.01$), and tests of simple effects indicated that accuracies were higher for bilateral presentations ($M = 90.3\%$ correct) than for either LVF ($M = 86.9\%$) or RVF ($M = 87.2\%$) conditions, which did not significantly differ from one another.
3.2.2. Lateralized texture discrimination—somatosensory modality

Effects of sex, handedness, and stimulation condition (right hand, left hand, dichaptic) were examined. Although there were no significant main effects of sex or handedness, the interaction proved significant ($F_{1,56} = 4.90, P<0.025$). Tests of simple effects showed right-handed females to be more accurate ($M=78\%$ correct) than left-handed females ($M=72\%$ correct), while males showed no handedness effect ($M=73\%$ and $75\%$ correct for right- and left-handed males, respectively). No significant differences were found as a function of whether the sandpaper was felt with two fingers from the right hand, the left hand, or with a finger from each hand.

3.2.3. Dichotic listening to consonant-vowel syllables—auditory modality

The findings from this task are presented in greater detail in Clarke et al. [11]. Tests for effects of sex, handedness, and ear (left, right) revealed significant main effects of handedness ($F_{1,56} = 9.99, P<0.01$) and ear ($F_{1,56} = 41.30, P<0.0001$). Right-handers tended to identify more stimuli ($M=53.1\%$ identified) than left-handers ($M=47.8\%$), and overall, subjects showed a right ear advantage ($M=56.8\%$ right ear items identified vs. $44.2\%$ for left ear items). A significant handedness by ear interaction ($F_{1,56} = 5.98, P<0.025$) indicated that the right ear advantage ($\%{\text{RE}}-\%{\text{LE}}$) was greater for right-handers ($17.3\%$) than for left-handers ($7.8\%$).

3.2.4. Lateralized lexical decision with associative priming—semantic facilitation

In order to examine effects of semantic relatedness, accuracies were determined for trials in which targets were English words. The variables were: sex, handedness, prime visual field, target visual field, and association (i.e. whether a target word was semantically related or unrelated to the preceding prime word). The $2\times 2\times 2\times 2$ ANOVA did not reveal any significant effects involving prime visual field, so the data were re-analyzed collapsing across this variable. Two significant main effects were found, that of target visual field ($F_{1,56} = 29.58, P<0.0001$) and of association ($F_{1,56} = 25.30, P<0.0001$). Accuracies were higher for RVF target presentations ($M=81.4\%$ correct) than for LVF presentations ($M=70.2\%$), and they were higher for associated prime-target pairs ($M=79.7\%$) than for unassociated pairs ($M=71.8\%$). The only significant interaction was that of handedness $\times$ target visual field $\times$ association ($F_{1,56} = 6.22, P<0.025$). As can be seen in Fig. 4, the simple interaction of target visual field $\times$ association was significant for right-handers ($F_{1,56} = 9.63$) but not for left-handers ($F_{1,56} = 0.18$). For right-handers, semantic facilitation (i.e. the performance advantage of associated pairs over unassociated pairs) was greater for LVF target presentations than for RVF targets. In order to determine whether priming in the LVF is significantly different for right- and left-handers, the simple interaction of handedness $\times$ association for LVF targets was tested and was found to be significant ($F_{1,56} = 6.16, P=0.011$). Semantic priming enhanced LVF performance for right-handers, but not for left-handers.

3.2.5. Other classification of handedness

Using the three handedness groups CRH, MH and CLH, we examined effects of handedness and sex on the overall laterality indices from the four tasks, as well as on an additional measure from the primed lexical decision task—the visual field difference in semantic facilitation. In selecting a method for deriving a laterality index, we took into consideration the need to correct (e.g. [9]) or not to correct (e.g. [34]) for overall performance. Consequently, we chose to use the simple difference formula ($R-L$) when this difference measure did not correlate significantly with overall performance across all subjects; otherwise, the laterality measure lambda [9] was used as it corrects for overall performance. Only the primed lexical decision task showed such a relationship ($r_{56} = -0.38, P<0.01$, and for all other tasks $-0.15 < r < 0.18$).

Once again, significant handedness effects were found for dichotic listening ($F_{2,54} = 4.07, P<0.025$) and for the

---

Fig. 4. Mean accuracies and standard errors for right-handers ($n=30$) and left-handers ($n=30$) on the primed lexical decision task when target words that were either associated or unassociated to a preceding prime word were presented in the LVF or RVF. *$P<0.05$; **$P<0.01$; ***$P<0.001$. 

Table 2
Summary of findings from four behavioral laterality tests in 60 subjects

<table>
<thead>
<tr>
<th>Laterality effect</th>
<th>Sex diff. in</th>
<th>Hand. diff. in</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lat. eff.</td>
<td>Int. cond.</td>
</tr>
<tr>
<td>1. Visual discrim.</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2. Texture discrim.</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3. Dichotic listen.</td>
<td>+</td>
<td>N/A</td>
</tr>
<tr>
<td>4. Primed lexical decision</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>

Presence (+) or absence (−) of significant effects are noted for the overall laterality effect (Lat. eff.) for each task, as well as for sex and handedness differences in the laterality effect and in performance for the interhemispheric condition (Int. cond.).

visual field difference in semantic facilitation ($F_{2,54} = 3.20, P < 0.05$). Interestingly, contrasts across the three handedness groups revealed a dissociation for these two findings. For the dichotic listening task, consistent-right-handers had significantly ($P < 0.01$) greater right ear advantages ($M = 17.3\%$) than did mixed-handers ($M = 4.2\%$), while consistent-left-handers had an intermediate value ($M = 11.9\%$) that was not significantly different from the other two groups. In contrast, the visual field difference for semantic facilitation was relatively large and leftward-biased in consistent-right-handers ($M = -10.5\%$ difference), which was significantly ($P < 0.025$) different from the smaller, rightward-biased value in consistent-left-handers ($M = 3.5\%$ difference). Here, mixed-handers showed the intermediate value ($M = -0.4\%$ difference) which did not differ significantly from the other two handedness groups.

3.2.6. Summary of behavioral findings

Table 2 summarizes the key findings from the four laterality tasks. Laterality effects were evident for the two tasks employing verbal stimuli (dichotic listening and primed lexical decision), with the right ear/VF advantages being consistent with left hemispheric specialization for these tasks. There were no sex differences in these laterality effects, but handedness effects were found. The findings suggest that behavioral hemisphere differences were more pronounced in right-handers than in left-handers for phonetic processing of CV syllables and for semantic priming. When consistency of handedness was taken into account, dissociations were found across the two tasks. For dichotic listening, right-handers were significantly more lateralized than those left-handed writers with mixed hand preferences. In contrast, visual field differences in semantic priming differed between right-handers and those subjects with consistent left hand preferences. Finally, there was no evidence for a difference between males and females or between right- and left-handers in interhemispheric functioning, as inferred from performances from the “interhemispheric” conditions of these tasks.

3.3. Anatomical-behavioral relationships

For each behavioral task, Pearson product–moment correlation coefficients were determined between each of the corpus callosum measures and (i) a laterality index, (ii) performance on the “interhemispheric” condition (where appropriate), (iii) performances on the unilateral conditions (i.e. right and left:VF, hand, or ear), (iv) the overall performance for the unilateral conditions (i.e. L + R), (v) an absolute laterality measure (that reflects degree of laterality irrespective of direction), and (vi) the difference between the interhemispheric and intrahemispheric conditions (i.e. a relative measure of interhemispheric advantage/disadvantage). No significant correlations were found for the latter three behavioral measures, and hence these results will not be presented further. In order to decrease the probability of obtaining spurious results without unduly sacrificing the power of detecting meaningful ones, a significance level of 0.01 was used (two-tailed). This was chosen over more conservative approaches for the reason that this study is a first attempt to investigate whether there are specific relationships between functionally-distinct callosal regions and both hemispheric and interhemispheric measures from several behavioral laterality tasks. This then is an exploratory study intended to generate hypotheses for confirmation in future experiments.

Midsagittal cerebral area did not correlate significantly with any of the behavioral measures. Significant relationships were found for non-normalized corpus callosum measures, but not for normalized callosal measures. The findings associated with each of the four behavioral tests follow.

3.3.1. Lateralized shape discrimination—visual modality

As can be seen from Table 3, the laterality index from the visual shape discrimination task correlated positively with total corpus callosum area and with the two midbody areas. An example of a scatterplot associated with one of these findings is shown in Fig. 5A. Note that there are
Table 3
Correlation coefficients between corpus callosum (CC) measures and behavioral measures from the lateralized visual shape discrimination task for 60 subjects

<table>
<thead>
<tr>
<th>Behavioral measures</th>
<th>RVF-LVF</th>
<th>Bi</th>
<th>LVF</th>
<th>RVF</th>
</tr>
</thead>
<tbody>
<tr>
<td>CC area measures</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total CC</td>
<td>0.33*</td>
<td>0.19</td>
<td>-0.16</td>
<td>0.13</td>
</tr>
<tr>
<td>Anterior-third</td>
<td>0.25</td>
<td>0.11</td>
<td>-0.15</td>
<td>0.07</td>
</tr>
<tr>
<td>Anterior midbody</td>
<td>0.38*</td>
<td>0.14</td>
<td>-0.26</td>
<td>0.06</td>
</tr>
<tr>
<td>Posterior midbody</td>
<td>0.41*</td>
<td>0.13</td>
<td>-0.23</td>
<td>0.12</td>
</tr>
<tr>
<td>Isthmus</td>
<td>0.16</td>
<td>0.22</td>
<td>-0.04</td>
<td>0.12</td>
</tr>
</tbody>
</table>

| CC linear measures  |         |     |     |     |
| Min. body width     | 0.26    | 0.15| 0.05| 0.31|
| Max. splenial width | 0.21    | 0.22| -0.02| 0.18|

Laterality index (RVF-LVF), bilateral (Bi), left visual field (LVF), right visual field (RVF).
*P<0.01.

Table 4
Correlation coefficients between corpus callosum (CC) measures and behavioral measures from the lateralized tactile discrimination task for 60 subjects

<table>
<thead>
<tr>
<th>Behavioral measures</th>
<th>Rh-Lh</th>
<th>Di</th>
<th>Lh</th>
<th>Rh</th>
</tr>
</thead>
<tbody>
<tr>
<td>CC area measures</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total CC</td>
<td>0.40*</td>
<td>0.11</td>
<td>-0.25</td>
<td>0.15</td>
</tr>
<tr>
<td>Anterior-third</td>
<td>0.36*</td>
<td>0.02</td>
<td>-0.31</td>
<td>0.05</td>
</tr>
<tr>
<td>Anterior midbody</td>
<td>0.37*</td>
<td>0.06</td>
<td>-0.24</td>
<td>0.13</td>
</tr>
<tr>
<td>Posterior midbody</td>
<td>0.40*</td>
<td>0.10</td>
<td>-0.05</td>
<td>0.33</td>
</tr>
<tr>
<td>Isthmus</td>
<td>0.27</td>
<td>0.09</td>
<td>-0.06</td>
<td>0.19</td>
</tr>
<tr>
<td>Splenium</td>
<td>0.24</td>
<td>0.19</td>
<td>-0.14</td>
<td>0.10</td>
</tr>
</tbody>
</table>

| CC linear measures  |       |     |     |     |
| Min. body width     | 0.32   | 0.02| 0.04| 0.25|
| Max. splenial width | 0.00   | 0.18| 0.04| 0.03|

Laterality index (Rh-Lh), dichhaptic (Di), left hand (Lh), right hand (Rh).
*P<0.01.

approximately as many subjects demonstrating a RVF advantage (i.e. positive laterality values) as there are that demonstrate a LVF advantage (negative values), consistent with the absence of an overall visual field difference for this task. And yet, the callosal measures tended to be smaller in those subjects who had superior LVF performances and tended to be larger in those individuals with superior RVF performances. The possible implications of this finding will be discussed below.

Also note that none of the splenium measures, nor any other callosal measure, correlated significantly with performance on the bilateral (i.e. interhemispheric) condition, even though the splenium is critical for cerebral visual interhemispheric transfer.

3.3.2. Lateralized texture discrimination—somatosensory modality

Anatomical–behavioral relationships for the lateralized texture discrimination task (Table 4) are similar to those found for the visual discrimination task. The laterality index correlated positively and significantly with total corpus callosum area, the two midbody regions, and, unlike the visual discrimination task, with the anterior third area as well. Examination of the scatterplots (e.g. Fig. 5B) shows a similar pattern of results to that found for the visual discrimination task.

Performance on the “interhemispheric” (dichhaptic) condition was once again unrelated to callosal measures.

3.3.3. Dichotic listening to consonant–vowel syllables—auditory modality

There were no significant relationships between any callosal measure and the laterality index for the dichotic listening task (Table 5). It is interesting that in contrast to the visual and texture discrimination tasks, dichotic listening did show a significant behavioral laterality effect, and yet individual variations in the laterality measure were unrelated to corpus callosum morphometry.

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Fig. 5. Relationships between posterior midbody corpus callosum size and laterality scores from the (A) visual and (B) tactile discrimination tasks. Least-squares regression lines are also shown.
Table 5
Correlation coefficients between corpus callosum (CC) measures and behavioral measures from the dichotic listening task for 60 subjects

<table>
<thead>
<tr>
<th>Behavioral measures</th>
<th>RE-LE</th>
<th>LE</th>
<th>RE</th>
</tr>
</thead>
<tbody>
<tr>
<td>CC area measures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total CC</td>
<td>-0.14</td>
<td>-0.18</td>
<td>-0.34*</td>
</tr>
<tr>
<td>Anterior-third</td>
<td>-0.15</td>
<td>-0.16</td>
<td>-0.35*</td>
</tr>
<tr>
<td>Anterior midbody</td>
<td>-0.14</td>
<td>-0.11</td>
<td>-0.29</td>
</tr>
<tr>
<td>Posterior midbody</td>
<td>-0.13</td>
<td>-0.08</td>
<td>-0.25</td>
</tr>
<tr>
<td>Isthmus</td>
<td>-0.08</td>
<td>-0.12</td>
<td>-0.21</td>
</tr>
<tr>
<td>Splenium</td>
<td>-0.05</td>
<td>-0.17</td>
<td>-0.21</td>
</tr>
<tr>
<td>CC linear measures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Min. body width</td>
<td>-0.11</td>
<td>-0.02</td>
<td>-0.17</td>
</tr>
<tr>
<td>Max. splenial width</td>
<td>0.23</td>
<td>-0.26</td>
<td>0.10</td>
</tr>
</tbody>
</table>

Laterality index (RE-LE), left ear report (LE), right ear report (RE). *P<0.01.

The dichotic listening task does not have an interhemispheric condition per se, that is, there is no condition in which stimuli that reach opposite hemispheres need to be compared. However, evidence cited above indicates that accurate report of left ear items, but not right ear items, is dependent on interhemispheric transfer in individuals with left hemisphere language specialization. The inferred interhemispheric condition of left ear accuracy did not correlate significantly with any callosal measure (Table 5). Similar negative results were obtained when correlations were determined only for right-handers, or only for those subjects demonstrating a right ear (left hemisphere) advantage on this task.

We predicted that right ear accuracy would not be related to callosal measures since right ear inputs are directly received by the left cerebral hemisphere and hence do not require interhemispheric transfer, at least for the majority of individuals in which phonetic processing is specialized to the left hemisphere. Yet surprisingly, it was specifically right ear scores that correlated significantly, and negatively, with total corpus callosum area and the anterior-third region (Table 5). Since 15% of the subjects demonstrated a reversed laterality effect, presumably reflecting right hemisphere specialization, we also determined correlations using “superior” and “inferior” ears scores rather than right and left ear scores. Similar findings were obtained, whereby callosal measures correlated significantly and negatively with superior ear scores (i.e. inferred non-interhemispheric condition) but were unrelated to inferior ear scores (i.e. inferred interhemispheric condition) [11]. Further exploratory analyses of each subgroup revealed similar significant correlational findings for right-handers (for total corpus callosum area, anterior-third, and anterior midbody) but not for left-handers, and for males (all corpus callosum area measures except for posterior midbody) but not for females [11].

3.3.4. Lateralized lexical decision with associative priming—semantic facilitation

Since this was the only task in which the simple laterality index (R–L) was significantly correlated with overall performance, the laterality index “lambda” which corrects for overall performance was used for correlations. None of the callosal measures correlated significantly with this laterality measure (Table 6).

The interhemispheric effect investigated in this task was that of interhemispheric semantic priming. Subjects were more accurate in correctly classifying a target stimulus as a word when it was preceded by a semantically related prime than when it was preceded by a semantically unrelated word. This was true for both within visual field and across visual field priming. Since semantic facilitation was effective in the cross-visual field conditions (i.e. LVF-prime/RVF-target and RVF-prime/LVF-target), interhemispheric integration must have occurred. Thus, the cross-visual field condition for associated prime-target pairs was considered as the interhemispheric condition for semantic facilitation. As can be seen in Table 6, none of the callosal measures were significantly correlated with performance in the interhemispheric condition, nor were they correlated with overall performance in LVF or RVF target conditions.

Additional anatomical-behavioral exploratory analyses were carried out that considered primed lexical decision measures and measures of the isthmus and minimum body

Table 6
Correlation coefficients between corpus callosum (CC) measures and behavioral measures from a primed lexical decision task for 60 subjects

<table>
<thead>
<tr>
<th>Behavioral measures</th>
<th>lambda</th>
<th>Assoc Cross-VF</th>
<th>LVF</th>
<th>RVF</th>
</tr>
</thead>
<tbody>
<tr>
<td>CC area measures</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total CC</td>
<td>0.02</td>
<td>-0.12</td>
<td>-0.08</td>
<td>0.03</td>
</tr>
<tr>
<td>Anterior-third</td>
<td>-0.13</td>
<td>-0.09</td>
<td>0.02</td>
<td>-0.04</td>
</tr>
<tr>
<td>Anterior midbody</td>
<td>0.04</td>
<td>-0.05</td>
<td>-0.06</td>
<td>0.04</td>
</tr>
<tr>
<td>Posterior midbody</td>
<td>0.07</td>
<td>-0.05</td>
<td>-0.05</td>
<td>0.04</td>
</tr>
<tr>
<td>Isthmus</td>
<td>0.14</td>
<td>-0.06</td>
<td>-0.12</td>
<td>0.10</td>
</tr>
<tr>
<td>Splenium</td>
<td>0.15</td>
<td>-0.17</td>
<td>-0.19</td>
<td>0.08</td>
</tr>
<tr>
<td>CC linear measures</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Min. body width</td>
<td>0.03</td>
<td>0.03</td>
<td>-0.02</td>
<td>0.08</td>
</tr>
<tr>
<td>Max. splenial width</td>
<td>0.18</td>
<td>-0.11</td>
<td>-0.10</td>
<td>0.12</td>
</tr>
</tbody>
</table>

Laterality index (lambda), cross visual field semantic priming condition (Assoc Cross-VF), left visual field targets (LVF), right visual field targets (RVF).
Table 7

Correlation coefficients are shown for all subjects and for individual subgroups between the laterality index from associated trials on the primed lexical decision task and the sizes of normalized isthmus area and of normalized minimum body width.

<table>
<thead>
<tr>
<th>Normalized measures</th>
<th>All subjects (n = 60)</th>
<th>Right Hdrs (n = 30)</th>
<th>Left Hdrs (n = 30)</th>
<th>Males (M) (n = 30)</th>
<th>Females (F) (n = 30)</th>
<th>Z (M-F)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isthmus area</td>
<td>-0.05</td>
<td>-0.04</td>
<td>-0.09</td>
<td>-0.52*</td>
<td>0.18</td>
<td>2.76*</td>
</tr>
<tr>
<td>Min. body width</td>
<td>-0.05</td>
<td>-0.11</td>
<td>-0.17</td>
<td>-0.48*</td>
<td>0.38</td>
<td>3.36**</td>
</tr>
</tbody>
</table>

Z-scores (Z) representing the difference in the correlations between males and females for each anatomical measure are also shown.

* For the female subgroup, one subject was excluded due to an outlying laterality score.

*P<0.01; **P<0.001.

width since (i) group differences were found for the isthmus and minimum body width, a finding shared by other studies [10,18,26,62,68], (ii) the isthmus appears to be the callosal region containing the highest concentration of fibers from posterior language (i.e. peri-Sylvian) areas, and (iii) isthmus measures have been shown to be related to anatomical hemispheric asymmetries in both Sylvian Fissure length and planum temporale area in males but not in females [2]. The anatomical–behavioral relationships examined in Table 6 were subsequently determined for right-handers, left-handers, males, and females separately. No significant (P < 0.01) correlations were found for either actual or normalized isthmus and minimum body width measures.

The laterality index presented in Table 6 included both associated and unassociated prime-target pairs. Since semantic relatedness affected performance, laterality indices were determined for associated and unassociated conditions separately. Isthmus and minimum body width measures were unrelated to the laterality index from the unassociated condition. When the laterality index from associated trials were considered, males showed significant, negative correlations with both the normalized isthmus and the normalized minimum body width measures (Table 7). In contrast to these negative correlations, the corresponding correlations for females were positive. This approached significance for normalized isthmus area (r = 0.38, 0.05 > P > 0.01) and was significant for normalized minimum body width (r = 0.47, P < 0.01). However, the correlations for females were largely due to a subject with an outlying laterality score (2.9 S.D. from the mean). When this subject was excluded, the correlations were not significant, although the differences between the correlations for males and females were significant (Table 7).

To determine whether or not such relationships were limited to the isthmus region, correlations were determined between the laterality index for associated pairs and all other callosal measures. No significant relationships were found (P > 0.05 in each case), suggesting that the laterality–callosal relationship is unique to the isthmus.

Table 8

Summary of anatomical–behavioral relationships indicating behavioral measures that correlated positively (pos), negatively (neg), or did not correlate (−) with callosal morphometry measures

<table>
<thead>
<tr>
<th>Laterality index</th>
<th>Interhem. cond.</th>
<th>LH</th>
<th>RH</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Visual discrimination</td>
<td>pos</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>2. Texture discrimination</td>
<td>pos</td>
<td>−</td>
<td>neg</td>
</tr>
<tr>
<td>3. Dichotic listening</td>
<td>−</td>
<td>neg</td>
<td>−</td>
</tr>
<tr>
<td>4. Primed lexical decision</td>
<td>neg*</td>
<td>−</td>
<td>−</td>
</tr>
</tbody>
</table>

LH and RH refer to left and right hemisphere conditions, respectively, based on side of stimulus presentation.

* Males only for associated prime-target pairs.

A summary of the anatomical–behavioral correlation findings for all four tasks is presented in Table 8.

4. Discussion

4.1. Individual differences in corpus callosum morphometry

Females had larger minimum body widths (actual and normalized measures) as well as larger normalized isthmus sizes compared to males. Larger minimum body widths in females has previously been reported [10]. The minimum body width is invariably found within the isthmus, and the isthmus has been known to be larger in females than in males when measured as percent of total corpus callosum area, but not when measured as actual area [62,68], which was found in the present study. Other studies have either found no significant sex difference in isthmus-related measures [4,26,49] or an effect that favored males [2,18]. However, except for Aboitiz et al. [2], all other studies did not measure relative isthmus area in the same manner as ourselves. Steinmetz et al. [62] and Witelson [68]. In Aboitiz et al.’s Chilean sample, actual isthmus area was larger in males than in females, while no
sex difference was found for the normalized measure. Because the isthmus region appears to be the primary locus for fibers from posterior language areas, a sexual difference in isthmus morphometry may be indicative of differences in hemispheric language organization between males and females [68]. Given this accumulating, although not conclusive, evidence for sex differences in the morphometry of the posterior body of the corpus callosum, future studies should take a more refined approach to examining the morphometric parameters that best characterize this putative sex difference. This endeavor will likely be aided by parallel studies investigating how fiber composition varies across different callosal regions, how this relates to anatomical asymmetries, and how it may differ for males and females. Indeed, Aboitiz et al. [1,2] found no sex differences in the number or types of fibers that cross the isthmus, or in planum temporale asymmetries, but there was a negative correlation between the two in males, and not in females.

Our failure to find handedness differences in callosal measures is consistent with the majority of studies that have examined this issue [28,35,46,47,55,62]. Those studies that did find handedness effects have suggested that the effect may depend on classifying subjects by consistency of hand preferences, rather than by writing hand or direction of hand preferences [26,68] (however, see [62]). Although we did not find overall handedness effects, we did replicate previous findings of a sex by handedness interaction in the size of the isthmus [18,26,68] when consistency of handedness was considered. These three other studies had samples with either very few subjects who had consistent left hand preferences [26] or no such subjects [18,68]. In turn, we found the sex by handedness effect for the isthmus only when consistent-right-handers and mixed-handers were considered, excluding consistent-left-handers. The intermediate isthmus sizes of consistent left-handers appeared to diminish the overall effect (however, see [62]). As for the interaction itself, the common finding for all four studies (our own and the three others) is that males exhibit a handedness effect, with isthmus measures being smaller in consistent-right-handed males than in mixed-handed males (this approached significance in the present study), while females do not show handedness differences in the isthmus, as shown in Fig. 6. Interestingly, this finding parallels the report that for males, but not females, isthmus area is smaller in individuals with greater anatomical hemispheric asymmetries of the planum temporale and Sylvian fissure [2]. Since our dichotic listening findings revealed larger laterality effects in consistent-right-handers than in mixed-handers, it appears that both behavioral (at least for dichotic listening) and anatomical hemispheric asymmetries are larger in males with smaller isthmus sizes.

We can only speculate as to why the isthmus is associated with hemispheric asymmetries only in males. Sex differences in hormonal influences is a possible factor. Findings in the rat indicate that perinatal hormonal environment can have marked effects on the ontogeny of the
corpus callosum [19,44]. Intrauterine hormonal influences may even contribute to individual differences in callosal development within a particular sex (cf. [23, p. 445]).

4.2. Corpus callosum size and excitatory callosal functions

The above findings could be interpreted as supporting an excitatory model of callosal function. That is, the larger isthmus in mixed-handed males may have allowed for more effective interhemispheric transfer of auditory signals in the dichotic listening task, resulting in smaller laterality effects than observed in right-handed males. However, mixed-handers had smaller right ear scores than right-handers rather than larger left ear scores. The smaller right ear advantages seen in the mixed-handers, who are left handed for writing, is more likely related to the well-established finding that hemispheric localization of language functions is more variable in left-handers than in right-handers. Thus, behavioral laterality measures may be related to differences in hemispheric competence and consequently to hemispheric asymmetries, with isthmus size being yoked to the anatomical asymmetries for ontogenetic reasons (e.g. through simultaneous growth; cf. [2,57]). This does not necessarily mean that individual variations in isthmus size is of no significance to callosal functions. As previously suggested, the larger isthmus in mixed-handed males than in right-handed males may serve increased demands on interhemispheric communication with increasing bilateral representation of language functions (cf. [68]).

4.3. Isthmus size and semantic-verbal functions

Correlational findings from the primed lexical decision task provide compelling support for the view that for males, but not females, isthmus size is associated with cerebral hemispheric differences for posterior language functions. Those males with strong RVF advantages, indicating strong left hemisphere advantages, tended to have relatively small isthmus and minimum body width measures. It is interesting that these anatomical–behavioral relationships were only apparent for the lexical decision condition with semantic facilitation. Previous findings from right-handed split-brain patients as well as from normal subjects indicate that both cerebral hemispheres can make lexical decisions, although the left hemisphere is usually superior [70]. Furthermore, our behavioral findings in right-handers suggest that the right hemisphere is particularly aided by semantic facilitation, consistent with previous findings [70]. In sum, isthmus size appears to be related to hemispheric differences in lexical functions under conditions in which the right hemisphere is “performing” at its optimal level.

4.4. Corpus callosum size and interhemispheric sensory transfer

We did not find evidence to support the hypothesis that performance on “interhemispheric” tasks of a particular sensory modality are related to the size of the corresponding sensory-specific callosal region (cf. [52]). Since performances on the “interhemispheric” conditions of our tasks were unrelated to any of our callosal measures, it could be that effective interhemispheric transfer of sensory stimulus information depends on a certain minimum amount of callosal connectivity, which presumably all of our subjects had. Indeed, multiple sclerosis patients with atrophied corpus calsums do exhibit behavioral indices of impaired interhemispheric functions [54]. Alternatively, effectiveness of sensory callosal transfer may depend on the number of large diameter callosal fibers, which is not correlated with callosal size [1]. Of course, individual differences in sensory interhemispheric transfer may still be related to some yet-to-be determined morphometric callosal measures.

4.5. Corpus callosum size and inhibitory callosal functions

The anatomical–behavioral correlational findings from the dichotic listening task were surprising. Previous findings from right-handed commissurotomized patients indicate that (i) the left hemisphere is exclusively specialized for the phonetic processing required in this difficult task, (ii) the ipsilateral auditory pathways are ineffective, causing the inputs from each ear to be lateralized to the contralateral hemisphere, and consequently (iii) the report of left ear items requires right-to-left interhemispheric transfer in order to reach the specialized left hemisphere processors, while the report of right ear items is not dependent on callosal pathways (e.g. [45,60,69]). Yet in our right-handed subjects, we found corpus callosum measures to be unrelated to left ear accuracies, which depend on callosal transfer, while total corpus callosum area and anterior corpus callosum regions correlated significantly and negatively with right ear report, which does not depend on callosal transfer. Because larger corpus callosum measures were associated with worse right ear performance, we have tentatively interpreted this finding as evidence for functional interhemispheric inhibition [11]. We posit that such inhibition or interference arises under the special circumstances where (i) one hemisphere is exclusively specialized for the task, (ii) both hemispheres simultaneously receive stimulus inputs and each proceeds to process them, and (iii) the non-specialized hemisphere is unsuccessful, with results that impede processing by the specialized hemisphere. For the dichotic listening task, the specialized phonetic processors may be localized in the
anterior left hemisphere [7], suggesting that such interference would probably originate from the homologous area in the right hemisphere and be conveyed along anterior callosal pathways. Since left ear auditory information reaches the left hemisphere via more posterior callosal pathways, both right and left ear reports should be affected by the inhibition. However, the accuracy of left ear report depends on additional factors, such as right hemisphere acoustic processing and subsequent interhemispheric transfer. Consequently, left ear scores can be expected to have a smaller, non-significant, association with interhemispheric inhibition.

4.6. Corpus callosum size and cerebral hemispheric arousal

The absence of behavioral laterality effects for the visual and tactile discrimination tasks suggest that neither cerebral hemisphere is generally superior at performing these two perceptually-oriented tasks, consistent with previous findings [29,39]. Despite the presumed functional equivalence between the hemispheres for performing these tasks, individual variations in the laterality indices were significantly correlated with corpus callosum measures. For these tasks, individuals with larger corpus callosums tended to have superior RVF and right hand (i.e. left hemisphere) performances, while those with smaller corpus callosums were likely to have superior LVF and left hand (i.e. right hemisphere) scores. We propose that these behavioral laterality—callosal morphometry relationships may well arise only in situations in which both hemispheres are similarly capable of processing the stimulus information, so that the behavioral laterality effects are primarily a reflection of individual differences in hemispheric arousal (cf. [36,41]). Levy et al. [41] cites behavioral, physiological and clinical evidence supporting the view that there are individual differences in the relative arousal levels of the left and right hemispheres. Unlike hemispheric specialization, hemispheric arousal is assumed to be invariant with stimulus or task parameters. The highly similar, although not identical, patterns of behavioral laterality—corpus callosum correlations in the visual and tactile discrimination tasks is consistent with this task-invariant feature of hemispheric arousal. In this view, the callosal areas associated with hemispheric arousal would tend to have a more anterior callosal representation than the more posteriorly located sensory functions. Laterality indices from the dichotic listening and primed lexical decision tasks are also presumably influenced by hemispheric arousal, but this influence is overshadowed by the pronounced effects of hemispheric specialization. Thus, we propose that the corpus callosum participates in the establishment and/or maintenance of a particular bias in hemispheric arousal within an individual, whereby left and right hemisphere biased individuals would tend to be associated with larger and smaller anterior callosums, respectively.

4.7. Corpus callosum size indexes multiple callosal functions

Table 9 presents a summary of the individual differences observed. The four behavioral laterality effects appear to tap different lateralized functions. In particular, this is true for the two language tasks, showing that phonetic and lexical-semantic processing are lateralized to different degrees. This is supported by the observation that handedness has a different effect on the laterality index in the two tasks: in dichotic listening, consistent-left-handers had an intermediate laterality index between right-handers and mixed-handers, whereas in primed lexical decision, mixed-handers had an intermediate laterality index between consistent-right and consistent-left-handers.

Table 9
Effects of sex (S), handedness (H), and the interaction (S × H) for behavioral laterality effects, relevant corpus callosum (CC) measures and the correlation between them

<table>
<thead>
<tr>
<th>Task</th>
<th>Behavioral lat. effect</th>
<th>CC morphometry</th>
<th>CC vs. behav. lat.</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>S</td>
<td>H</td>
<td>S × H</td>
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<tr>
<td>1. Visual discrim.</td>
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<td>2. Texture discrim.</td>
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<td>3. Dichotic listening</td>
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<tr>
<td>4. Lexical decision</td>
<td></td>
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</tr>
</tbody>
</table>

1 Handedness × ear: right-handers vs. mixed-handers.
2 Sex difference in relation of anterior CC to right ear score.
3 Handedness difference in relation of anterior CC to right ear score.
4 Handedness × visual field × association: difference between right-handers and consistent-left-handers.
5 Sex difference in isthmus for right-handers vs. mixed-handers.
6 Sex difference in relation of isthmus size to laterality index for associated pairs.
In our data, the presence of a behavioral laterality effect (found only for the dichotic listening and lexical decision tasks) did not imply the presence of a correlation between that effect and callosal morphometry (found only for the visual shape and tactile tasks), arguing against the ontogenetic callosal-elimination hypothesis of Galaburda et al. [21] Alternatively, an individual difference (sex or handedness) in a behavioral laterality effect does not imply the same individual difference in callosal morphometry or in the relation between anatomy and behavior. Finally, when significant correlations between behavioral laterality effects and callosal morphometry do occur, they can involve different corpus callosal regions for different tasks.

The absence of any significant relationships between callosal morphometry and performances on the interhemispheric conditions of our tasks suggests that corpus callosum size is not a reliable index of individual differences in interhemispheric transfer of sensory information. Instead, the behavioral laterality–callosal morphometry findings that were significant point to a relationship between corpus callosum size and higher-order “associative” functions of the corpus callosum. We have proposed that these functions may include: interhemispheric support of bilateral language representation, interhemispheric inhibitory control, and interhemispheric influences that contribute to hemispheric differences in arousal. Recent findings on the fiber composition of the human corpus callosum are consistent with the proposed relationship between corpus callosum size and associative, but not sensory, functions. Midsagittal corpus callosum area in humans is unrelated to the number of large diameter callosal fibers (> 3 μm) which have been implicated in sensory interhemispheric transfer, while corpus callosum area is related to the number of smaller diameter fibers which appear to be most prevalent between cortical association areas [1] (see also [38]).

In our model of higher-order callosal functions, the corpus callosum conveys co-residing and channel-specific excitatory and inhibitory control codes, although the proportion of each may vary over different callosal regions. The corpus callosum regions involved and the relative participation of the resident inhibitory and excitatory channels are largely dependent on the cortical localization of the functions required to perform a particular task.

Our study is limited by the inherent problems in interpreting correlational findings, and the potential pitfalls of callosal-phenology. However, the correlational approach permits an initial investigation of whether corpus callosum anatomy and behavioral laterality measures are related in normal living subjects. Given that such relationships appear to exist, we have presented models of interhemispheric functioning and hemispheric specialization that are compatible with these findings. The test of these models will depend on future parallel investigations from experimental and from clinical studies carried out in parallel at the behavioral, physiological and anatomical levels.

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