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Sexual dimorphism in the human corpus callosum: an extension and replication study

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Summary. Using a new sample of 16 human brains (F = 8, M = 8), it was found that the splenial portion of the corpus callosum was larger and more bulbous in females than in males. In addition, the total area of the corpus callosum was both absolutely and relatively larger in females than in males, with the relative measurements (i.e., to brainweight) differing significantly. This was also true when using exponential values of brainweight commensurate with the areas and linear distances of the corpus callosum. These results, which replicate the findings of earlier work, were found by the two authors using different methods, and working independently of each other. We believe these findings provide a partial anatomical basis for purported gender differences in cognitive task behaviour, and are related to early gonadal steroidal influences during prenatal development.

Key words: Corpus callosum – Sexual dimorphism – Splenium – Gonadal steroids

Sexual dimorphism in the human brain has been extensively reviewed by Swaab and Hofman (1984) but for the most part little of substance has been unequivocably demonstrated, a matter well-appreciated by Mall's (1909) review, and Papez's (1927) study. More recently, Swaab and Fliers (1985) have reported a major difference in both the volume of the hypothalamic preoptic area, and their cell numbers, a finding indicating that these variables are approximately 2.2 to 2.5 times as large in males than in females. In an earlier paper, de Lacoste-Utamsing and Holloway (1982) reported a sexually dimorphic difference favoring females in the corpus callosum which interconnects the two cerebral hemispheres. Baack et al. (1982) suggested such a dimorphism was present by age 26 weeks prenatal, an observation more recently confirmed by de Lacoste et al. (in press). Such evidence suggests that both reproductive and non-reproductive (cognitive) behaviour patterns have some underlying dimorphic neural basis. Purported gender differences in cognitive tasks have been reported by Kimura and Harshman (1984), Witelson (1976), Harris (1978), and the results and problems extensively reviewed by McGlone (1980) and Kahn and Cataio (1984). Nonverbal differences have been exhaustively assessed by Hall (1984). Most recently, Witelson (1985) has provided evidence that differences between left and right handedness could provide a basis for callosal differences, as she found no significant sex effect. While handedness may indeed play a role in the size of the corpus callosum, we still find sex effects to be strong in autopsy cases unselected for handedness. (As we will show in the discussion section, there are some differences in Witelson's data).

It remains a fact, however, that most studies have been based on small sample sizes, and replication studies must play an important role in demonstrating the underlying neuroanatomical dimorphisms. In this paper, we report upon one such replication study involving the corpus callosum, and extend our analysis to provide relative measurements using exponential values of brain size commensurate with our callosal measurements.

Methods and results

Whole normal brains of both sexes ($n = 16$: F = 8; M = 8) were obtained from embalmed caucasian and black cadavers of the Willed-Body Program at the University of Texas Health Science Center in Dallas and weighed immediately, following removal of the falx cerebri and of the meninges exclusive of the pia matter. (Originally, the sample size was 17, including 9 females, one of which we deleted as the brain evidenced extreme atrophy.) The brains were stored in 10% formalin but rinsed in tap water for at least 24 hours prior to sectioning. Following a midsagittal cut precisely through the cerebral aqueduct, Kodachrome slides were taken of the medial aspect of the brain with a mm rule and autopsy I.D. # placed in the same plane. Sex of the brains was unknown at the time. One of us (MCL) traced the contours of the callosa directly from photographic (2 – 3 ×)

Table 1. Student t-tests for significant differences in the area of the human corpus callosum

Variable	n	Mean	SD	SE	t-values	p (2-tailed)
Brainweight						
Female	8	1202.0	126.95	44.8	0.61	0.550
Male	8	1248.0	170.21	60.18		
Age						
Female	8	73.0	10.73	3.79	−1.53	0.149
Male	8	63.7	13.33	4.71		
cc Area (MCL)						
Female	8	711.67	132.02	46.68	−1.32	0.207
Male	8	620.08	144.58	51.11		
cc Area (RLH)						
Female	8	770.05	133.03	47.03	−2.36	0.033
Male	8	619.90	121.45	42.94		
cc Area (RLH-MCL)						
Female	8	755.19	111.22	39.24	−2.35	0.034
Male	8	620.55	117.38	41.50		
cc Area (RLH_2)[a]						
Female	8	740.51	104.18	36.83	−2.14	0.051
Male	8	613.14	132.49	46.84		
cc Area[b] (average of 4 measurements)						
Female	8	744.35	113.52	40.14	−2.11	0.054
Male	8	618.42	125.28	44.29		

[a] These represent the average of two separate measurements; [b] i.e., the average of (MCL), (RLH-MCL), (RLH), and (RLH_2). CC area is the total corpus callosal area: MCL refers to MCL measurements; RLH refers to RLH measurements. RLH-MCL refers to MCL's digitizing of RLH's 1st set of measurements; and RLH_2 refers to RLH's 2nd set of measurements. The male range in brainweight was 936 – 1515 g; in females, 1030 – 1350 g. Male age varied between 35 – 81 years; females between 53 – 87 years. Areas are measured in mm^2. SD is the standard deviation, and SE is the standard error. In two comparisons (RLH, and RLH-MCL), the differences are significant at less than the 0.05 level. In RLH_2 and the average of the four measurements, the differences are slightly over the 0.05 level. In all cases, the female corpus callosal area is absolutely larger than the male counterpart, although the male brainweight is higher

Table 2. Student t-tests for significant differences in dorso-ventral splenial distance

Variable	n	Mean	SD	SE	t-value	p (2-tailed)
Splenial DV (RLH_1)						
Female	8	1.31	0.13	0.05	−2.67	0.018
Male	8	1.06	0.22	0.08		
Splenial DV (RLH_2)						
Female	8	1.31	0.12	0.04	−3.14	0.007
Male	8	1.04	0.21	0.07		
Splenial DV (MCL)						
Female	8	1.40	0.18	0.06	−4.67	0.000
Male	8	0.98	0.18	0.06		
Splenial DV (Av.) (Average of 3 measurements, 2 RLH, 1 MCL)						
Female	8	1.33	0.09	0.03	−4.03	0.001
Male	8	1.03	0.20	0.07		

Dorsoventral splenial distances were measured in cm, using a vernier caliper. Splenial DV ($RLH_{1,2}$) refers to RLH's measurements; MCL refers to MCL's measurements. The average of the three measurements is also given. In all cases, the differences are significant at less than the 0.02 level

Table 3. Student t-tests for significant differences in ratio variables

Variable	n	Mean	SD	SE	t-value	p (2-tailed)
$Brainweigth^{0.333}$						
Females	8	10.59	0.38	0.13	0.56	0.582
Males	8	10.72	0.50	0.18		
$Brainweight^{0.666}$						
Females	8	112.39	7.96	2.81	0.59	0.566
Males	8	115.15	10.60	3.75		
Av. cc/$Brainweight^{0.666}$($\times 100$)						
Females	8	662.27	88.70	31.36	−2.99	0.010
Males	8	534.93	81.35	28.76		
Av. Splenial DV/$brainweight^{0.333}$($\times 100$)						
Females	8	12.65	0.95	0.33	−4.75	0.000
Males	8	9.55	1.58	0.56		
Av. cc/Brainweight						
Females	8	0.6213	0.086	0.030	−3.21	0.006
Males	8	0.4954	0.071	0.025		
Av. Splenial DV/brainweight						
Females	8	0.0011	0.000	0.000	−4.86	0.000
Males	8	0.0008	0.000	0.000		
(Av. Splenial DV/$braingweight^{0.333}$)/(Av. cc/$braingweight^{0.666}$)						
Females	8	0.0193	0.002	0.001	−0.82	0.425
Males	8	0.0181	0.003	0.001		

Table 3 uses both the total brainweights, and those made commensurate with the variable measured (i.e., $brainweight^{0.666}$) for total cc area, and $brainweight^{0.333}$ for dorsoventral splenial distance. (These two ratios were multiplied by 100). Using exponential values for brainweight does not change the lack of significant differences between male and female values. These tests indicate that relative to brainweight, whether total or exponential, both the average cc area and dorsoventral splenial distances are significantly larger in females at less than the 0.01 level. Note, however, that the ratio of splenial distance divided by corpus callosal area, corrected for brainweight, does *not* show a significant difference between males and females, although values for females are higher

projection of the slides onto a graphics tablet connected to a tektronix graphics terminal attached to a timesharing computer, which computed the cross-sectional surface areas. The slides were then sent to RH who had no knowledge of either sex or brain weights. RH used an Omega enlarger to project the slides (approximately 2 – 3 times), onto bond paper, tracing the outline of the corpus callosum. These tracings were then measured using a Tamaya Planix-7 digital planimeter. In addition, RH measured the dorsoventral splenial widths. RH then sent his tracings to MCL who digitized them on the above device. After an 8-month interval, the slides were returned to RH for a second set of measurements, and MCL measured the dorsoventral splenial widths from her tracings. Dorsoventral splenial width is the maximum distance between two parallel lines drawn at tangents to the dorsal and ventral splenial surfaces. These lines are usually drawn parallel to the axis of the body just anterior to the splenium. Thus, we report herein the results of four individual measurements, two acquired at Dallas, and two in New York.

Table 4. Student t-tests on pairs of measurements, sexes combined

Variables	n	$\bar{x}$	SD	t	r	2-tailed P	Differ. (mean)
Splenial (RLH)	16	1.18	0.22	−0.13	0.77	0.898	−0.0058
Splenial (MCL)	16	1.19	0.28				
CC Area (MCL)	16	665.87	141.86	−1.39	0.831	0.184	29.10
CC Area (RLH-MCL)	16	694.78	145.44				
CC Area (MCL)	16	65.87	141.86	1.23	0.866	0.236	21.99
CC Area (RLH_1)	16	687.87	130.52				
CC Area (MCL)	16	665.87	141.86	0.71	0.902	0.488	10.95
CC Area (RLH_2)	16	676.82	132.60				
CC Area (RLH_1)	16	687.87	130.52	0.90	0.931	0.381	11.05
CC Area (RLH_2)	16	676.82	132.60				

The variables are as described in Tables 1 and 2, providing the mean $\bar{x}$, SD (standard deviation of the differences between two observers' measurements). The two-tailed p values indicate no significant differences between pairs of measurements. The r values (correlation coefficients) are all significant at less than the 0.003 level. The differences between means are very small, the average being well-less than 10%, although the SDs of the differences are close to 10%. Units are as in Tables 1 and 2

A quantitative analysis was then performed using student t-tests from the SPSSX package (SPSSX, 1983), as reported in Tables 1 – 4. In addition, an Anova subroutine was used to assess the effects of age and sex on callosal areas (Tables 5).

As reported earlier (de Lacoste-Utamsing and Holloway, 1982), the *absolute* values of both total corpus callosal area and dorsoventral splenial width were larger in females, but the former were not significant below the $p = 0.05$ level (Table 1). Table 2 shows that the splenial widths are significantly larger in females. However, the ratios of total corpus callosal area to brain weight, and the splenial width divided by brain weight were all significantly different at a level lower that $p = 0.05$, as seen in Table 3. (Since the two measurements used were either an area (cc area) or a linear distance measured by calipers (dorsoventral splenial distance), and the control variable a volume or weight (brainweight), we have also used exponential values of brainweight for our relative measurements or ratios. The two-thirds power of brainweight should provide a more commensurate measurement to use with an areal measurement, and the one-third power of brainweight should provide a control more commensurate with splenial distance.) These corrective ratios are necessary given (1) that there is an initial dimorphism in brain weight favoring males, and (2) the female average age was slightly higher than in males. As there is well-documented knowledge of a loss of brainweight with age (e.g. Dekaban and Sadowsky, 1978) these ratios are justified.

Table 5. Anova analyses of both age and sex effects

Variable	Covariate	Main effect	F-ratio	Signif. of F	Multiple R
Brainweight	Age		2.050	0.176	0.370
		Sex	0.009	0.928	
CC area (MCL)	Age		7.081	0.020	0.746
		Sex	9.223	*0.010*	
CC area (RLH)	Age		2.750	0.121	0.760
		Sex	14.975	*0.002*	
CC area (RLH-MCL)	Age		1.654	0.221	0.720
		Sex	12.366	*0.004*	
CC area (RLH_2)	Age		3.199	0.097	0.747
		Sex	13.236	*0.003*	
CC area (Av.)	Age		3.984	0.067	0.764
		Sex	14.285	*0.002*	
CC area (Av.)/ Brainweight	Age		2.355	0.149	0.793
		Sex	19.744	*0.001*	
CC area (Av.)/ $Brainweight^{0.666}$	Age		1.553	0.235	0.790
		Sex	20.063	*0.001*	
Splenial DV (Av. of 3 meas.)	Age		0.001	0.979	0.790
		Sex	21.515	*0.000*	
Splenial DV/ of 3 meas.)	Age		0.001	0.979	0.790
		Sex	21.515	*0.000*	
Splenial DV/ $Brainweight^{0.333}$	Age		0.363	0.557	0.815
		Sex	25.323	*0.000*	
Splenial DV/ CC area (Av.)	Age		3.664	0.078	0.475
		Sex	0.127	0.727	

Analysis of variance results using the classic experimental approach which assesses separately the covariate effects (age), then main effects of factors (sex), adjusting for each other. (See SPSSX 1983, p. 444). Age does not appear to be a significant covariate effect in this sample, as can be seen by the strong F-ratios for sex. The corrected ratios show a strong sex effect, i.e., either cc area or dorsoventral splenial distance divided by its relevant exponential value of brainweight

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