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Morphometry of the adult human corpus callosum: lack of sexual dimorphism*

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INTRODUCTION

A major sexual dimorphism in the mid-sagittal cross-section of the adult human corpus callosum was described by de Lacoste-Utamsing & Holloway (1986), the splenium in female brains being larger and more bulbous than in the brains of males. The implications of such a large difference for neurobiology are considerable. The initial series reported was small, comprising five female and nine male brains, although some of the differences recorded achieved statistical significance at the 0·1% level. Subsequently the same authors extended their observations to 38 fetal and a further 16 adult brains and found sexual dimorphism during development and in adulthood (de Lacoste, Holloway & Woodward, 1986; Holloway & de Lacoste, 1986). Yoshi *et al.* (1986) also found that the splenium was more bulbous in females. Their study included 19 female and 14 male brains. Sexual dimorphism of the splenium has also been described in 15 pongid brains but not in other non-human primate species (de Lacoste & Woodward, 1988).

However, Bell & Variend (1985), who examined 44 brains, (28 male, 16 female) from children ranging in age from term infants to 14 years found no evidence of sexual dimorphism in the corpus callosum. Witelson (1985), in a study of the corpus callosum with respect to handedness, noted in passing that she was unable to detect any sexual dimorphism in the corpus callosum in a sample of 42 adult subjects. Studies by Weber & Weis (1986), Byne, Bleier & Houston (1988) and Demeter, Ringo & Doty (1988) also failed to find a difference between the sexes. These three groups of workers examined a total of 108 brains.

In view of the uncertainty concerning the existence of a major anatomical difference between the brains of men and women, we have studied 33 adult human brains, 17 male and 16 female, using a variety of morphometric approaches to see whether we could detect such a difference.

MATERIALS AND METHODS

Twenty eight brains were removed from dissecting room subjects preserved by perfusion–fixation with a solution containing 7% formaldehyde, 40% ethanol, 13% glycerine and 0·1% Panacide (an anti-fungal agent) via the femoral arteries. Five were

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right half-brains which had been fixed by flotation in 10% buffered formalin after the whole brain, obtained at autopsy, had been divided in the mid-sagittal plane and the left half-brain taken for biochemical studies. The right cerebral hemisphere was removed from the cadavers by a mid-sagittal slice through the corpus callosum, and a slice at right angles through the upper mid-brain. The latter incision only was necessary for the half-brains as the former had already been made. Fragments of the septum pellucidum were trimmed away with scissors and the hemispheric weight recorded on an Oertling electronic balance. Diseased and grossly atrophic brains were excluded, as were those specimens in which the corpus callosum was damaged during dissection. There were 33 brains (17 male, 16 female) for which data could be analysed morphometrically.

Photographs were taken of the medial surface of the hemisphere with a millimetre scale in the same plane as the cut surface of the corpus callosum, Black and white photographic prints were prepared at magnifications of 1·5 to 2·4. The image magnification was calculated for each photograph by direct measurement. The outline of the corpus callosum was then transferred to tracing paper and this outline was used for subsequent morphometric analysis. Each author independently traced the corpus callosum without knowing the sex of the subject. Both tracings were measured in every case, using a digitiser tablet and Graphic Information Systems 5040 series microcomputer using a specially written BASIC program. The following measurements were made for each corpus callosum: length (CCL), area (CCA) and circumference (CCC); area (SPA) and circumference (SPC) of the posterior fifth, which was taken to represent the splenium; maximum width of the splenium (SPW). A form factor defined as $4\pi A/C^2$, where A is the area and C the circumference of the area in question, was calculated for the whole corpus callosum (CCFF) and for the splenium (SPFF). This form factor has extreme possible values of 0 (straight line) and 1 (circle), and measures the 'circularity' of an area.

CCFF, SPFF and the ratios CCW/CCL and SPA/CCA are dimensionless and do not need correction for hemispheric weight. The weight (W) of similar objects is proportional to the cube of linear dimension (L^3), while their cross-sectional area, A, is proportional to L^2. It follows that

$$W \propto L^3 \propto A \times L \propto A\sqrt{A} = A^{\frac{3}{2}}.$$

It is possible therefore to correct individual measurements to the mean hemispheric weight for all 33 brains by the implied formulae

$$L_c = L_{uc}(W/w)^{\frac{1}{3}}$$
$$A_c = A_{uc}(W/w)^{\frac{2}{3}}$$

where L_c and A_c are corrected lengths and areas, L_{uc} and A_{uc} are uncorrected lengths and areas, W is the mean hemispheric weight (507·25 g), and w the weight of the individual hemisphere. On average, the ratio W/w is greater than unity for female brains and less than unity for male brains. The effect of the correction formula is therefore to increase the measurements for the female brains, and decrease them for the male brains. Means of uncorrected and corrected measurements for male and female brains were compared by t tests.

RESULTS

Table 1 lists means and standard deviations of the measurements made by each observer. The means were closely concordant for all measurements, paired t tests

Table 1. *Reproducibility of measurements made on separate tracings by two observers (AD and JJG). Means, standard deviations and t values for comparison of means. Absolute t values are all much less than critical value for P = 0·05*

	Observer: AD		Observer: JJG		
Measurement	Mean	SD	Mean	SD	*t* value
CCL (mm)	74·98	5·31	75·04	5·39	−0·105
CCC (mm)	205·1	17·97	206·1	17·62	−0·963
CCA (mm²)	637·3	120·5	639·0	124·0	−0·625
CCFF	0·1919	0·0352	0·1895	0·0318	0·053
SPL (mm)	15·03	1·07	15·04	1·07	−0·039
SPC (mm)	55·68	4·77	55·74	4·77	−0·011
SPA (mm²)	181·1	36·1	181·0	34·2	0·069
SPFF	0·7353	0·1097	0·7344	0·1160	0·011

Table 2. *Comparison of age, sex and measurements for female and male brains*

	Male brains		Female brains		
	Mean	SD	Mean	SD	*t* value
Age	74·4	11·3	82·0	7·1	—
Hemispheric weight (g)	535·8	46·1	476·0	60·0	—
	Uncorrected measurements				
CCL (mm)	75·9	5·8	74·1	4·9	0·96
CCC (mm)	207	17	204	18	0·49
CCA (mm²)	656	130	621	112	0·83
CCW (mm)	11·5	2·0	11·1	2·1	0·56
CCW/CCL	0·149	0·026	0·144	0·028	0·53
SPA/CCA	0·298	0·031	0·276	0·022	2·35
SPC (mm)	56·9	5·2	54·5	3·9	1·50
SPA (mm²)	192	39	170	27	1·88
CCFF	0·191	0·028	0·189	0·039	0·17
SPFF	0·744	0·103	0·724	0·123	0·51
	Corrected measurements				
CCL (mm)	74·6	5·6	75·8	4·3	−0·69
CCC (mm)	204	17	209	17	−0·84
CCA (mm²)	631	114	646	100	−0·40
CCW (mm)	11·5	1·9	11·4	2·0	0·15
SPC (mm)	55·9	5·1	55·1	4·6	0·47
SPA (mm²)	185	34	172	35	1·08

showing no difference between the two observers. Inter-observer reproducibility was therefore considered acceptable and the means of the two determinations were used in subsequent analysis. Consistency of the same observer on separate occasions was not assessed.

Table 2 lists means, standard deviations and *t* values of uncorrected and corrected measurements for male and female brains, as well as giving age and hemispheric weight data. For 31 degrees of freedom, the absolute value of *t* should exceed 2·04 to be significant at the 5% level (two tailed). The only measurement for which this was true was the ratio SPA/CCA, SPA being relatively larger in male brains.

DISCUSSION

The brains we have studied are from relatively aged subjects. As the brain ages its weight decreases, gyri shrink, sulci and ventricles become larger. This atrophy proceeds slowly to the age of 60 and more rapidly thereafter. Neuronal loss occurs in many parts of the brain, although some areas are more susceptible than others. In the cerebral cortex many neurons have been lost by the ninth decade (Brody, 1955). Neuronal loss proceeds even in the absence of overt dementia. The corpus callosum, via its cortical radiations, links the neopallium of the two hemispheres, and the loss of cortical neurons is likely to cause secondary loss of callosal fibres, those of the splenium as a consequence of loss in the occipital cortex. Specific studies of age-related changes in the corpus callosum are hard to find, but atrophy, as measured by decreasing weight, proceeds *pari passu* in men and women (von Braunmühl, 1957), and there are no data suggesting sex differences in the pattern of cortical atrophy. We believe that the age of our subjects is not likely to have obscured sex differences in the corpus callosum, but recognise that studies of younger subjects would be desirable. Neither Holloway & de Lacoste (1986) nor Yoshi *et al.* (1986) give specific age data.

It is well known that the brains of men are larger and heavier than those of women. This presents a difficulty for studies of sexual dimorphism, in that real differences between the brains of men and women may be obscured, or spurious differences created, by this difference in size. The question arises whether it is proper to attempt correction for brain weight. Correction reflects the theoretical model of relationships between brain weight and the quantities under consideration, and the model may not be correct. Corrected data must therefore be interpreted with caution, even scepticism. We have, however, preferred to include corrected data as some authors believe that corrections of the kind we have made may reveal biologically significant relationships (Holloway & de Lacoste, 1986).

Using techniques comparable to those of de Lacoste & Holloway, we have found no difference between the sexes in the morphology of the adult human corpus callosum. The only measurement, apart from hemispheric weight, to differ significantly (SPA/CCA; $P < 0{\cdot}05$) between the sexes did so in the opposite direction to that expected from the studies of de Lacoste & Holloway. The circularity form factor permitted quantitation of splenial bulbosity and did not support the qualitative assessment of de Lacoste & Holloway. Our findings agree with several published studies relating to human material. Taken together, our own studies and those of Bell & Variend (1985), Weber & Weis (1986), Byne *et al.* (1988) and Demeter *et al.* (1988) refer to 105 brains from neonates to subjects in the tenth decade of life. The magnetic resonance imaging study by Byne *et al.* has the advantage of measuring the intact living brain. There is no conclusive evidence for major sexual dimorphism in the human corpus callosum, of the order described originally by de Lacoste-Utamsing & Holloway (1986). This is important to investigators interested in the lateralisation of cerebral function, brain sex and cognate matters. The non-human primate studies of de Lacoste & Woodward (1988) concerned 56 brains representing 34 species. There was no sex dimorphism of the corpus callosum of ceboids or cercopithecoids. Data for strepsirrhines were ambiguous but for 15 pongids they reported significant differences in the ratios of callosal and splenial area to brain weight. Replication of these observations would clearly be of interest. Here, as with human brains, only large critically conducted studies will exclude the possibility of minor variation of the corpus callosum between the sexes.

SUMMARY

Morphometric analysis of the corpus callosum of 33 human brains (17 male, 16 female) showed no sexual dimorphism, whether or not any correction was made for brain weight.

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