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No Sex-Related Differences in Human Corpus Callosum Based on Magnetic Resonance Imagery

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Recent studies have reported sex-related differences in the morphology of the human corpus callosum in cadaver brains. To further investigate these reports, sagittal magnetic resonance image scans from 40 male and 40 female subjects were used to compare callosal morphology. Relative callosal measurements were calculated by morphometric analysis. Significant sex-related differences were not found for callosal areas, maximal callosal width, or callosal curvature. These results indicate the need for further study before claims of sex-related differences can be accepted.

Oppenheim JS, Lee BCP, Nass R, Gazzaniga MS: No sex-related differences in human corpus callosum based on magnetic resonance imagery. Ann Neurol 21:604–606, 1987

Neuropsychological studies suggest that males show greater cerebral lateralization of language and spatial skills, whereas females evidence greater bilateralization of function, particularly for language [1]. Sex-related anatomical differences between the cerebral hemispheres have also been reported. Wada and associates [8] found that the left planum temporale—a brain region closely associated with language skills [2]—is likely to be larger in adult men than in adult women.

Recent interest has focused on morphological sex-related differences of the corpus callosum. deLacoste-Utamsing and Holloway [6] reported greater splenial width and area (the posterior fifth of the callosum), but not greater callosal length, in 5 female versus 9 male cadaver brains. In addition, the total cross-sectional area, although indistinguishable as an absolute value, was larger in the females when calculated relative to brain weight.

Witelson [9], who examined 12 male and 21 female cadaver brains, found no sex-related difference in callosal or splenial areas. Consistent with the previous finding [6], however, females had a larger callosal area only when calculated relative to brain weight. Witelson also reported that ambidextrous subjects had a slightly larger callosal area than those who were right-handed (0.75 cm^2), but this difference was unrelated to sex.

deLacoste-Utamsing and Holloway [6] defined the splenium by dividing the maximal callosal length into fifths and calculating the area of the most posterior fifth. They argued that the female splenium is more bulbous, but offer no quantitative evidence. Alternatively, a larger splenium might be observed if the callosum had a greater curvature. Since the area subtended by an arc increases with the curvature of the arc, a callosum with a greater curvature should be subtended by a larger area.

The poor replication and uncertain interpretation of these earlier studies indicated the need for a larger study. Magnetic resonance imagery (MRI) offers the advantage of an in vivo analysis on a larger number of subjects. In this study, MRI was used to examine callosal morphology for several sex-related differences.

Method

The sagittal images evaluated were produced by a 0.5-T Teslacon MRI system at the Cornell University Medical Center (see [5]). The subjects, 40 men and 40 women, were patients at the New York Hospital–Cornell Medical Center, and were suffering from diseases that did not involve either the cerebral hemispheres or the corpus callosum. The MR images had a nominal in-phase resolution of 1.0 × 1.3 mm, enabling detailed observation of callosal morphology.

Tracings of the MR images were enlarged, and morphometric area measurements were made using a Zeiss MOP-3 X;Y image digitizer. The methods of measurement previously employed [6, 9] were not accurately described; however, a similar method was estimated. Measured areas were determined as follows (Figure). A straight line (line A) was drawn through the most inferior borders of the splenium and rostrum. From this line, perpendicular lines were drawn

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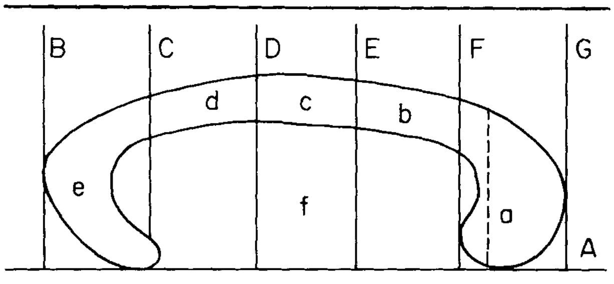

Method of measurement. (See text for further description.)

at the anterior edge of the rostrum and at the caudal end of the splenium (lines B and G). The length of line A between lines B and G represented the maximal callosal length. This length was divided by five and further perpendicular lines were then drawn (lines C, D, E, and F) to then divide the callosum into five areas (a, b, c, d, e). Measurements were also made of the total callosal area and of the area beneath the callosum but above line A (area f). In places where the splenium or rostrum curved from an external subregion into an internal subregion (e.g., from BC to EF), the brain region involved was still considered to be part of the external subregion.

Since size reduction of the MR images and enlargement of the tracings made ascertainment of absolute callosal areas difficult, all areas were calculated as a percentage of the total callosal area for each subject. Splenium width was measured perpendicular to line A at the point in area a where the inferior to superior width was greatest (see dotted line in the Figure). Again, because of enlargement differences, this width was expressed as a percentage of maximal callosal length. Since both deLacoste-Utamsing and Holloway [6] and Witelson [9] agree that there are no sex-related differences associated with either total callosal area or maximal callosal length, a sex-related difference in splenium size or width should be evident when expressed as a percentage of the total area or length.

Results

The Table shows the mean measurements obtained from 80 subjects (40 male, 40 female) for each of the callosal fifths as well as the area beneath the callosum and the maximal splenial width. The values for callosal areas a through f are expressed as the mean of the percentage of total callosal areas. The mean widths were calculated as percentages of the maximal callosal lengths.

Although both splenial area and width tended to be larger in females, no significant sex-related differences for any of the measurements were found ($p > 0.05$).

Discussion

The results of this study reveal no sex-related difference in the percentage of callosum occupied by the splenium or any of the other callosal fifths, splenial width, splenial shape, or callosal curvature. deLacoste-Utamsing and Holloway's report of sex-related differences in splenial parameters must be viewed in the context of their small sample size as well as in the context of Witelson's (and the present) failure to confirm these findings in larger samples.

deLacoste-Utamsing and Holloway [6] found that females had a larger callosum only when size was calculated relative to brain weight. In other words, male brains weighed more than female brains. Such sex-related differences in brain weight are well known (see [4]), and it is not clear that this should be related to callosal area. Because in vivo brain weight was not quantified, we could not test this finding.

Our examination of callosal curvature also failed to confirm the possibility of a sex-related difference in the area subtended by the callosum (area f). deLacoste-Utamsing and Holloway have claimed that impartial

Statistical Results

	Callosal Areas[a]						
		Body					
	a (splenium)	b	c	d	e (anterior)	f (subcallosum)	Width
Male							
Mean (%)	30.4	11.4	12.6	13.0	31.2	150.6	23.7
SD	4.05	2.59	1.77	2.44	3.64	32.27	4.15
Female							
Mean (%)	31.2	11.0	12.4	13.2	30.4	148.5	24.1
SD	3.39	1.69	1.92	2.90	3.72	36.31	2.55
t (df = 78)	−0.923	0.968	0.551	−0.436	0.985	0.270	−0.516
p	NS	NS	NS	NS	NS	NS	NS
Standard error	0.834	0.488	0.413	0.599	0.822	7.68	0.770

[a]See text and Figure for description of areas.

SD = standard deviation; NS = not significant.

observers could categorize callosal outlines according to sex based on the marked bulbous morphology of the corpus callosum in females (versus the cylindrical shape in males). A similar qualitative test was conducted by a single observer who was familiarized with the previous morphological criteria. His scores were at chance level (23 of 40 were sorted incorrectly). Furthermore, he was no better at sorting either the female or male callosal outlines.

deLacoste-Utamsing and Holloway argued that a larger splenium would correlate with a larger number of interhemispheric fibers and less lateralization of function. However, callosal area is dependent not only on the total number of crossing fibers, but also on the density of these fibers. Tomasch [7] found great variance in the distribution of fiber densities across the human corpus callosum. Therefore, further cadaver investigations of sex-related callosal differences should incude measurements of axonal densities.

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Symptomatic Atlantoaxial Dislocation in Down's Syndrome

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Four patients with Down's syndrome suffered compression of the spinal cord secondary to atlantoaxial dislocation. All four developed inability to walk and quadriparesis, with signs of cervical myelopathy. It is important to recognize this potentially fatal complication of the syndrome. Immediate immobilization of the neck, followed by cervical roentgenograms, should be done in any patient with Down's syndrome who presents with neck pain, torticollis, urinary incontinence, or loss of ambulation. Surgical repair with fusion of the first and second cervical vertebrae can be carried out later.

Chaudhry V, Sturgeon C, Gates AJ, Myers G: Symptomatic atlantoaxial dislocation in Down's syndrome. Ann Neurol 21:606–609, 1987

Although asymptomatic subluxation of the atlantoaxial joint has been estimated to occur in 9.5 to 20% of persons with Down's syndrome [2, 7, 8, 9], symptomatic dislocation has been reported infrequently. An extensive search of the literature revealed only 15 instances of this complication since its first description by Tischler and Martel [12] in 1965.

We report 4 cases in patients with Down's syndrome who presented with quadriparesis and incontinence. All had cervical myelopathy secondary to dislocation of the first and second cervical vertebrae.

Case Reports

Patient 1

A 7-year-old girl was diagnosed at birth as having Down's syndrome and had characteristic phenotypic features. She had an endocardial cushion defect requiring repair of her atrioventricular canal at the age of 9 months. Her developmental milestones were all delayed. Six to seven weeks before admission, she developed an infection of the upper respiratory tract followed by neck pain and inability to walk. She held her head in an extended position and fell down whenever she tried to stand up. Cervical spine roentgenograms were interpreted as normal. She was treated with anti-

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