NeuroReport 6, 1002–1004 (1995)

Corpus callosum and brain volume in women and men

Helmuth Steinmetz,[CA] Jochen F. Staiger, Gottfried Schlaug, Yanxiong Huang and Lutz Jäncke[1]

Department of Neurology and [1]Institute of General Psychology, Section of Cybernetical Psychology and Psychobiology, Heinrich-Heine-Universität, PO Box 101007, D-40001 Düsseldorf, Germany

[CA] Corresponding Author

USING high-resolution *in vivo* magnetic resonance morphometry we measured the midsagittal area of the corpus callosum and total forebrain volume in 120 healthy young adults (mean age (± s.d.) 25.7 ± 4.7 years). The forebrain volume-adjusted size of the corpus callosum was larger in women than in men (32 mm² mean difference; $p = 0.011$). Handedness had no effect in this measurement. The morphometric data confirm a gender difference in cerebral structural organization.

Key words: Brain anatomy; Corpus callosum; Gender differences; Handedness; Laterality; Magnetic resonance imaging; Sex characteristics

Introduction

Gender differences in the anatomy of the human corpus callosum have been a matter of long-standing dispute. Although there is indeed increasing evidence for sexual dimorphism of callosal shape from both post-mortem investigations[1–4] and magnetic resonance (MR) imaging,[4–7] no consistent sex difference has emerged for callosal size when brain weight was statistically controlled.[3,8,9] However, influences of patient age, terminal illness, brain fixation and sample heterogeneity could not be excluded in the post-mortem investigations, and the *in vivo* imaging studies did not take brain weight or volume into account. Thus, a number of confounding variables may have contributed both to possible false-positive or false-negative results in previous reports. We used high-resolution *in vivo* MR morphometry of callosal size and forebrain volume in 120 young healthy adults.

Materials and Methods

Participants. The study participants were recruited through announcements in the local Medical School specifically calling for participation in a study comparing left- and right-handers, men and women. Following informed consent, 120 consecutive persons reporting no neurological or psychiatric illness, failure in elementary school, or claustrophobia were studied. Most of them were university students or medical faculty members who were paid for their participation. Handedness was determined with the Hand Dominance Test.[10] This paper and pencil test of hand motor skill consists of three dexterity tasks (tracing lines, dotting circles, tapping on squares) each to be performed with maximal speed and precision over 15 s, with each hand. Laterality coefficients (R–L)/(R+L) were calculated. Negative values indicated left-handedness and positive values, right-handedness.[10,11] According to these measurements, there were 29 left-handed women, 29 left-handed men, 20 right-handed women, and 42 right-handed men.

In vivo MR morphometry. This technique has been described previously in detail.[7] Briefly, we employed a volumetric fast low-angle shot MR sequence (1.00 mm × 1.00 mm × 1.17 mm image voxel size) with sagittal slice orientation (128 contiguous slices covering the entire brain). The total cross-sectional corpus callosum area (CCA) was measured on the midsagittal slice by a blinded observer (interobserver reliability: $r = 0.96$ as calculated according to the formula of Bartko and Carpenter[12] for observers J.F.S. and G.S.; $n = 40$; $p < 0.001$). In addition, forebrain volume was measured using MR image segmentation, that is, a computerized, step-wise, interactively controlled procedure which removes all tissue and fluid not corresponding to brain gray or white matter from each image slice (Fig. 1).[13] The hindbrain was removed by a cut-off line spanning from the base of the mamillary bodies to the upper margin of the posterior commissure.

Statistical analysis: For each gender orthogonal linear and quadratic regression analyses were performed with forebrain volume as independent and CCA as dependent variables. Because significant linear correlations emerged (Table 1), forebrain volume as a source of variance was partialled out[14] by calculating the linearly adjusted callosal area measure CCA′. Since gender and handedness differences in callosal morphology have been described,[1–7,15] two-way analyses of variance (ANOVA) were performed for CCA′ with gender and handedness as between-subject factors.

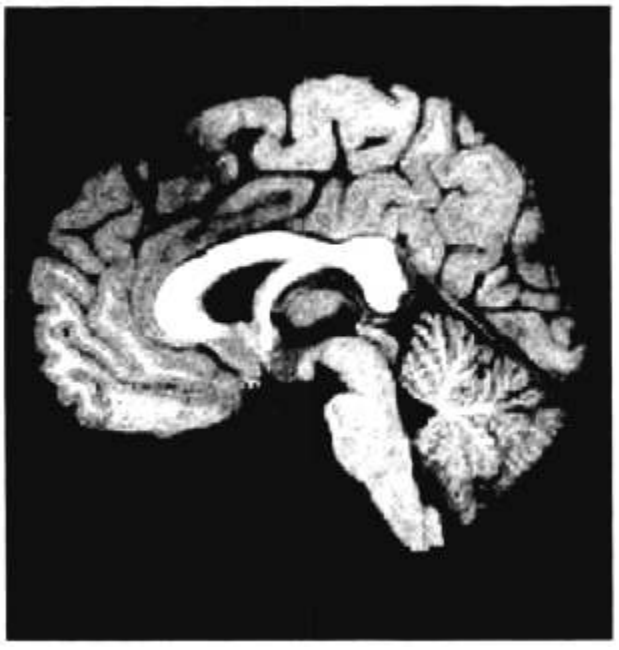

FIG. 1. Midsagittal MR image containing cross-section of the corpus callosum (pixel size: 1.00 mm × 1.00 mm; slice thickness: 1.17 mm). All non-brain tissue has been removed for the purpose of brain volumetry.

Table 1. Linear correlations (Pearson correlation coefficients) between body height, forebrain volume and absolute midsagittal corpus callosum area (CCA)[a]

	Women (n = 49)		Men (n = 71)	
	Forebrain volume	CCA	Forebrain volume	CCA
Forebrain volume	—	0.57**	—	0.42**
Body height	0.30*	0.11	0.04	−0.21

**$p < 0.001$; *$p = 0.030$.
[a]For all comparisons, orthogonal quadratic correlations were also calculated but did not provide additional explanations regarding CCA variation ($p > 0.10$).

Results

The gender differences in body height and brain volume observed in our sample (Table 2) corresponded to those in a large North American post-mortem series of 22- to 30-year-old men and women compiled 20 years ago by Dekaban and Sadowsky.[16] With respect to the forebrain volume-adjusted midsagittal callosal area (CCA'), the ANOVA revealed a main gender effect [$(F(1,116) = 6.597$, $p = 0.011$], no handedness effect [$F(1,116) = 2.193$, $p = 0.141$], and no handedness by gender interaction [$F(1,116) = 0.002$, $p = 0.964$] (Table 3). There were only weak or non-existent correlations between forebrain volume and body height (Table 1). This confirms the view of others[17] that body height is an unsuitable parameter for normalizing brain morphometric data.

Table 2. Anthropometric data (mean ± s.d.) for 120 adults studied with *in vivo* MR brain morphometry

	Women (n = 49)	Men (n = 71)	Gender effect*
Age (years)	26.3 ± 4.8	25.3 ± 4.5	n.s.
Height (cm)	169.8 ± 6.0	180.7 ± 6.3	$p < 0.001$
Forebrain volume (ml)	986 ± 100	1084 ± 107	$p < 0.001$

*according to two-sample t-tests with degrees of freedom = 116; n.s., not significant.

Table 3. Mean midsagittal corpus callosum area (± s.d.) in women and men: absolute (CCA) and forebrain volume-adjusted measurements (CCA')

	Women (n = 49)	Men (n = 71)	Gender effect
CCA (mm^2)	664 ± 81	663 ± 82	n.s.
CCA' (mm^2)	682 ± 69	650 ± 74	$p < 0.011$*

*According to two-way ANOVA; n.s., not significant.

Discussion

This is the first study reporting *in vivo* measurements of the corpus callosum adjusted for variation attributable to brain volume. Our finding of an increased relative callosal size in women concurs with two previous post-mortem studies of smaller samples by Holloway *et al.*[2,18] What are the implications of this finding? According to Aboitiz *et al*[9,19] the packing density of fibres in the human corpus callosum does not differ between genders or change with midsagittal callosal area. If this is correct, one possible interpretation of our data is a higher percentage of callosal neurons, or increased axonal branching of these neurons, in the female brain. This would support the notion that callosal connectivity may be stronger in women because of a more bilateral representation of cognitive functions.[1,3] However, explanations focused on such possible differences in cortico-cortical connectivity rest on the assumption that neuronal packing densities are equal in the unequally sized brains of men and women. That this is not necessarily the case is suggested by one post-mortem study that has calculated very similar total numbers of cortical neurons for both sexes, despite smaller female brains.[20] In contrast, Pakkenberg and colleagues found no gender difference in neuronal density.[21] In either case, whether explaining the present finding by a gender difference in interhemispheric connectivity or in neuronal spacing, the data suggest an intriguing divergence of structural brain organization that calls for further clarification by post-mortem studies. The timing of factors leading to such differences will also have to be clarified, particularly because it has recently been suggested that the corpus callosum may continue to grow throughout the first decades of human life[22–24] and that decreases in callosal size occurring later may differ between the sexes.[23,25]

Conclusion

Using *in vivo* MR morphometry in 120 healthy young adults we found a gender difference in the forebrain volume-adjusted size of the corpus callosum. In principle, this finding can be explained by gender differences in callosal fibre density, cerebral neuronal density or transcallosal interhemispheric connectivity. The prenatal or postnatal mechanisms creating the difference are unknown, as are the functional implications. Our study illustrates that *in vivo* morphometry alone does not provide meaningful results and has to be complemented by post-mortem anatomical investigations of the relationship between microstructure and macrostructure.

ACKNOWLEDGEMENTS: This study was supported by grants from the Deutsche Forschungsgemeinschaft (SFB 194/A7) and the Hermann-und-Lilly-Schilling-Stiftung (H.S.). The authors also thank Professor U. Mödder, Institute for Diagnostic Radiology, Heinrich-Heine-Universität Düsseldorf, for providing them time in the MR facility, and Professor K. Zilles, C. & O. Vogt Brain Research Institute, Heinrich-Heine-Universität Düsseldorf, for particularly helpful discussions.

References

1. de Lacoste-Utmasing C and Holloway RL. *Science* **216**, 1431–1432 (1982).
2. Holloway RL and de Lacoste MC. *Hum Neurobiol* **5**, 87–91 (1986).
3. Witelson SF. *Brain* **112**, 799–835 (1989).
4. Clarke S, Kraftsik R, van der Loos H *et al. J Comp Neurol* **280**, 213–230 (1989).
5. Allen LS, Richey MF, Chai YM *et al. J Neurosci* **11**, 933–942 (1991).
6. Habib M, Gayraud D, Oliva A *et al. Brain Cognition* **16**, 41–61 (1991).
7. Steinmetz H, Jäncke L, Kleinschmidt A *et al. Neurology* **42**, 749–752 (1992).
8. Witelson SF and Kigar DL. Anatomical development of the corpus callosum in humans: a review with reference to sex and cognition. In: Molfese DL and Segalowtiz SJ, eds. *Brain Lateralization in Children: Developmental Implications.* New York: Guilford Press, 1988: 35–57.
9. Aboitz F, Scheibel AB and Zaidel E. *Brain* **115**, 1521–1541 (1992).
10. Steingrüber HJ. *Z Exp Angew Psychol* **18**, 337–357 (1971).
11. Jäncke L, Schlaug G, Huang Y *et al. NeuroReport* **5**, 1161–1163 (1994).
12. Bartko JJ and Carpenter WT. *J Nerv Ment Dis* **163**, 307–317 (1976).
13. Huang Y, Knorr U, Schlaug G *et al. J Cereb Blood Flow Metab* **13** (Suppl. 1), S315 (1993).
14. Pedhazur EJ. *Multiple Regression in Behavioral Research: Explanation and Prediction.* New York: Holt Rinehart and Winston, 1982.
15. Witelson SF and Goldsmith CH. *Brain Res* **545**, 175–182 (1991).
16. Dekaban AS and Sadowsky D. *Ann Neurol* **4**, 345–356 (1978).
17. Peters M. *Can J Psychol* **45**, 507–522 (1991).
18. de Lacoste MC, Adesanya T and Woodward DJ. *Biol Psychiat* **28**, 931–942 (1990).
19. Aboitz F, Scheibel AB, Fisher RS *et al. Brain Res* **598**, 143–153 (1992).
20. Haug H. *Am J Anat* **180**, 126–140 (1987).
21. Pakkenberg B, Evans SM, Moller A *et al. Soc Neurosci Abstr* **16**, 1134 (1990).
22. Hayakawa K, Konishi Y, Matsuda T *et al. Radiology* **172**, 171–177 (1989).
23. Cowell PE, Allen LS, Zalatimo NS *et al. Dev Brain Res* **66**, 187–192 (1992).
24. Pujol J, Vendrell P, Junqué C *et al. Ann Neurol* **34**, 71–75 (1993).
25. Witelson SF. *N Engl J Med* **325**, 211–212 (1991).

Received 13 February 1995; accepted 25 February 1995