

# Gender-related differences in the morphometry of the corpus callosum: MRI study



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## ABSTRACT

**Background:** The size and shape of the adult corpus callosum (CC) may vary with gender. There is, however, less literature available on data involving the morphometry of CC among the Indian population. **Aims and Objectives:** To measure the size of CC using magnetic resonance imaging (MRI) scans of normal Indian adult females and males and identify gender-related differences, if any. **Materials and Methods:** The dimensions of CC were measured on MRI scans on a midsagittal section view belonging to 150 (59 females, 91 males) normal Indian adults (North India) using e-measurement tools. The measurements included the maximum length and height of CC, the thickness of various parts of CC, the CC index (CCI), and the distance of CC from the frontal and occipital poles of the cerebral hemisphere. The study was carried out in the Department of Anatomy in collaboration with the Department of Radiodiagnosis, King George's Medical University, U.P., Lucknow, India. The data was analyzed using the statistical package for social sciences, 23<sup>rd</sup> version. Means were compared for significant differences using the independent unpaired t-test. **Results:** The mean length of the CC was found to be  $6.94 \pm 0.63$  cm; mean height was  $2.57 \pm 0.43$  cm; the mean thickness of the genu was  $9.16 \pm 2.26$  mm; the mean thickness of the body was  $5.09 \pm 0.99$  mm; the mean thickness of splenium was  $9.10 \pm 2.22$  mm; the mean distance from the frontal pole was  $3.66 \pm 0.35$  cm; the mean distance from the occipital pole was  $5.70 \pm 0.74$  cm; and the mean CCI calculations showed to be  $3.37 \pm 0.56$ . All measurements were found to be greater in males as compared to females except mean height (males  $2.56 \pm 0.47$  cm; females  $2.59 \pm 0.37$  cm) and mean thickness of the body (males  $5.04 \pm 0.94$  mm; females  $5.17 \pm 1.06$  mm). A statistically significant difference was observed in the distance of CC from the frontal pole in our population with respect to gender ( $P=0.03$ ). **Conclusion:** Based on observations made in the study, normative data of CC measurements was generated, and it was found that there was no significant gender-related difference in the morphology of CC; the only significant difference was in the distance of the genu from the frontal pole, which was greater in females as compared to males.

**Key words:** Magnetic resonance imaging; Morphometry; Corpus callosum; Cerebral hemisphere

## INTRODUCTION

The corpus callosum (CC) is an important inter-hemispheric commissural tract in the human brain with about 250–300 million fibers that connect and correlate the activities of the left and right cerebral hemispheres. It is about 10 cm long and consists of the rostrum, genu, body, and splenium. The rostrum is the narrowest

part, the genu is the anterior projecting part about 4 cm from the frontal pole, the body (trunk) is the main part of the CC, and the splenium is the thickened posterior end of the CC that lies about 6 cm from the occipital pole.<sup>1</sup> Researchers have been interested in CC dimensions, morphology, and sex-related variables because previous studies have found differences in CC size according to race or ethnicity in various regions of the world.<sup>2</sup>

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Using magnetic resonance imaging (MRI), various studies have assessed the dimensions of CC, including size, diameter, age-related morphology, and gender-related variations.<sup>3</sup> Several studies have reported that CC can be altered with respect to size and shape or both, in many psychiatric illnesses like bipolar disorders, Alzheimer's disease, schizophrenia, Niemann-Pick disease, dyslexia, multiple sclerosis, and Williams syndrome.<sup>4,5</sup> In disorders such as dyslexia, down's syndrome, depression, schizophrenia, and HIV/AIDS, the morphology of CC may be altered, according to some researchers.<sup>6-8</sup>

The anatomy of CC has thus received more interest due to increasing surgical interventions like colostomies and treatments for some forms of epilepsy.<sup>9</sup> Few studies have been conducted to date in the East Asian and Indian populations, where they found that no sexual dimorphism was noticed in any of the studied parameters. Studies have also reported age-related shrinkage of the anterior half of the CC, which could be attributed to the atrophic alterations of the brain.<sup>10</sup> Therefore, the size of the CC is a sensitive predictor of the cerebral cortical state, as it might reflect cerebral cortical abnormalities.<sup>11</sup> These measurements can provide the normal values and, thus, would help to establish standard reference values in this population and also compare gender-related differences for comparative evaluation, if any.

Thus, we proposed to make a detailed morphometric measurement of CC among normal Indian adults in the North Indian Population (Lucknow Region). The aim of our study was to measure various dimensions of CC in normal adult Indian males and females of the Lucknow region and to identify gender-related differences, if any.

### Aims

To identify gender-related differences, if any, in the size and morphology of the CC among the Indian population.

### Objectives

- To measure the maximum length, height and thickness of various parts of the CC, including the genu, body, and splenium.
- To measure the distance of CC from the frontal and occipital poles of the cerebral hemisphere.
- To compare the measurements of CC between males and females.
- To determine the Corpus Callosum Index (CCI).

## MATERIALS AND METHODS

This is a cross-sectional observational study that was carried out in the Department of Anatomy in collaboration with

the Department of Radiodiagnosis, King George's Medical University (KGMU), Lucknow. The duration of the study was 12 months. Informed consent from patients and clearance from the institutional ethics committee of our university were obtained (Ref. Code: 90<sup>th</sup> ECM II B IMR-S/P6).

MRI cans (reported as radiologically normal) belonging to 150 adults (91 males and 59 females) of the Lucknow region who were referred to the Department of Radiodiagnosis (KGMU) for MRI of the brain were randomly selected retrospectively.

### Inclusion criteria

The inclusion criteria comprised all the patients referred for suspected or known central nervous system diseases with no neurological signs, no intracranial lesions, mass, or head injury on MRI and all MRI, scans that were reported radiologically normal (specific region of interest).

### Exclusion criteria

The exclusion criteria comprised the presence or documentation of any pathological process distorting the anatomy of the CC (e.g., hydrocephalus or tumor), when the entire CC was not captured on a single slice or oblique imaging plane, and if images were of poor quality.

Two independent observers evaluated cerebral images to exclude deviations from the normal state, measurements of CC were made, and morphometric indices were calculated.

Various parameters of CC measured using mid-sagittal MRI scans included:

1. Maximum Length  $L_{max}$  (in cm): Distance between the anterior edge of the genu and the posterior edge of splenium (Figure 1).
2. Maximum Height  $H_{max}$  (in cm): A line extending from the inferior ends of the rostrum to the splenium. Another parallel line was drawn at the top of the CC; the distance between these lines was then measured (Figure 2).
3. Distance of genu from frontal pole (DfFP) (in cm) (Figure 3).
4. Distance of splenium from occipital pole (DfOP) (in cm) (Figure 3).
5. Thickness, height, and width of individual parts of the CC at its maximum level (genu, rostrum, body, and splenium) (Figure 4):
  - The thickness of Genu and  $T_g$  (in mm)
  - The thickness of Body,  $T_b$  (in mm)
  - The thickness of Splenium,  $T_s$  (in mm)
6. CC index (CCI): Obtained from the division of the total height of individual parts of CC by the maximum

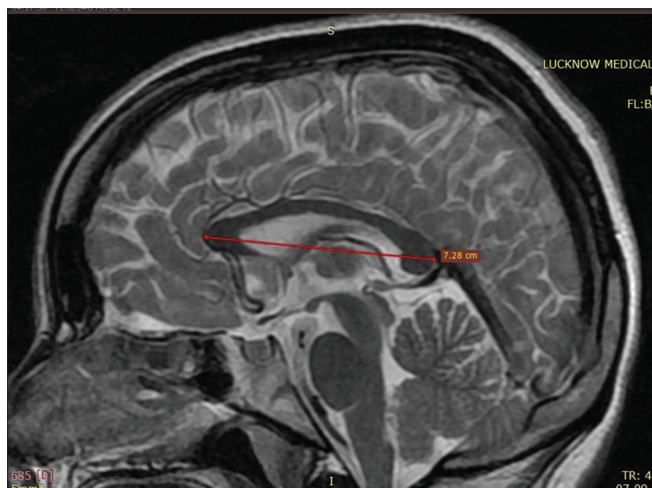


Figure 1: Maximum length  $L_{max}$  (in cm)



Figure 2: Maximum height  $H_{max}$  (in cm)

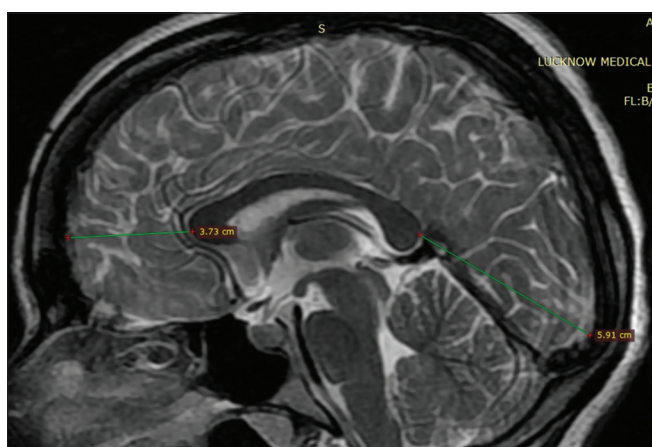


Figure 3: Distance of genu from frontal pole DfFP (in cm) and distance of splenium from occipital pole DfOP (in cm)

$$\text{length of CC, } (T_g + T_b + T_s) / L_{max}$$

The various dimensions of CC were described using descriptive statistics as mean±SD, along with minimum and maximum values for all parameters. The observations

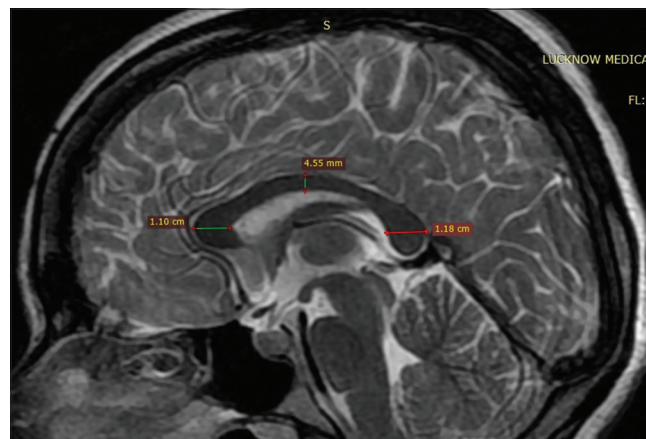


Figure 4: Thickness of genu,  $T_g$  (in mm), thickness of body,  $T_b$  (in mm) and thickness of splenium,  $T_s$  (in mm)

Table 1: Demographic profile of study population

| S. No. | Gender  | No. of subjects | Percentage |
|--------|---------|-----------------|------------|
| 1.     | Females | 59              | 39.3       |
| 2.     | Males   | 91              | 60.7       |
|        |         | 150             | 100.0      |

from males and females were compared for significant differences (if any) using the independent unpaired t-test. The data was statistically analyzed using the statistical package for social sciences (SPSS) version 23. Thereafter, conclusions and interpretations were drawn from the analyzed data.

## RESULTS

The data were statistically analyzed using SPSS. Table 1 provides the demographic profile of the concerned study population.

In our study, the mean length was found to be  $6.94 \pm 0.63$  cm; the mean height was  $2.57 \pm 0.43$  cm; the mean thickness of the genu was  $9.16 \pm 2.26$  mm; the mean thickness of the body was  $5.09 \pm 0.99$  mm; the mean thickness of the splenium was  $9.10 \pm 2.22$  mm; the mean distance from the frontal pole was  $3.66 \pm 0.35$  cm; the mean distance from the occipital pole was  $5.70 \pm 0.74$  cm; and the mean CCI calculations showed to be  $3.37 \pm 0.56$  (Table 2).

All measurements were found greater to be in males as compared to females except mean height (males  $2.56 \pm 0.47$  cm; females  $2.59 \pm 0.37$  cm) and mean thickness of body (males  $5.04 \pm 0.94$  mm; females  $5.17 \pm 1.06$  mm) (Table 2).

Statistical analysis revealed differences in the majority of CC dimensions with respect to gender, but they were not

**Table 2: Mean values of individual parameters with respect to gender differences**

| S. No. | Gender                | n   | Min.   | Max.  | Median | Mean | SD   | (95% CI)    |             |  |
|--------|-----------------------|-----|--|-------|--------|------|------|-------------|-------------|--|
|        |                       |     |  |       |        |      |      | Lower bound | Upper bound |  |
| 1.     | L <sub>max</sub> (cm) |     |  |       |        |      |      |             |             |  |
|        | Female                | 59  | 5.06   | 8.40  | 6.96   | 6.87 | 0.65 | 6.71        | 7.04        |  |
|        | Male                  | 91  | 5.19   | 8.23  | 7.11   | 6.98 | 0.62 | 6.85        | 7.11        |  |
|        | Total                 | 150 | 5.06   | 8.40  | 7.00   | 6.94 | 0.63 | 6.84        | 7.04        |  |
|        |                       |     | “t”=-1.037; P=0.301  |       |        |      |      |             |             |  |
| 2.     | H <sub>max</sub> (cm) |     |  |       |        |      |      |             |             |  |
|        | Female                | 59  | 1.69   | 3.46  | 2.56   | 2.59 | 0.37 | 2.49        | 2.68        |  |
|        | Male                  | 91  | 1.29   | 4.80  | 2.50   | 2.56 | 0.47 | 2.47        | 2.66        |  |
|        | Total                 | 150 | 1.29   | 4.80  | 2.52   | 2.57 | 0.43 | 2.50        | 2.64        |  |
|        |                       |     | “t”=0.372; P=0.711   |       |        |      |      |             |             |  |
| 3.     | T <sub>g</sub> (mm)   |     |  |       |        |      |      |             |             |  |
|        | Female                | 59  | 4.08   | 12.90 | 9.13   | 8.82 | 2.15 | 8.27        | 9.37        |  |
|        | Male                  | 91  | 1.07   | 13.30 | 9.51   | 9.38 | 2.31 | 8.90        | 9.85        |  |
|        | Total                 | 150 | 1.07   | 13.30 | 9.16   | 9.16 | 2.26 | 8.80        | 9.52        |  |
|        |                       |     | “t”=-1.483; P=0.140  |       |        |      |      |             |             |  |
| 4.     | T <sub>b</sub> (mm)   |     |  |       |        |      |      |             |             |  |
|        | Female                | 59  | 2.84   | 8.68  | 5.07   | 5.17 | 1.06 | 4.90        | 5.44        |  |
|        | Male                  | 91  | 2.55   | 7.61  | 5.09   | 5.04 | 0.94 | 4.85        | 5.23        |  |
|        | Total                 | 150 | 2.55   | 8.68  | 5.09   | 5.09 | 0.99 | 4.93        | 5.25        |  |
|        |                       |     | “t”=0.771; P=0.442   |       |        |      |      |             |             |  |
| 5.     | T <sub>s</sub> (mm)   |     |  |       |        |      |      |             |             |  |
|        | Female                | 59  | 1.22   | 11.80 | 9.36   | 8.80 | 2.25 | 8.22        | 9.37        |  |
|        | Male                  | 91  | 1.13   | 14.80 | 9.17   | 9.30 | 2.20 | 8.85        | 9.75        |  |
|        | Total                 | 150 | 1.13   | 14.80 | 9.26   | 9.10 | 2.22 | 8.75        | 9.46        |  |
|        |                       |     | “t”=-1.367; P=0.174  |       |        |      |      |             |             |  |
| 6.     | DfFP (cm)             |     |  |       |        |      |      |             |             |  |
|        | Female                | 59  | 2.95   | 4.72  | 3.54   | 3.58 | 0.35 | 3.49        | 3.67        |  |
|        | Male                  | 91  | 2.21   | 4.56  | 3.72   | 3.71 | 0.35 | 3.63        | 3.78        |  |
|        | Total                 | 150 | 2.21   | 4.72  | 3.66   | 3.66 | 0.35 | 3.60        | 3.71        |  |
|        |                       |     | “t”=-2.189; P=0.030  |       |        |      |      |             |             |  |
| 7.     | DfOP (cm)             |     |  |       |        |      |      |             |             |  |
|        | Female                | 59  | 4.13   | 7.80  | 5.55   | 5.59 | 0.61 | 5.43        | 5.75        |  |
|        | Male                  | 91  | 2.21   | 6.93  | 5.83   | 5.78 | 0.81 | 5.61        | 5.95        |  |
|        | Total                 | 150 | 2.21   | 7.80  | 5.73   | 5.71 | 0.74 | 5.59        | 5.82        |  |
|        |                       |     | “t”=-1.539; P=0.126  |       |        |      |      |             |             |  |
| 8.     | CCI                   |     |  |       |        |      |      |             |             |  |
|        | Female                | 59  | 2.16   | 4.56  | 3.42   | 3.33 | 0.58 | 3.18        | 3.48        |  |
|        | Male                  | 91  | 1.93   | 4.59  | 3.48   | 3.40 | 0.55 | 3.29        | 3.52        |  |
|        | Total                 | 150 | 1.93   | 4.59  | 3.46   | 3.37 | 0.56 | 3.28        | 3.46        |  |
|        |                       |     | “t”=-0.819; P=0.414, CCI: CC index, DfFP: Distance of genu from frontal pole, DfOP: Distance of splenium from occipital pole |       |        |      |      |             |             |  |

statistically significant ( $P>0.05$ ). A significant difference ( $P=0.03$ ) was observed only in the DfFP (Table 2).

## DISCUSSION

The main commissure bridging the brain hemispheres is called the CC, and hence, it has always been the subject of considerable study and discussion, particularly with regard to how its morphology relates to different aspects of neurological function. From rostral to caudal, the CC can be structurally divided into the rostrum, genu, body, and splenium. However, the callosal fibres' functional topography is still not fully known.<sup>1</sup>

Suganthi et al., reported length of CC to be more in males with statistical significance ( $P=0.03$ ), whereas no

other parameters of their study showed significant gender differences.<sup>3</sup> Gupta et al., (2008) also reported a larger length of CC in males among their studied MRI group ( $7.57\pm 0.62$ ).<sup>10</sup> In our study, the length of the CC was found to be greater in males than females but was not statistically significant. Mourgela et al., found that males had greater longitudinal dimensions of the genu and length of the CC, whereas females had greater longitudinal dimensions of the splenium.<sup>2</sup> Gupta et al., (2009) reported similar findings as larger length and height of CC in males, whereas splenial width was found to be more in females.<sup>12</sup> These findings were similar to our study except for the thickness of splenium. Yasin and Farahani did not find any statistically significant differences in CC size in either gender.<sup>13</sup>

Karakaş et al., reported mean values for the genu, body, and splenium widths, maximal CC heights and lengths, as

well as many other third and lateral ventricle parameters, from 52 MR images of healthy adults. In their study, the mean widths of the genu, body, splenium, and height of the CC were larger in females than in males.<sup>14</sup> However, in our study, all the measurements were found to be greater in males as compared to females except mean height (males  $2.56 \pm 0.47$  cm; females  $2.59 \pm 0.37$  cm) and mean thickness of the body (males  $5.04 \pm 0.94$  mm; females  $5.17 \pm 1.06$  mm). Mohamed et al., reported that the thickness of the CC body, splenium and CCI was greater in females than males, with a significant difference at  $P=0.000$ ,  $0.011$ , and  $0.031$ , respectively.<sup>15</sup> They also showed a positive linear relationship between the AP length of the CC and the fronto-CC length. These findings were not consistent with our study. There wasn't any statistically significant difference across gender with respect to CCI in our study; however, the value of the mean CCI was higher in males than females. Arda and Akay showed CC and splenium lengths were greater in males as compared to females ( $P=0.029$  for both), which was similar to our findings though not statistically significant in our study.<sup>16</sup>

Mohammadi et al., evaluated 100 normal mid-sagittal brain MRI scans to estimate the size of CC and discover its gender- and age-related variances in the northern region of Iran.<sup>17</sup> A multivariate linear regression revealed a positive linear connection between the distance of the CC from the frontal and occipital poles. In addition, there was a statistical correlation between brain size and the longitudinal dimensions of CC. Thus, the authors inferred that the diverse dimensions of the brain fluctuate in tandem with one another. Hence, to maintain the symmetry of the human brain, the size and proportions of CC could fluctuate. There was another study by Jain et al., which included cranial MRI scans of 121 normal individuals. It was done to assess the variations in the thickness and bending angle of the CC in relation to age and gender. But the authors concluded that the distances of the genu and splenium from the frontal and occipital poles, respectively, did not differ statistically.<sup>18</sup> Patra et al., dissected 50 formalin-fixed human brains in the midsagittal plane to examine the distances of CC from the frontal and occipital poles in order to determine its topographic position within the cerebral hemispheres.<sup>19</sup> Contrary to our findings, they found that the distance from the occipital pole to the posterior-most point of the CC showed a statistically significant ( $P<0.05$ ) gender difference. Another study by Poleneni et al., aimed to study the topographical position of CC in relation to the brain using 40 formalin-fixed, full brain specimens.<sup>20</sup> They also measured the distance of CC from the frontal pole to the genu and the distance of CC from the occipital pole to the splenium, but didn't compare them across genders.

Our study revealed a unique finding of a statistically significant difference ( $P=0.03$ ) for the DfFP with respect to gender, while the distance of the splenium from the occipital pole did not reveal any statistically significant gender-related difference. We infer that this parameter has not been explored in the majority of the other published studies to our knowledge, and in addition, there are limited cadaveric studies involving this parameter. Hence, our findings would add to the existing information pool of normal morphometric and morphologic data regarding CC. This may be of value to any/all upcoming surgical procedures and thus may be further explored in upcoming similar studies.

All of the aforementioned measurements would therefore aid in establishing standard reference values in the particular population, including gender-related disparities. A study of normal morphometry will aid in the identification of changes in the structure of the CC during the description of the CC in order to analyze deviations from the standard. This information may be valuable in connection with a variety of diseases, possibly allowing for a more accurate diagnosis, which may positively affect the therapy, provide a better prognosis, and aid in the planning of any surgical treatments relevant to the affected areas. More recent developments have now been targeted on MRI-guided stereotactic laser ablation of particular callosal tissues. Individual CC pieces can be identified by applying the anatomical values and ratios to MRI films. This facilitates a more precise callosotomy and lessens the neuropsychological aftermath of the procedure.

#### Limitations of the study

Further research should be conducted to estimate disparities among ethnicities and races and to generate normative values for each population. Due to limitations of time and resources, we were unable to include a larger population size, and therefore, we did not group the subjects on the basis of age. Hence, the present study could have an extension wherein the same parameters could be studied in a much larger sample size for better standardization of the normative data; also, the age of subjects can be taken into consideration, and the various parameters could be compared across age and gender amongst various ethnicities to get a more thorough comparative analysis.

#### CONCLUSION

This was a comprehensive study design whereby normal morphometric CC measurements using MRI images of 150 healthy subjects were determined. It utilized mostly the same parameters used in the previous studies for CC measurements. Some of our results were comparable to

previous studies, whereas others were uniquely different. We attempted to create a reference nomogram for normal measurements of CC in males and females.

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**GS**- Design of study, concept, implementation of study protocol, data analysis, coordination and manuscript review and revision, literature survey; **AK**- Concept, design, clinical protocol, data collection; **NK**- Review manuscript and manuscript revision; **NA**- Statistical analysis and interpretation, manuscript preparation and submission of article

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