Magnetic Resonance Imaging-Based Morphometric Assessment of Sexual Dimorphism of Corpus Callosum

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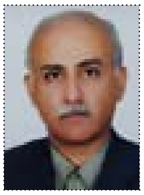
Citation: Abdolmaleki A, Mastery Farahani R, Ghoreishi SK, Shaerzadeh F, Aliaghaei A, Mirjavadi SH, et al. Magnetic Resonance Imaging-Based Morphometric Assessment of Sexual Dimorphism of Corpus Callosum. Anatomical Sciences. 2016; 13(2):117-124.



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Article info:
Received: 29 Oct. 2015
Accepted: 19 Feb. 2016
Available Online: 01 Jul. 2016

Key Words:
Magnetic resonance imaging, Corpus callosum, Sexual differences

ABSTRACT

Introduction: Interhemispheric transmission of signal is done by corpus callosum (CC) as the largest fiber tract in brain. CC comprised 5 segments of rostrum, genu, body, isthmus, and splenium. Contradictory reports exist about sexual dimorphism of CC. We designed this study to assess probable sexual differences of CC and its different parts in men and women.

Methods: We analyzed magnetic resonance (MR) images of 68 females and 60 males in midsagittal view by PmsDViewer software. Data were analyzed by Student t test. These cases had no neurologic and pathologic diseases.

Results: MRI anthropometric analysis indicates that all segments of CC are larger in men compared to women. Moreover, our results also revealed that although all segments of CC were bigger in men, this increase in size was more prominent in the anterior segments of CC.

Conclusion: These findings indicate gender-related differences regarding CC segments. Notably, brain size as an interfering variable was eliminated in this study.

1. Introduction

The most important and largest connecting fiber tract which communicates two cerebral hemispheres of brain is corpus callosum (CC). Histologically, this structure consists of approximately 180 million fibers [26] that functionally integrates activities of the two hemispheres by transferring sensory

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and higher processed information. It also supports primary cognitive abilities, including memory, attention, language, and intelligence [10].

For the first time, Nottebohm and Arnold proved sexual dimorphism in the vocal control area of the songbird brain in 1976 [22]. After that, in the early eighties, a pioneering study indicated sexual dimorphism of the CC emphasizing the fact that women callosal splenium is larger and more bulbous than its counterpart in men [7]. However, further studies indicated that relative to cerebral volume, amygdala, hypothalamus, and fronto-medial cortex in male brain have larger sizes than those in women [12]. Moreover, it was found that overall white matter mass in men, compared to women, was larger [18]. Additionally, although postmortem studies indicate the gender-related differences of various segments of CC [16], published studies on morphological sex differences in CC volume are controversial.

In this line, whilst some results showed a gender-related differences in CC size [1, 3, 8, 17, 23, 24] others reported no significant sex difference in the size of the CC [5, 19, 20, 27]. These findings emphasized that relative to brain size, the midsagittal cross-sectional area of CC in females is usually larger than that in males [1, 23, 24, 27]. In fact, since women tend to have smaller brains, sex differences in callosal anatomy are explained by sex differences in brain volume [28].

Therefore, as a novelty in the present study we accounted for the brain size as an interfering variable and used magnetic resonance imaging (MRI)-based morphometric assessment to clarify gender-related changes in different segments of CC [9].

2. Materials and Methods

Participants

A total of 128 normal subjects (68 females and 60 males) without previous brain damage or history of neurological problems (confirmed by neurologists and radiologists) were selected from Imam Khomeini Hospital in Tehran, Iran. The present study approved by Ethics Committee of Shahid Beheshti University of Medical Sciences. The study was conducted in accordance with the World Medical Association Declaration of Helsinki. Data were collected over a period of 5 months. Evidently, the size of CC remains to be relatively stable at least through the seventh decade [8, 17, 24] and most of previous studies showed that CC is relatively resistant to age-related shrinkage in adults from the third to seventh decade of life [17, 24] so the age of the participants was in the range of 20 to 80 years.

Imaging and analysis procedure

Corpus callosum has 5 segments of rostrum, genu, body, isthmus, and splenium. Frontal lobes of two hemispheres are connected by "genu" and parts of "body." Rest of the "body" is responsible for connection of parietal lobes. Isthmus contains some fibers of the parietal and temporal lobes. Splenium also connects the anterior temporal and occipital lobes of the two hemispheres to each other.

MRI without ionizing radiation and excellent anatomical resolution provides unprecedented opportunity to obtain in vivo neuroanatomical information [10]. The type of images were T2 and were taken with 3T intensity. Then, MRI images were analyzed using PmsDViewer software. CC was divided into 5 regions based on Witelson's scheme: Region I, as the most anterior segment, covers the first sixth of the CC and contains fibers projecting into the prefrontal region. The rest of the anterior half of the CC is region II that contains fibers projecting to premotor and supplementary motor cortical areas. Region III was defined as the posterior half part minus the posterior third and comprised the fibers projecting into the primary motor cortex. Region IV, that is the posterior one-third minus posterior one-fourth, refers to the primary sensory fibers. Callosal parietal, temporal, and occipital fibers cross the CC through region V, which is defined as the posterior one-fourth.

We assessed 5 criteria, including area of rostrum and genu (ARG) to the area of corpus callosum (ACC) (ARG/ACC), area of anterior midbody (AAMB) to ACC (AAMB/ACC), area of posterior midbody (APMB) to ACC (APMB/ACC), area of isthmus (AI) to ACC (AI/ACC), and area of splenium (AS) to ACC (AS/ACC).

Data analysis

All obtained data are presented as mean±SEM. The Student t test was used to compare the means between groups. The significance value was set at $P<0.05$.

3. Results

The ARG/ACC ratio

The average ratio of the area of rostrum and genu to the total area of corpus callosum in male brains was significantly higher (Figure 1) compared to that in female brains ($P<0.005$). The average ARG/ACC ratio for men was 163.54±32.41 and about 149.25±22.16 for the women. The results showed that rostrum and genu have occupied more area midsagittal view in men brains compared to that in women brains.

The AAMB/ACC ratio

As shown in Figure 2, the average AAMB/ACC ratio in male brains was higher than that in female brains. The difference was statistically significant (P<0.001). The AAMB/ACC mean values calculated for men and women were 160.14±49.62 and 135.08±27.64, respectively.

The APMB/ACC ratio

The average APMB/ACC ratio in male brains was higher than that in female brains. This difference was statistically significant (P<0.04) indicating that posterior midbody occupied larger area of total ACC in male brains compared to female brains (Figure 3). The average APMB/ACC values were 68.49±14.19 and 61.59±12.39 for males and females, respectively.

The AI/ACC ratio

As shown in Figure 4, the average AI/ACC ratio in the male brains was higher than that in the female brains. This difference was statistically significant (P<0.02). The AI/ACC average values calculated for the male and female brains were 34.07±9.389 and 29.43±7.38, respectively.

The AS/ACC ratio

The average AS/ACC ratio in male brains was significantly higher than that in female brains (P<0.03) indicating that isthmus occupied more area of CC in male brains (Figure 5). The AS/ACC ratio mean values in men subjects was 220.69±40.16 and it was about 201.02±31.66 in women subjects.

4. Discussion

Regarding the important role of CC to transfer information between two cerebral hemispheres as well as many controversial reports about sex-related differences of CC, we decided to measure the ratio of 5 segments of CC, including rostrum and genu, anterior midbody, posterior midbody, isthmus, and splenium to the total area of CC in a gender-related manner using MRI-based morphometric assessment. Our results revealed that all 5 segments of CC were bigger in men, however this increase was more pronounced in the anterior segments of CC.

In the literature on sexual dimorphism of CC, considering the brain size is one of the most important factors. It is believed that CC length, shape, and area in women brains are different from men because of women's smaller brain size, although there are many controversial reports in this regard [2, 6, 7, 14]. Several lines of evidence indicate that unadjusted callosal size is larger in males, and differences may disappear after statistically correcting brain size [3]. In this regard, Bishop et

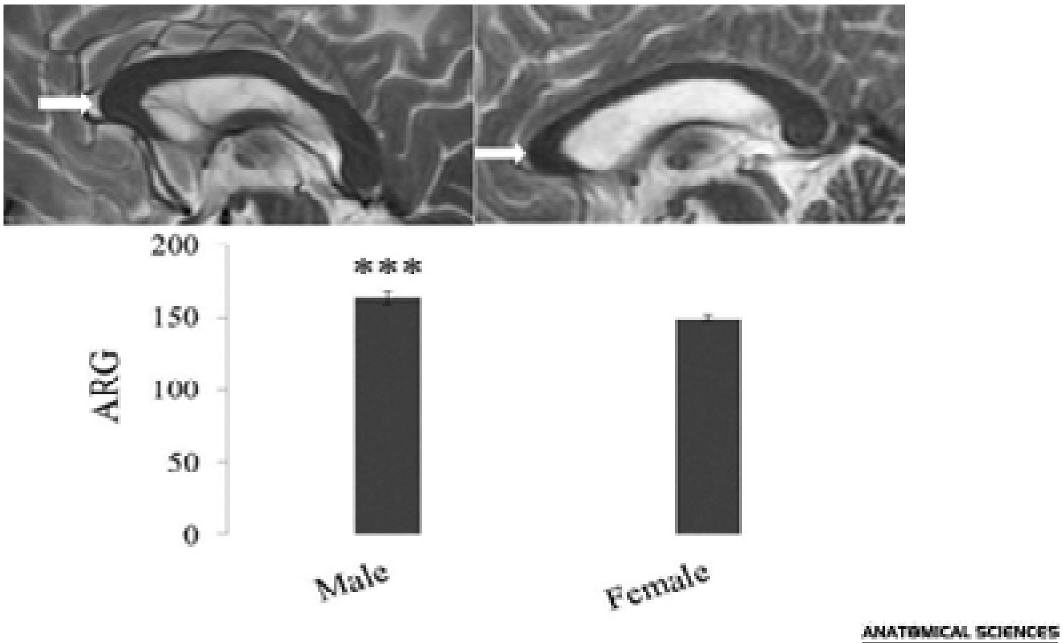

Figure 1. Evaluation of total area of rostrum and genu (ARG) to total area of corpus callosum (ACC) in male and female brains. ARG is shown by white arrow. This figure indicates larger area of ARG in men compared to that in women.

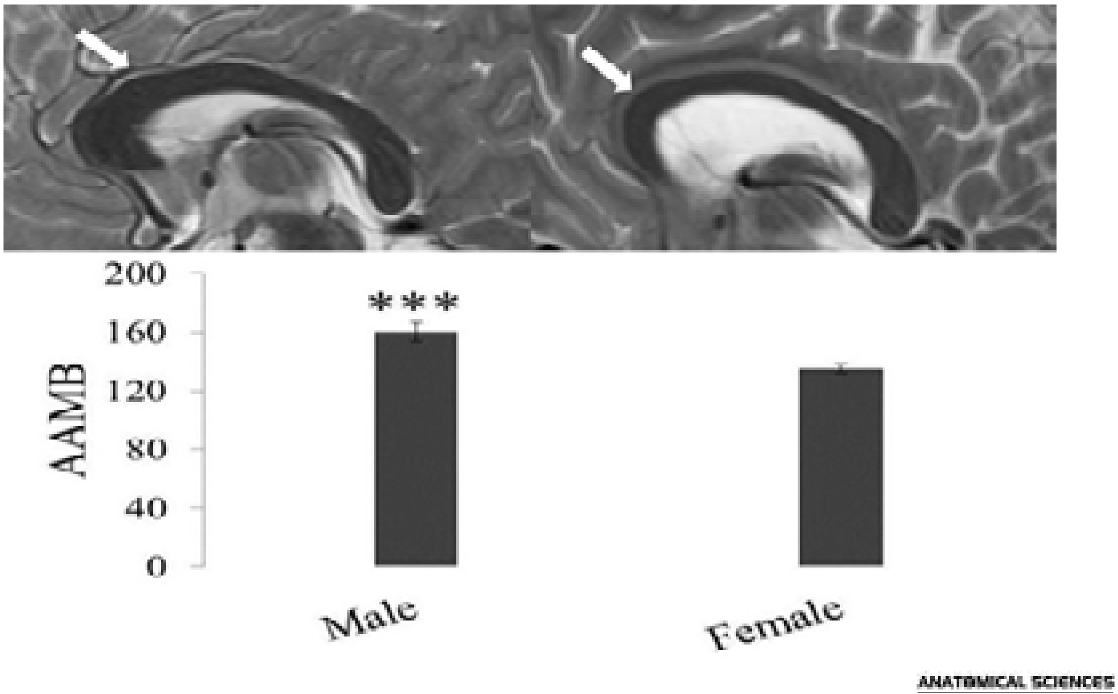

Figure 2. Ratio of area of anterior midbody (AAMB) to total area of corpus callosum (ACC) in male and female brains.

al. and Luders et al. have reported no gender-related differences in the size and other parameters of CC between male and female brains [3, 21]. Moreover, Davatzikos findings indicated that most morphological parameters of CC were similar in both sexes [13]. Takeda et al. have also reported no sexual-relative differences in the size of CC in brains of Japanese subjects [25]. And finally, in Giedd et al. study, no sexual dimorphism was observed [10] consistent with many other investigators who found no particular link to sex.

However, Witelson and Clarke et al. reported greater width of trunk and larger isthmus in females as well as larger genu and anterior trunk in male brains [4, 29]. Also, Sullivan et al. have found that proportional callosal area (corpus callosum area/brain size) is larger in women [24]. In line with those finding, our results indicated that ratios of several areas of CC to its total area is associated with gender. Our findings clearly showed statistically significant sexual differences in all segments of CC in

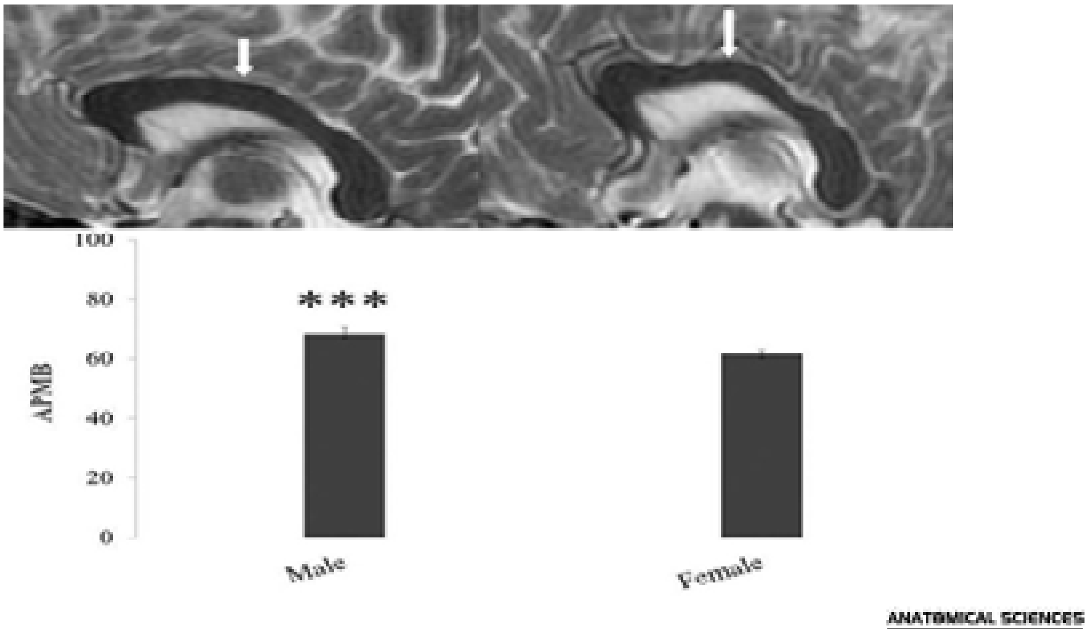

Figure 3. Ratio of area of posterior midbody (APMB) to total area of corpus callosum (ACC) in male and female brains.

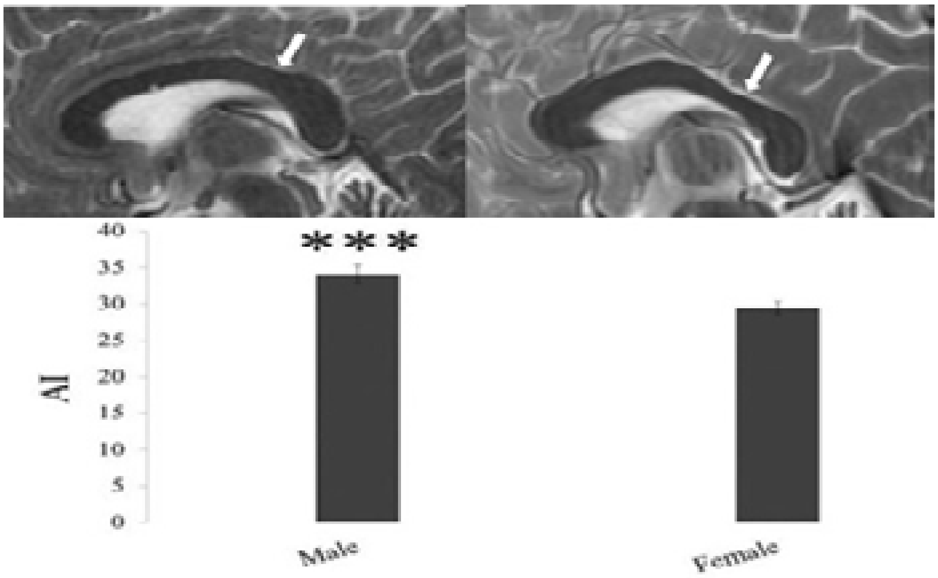

Figure 4. Ratio of area of isthmus (AI) to total area of corpus callosum (ACC) in male and female brains.

which CC size for men in midsagittal view was greater than that in female.

Among the 5 segments of CC, splenium has received more attention than other parts in almost all studies on sexual dimorphism [13]. As mentioned above, some studies have reported greater splenial width and area in females [2, 6, 7, 14, 15]. Bishop and Wahlstein based on 19 independent studies of human CC concluded that there was insufficient evidence to support the presence of sex-related differences in the size or shape of the splenium, irrespective of difference in the overall brain size in two sexes [3]. Additionally, Luders et al. suggested that effect of individual variations in callosal size was large enough to outrange any effect of splenial size differences between males and females [21]. Interestingly, in contrast with previous reports, our data revealed significant sexual difference with regard to splenium part of CC in a way that men have larger splenia compared to women. One possible reason for this discrepancy in

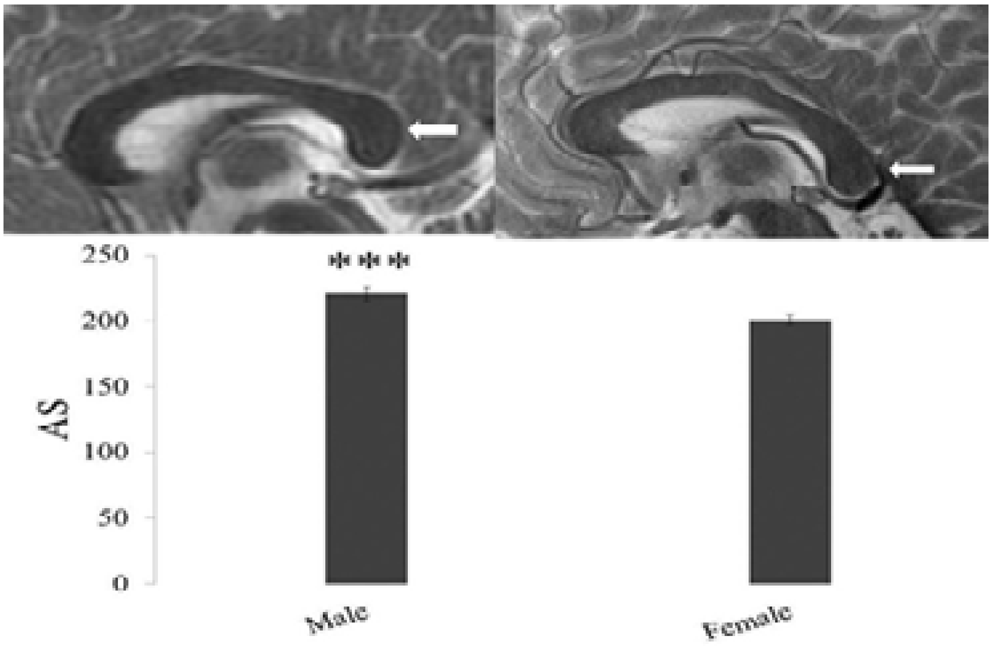

Figure 5. Ratio of area of splenium (AS) to total area of corpus callosum (ACC) in male and female brains.

results could be related to our way of assessment. We measured proportional callosal area to the total area of CC and therefore omitted this interfering variable from our results.

Based on our results, there are sexual-related differences between men and women with regard to areas of CC (accounting for the brain size). Our results indicate that all segments of CC in midsagittal view are greater in male brains than those in female brains.

Acknowledgements

The current research hasn't received any financial support.

Conflicts of Interests

The authors declared no conflict of interest.

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