Animal Cells and Systems
Vol. 15, No. 4, December 2011, 274–278

Taylor & Francis
Taylor & Francis Group

Effects of age and gender on spatial orientation of human corpus callosum in healthy Koreans

Seung Jun Hwang[a], Chan Park[a], Hea Nam Hong[a], Ji Yeon Ryu[b], In Sung Park[c] and Im Joo Rhyu[c]*

[a]*Department of Anatomy and Cell biology, College of Medicine, University of Ulsan, 388-1 Pungnap-2 Dong, Songpa-Gu, Seoul, 138-736, Republic of Korea;* [b]*Hanil General Hospital, Neurology, 388-1 Sangmoon-Dong, Dobong-Ku, Seoul, 132-703, Republic of Korea;* [c]*Korea University, College of Medicine, Anatomy, 126-1 Anam Dong, SungBuk, Seoul, 136-705, Republic of Korea*

(*Received 7 March 2011; received in revised form 12 April 2011; accepted 20 May 2011*)

The changes in the corpus callosum (CC) with age and gender remain largely subject to dispute, which might come from the different strategies for analyzing the size and shape of CC. We have investigated this issue by measuring some variables reflecting the spatial orientation of CC on magnetic resonance imaging in Koreans, which minimize individual variances in the brain. The subjects were composed of young adults in their twenties (51 male, 59 female) and elderly adults in their sixties and seventies (60 male, 71 female). The total area of CC, length and height of CC, the central angle and the four angles suggested by Oka et al. were measured. The whole area and the central angle of CC were not significantly affected by age and gender. The height and length of CC were significantly greater in elderly people. The angle connecting genu, upper notch of pons and splenium was significantly larger in the elderly group. Furthermore, all four angles were significantly different between male and female subjects. These results confirm that the spatial orientation of CC is influenced by age and gender.

Keywords: corpus callosum; gender; aging; spatial orientation; angle; magnetic resonance imaging; Korean

Introduction

The corpus callosum (CC) is the largest structure among commissural fibers connecting both cerebral hemispheres to exchange information. It has been proposed that the role of the CC is to coordinate many neurological behaviors, and the CC in human is known to contain 200–350 million nerve fibers (Sperry 1982).

Many studies have examined the correlation of CC with gender (DeLacoste-Utamsing and Holloway 1982; Clarke et al. 1989), language dominance (Clarke et al. 1993) and hand preference (Witelson and Goldsmith 1991), and neurological problems such as autism (Piven et al. 1997), schizophrenia (Panizzon et al. 2003), epilepsy (Hermann et al. 2003) and dyslexia (Hynd et al. 1995) have been suggested to be related to the morphology and function of CC.

Sexual dimorphism of the CC is one of the long-standing issues. Some studies reported gender difference in size and shape (DeLacoste-Utamsing and Holloway 1982; Sullivan et al. 2001; Allen et al. 2003), whereas others failed to reveal gender difference in CC morphology (Bishop and Wahlsten 1997). This controversy might come from different analysis strategies and a lack of standards for the size and shape of CC (Dubb et al. 2003). In addition to size, the effect of gender on the spatial orientation of CC was evaluated through adult magnetic resonance imaging (MRI) analysis by Oka et al., who reported that the splenium of CC is lower in males than in females (Oka et al. 1999), and Hwang et al. reported that male neonates have significantly greater heights of CC compared with female neonates based on ultrasonographic studies (Hwang et al. 2004).

In addition to the effect of gender, there have been some controversies on the effect of aging on the changes in CC. Witelson reported that aging led to a reduction in area (Witelson 1989), and others found that the reduction in area was followed by decreasing length as well (Byne et al. 1988; Allen et al. 1991). On the other hand, an increased length of CC with aging has also been reported (Sullivan et al. 2002; Suganthy et al. 2003). Furthermore in addition to increased length of CC with aging, an increased height of the CC was also observed by Takeda et al. (2003).

The above reports suggest that length and angle are useful parameters for characterizing CC, in addition to area and thickness, which have been employed in many studies. Individual differences could be minimized if we measure angular parameters, because they are determined by the relative configuration of neighboring structures. Therefore, we investigated the effect of aging and gender on the CC with linear and angular parameters in neurologically healthy Koreans.

*Corresponding author. Email: irhyu@korea.ac.kr

ISSN 1976-8354 print/ISSN 2151-2485 online

http://dx.doi.org/10.1080/19768354.2011.607512
http://www.tandfonline.com

Materials and methods

Subjects

This study included 241 subjects, comprising mixed healthy young and old Korean adults (Table 1). After volunteers were given an explanation of the study's purposes and methods, brain images were obtained by MRI, showing healthy profiles after neurological examination and minimal mental status examination. Inclusion criteria were no neurological signs, no intracranial lesions on MRI, and no history of neurological illness, current or past psychiatric illness, alcoholism, or drug addiction problems.

MRI protocol

Magnetic resonance imaging was performed on 1.5-tesla Magnetom vision (Siemens, Erlangen, Germany). The following parameters were used for the volumetric acquisition: TR = 9.7 ms, TE = 4 ms, flip angle 12 degrees; slice thickness: continuous 1.5 mm, matrix 512×512. The files were saved as a DICOM format and imported into V-work 3.5 program (Cybermed LTD, Seoul Korea). The midsagittal slice of each brain image volume was manually extracted and saved for further analysis (Figure 1).

To measure area and length, the midsagittal section image was imported into Adobe Photoshop 7.0 and processed for further analysis. The processed image was transferred to Scion Image (Scion Corporation), and length (L), height (H), whole area of CC (S) and some angles of CC were measured as follows (Figure 2). A line (L) was drawn through the inferior borders of the splenium and genu, and a second (H) line was drawn vertical to this base line (L) to the highest point of CC. The CC was inscribed into he minimum rectangle. The apex angle (CA) of the isosceles triangle was estimated based on the method of Tomaiuolo et al. (2002): it was measured by calculating the value of the vertex angle of the isosceles triangle which had the same base and height of the minimum rectangle circumscribing the CC (Figure 2A).

To understand the spatial characteristics of the CC, four angles (A, B, C, D) were measured (Figure 2B) according to Oka et al. (1999) with a minor modification. The upper notch of the pons was used for the analysis point. Four lines (1–4) were drawn as in Figure 2B; a line (1) connecting the inferior margin of genu and splenium of CC, a line (2) connecting the analysis point and the inferior margin of genu, a line (3) connecting the analysis point and the inferior margin of splenium, and a line (4)extrapolated to the dorsal of the brain stem. Angle A is the upper side between line 2 and line 3 at the upper notch of the pons. Angle B is the anterior upper angle between line 1 and line 4. Angle C is the anterior lower angle between line 1 and line 3. Angle D is the anterior upper angle between line 2 and line 4.

Table 1. Subject summary.

	Male	Mean age	Female	Mean age	Total
Age	*n*		*n*		*n*
20–30	51	24.6 ± 2.9	59	24.9 ± 2.8	110
60–75	60	69.3 ± 3.4	71	68.7 ± 3.3	131
Total	111		130		241

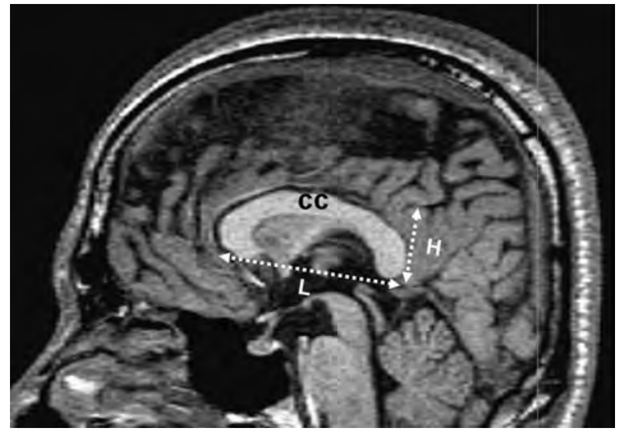

Figure 1. Midsagittal image of human MRI. The huge white mater in the center of the MRI is the corpus callsoum (CC); the length (L) and height (H) were defined as shown to measure CC.

Statistical analysis

The data collection was undertaken by a double-blind method. Total area of CC, length and height of CC, central angle and the four angles were reported as mean ± standard deviation for continuous variables and number for categorical variables. Because most of the measures for CC were not shown to have a non-normal distribution by the Kolmogorov-Smirnov goodness-of-fit test, they were compared by parametric analysis using a two-way ANOVA test. All reported P values are two-sided, and P values of less than 0.05 were considered to indicate statistical significance. The SPSS program (for Windows, version 10.0.5) was used for the statistical analysis.

Results

Effect of age

ANOVAs performed for individual parameters revealed that the variables width ($F(1, 237) = 53.93$, $P < 0.001$),

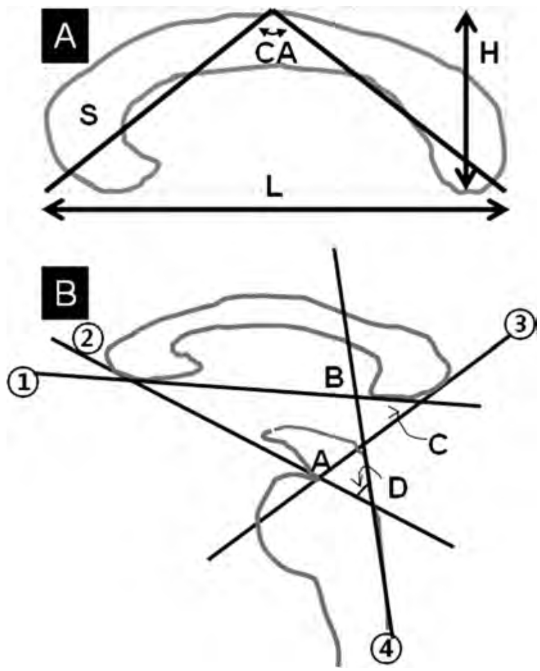

Figure 2. Schematic presentation of the parameters observed. On the midsagittal section (A), the total area (S) of corpus callosum (CC), height (H) and width (W) were measured with Scion Image. The CC was inscribed into the minimum rectangle. The vertex angle of the isosceles triangle was estimated (CA). To understand the spatial characteristics of CC, four angles were measured (B) after Oka et al. (1999). The upper notch of the pons was used for the analysis point. Four lines were drawn as in B: line 1 connecting the inferior margin of genu and splenium of CC, line 2 connecting the analysis point and the anterior inferior margin of genu, line 3 connecting the analysis point and the posterior inferior margin of splenium, and line 4 was extrapolated to the dorsal of the brain stem.

height ($F_{1,237} = 19.83$, $P < 0.001$), A ($F_{1,237} = 70.69$, $P < 0.001$), and D ($F_{1,237} = 19.42$, $P < 0.001$) were significantly larger in the old group than in the young group. On the other hand, the variable C ($F_{1,237} = 46.35$, $P < 0.001$) was significantly smaller in the old group than in the young group. The variables S ($F_{1,237} = 2.82$, $P = 0.09$), B ($F_{1,237} = 1.30$, $P = 0.25$) and CA ($F_{1,237} = 0.45$, $P = 0.50$) showed no significant difference between old and young groups (Table 2).

Effect of gender

ANOVAs indicated that the variables width ($F_{1,237} = 8.72$, $P = 0.003$) and C ($F_{1,237} = 25.70$, $P < 0.001$) were significantly larger in male subjects than in female subjects. On the other hand, the variables A ($F_{1,237} = 7.52$, $P = 0.007$), B ($F_{1,237} = 8.25$, $P = 0.004$) and D ($F_{1,237} = 4.34$, $P = 0.038$) were significantly smaller in male subjects than in female subjects. The variables S ($F_{1,237} = 1.21$, $P = 0.27$),

Table 2. Effects of age and gender on the parameters of the corpus callosum.

	Young		Old		P value		
Region	Men ($n = 51$)	Women ($n = 59$)	Men ($n = 60$)	Women ($n = 71$)	Age	Gender	Age × gender
S (mm^2)	674.01 ± 122.75	630.72 ± 114.87	621.11 ± 125.78	627.61 ± 144.66	0.094	0.271	0.137
L (mm)	70.35 ± 4.36	66.48 ± 6.27	73.64 ± 5.44	73.40 ± 5.11	< 0.001	0.003	0.010*
H (mm)	25.77 ± 3.04	25.28 ± 2.92	27.87 ± 4.10	27.22 ± 3.68	< 0.001*	0.209	0.867
A (°)	100.54 ± 5.75	101.09 ± 7.12	106.58 ± 10.08	111.35 ± 6.16	< 0.001	0.007	0.031*
B (°)	78.48 ± 4.02	80.77 ± 4.34	78.55 ± 3.88	79.43 ± 4.66	0.255	0.004*	0.203
C (°)	51.34 ± 4.80	49.15 ± 6.21	48.00 ± 5.22	43.46 ± 4.13	< 0.001*	< 0.001*	0.077
D (°)	50.29 ± 4.22	50.98 ± 4.84	52.37 ± 4.37	54.18 ± 4.88	< 0.001*	0.038*	0.353
CA (°)	107.82 ± 5.91	106.75 ± 5.57	106.19 ± 6.64	107.32 ± 5.99	0.502	0.972	0.163

Means ± SD. S, whole area of corpus callosum; L, width of corpus callosum; H, height of corpus callosum. Angles A, B, C, D and CA (central angle) are illustrated in Figure 2.
*Two-way ANOVA showed statistical significance with $P < 0.05$.

height ($F_{1,237}=1.58$, $P=0.20$), and CA ($F_{1,237}=0.001$, $P=0.97$) showed no significant difference between men and women (Table 2).

Effect of age by gender

ANOVAs revealed a significant gender by age interaction between age and gender in the variables width ($F_{1,237}=6.79$, $P=0.010$) and A ($F_{1,237}=4.72$, $P=0.031$) (Table 2). On the other hand, the variables S ($F_{1,237}=2.22$, $P=0.13$), height ($F_{1,237}=0.02$, $P=0.86$), B ($F_{1,237}=1.63$, $P=0.20$), C ($F_{1,237}=3.15$, $P=0.077$), D ($F_{1,237}=0.86$, $P=0.35$) and CA ($F_{1,237}=1.95$, $P=0.16$) showed no significant interaction between aged and gender (Table 2).

Discussion

There are many studies which have investigated the effects of aging and gender on CC, and they have been focused mainly on the size of CC. In this study, however, we analyzed the difference in spatial arrangement of CC according to age and gender. The spatial orientation of CC is a relative parameter to reflect the relationship among the neighboring brain structures, whereas the area of CC implies a direct functional correlation. Because the size could be affected by age, constitution and environment, careful consideration is required to normalize the data when absolute parameters such as area and volume are used. However, angular parameters are relative and contains an inherent control for individual differences because of the above features. Therefore, the use of angular parameters adopted in this study could be a useful approach in evaluating CC morphology (Oka et al. 1999).

In the present study, we failed to observe difference in whole CC size (S) between young and old age groups. Previous studies reported that the area of CC is decreased with aging (Weis et al. 1993; Parashos et al. 1995) whereas other studies reported that the size of CC is relatively stable up to the seventies (Driesen and Raz 1995; Sullivan et al. 2001). Lee et al. reported no difference in CC volume between the twenties and the forties in Koreans (Lee et al. 2009), in partial agreement with our present results, although the age distribution of the subjects is slightly different.

In the present study, the length and height of CC were found to be increased in the sixties and seventies age-group, in good agreement with previous reports (Sullivan et al. 2002; Suganthy et al. 2003; Takeda et al. 2003). In addition, the degree of lengthening of CC was more remarkable in women than men; however, some studies have reported that the length of CC is reduced in women (Byne et al. 1988; Hopper et al. 1994). A lengthening of CC in the elderly group was found in this study, but the total area of CC was not different between young and old groups, which could suggest that the white matter of the cortical neuron might be spared during spatial changes of CC with aging. Furthermore senile neuronal atrophy may mainly occur in somas and be less affected in axons, which should be confirmed by future experiments. The CC is located just above the lateral ventricles. The enlargement of lateral ventricles during aging has been suggested to relate to spatial changes of CC (Pfefferbaum et al. 2000; Takeda et al. 2003).

We have analyzed some angular parameters to understand the spatial organization of CC with aging, and found that angles A and D were significantly larger in the old-age group, although angle C was smaller in the old-age group. Considering the geometry involved it is highly likely that the increase in the length of CC shifts line 1 anteriorly and line 3 posteriorly, which is supported by the results of this study. The change of angle A with aging was more evident in women than men, which is a parallel finding of a lengthening pattern. The central angle (CA) and angle B did not show any difference in young and old groups. The wider CA in William's syndrome has been suggested to be associated with premature termination of brain development and overall reduction of parieto-occipital area (Tomaiuolo et al. 2002). In the present study, we showed that the CA of CC was stable with aging, which might be used as a diagnostic parameter for evaluating abnormal brain development and atrophy.

Sexual dimorphism in the corpus callosum is the subject of a long-standing dispute (DeLacoste-Utamsing and Holloway 1982; Bishop and Wahlsten 1997; Hwang et al. 2004), being focused mainly on the size and shape of CC. In the present study, we failed to observe any gender difference in the total area of CC. We focused on the spatial organization of CC, which was investigated by the four angles suggested by Oka et al. (1999). The angles A, B and D were larger in the female group, whereas the angle B was larger in males, indicating that CC has a different spatial distribution according to gender, in good agreement with the study by Oka et al. (1999). Nevertheless Oka et al. reported that males had larger angles of A and C in their CC, whereas female CC showed larger angles of B and D. The different trend of the angle A might have been due to differences in composition of the subjects; the subjects of this study were young (20–30 years) and aged individuals (60–75 years), whereas the age range of the subjects of the study by Oka et al. was 20–50 years old (Oka et al. 1999). Based on the angular differences in male and female subjects, we can deduce that lines 3 and 4 were shifted counter-clockwise. This spatial difference might have resulted from differential development of the cerebral cortex, interhemispheric connectivity and laterality of neurocognitive functions between men and women (Oka et al. 1999; Ullmann et al. 2008).

In this study, we demonstrated the expansion of spatial dimensions of CC with aging. Also, we confirmed that the spatial orientation of CC is different according to gender. These results suggest that spatial orientation could be an important factor in studies of the corpus callosum.

Acknowledgement

This study was supported by Brain Korea 21 to IJR, and by a grant from the Asan Institute for Life Sciences to SJH.

References

Allen LS, Richey MF, Chai YM, Gorski RA. 1991. Sex differences in the corpus callosum of the living human being. J Neurosci. 11:933–942.

Allen JS, Damasio H, Grabowski TJ, Bruss J, Zhang W. 2003. Sexual dimorphism and asymmetries in the gray-white composition of the human cerebrum. Neuroimage. 18:880–894.

Bishop KM, Wahlsten D. 1997. Sex differences in the human corpus callosum: myth or reality? Neurosci Biobehav Rev. 21:581–601.

Byne W, Bleier R, Houston L. 1988. Variations in human corpus callosum do not predict gender: a study using magnetic resonance imaging. Behav Neurosci. 102: 222–227.

Clarke S, Kraftsik R, Van der Loos H, Innocenti GM. 1989. Forms and measures of adult and developing human corpus callosum: is there sexual dimorphism? J Comp Neurol. 280:213–230.

Clarke JM, Lufkin RB, Zaidel E. 1993. Corpus callosum morphometry and dichotic listening performance: individual differences in functional interhemispheric inhibition? Neuropsychologia. 31:547–557.

DeLacoste-Utamsing C, Holloway RL. 1982. Sexual dimorphism in the human corpus callosum. Science. 216:1431–1432.

Driesen NR, Raz N. 1995. The influence of sex, age, and handedness on corpus callosum morphology: a meta-analysis. Psychobiology. 23:240–247.

Dubb A, Gur R, Avants B, Gee J. 2003. Characterization of sexual dimorphism in the human corpus callosum. Neuroimage. 20:512–519.

Hermann B, Hansen R, Seidenberg M, Magnotta V, O'Leary D. 2003. Neurodevelopmental vulnerability of the corpus callosum to childhood onset localization-related epilepsy. Neuroimage. 18:284–292.

Hopper KD, Patel S, Cann TS, Wilcox T, Schaeffer JM. 1994. The relationship of age, gender, handedness, and sidedness to the size of the corpus callosum. Acad Radiol. 1:243–248.

Hwang SJ, Ji EK, Lee EK, Kim YM, Shin DY, Cheon YH, Rhyu IJ. 2004. Gender differences in the corpus callosum of neonates. Neuroreport. 15:1029–1032.

Hynd GW, Hall J, Novey ES, Eliopulos D, Black K, Gonzalez JJ, Edmonds JE, Riccio C, Cohen M. 1995. Dyslexia and corpus callosum morphology. Arch Neurol. 52:32–38.

Lee BY, Sohn JH, Choi MH, Lee SJ, Kim HS, Yang JW, Choi JS, Yi JH, Tack GR, Chung SC. 2009. A volumetric study of the corpus callosum in 20s and 40s Korean people. Brain Struct Funct. 213:463–467.

Oka S, Miyamoto O, Janjua NA, Honjo-Fujiwara N, Ohkawa M, Nagao S, Kondo H, Minami T, Toyoshima T, Itano T. 1999. Re-evaluation of sexual dimorphism in human corpus callosum. Neuroreport. 10:937–940.

Panizzon MS, Hoff AL, Nordahl TE, Kremen WS, Reisman B, Wieneke M, Harris D, Goodman C, Espinoza S, Liu W, Lim K. 2003. Sex differences in the corpus callosum of patients with schizophrenia. Schizophr Res. 62:115–122.

Parashos IA, Wilkinson WE, Coffey CE. 1995. Magnetic resonance imaging of the corpus callosum: predictors of size in normal adults. J Neuropsychiatry Clin Neurosci. 7:35–41.

Pfefferbaum A, Sullivan EV, Swan GE, Carmelli D. 2000. Brain structure in men remains highly heritable in the seventh and eighth decades of life. Neurobiol Aging. 21:63–74.

Piven J, Bailey J, Ranson BJ, Arndt S. 1997. An MRI study of the corpus callosum in autism. Am J Psychiatry. 154:1051–1056.

Sperry R. 1982. Some effects of disconnecting the cerebral hemispheres. Science. 217:1223–1226.

Suganthy J, Raghuram L, Antonisamy B, Vettivel S, Madhavi C, Koshi R. 2003. Gender- and age-related differences in the morphology of the corpus callosum. Clin Anat. 16:396–403.

Sullivan EV, Rosenbloom MJ, Desmond JE, Pfefferbaum A. 2001. Sex differences in corpus callosum size: relationship to age and intracranial size. Neurobiol Aging. 22:603–611.

Sullivan EV, Pfefferbaum A, Adalsteinsson E, Swan GE, Carmelli D. 2002. Differential rates of regional brain change in callosal and ventricular size: a 4-year longitudinal MRI study of elderly men. Cereb Cortex. 12:438–445.

Takeda S, Hirashima Y, Ikeda H, Yamamoto H, Sugino M, Endo S. 2003. Determination of indices of the corpus callosum associated with normal aging in Japanese individuals. Neuroradiology. 45:513–518.

Tomaiuolo F, Di Paola M, Caravale B, Vicari S, Petrides M, Caltagirone C. 2002. Morphology and morphometry of the corpus callosum in Williams syndrome: a T1-weighted MRI study. Neuroreport. 13:2281–2284.

Ullmann MT, Miranda RA, Tavers ML. 2008. Sex differences in the neurocognition of language. In: Becker JB, Berjley KJ, Geary N, Hampson E, Herman JP, Young EA, editors editors. Sex difference in the brain – from genes to behavior. Oxford: Oxford University Press. p. 291–309.

Weis S, Kimbacher M, Wenger E, Neuhold A. 1993. Morphometric analysis of the corpus callosum using MR: correlation of measurements with aging in healthy individuals. Am J Neuroradiol. 14:637–645.

Witelson SF. 1989. Hand and sex differences in the isthmus and genu of the human corpus callosum. A postmortem morphological study. Brain. 112:799–835.

Witelson SF, Goldsmith CH. 1991. The relationship of hand preference to anatomy of the corpus callosum in men. Brain Res. 545:175–182.