The Relationship of Age, Gender, Handedness, and Sidedness to the Size of the Corpus Callosum

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Objectives. We correlated the area and size of the corpus callosum, as measured by MR imaging, with the individual's handedness, sidedness, age, and gender.

Materials and Methods. A total of 117 patients (59 male, 58 female) aged 15–75 years were selected for this study. This included 12 persons who were either left-handed or ambidextrous. Each patient was tested extensively to determine handedness and sidedness. Callosal areas and thickness were measured and correlated with brain size.

Results. The body of the corpus callosum decreases in size with age and is larger in right-handed persons. The cross-sectional areas of the genu, splenium, and corpus callosum, overall, do not vary significantly with respect to age, gender, sidedness, or handedness.

Conclusions. The size of the corpus callosum consistently decreases with age. Otherwise, few statistical differences in callosal size relate to gender, sidedness, or handedness.

Key Words. Corpus callosum; corpus callosum, MR; brain, growth and development; brain, MR.

The corpus callosum has been the subject of numerous conflicting studies as to its variation in size with handedness, gender, or age. For instance, Witelson [1] found the corpus callosum to be significantly larger (11%) in left-handed and ambidextrous persons, but Kertesz et al. [2] found no significant differences in callosal size based on handedness. DeLacoste-Utamsing and Holloway [3] found the splenium to be larger in females, whereas Kertesz et al. [2] found no significant difference between genders in the size of the splenium. Hayakawa et al. [4] found the callosal size to decrease in both sexes between ages 40 and 60. Few studies of the size of the corpus callosum, however, have used the excellent anatomic depiction offered by MR imaging, and no attempt has been made to define the relationships of age, gender, handedness, and sidedness to callosal size. Finally, no one has attempted to correlate callosal size with the circumference of the

Received October 15, 1993 and accepted for publication after revision June 27, 1994.

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***Acad Radiol* 1994;1:243–248**

head when comparing different age groups and sexes. We adopted these goals, using MR imaging measurements, for this study.

MATERIALS AND METHODS

A total of 117 patients (59 male, 58 female) with normal findings on MR images of the brain were asked to participate in this study after a review of their scans. Older patients with more atrophy and aging changes than expected for their age were excluded. The selection of patients ensured a representative cross-section of ages between 15 and 75 years for each gender, with approximately 12 male and 12 female patients per decade. Examinations were performed on a Siemens 1.0-T Somatom scanner (Seimans Medical Systems, Iselin, NJ). Each subject was asked to complete a test that determined handedness and sidedness by using questions and activities involving hand, eye, and ear preference. These results were scored for both handedness and sidedness on a scale of 0–10, with 0 indicating a strong right-handed and right-sided person, and 10 for a predominantly left-handed and left-sided person.

To test handedness and sidedness, we gave each subject a handedness test composed of two parts. The first part was a questionnaire the patient filled out about hand preference in activities such as writing, throwing a ball, brushing teeth, and holding a spoon [3, 5–8]. The patients also answered questions on history of handedness for themselves and their families. Questions pertaining to laterality and sidedness in general were included. The second part of the test was active performance, using a fork, cutting with scissors, throwing a punch, initiating a handshake, and picking up objects. As a double check, a test was given that involved a time limit on making perfect Xs with each hand [6]. Eye preference and ear preference also were determined to decide general sidedness (laterality).

Each test was scored and then converted into two numbers for each patient. The first score was derived from all questions involving the hand and its use. This was the handedness score. The second score was derived from the handedness score and the questions involving the eye, ear, and foot. Each question or action was assigned a value of 0, 5, or 10. Zero was assigned for an action carried out by the right hand, 5 for an action carried out by both hands, and 10 for an action carried out by the left hand. The total scores were added up separately for handedness and sidedness, each ranging from 0 to 10 for each subject. Zero to 4 was scored as right-handed and right-sided, 6–10 was scored as left-handed and left-sided, and 4–6 (noninclusive) was considered ambidextrous. The corpus callosum was evaluated on a midline sagittal T1-weighted MR image. Diameters were measured at five points: the widest part of the genu, the widest part of the splenium, and three equidistant points through the callosal body. These points were determined by digitally dividing the anteroposterior length of the corpus callosum into four equal parts and measuring the thickness of the callosal body at the three resulting division lines (Fig. 1). Total and segmental areas from these four callosal parts also were calculated directly from the digitized image. The axial cross-sectional area of the brain was measured at the level of the callosal body. Segmental diameters and segmental and total areas were calculated for the entire studied population and separately for the two genders, those 45 years of age or older versus those under 45, and right-handed/sided versus nonright-handed/sided and versus the entire patient population. Last, the above analyses were repeated after dividing the diameter or callosal area by the cross-sectional area of the brain at the level of the body of the corpus callosum. $P < 0.05$ was considered statistically significant. Stepwise linear regression was done to evaluate the relationship of age, gender, and handedness/sidedness to callosal size.

RESULTS

Because of the small number of study participants, results for left-handed and ambidextrous persons were combined into a single "nonright" category. One hundred four patients were right-sided and 106 were right-

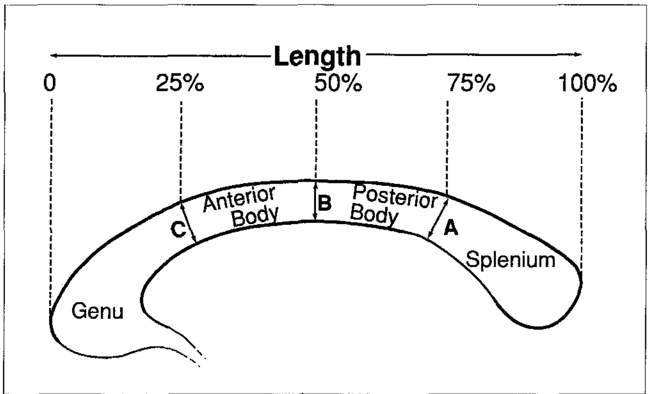

FIGURE 1. A diagram of the corpus callosum shows how the corpus callosum was divided into four equal parts with the thicknesses measured at these points.

handed, versus only 13 nonright-sided and 11 nonright-handed patients. The age of the nonright subjects ranged from 15 to 69 years, and the group included only three females and three over the age of 45. For the combined handedness and sidedness score, 105 subjects were right-handed and only 12 were nonright-handed. Patients were divided by age into two groups: those 45 or younger (n = 60) and those older than 45 years (n = 57). In addition, patients older than age 65 years were analyzed further separately.

The corpus callosum tended to be longer in nonright versus right-handed and right-sided subjects (Table 1). However, after correction for the brain area, this difference was not statistically significant. After correction for brain size, significant differences were found in the thickness of the anterior, mid, and posterior body of the corpus callosum. Generally, the thickness of the callosal body was greater in the right-handed and right-sided subjects than in their nonright counterparts. After correction for brain area, we found no statistically significant variation in the size of the genu and splenium of the corpus callosum between right- and nonright-handed and -sided subjects. The overall callosal area, after correction, was significantly larger in right-sided persons. The overall area of the anterior and posterior portions of the callosal body also was significantly greater in right-handed and right-sided persons than in the nonright-handed and nonright-sided persons (Table 2).

There was a generalized decrease in the segmental callosal thickness (Table 1) and segmental areas (Table 2) with aging after correcting for each patient's brain area. This decrease was most remarkable in the overall length/area and in the anterior body. The callosal length measured an average 7.44 cm in those patients aged 45 years or younger versus 7.32 cm in those older than 45 years (P = 0.012). The mean length for those patients aged greater

TABLE 1: Callosal Thickness in 117 Subjects

	n	Callosal Length (cm)	Thickness Genu (cm)	Thickness Body			Thickness Splenium (cm)
				C (cm)	B (cm)	A (cm)	
Handedness and Sidedness							
Right							
Sided	104	7.30	1.20	0.70[a, b]	0.70[a, b]	0.60[a, b]	1.20
Handed	106	7.30	1.20	0.70[a, b]	0.70[a, b]	0.60	1.20
Combined	105	7.30	1.20	0.70[a, b]	0.70[a, b]	0.60[a, b]	1.20
Nonright							
Sided	13	7.50	1.30	0.60[a, b]	0.60[a, b]	0.50[a, b]	1.20
Handed	11	7.70	1.30	0.60[a, b]	0.60[a, b]	0.50	1.20
Combined	12	7.55	1.30	0.60[a, b]	0.55[a, b]	0.50[a, b]	1.20
Age							
≤ 45 years	60	7.44[a, c]	1.20	0.69[c]	0.68	0.58	1.23
Right sided	51	7.41	1.19	0.71[a, c]	0.70[c]	0.60	1.23
Right handed	52	7.40	1.19	0.71[a, c]	0.70[c]	0.59	1.23
Right combined	51	7.41	1.19	0.71[a, c]	0.70[c]	0.60	1.23
> 45 years	57	7.32[a, c]	1.20	0.59[c]	0.63	0.53	1.23
Right sided	53	7.31	1.20	0.60[a, c]	0.64[c]	0.54	1.24
Right handed	54	7.31	1.20	0.60[a, c]	0.64[c]	0.53	1.24
Right combined	54	7.31	1.20	0.60[a, c]	0.64[c]	0.53	1.24
> 65 years	25	7.28[a]	1.15[a]	0.54[a]	0.59[a]	0.52[a]	1.21
Gender							
Total male	59	7.52[d]	1.22	0.64	0.66	0.54[a, d]	1.26
Right sided	51	7.50[d]	1.20	0.66	0.68	0.55	1.26
Right handed	50	7.48	1.21	0.65	0.67	0.54[a, d]	1.26
Right combined	49	7.49[d]	1.20	0.65	0.68	0.55	1.26
Total female	58	7.23[d]	1.18	0.65	0.65	0.58[a, d]	1.21
Right sided	53	7.24[d]	1.19	0.65	0.66	0.58	1.21
Right handed	56	7.24	1.19	0.65	0.66	0.58[a, d]	1.21
Right combined	56	7.24[d]	1.19	0.65	0.66	0.58	1.21

[a] Statistically significant (p<.05) after correction for brain size.
[b] Right significantly different from nonright.
[c] ≤ 45 years of age significantly different from >45.
[d] Males significantly different from females.
A; B, C: Thickness (cm) posterior, mid, and anterior callosal body, respectfully.

TABLE 2: Callosal Area in 117 Subjects

	n	Callosal Area (cm^2)	Area Genu (cm^2)	Anterior Body Area (cm^2)	Posterior Body Area (cm^2)	Max Splenium Area (cm^2)
Handedness and Sidedness						
Right						
Sided	104	7.01[a, b]	2.46	1.17[a, b]	1.05[a, b]	2.36
Handed	106	7.01	2.46	1.17[a, b]	1.05	2.36
Combined	105	7.01[a, b]	2.46	1.17[a, b]	1.05[a, b]	2.36
Nonright						
Sided	13	6.99[a, b]	2.44	1.06[a, b]	0.97[a, b]	2.46
Handed	11	6.99	2.44	1.08[a, b]	1.03	2.46
Combined	12	6.91[a, b]	2.35	1.07[a, b]	1.03[a, b]	2.35
Age						
≤ 45 years	60	7.27	2.52	1.21	1.12[c]	2.42
Right sided	51	7.34	2.54	1.24[c]	1.14	2.41
Right handed	52	7.30	2.53	1.24[c]	1.14[c]	2.40
Right combined	51	7.34	2.54	1.24[c]	1.15[c]	2.41
> 45 years	57	6.98	2.44	1.12	1.00	2.42
Right sided	53	7.01	2.45	1.12[c]	1.01	2.43
Right handed	54	7.01	2.45	1.12[c]	1.00[c]	2.43
Right combined	54	7.01	2.45	1.12[c]	1.00[c]	2.43
> 65 years	25	6.77	2.33	1.06[a]	1.00	2.41
Gender						
Total male	59	7.17	2.52	1.17	1.07	2.41
Right sided	51	7.23	2.54	1.20	1.10	2.40
Right handed	50	7.18	2.54	1.19	1.08	2.38[a, d]
Right combined	49	7.22	2.55	1.20	1.08	2.40
Total female	58	7.08	2.44	1.16	1.05	2.43
Right sided	53	7.12	2.45	1.16	1.06	2.44
Right handed	56	7.12	2.45	1.16	1.06	2.44[a, d]
Right combined	56	7.12	2.45	1.16	1.06	2.44

[a] Statistically significant ($P<.05$) after correction for brain size.
[b] Right significantly different from nonright.
[c] ≤ 45 years of age significantly different from >45.
[d] Males significantly different from females.

than 65 years was 7.28 cm, which also was significantly decreased from the younger patients ($P = 0.045$). Similarly, the thickness of the anterior callosal body decreased from 0.69 cm in patients younger than or equal to 45 years to 0.59 and 0.54 cm in patients older than 45 and 65 years, respectively ($P = 0.028$, $P = 0.0003$). Similar aging changes were found in the overall callosal and anterior body areas. Although decreases with age were seen in the genu and posterior callosal body, these changes were not found to be statistically significant after correcting for each patient's brain area.

The callosal length was significantly longer in males, including those who were right-sided, compared with females. However, the overall callosal area, after correction for brain area, was not significantly different between genders. The posterior callosal body of males was significantly thinner than in females. However, the segmental area of the anterior and posterior callosal body, after correction for the brain area, was not significantly different between genders. We found no difference in the maximum thickness of the splenium between genders. However, the cross-sectional area of the splenium in right-handed males was smaller than that in right-handed females.

DISCUSSION

The corpus callosum and its role as the main interhemispheral commissural pathway have been the subject of numerous studies dealing with laterality and handedness. The corpus callosum is believed to play a key role in cerebral dominance. The inhibitory action of the dominant hemisphere over the subordinate hemisphere is carried out via the corpus callosum [5, 9]. The resulting dominance of one hemisphere over the other creates, except for ambidexterity, a dominant handedness and sidedness in each person [5, 10]. Three factors affect the size of the corpus callosum: gender, age, and handedness and sidedness.

Handedness

The terms "handedness" and "sidedness" refer to the fundamental neuroanatomic and psychologic aspects of motor coordination wherein a person uses one hand or side in preference to the other. Studies done by Hecaen [5] and Luria [11] have shown that 60% of left-handed individuals have language functions governed by the left hemisphere and visuospatial functions by the right hemisphere. Compared with this, nearly 99% of right-handed individuals have language functions in the left and visuospatial functions in the right hemisphere. Other studies have shown that left-handed individuals have greater bihemispheric representation of cognitive functions than do right-handed individuals [12]. As a result, left-handed individuals may have less consistent lateralization of language and visuospatial functions. To have coordination between hemispheres, it has been theorized that left-handed individuals require a greater number of fibers connecting the two sides. As a result, it has been suggested that the size of the corpus callosum should be larger in left- than in right-handed individuals.

Several studies done by Witelson [1, 13, 14] and Denenberg et al. [15] have shown that the total collosal area, and particularly the isthmus part of the corpus callosum, was larger by 11% to 38% in nonconsistent right-handed individuals (left-handed and ambidextrous persons) compared with consistent right-handed individuals. Habib [16] also showed a difference of 11% between the two groups for males. The isthmus is composed of the fibers connecting the parietotemporal fibers of two sides, which mediate the cognitive functions like language and are asymmetrically distributed [13, 16]. These studies, therefore, support the hypothesis that variation in callosal anatomy relates to variation in functional asymmetry [17].

Our data and studies by Kertesz and others [2, 18–22], however, contradict the results of the studies of Witelson and Habib. We found that the absolute size of the body of the corpus callosum and overall callosal area was larger in consistently right-handed than in nonright-handed individuals, although these differences were reduced after correction for the size of the brain. The conflict between the findings of Witelson [1, 13, 14] and Habib [16] and those of Kertesz [2] and our study may be explained by differing study design. Witelson used postmortem sections of the brains of mostly elderly patients, and his sample size was small. MR imaging and postmortem examinations may not be comparable because of the effects of cell death and formalin fixation and because correction for brain size was not done.

Sexual Dimorphism

Evidence of sexual dimorphism of the corpus callosum was first reported by DeLacoste-Utamsing and Holloway [3], who reported that the splenium on MR imaging was smaller in females. The studies that demonstrated females to have a larger corpus callosum than males inferred that females require more interhemispheric connections because of less lateralization of cognitive function. This inference was supported by Hines et al. [22], who, using female subjects only, showed that the posterior part of the corpus callosum, particularly the splenium, had a negative correlation with language lateralization.

Other investigators [1, 2, 13, 19, 20, 23–28] have found no difference in the size of the splenium between genders, although they did find the areas of the genu, body, and the total corpus callosum were larger in males than in females. However, although our data showed no difference for right-handed and right-sided men versus women with respect to splenial thickness, right-handed women had a statistically larger splenial area compared with their male counterparts (2.44 vs 2.38, $P < 0.05$).

Effects of Aging on Corpus Callosum

Our study showed a general decrease in thickness and length of the corpus callosum with aging. The decrease in thickness was most marked in persons greater than age 65 years in whom the decrease was significant in all portions of the corpus callosum (Table 1). For instance, the thickness of the anterior callosal body decreased from 0.69 cm in patients aged 45 years or younger to 0.54 cm for those greater than 65 years ($P < 0.0003$).

Hayakawa et al. [4] have shown that the thickness of the corpus callosum decreases with increasing age in both genders. Witelson [14] has shown a similar decrease but only in males. Allen et al. [29] showed a decrease in thickness of the anterior two thirds of the corpus callosum (which carry axons from frontal, premotor, and motor cortices) only, with the posterior one third (which carries axons from somesthetic, parietal, occipital, and temporal cortices) remaining unchanged.

The decreasing callosal size in older patients could be expected because of the generalized atrophy of cortical neurons that occurs with advancing age. Atrophy not only causes a decrease in the amount of gray matter but also a loss of white matter. This loss of white matter is due to a quantitative decrease in myelinated fibers and water [30]. This decrease in neuronal size, number of myelinated fibers, and the amount of myelination with aging is responsible for the decrease in size of the corpus callosum.

In conclusion, our study shows that the body of the corpus callosum decreases in size with age, especially in persons greater than age 65 years. In addition, the body of the corpus callosum is increased in size in right-handed persons. After correcting for brain area, the cross-sectional areas of the genu, splenium, and the corpus callosum overall do not vary significantly with age, gender, sidedness, or handedness.

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