Sexual dimorphism in the human corpus callosum after controlling for brain size

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Introduction

De Lacoste-Utamsing and Holloway (*Science*, 216:1431-1432, 1982) first suggested that on average, relative to brain size, the corpus callosum (CC) mid-sagittal cross-sectional area (CCA) in females is larger than in males. On the other hand, Bishop and Wahlsten (*Neurosci Biobehav Rev*, 21:581-601, 1997) performed a meta- analysis of 49 studies published before 1994 and came to the conclusion that there is no evidence suggesting a significant sex difference in the size of the CC. Regardless, it has been contended by many authors including in recent papers (Bruner et al., *J Anat*, 220:417-21, 2012) that any observed differences are not gender-specific but brain-size-specific. The idea is that as brain size increases, the CCA does not keep pace, such that subjects with larger brain size have a relatively smaller CCA regardless of their gender. Peters notes (*Can J Psychol*, 42:313-324, 1988) that: "... there is no reason to assume that whatever can or cannot be said about sex differences in corpus callosum parameters cannot also be said more generally about large and small brains." Hitherto this point has not been refuted. In the current paper, noting that there is a substantial overlap between brain size distributions in males and females, we compared the CCA between two groups of young adult females and males that had been closely matched for brain size. Therefore, any observed difference between CCA cannot be attributed to groups having different average brain sizes. As far as we are aware, none of the previous studies have used subjects matched for brain size in investigating the current question. We utilized brain images from the public domain OASIS database and have made our CC segmentations and area measurements available publicly (http://www.nitrc.org/projects/art) to facilitate independent analyses of the data. It is hoped that the availability of this completely transparent and easily accessible dataset would help in resolving this longstanding debate in the scientific community.

Methods

MRI volumes: The OASIS structural MRI scans are 3D sagittal T1-weighted volumes of matrix size: 256×256×128 and voxel size: 1×1×1.25 mm^3. Each volume is the post registration average of 3 or 4 independently acquired MP-RAGE scans with TR: 9.7 ms; TE: 4.0 ms; TI: 20 ms; TD: 200 ms; and flip angle: 10˚; obtained using a 1.5 Tesla Siemens Vision scanner (Erlangen, Germany). Subjects: We analyzed scans from 74 (37 males, 37 females, ages: 18-29 yrs) right-handed subjects in the OASIS cross-sectional database. An automated algorithm was used to select these subjects (from a total of 416 scans) so that the cohort included male and female pairs whose intracranial capacity (ICC) defined as the two-third power of the intracranial volume did not differ by more than 1 cm^2. CC Segmentation: We used a fully automated method to find the mid-sagittal plane (MSP) of the MRI volumes to bring the head yaw and roll angles as close as possible to zero. In addition, the anterior commissure (AP) and posterior commissure (PC) were located on the MSP using a fully automated model-based method. Using this information, the original MRI volume was re-sliced to obtain a single 2D image of matrix size: 512×512 and pixel size: 0.5×0.5 mm^2 representing the true AC-PC aligned MSP (Figure 1). Using *a priori* information a rectangular CC search region was indentified on the MSP as shown in Figure 1. Finally, a multi-atlas model-based segmentation method using the Automatic Registration Toolbox (ART) non-linear registration algorithm was used to locate the CC within the search region as shown in Figure 1. Our serial implementation of the entire segmentation process with 38 atlases takes less than one minute on a Linux workstation with 2.4 GHz clock speed. Statistical analysis: One-way analysis of covariance (ANCOVA) was performed using the SPSS 15.0 for Windows software with sex (F or M) as the fixed between-subject factor, age and ICC as covariates, and CCA as the dependent variable. Statistical significance was tested at the level of α=0.05 (two-tailed).

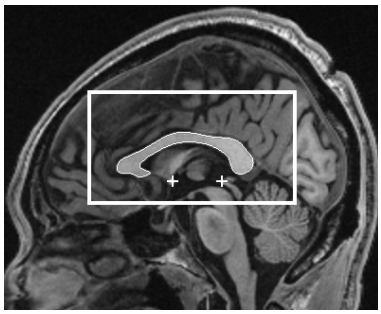

Figure 1: Automatically detected mid-sagittal slice, AC/PC landmarks, and rectangular CC search region.

Results

The mean (±SD) ICC was 133.43 (±5.64) cm^2 in females and 133.47 (±5.63) cm^2. Age was not associated with CCA [t(70)=1.52; p=0.133]. However, ICC was associated with CCA [t(70)=2.32; p=0.023]. Most significantly, when males and females were matched for ICC, mean female CCA was significantly greater than mean male CCA [t(70)=3.69; p<0.0005]. Estimated marginal means for the CCA correcting for age and ICC were 674 cm^2 in females and 610 cm^2 in males.

Discussion and Conclusions

We were able to confirm that there is a sexual dimorphism in the CCA, being larger in females in comparison to males by approximately 10% in young adults. There was no significant linear tendency for the CCA to decrease with age. This is expected in the age range considered. However, other studies have shown a steady decline in CCA with age in older adults after the age of approximately 65. Not surprisingly, larger brains tended to have larger CCA. The most significant contribution of the current study is that we compared the CCA between two groups of young adult females and males that had been closely matched for brain size. Therefore, the observed difference between CCA cannot be attributed to groups having different average brain sizes. As far as we are aware, this is the first study to use subjects matched for brain size in investigating sexual dimorphism in human CC.