

Research report

A quantitative MRI study of the corpus callosum in children and adolescents

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Accepted 31 October 1995

Abstract

Total midsagittal area and seven subdivisions of the corpus callosum were measured on magnetic resonance images of 114 healthy boys and girls, aged 4 to 18. Striking variability of size was noted for all measures. Total midsagittal corpus callosum area increased in a robust and linear fashion from ages 4 to 18 (slope = 13.1 mm²/year, $P = 0.0001$ and slope = 11.1 mm²/year, $P = 0.0001$ for females and males, respectively). Posterior and mid regions demonstrated greater age-related changes than anterior regions with the rostrum and genu (anterior regions) having reached adult sizes in the youngest of our subjects. There were no significant effects of sex for any measures. These findings support anatomical studies indicating ongoing myelination of higher association areas throughout adolescence, but raise intriguing questions about anterior-posterior gradients of interhemispheric myelination.

Keywords: Adolescent; Child; Corpus callosum; Development; MRI; Myelination; Sex

1. Introduction

The corpus callosum (CC) is the main interhemispheric commissure of the brain consisting of approximately 180 million fibers [55], most of which connect homologous cortical areas. Studies of acallosal subjects, subjects with brain lesions or commissurotomies, and animal research indicate an integral role for the CC in unifying sensory fields [6,51], organizing bimanual motor output [69], aiding memory storage and retrieval [68], allocating attention and arousal [36], facilitating language and auditory functions [13], and perhaps also in consciousness itself [32]. In general, the CC is thought to integrate the activities of the two hemispheres by transferring sensory and higher processed information. As task difficulty increases, the integrated activity of both hemispheres becomes more important [23,37], and both creativity and intelligence have been linked to interhemispheric integration [8].

The CC, although notably absent in marsupials and monotremes, is present in most animals from insectivores to higher primates. Across many species, CC size is ap-

proximately proportional to the size of the neocortex and appears to have evolved in parallel [34,44]. Magnetic resonance imaging (MRI) studies reveal that CC development in humans begins approximately 8 weeks after conception with the formation of the anterior curve, or genu, followed by the body and then posterior bulb, or splenium. The rostrum is the exception to this general anterior to posterior trend, forming last at about 20 weeks [4].

With the maximum number of axons crossing the CC obtained in utero [35], postnatal changes are largely determined by the degree of myelination of those fibers. Consistent with observed features of infant development, interhemispheric connections between the pre- and post-central gyri, which subservise basic motor and sensory functions, myelinate at about three months resulting in a thickening of the genu [4]. The next major morphologic change of the CC occurs at approximately 4–6 months with a thickening of the splenium as interhemispheric connections of the visual and visual association areas myelinate allowing binocular vision and visual accommodation [16]. Subsequent morphologic changes, most likely related to ongoing myelination of interhemispheric fibers from association areas, are more subtle and less well characterized.

Quantitative neuroanatomic data is particularly sparse for ages 4 to 18. Mortality is low, with accidents the

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leading cause of death, and autopsies are rarely performed. A review of postmortem studies of CC anatomy in infants and children from 1906 to 1989 [65] cataloged just 5 studies with a total of only 11 subjects aged 4 to 18.

A seminal study by Yakovlev and Lecours (1967) [67], regarding regional myelogenetic cycles, indicated myelination of the great cerebral commissures (which includes the CC) reached adult levels between the ages of 7 and 10. However, more recent MRI studies including subjects from ages 4 to 18 have generally found increasing callosal area through the third decade [2,14,43,46]. These studies are limited by their use of clinically referred subjects and having too few pediatric subjects to adequately characterize the highly variable and heterochronous developmental data.

Interest in the morphologic development of the CC from ages 4 to 18 stems from observed changes in capacities subserved by the CC in normal development and from implications of dysfunctional integration in childhood neuropsychiatric disorders such as developmental interhemispheric disconnection syndromes [30], attention-deficit/hyperactivity disorder (ADHD) [20,26], dyslexia [25,43], and early onset schizophrenia [7,47].

In the present study we examine the relationship between age, sex, and CC morphometry across ages 4 to 18 to characterize normal developmental changes and provide a control group from which to examine developmental hypothesis of neuropsychiatric disorders. At issue are whether CC area continues to increase throughout adolescence or reaches adult levels at earlier ages, whether there are regional differences in patterns of CC maturation, and whether these patterns are sexually dimorphic.

2. Materials and methods

2.1. Subjects

MRI, with its lack of ionizing radiation and excellent anatomical resolution, provides unprecedented opportunity to obtain *in vivo* neuroanatomical information of children and adolescents. However, the practice of assessing normal development from scans of children that have been interpreted as normal by radiologists is less than ideal since many indications for clinical MRI scans, such as head trauma or seizures, occur in higher frequency in children with neuropsychiatric disorders such as ADHD [54]. Also, it is conceivable that a small, but perhaps meaningful, percentage of clinically 'normal' children may have abnormal scans and excluding these children may introduce a bias when comparing to clinical groups. To avoid these possible confounds subjects in this study were recruited directly from the community and underwent extensive medical and neuropsychiatric screening prior to scanning.

From 624 responses to local newspaper advertisements and notices, 234 cases were excluded by telephone screen-

ing due to a history of learning disability or ADHD in the child, sibling, or first degree relative; special educational services needed in school; or ongoing medical, neurologic, or psychiatric disorders. Of the remaining 390, 187 were excluded based upon replies to questionnaires mailed to the parents including the Child Behavior Checklist [1], medical history form and Conners [48] Item Parent Questionnaire [12] or to the child's teachers, including the Conners [39] Item Teacher Questionnaire [22] and a school behavior assessment. The remaining 203 subjects were brought into the clinic for assessment which included: a physical and neurological examination; the 12 handedness items from the Physical and Neurological Examination for Subtle Signs (PANESS) [18]; structured interviews of the parents and child using the Child and Parent Diagnostic Interview for Children—Revised [61]; a clinical interview by a board-certified child psychiatrist (JNG) including family history assessment; Vocabulary, Block Design, and Digit Span subtests of the Wechsler Intelligence Scale for Children—Revised (WISC-R) [57] for subjects under 16 years of age or the Wechsler Adult Intelligence Scale—Revised (WAIS-R) [58] for subjects 16 or older; spelling subtest of the Wide Range Achievement Test—Revised [31]; and Reading Cluster Score (consisting of Letter–Word Identification, Word Attack, and Passage Comprehension subtests) of the Woodcock-Johnson Psycho-educational Battery [66]. Individuals with physical, neurological, or lifetime history of psychiatric abnormalities or learning disabilities, or who had any first degree relatives or greater than 20% of second degree relatives with major psychiatric disorders were excluded. In accordance with assumptions of statistical independence only one child per family was included in this data set.

125 subjects met all of the above criteria and returned for the scanning procedure. Four failed to complete the scan because of excessive anxiety or claustrophobia, and seven had excessive motion artifact which precluded accurate measurement resulting in a final sample size of 114. Sample characteristics are presented in Table 1.

There were no significant sex differences for age, height, weight, handedness, Tanner stage, Woodcock Johnson Reading Cluster Score, or WISC-R Block Design, Digit Span, or Vocabulary subtests. Subject means were above

Table 1
Characteristics of MRI subjects, ages 4–18 ($n = 114$)

	Female	Male
Sample size	50	64
Age (years)	10.8 (4.0)	11.1 (3.6)
Height (cm)	143.9 (21.6)	153.8 (19.1)
Weight (kg)	39.6 (16.1)	45.7 (16.7)
Tanner stage	2.2 (1.6)	2.2 (1.6)
Handedness	92% right-handed	92% right-handed
Vocabulary	12.9 (2.5)	13.8 (2.8)
Block design	12.9 (3.6)	13.1 (3.6)
Digit span	11.7 (2.8)	11.2 (2.9)

average population means (10 ± 3) on Vocabulary, Block Design, and Digit Span subtests. Our strict inclusion criteria make this outcome likely, although it does limit the generalizability of these findings. Volumetric cortical and subcortical measures for most of the subjects of this report have been reported elsewhere [21].

The protocol was approved by the Institutional Review Board of the National Institute of Mental Health. Written consent from the parents and assent from the child were obtained.

2.2. MRI protocol

All subjects were scanned on a GE 1.5 Tesla Signa scanner. T1-weighted sagittal images with slice thickness of 1.5 mm in the axial and sagittal planes and 2.0 mm in the coronal plane were obtained using three-dimensional spoiled gradient recalled echo in the steady state. Imaging parameters were TE = 5 ms, TR = 24 ms, flip angle = 45 degrees, acquisition matrix = 192×256 , number of excitations = 1, and field of view = 24 cm.

Vitamin E capsules, wrapped in gauze and placed in each auditory meatus, were used to help standardize head placement. A third capsule was taped to the lateral aspect of the left inferior orbital ridge. The vitamin E capsules are readily identifiable with our scanning parameters, and the three capsules were used to define a reference plane for our images. The patient's head was aligned in a head holder so that a narrow guide light passed through each of the vitamin E capsules. Foam padding was placed on both sides of the patient's head to minimize head movement. A sagittal localizing plane was acquired, and from this, a multi-echo axial series was obtained to assure that one of the axial slices contained all three of the capsules. If no slice clearly contained all three capsules, the patient was realigned until this criterion was met. An additional criterion, to control for tilt within the coronal plane, was the alignment of each subject's nose at '12:00' position. It should be noted that these alignment criteria were based on external landmarks only and did not guarantee standardization of internal structures.

Subjects were scanned in the evening to promote their falling asleep in the scanner. Younger children were allowed to bring blankets or stuffed animals into the scanner and have their parents read to them. No sedation was used.

2.3. Image analysis

All scans were evaluated by a clinical neuroradiologist. Two subjects were noted to have areas of increased T2 signal intensity; one in the left semiovale and one in the right parietal lobe. Both subjects were retained in the data set. Images were transferred to a Macintosh II FX computer workstation and analyzed with an image analysis program (Image 1.46) developed at the NIH [45].

Using the 3-D data set, a line was drawn to bisect the

cerebral hemispheres in the axial plane. From this line, a midsagittal image was reconstructed. Criteria to confirm a midsagittal orientation were patency of the cerebral aqueduct, presence of the septum pellucidum, and distinctness of the thalamus.

From the midsagittal slice, an elliptical region of interest encompassing the corpus callosum was drawn and within this region a supervised thresholding technique was used to determine the x - y coordinates of the CC perimeter. These coordinates were transferred to an SPARC 10 computer workstation for further analysis. All measures were made by the same rater (ACV) who was blind to subject age or sex. Twenty scans were randomly entered into the data set to be measured twice to determine intrarater reliability, which yielded an average ICC of 0.92 for the seven subdivisions.

An automated algorithm written in C language (by JCR) was used to analyze the CC perimeter x - y coordinates. The program, which is available upon request, uses radial distances to compute the areas of seven CC subregions. The subregions are illustrated in Fig. 1 and based on a technique by Witelson [64].

Total cerebral hemisphere volume was quantified using a previously described [52] image analysis technique that allows prior knowledge of brain anatomy to supplement the sometimes ambiguous MRI signal intensity characteristics. A 'standard' brain image was modeled as an elastically deformable template which then conformed to the individual brain image being analyzed by successive iterations of an energy minimization function enforcing constraints on curvature and topology. After this procedure the brains were examined and edited in the axial plane slice by slice by experienced raters to remove remaining artifacts such as patches of dura or eyeballs. Intraclass correlations (ICC) for the volumes of the edited brains were 0.99 for

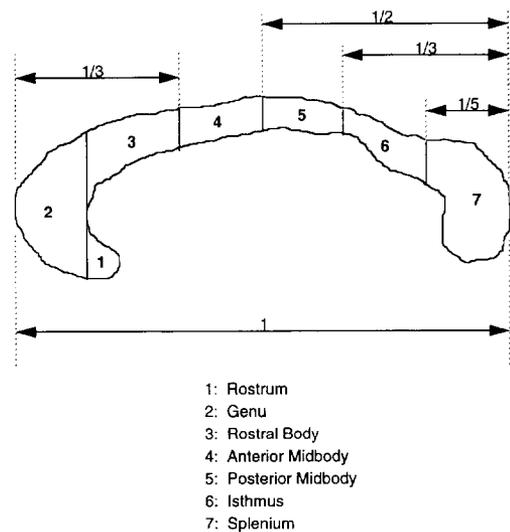


Fig. 1. Schematic of corpus callosum subdivisions (adapted from Witelson [64]).

Table 2
Linear regression by age and sex for total area and seven subdivisions of the corpus callosum in 114 healthy children and adolescents, ages 4–18

	Female <i>n</i> = 50		Male <i>n</i> = 64		Combined (M + F) <i>n</i> = 114	
	Slope (mm ² /year)	<i>P</i>	Slope (mm ² /year)	<i>P</i>	Slope (mm ² /year)	<i>P</i>
Total corpus callosum	13.1	0.0001	11.1	0.0001	12.2	0.0001
Rostrum	1.3	0.12	0.7	0.46	1.0	0.11
Genu	0.3	0.67	0.5	0.40	0.4	0.37
Rostral body	1.8	0.08	0.9	0.31	1.4	0.04
Anterior midbody	1.6	0.0001	1.0	0.005	1.3	0.0001
Posterior midbody	1.7	0.0003	1.2	0.004	1.4	0.0001
Isthmus	1.7	0.0001	2.1	0.0001	1.9	0.0001
Splenium	4.7	0.0001	4.8	0.0001	4.8	0.0001

interrater reliability and 0.95 by comparison to volumes derived from more conventional slice by slice hand tracing through all axial slices on which brain matter was visible.

2.4. Statistical analysis

Age effects were tested with linear regression models [49]. Males and females were analyzed separately and in combination to allow comparison with previous reports.

Since total cerebral volume was 9% larger in males (*t* = 5.1, *P* = 0.0001), sex differences were analyzed using

ANOVA and then ANCOVA to adjust for total cerebral volume. The relative merits of using absolute or adjusted values of brain structure sizes are a source of continuing debate, although both approaches have potential utility [3,38].

Differences between males and females on the demographic variables (age, height, weight, Tanner stage, and cognitive measures) were examined with *t*-tests and chi square for handedness. All *P*-values from statistical tests are two-tailed.

To assess the effects of handedness on CC morphology

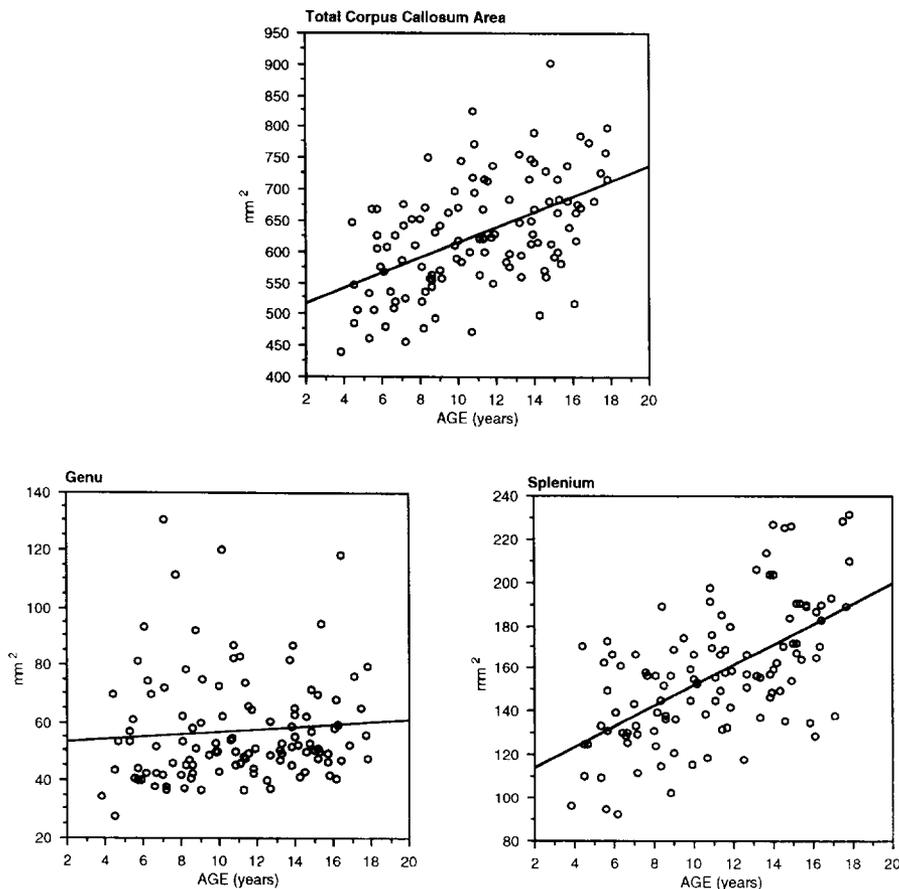


Fig. 2. Scatterplots of midsagittal area (mm²) by age for total corpus callosum area, genu (anterior-most region), and splenium (posterior-most region) for 111 healthy children and adolescents, aged 4–18.

Table 3
Means and standard deviations of total corpus callosum area (mm²) and 7 subregions in 114 healthy children and adolescents, ages 4–18

	Female <i>n</i> = 50 Mean (S.D.)	Male <i>n</i> = 64 Mean (S.D.)
Rostrum	57 (20)	68 (26)
Genu	67 (23)	57 (18)
Rostral body	142 (28)	149 (24)
Anterior midbody	72 (12)	75 (11)
Posterior midbody	67 (12)	67 (12)
Isthmus	58 (13)	60 (15)
Splenium	154 (29)	159 (31)
Total	617 (94)	635 (84)

2 to 1 age- and sex-matched controls for each of the ten adextrals was chosen for a separate group comparison.

3. Results

Total corpus callosum area increases in a robust and linear fashion from ages 4 to 18 (slope = 13.1 mm²/year, $P = 0.0001$ and slope = 11.1 mm²/year, $P = 0.0001$ for females and males, respectively). The slopes do not differ between males and females on any region. The age related increases were driven by the four posterior-most regions which showed highly significant changes ($P \leq 0.005$) for both sexes (see Table 2).

As can be seen from the scatterplots contained in Fig. 2 measures demonstrated a high degree of variability. Scatterplots of the anterior-most and posterior-most regions are presented to highlight the anterior-to-posterior gradient of maturational changes. Goodness-of-fit regression models of the CC regions and total indicated that the relationships with age were primarily linear and that no higher degree polynomial should have been considered.

Means and standard deviations of each region and total are presented for each sex in Table 3.

A two way repeated measures ANOVA (sex by CC region) did not reveal a significant effect for sex ($F = 1.17$, $P = 0.28$) nor for sex by region interaction ($F = 0.08$, $P = 0.52$). Similarly, an ANCOVA (controlling for total cerebral volume) showed no significant effect of sex ($F = 0.07$, $P = 0.79$).

We did not have enough non right-handed subjects to meaningfully assess the effect of handedness on CC morphology. However, there were no significant differences between 10 adextrals and 20 age and sex matched controls for any CC region.

4. Discussion

There is striking individual variation in CC morphology with as much as a two-fold area difference among subjects of the same age, sex, and height. This large variability

requires large samples or longitudinal study designs to adequately characterize developmental patterns. Results of small sample studies, for this and other highly variable brain structures, should therefore be interpreted cautiously.

Total midsagittal area of the corpus callosum increased robustly across this age span for both sexes, although significant increases were limited to mid and posterior regions. Relationships with age were all linear, no higher order regression polynomial coefficients were significant. The predominance of maturational changes in the posterior sections of the corpus callosum across this age span suggests the anterior sections may have already reached their adult sizes in the preschool years. This possibility was explored by comparing our pediatric data to scans on 23 adults subjects aged 20–40, acquired and analyzed in an identical manner. There were no differences between the child and adult means in the rostrum or genu. This is in contrast to the remaining mid and posterior sections which were significantly smaller for the pediatric group. This supports the notion that the rostrum and genu plateau at adult sizes early in development.

Ongoing development of the splenium, isthmus, and body of the CC is consistent with continued maturation of higher association areas well into adulthood, since a large proportion of callosal fibers emanate from these [42]. Postmortem data on patterns of interhemispheric myelination are not available for our age group. However, based upon EEG patterns of posterior-to-anterior maturation [53] we had expected changes in the anterior-most regions as well. Perhaps the increasing frontal connectivity patterns of adolescence involve predominantly intrahemispheric, as opposed to interhemispheric, structures. This unexpected anterior-to-posterior gradient of CC maturation, which mirrors the in utero development, raises intriguing questions about anterior/posterior patterns of interhemispheric myelination and connectivity during normal development.

Sexual dimorphism of the CC was first suggested in a report describing the splenium as rounder and more bulbous in females [17], notable as the first report of sexual dimorphism in the human brain not related to a reproductive function. In the present study no sexual dimorphism was observed, consistent with the many investigators finding no particular link to sex [5,10,40,59,60,62,63]. Other studies have found sexual dimorphism and argue that differences in measurement technique, MRI acquisition, or subject selection may account for the discrepancies [11,14,15,24].

No effects of handedness or sex by handedness interactions were found in this study but due to the small number of adextrals (5 males, 5 females) no conclusions can be drawn.

The size of the corpus callosum is determined by the number and size of its constituent axons, degree of myelination, packing density, vasculature, and extravascular fluid. Quantitative electron microscopy studies in the rhesus monkey [35] indicate that new callosal axons do not

develop postnatally. The most likely candidate for age-related increase in size is myelination. Electrophysiological, MRI, and postmortem studies all indicate that myelogenesis of the CC continues throughout childhood. By adulthood, most of the fibers are myelinated and diameters vary from 0.08 microns to greater than 5 microns with conduction velocities ranging from 1 m/s to 10 m/s [19,56].

The contributions of glial cells to CC size are difficult to determine. Unlike neurons, glial cells undergo a constant cycle of proliferation and cell death. Reports of glial cell/neuron ratios range from 1.7 to 10 [9]. Both metabolic activity and neuronal cell death are thought to influence glial proliferation [30] although the relationship between glial cell volume and the size, number, or activity of neurons is not well characterized.

Factors contributing to a decrease in the size of the CC are loss of neuronal number through cell death or axonal retraction [11,27–29]. The balance between decreasing number and increasing size determines the eventual size of the region.

Genetic influence on CC size is indicated by the greater similarity in CC morphology in monozygotic twins [41]. In rats, an enriched early environment was shown to increase CC size [33]. Hormones, nutrition, and other external factors such as infections, toxins, trauma, or stress may also have a role [30]. These factors were not addressed in the present study.

While many basic elements of adult cognition are in place around age 12, speed, capacity, and ability on mental tasks, especially those of higher order, can continue to improve well into adulthood [50]. The present data support the conclusion of Pujol et al. [43] that the CC is "part of the highest order-latest maturing neural network of the brain". Because of hypothesized abnormalities in connectivity in these areas we anticipate that these normative developmental data will be of importance for our ongoing studies of CC development in pediatric neuropsychiatric disorders.

Acknowledgements

Work supported in part by a grant from the Gulston Foundation.

References

- [1] Achenbach, T.M. and Edelbrock, C.S., *Manual for Child Behavior Checklist and Revised Behavior Profile*, Department of Psychiatry, University of Vermont, Burlington, VT, 1983.
- [2] Allen, L.S., Richey, M.F., Chai, Y.M. and Gorski, R.A., Sex differences in the corpus callosum of the living human being, *J. Neurosci.*, 11 (1991) 933–942.
- [3] Arndt, S., Cohen, G., Alliger, R.J., Swayze, V.W. and Andreasen, N.C., Problems with ratio and proportion measures of imaged cerebral structures, *Bull. Clin. Neurosci.*, 55 (1991) 131–136.
- [4] Barkovich, A.J., Normal development of the neonatal and infant brain. In A.J. Barkovich (Ed.) *Pediatric Neuroimaging*, Raven Press, New York, 1990, pp. 5–34.
- [5] Bell, A.D. and Variend, S., Failure to demonstrate sexual dimorphism of the corpus callosum in childhood, *J. Anat.*, 143 (1985) 143–147.
- [6] Berlucchi, G., Interhemispheric asymmetries in visual discrimination: a neurophysiological hypothesis, *Doc. Ophthalmol. Proc. Ser.*, 30 (1981) 87–93.
- [7] Bigelow, L.H., Nasrallah, H.A. and Rauscher, F.P., Corpus callosum thickness in chronic schizophrenia, *Br. J. Psychiatry*, 142 (1983) 284–287.
- [8] Bogen, J.E. and Bogen, G.M., The other side of the brain, *Bull. Los. Ang. Neurol. Soc.*, 34 (1969) 73–220.
- [9] Brizzee, K.R., Vogt, J. and Kharetehko, X., Postnatal changes in glia neuron index with a comparison of methods of cell enumeration in the white rat, *Prog. Brain Res.*, 4 (1964) 136–149.
- [10] Byne, W., Bleier, R. and Houston, L., Variations in human corpus callosum do not predict gender: a study using magnetic resonance imaging, *Behav. Neurosci.*, 102 (1988) 222–227.
- [11] Clarke, S., Kraftsik, R., Van Der Loos, H. and Innocenti, G.M., Forms and measures of adult and developing human corpus callosum: is there sexual dimorphism? *J. Comp. Neurol.*, 280 (1989) 213–230.
- [12] Conners, C.K., Rating scales in drug studies with children, *Psychopharmac. Bull.*, 24 (1973).
- [13] Cook, N.D., *The Brain Code. Mechanisms of Information Transfer and The Role of The Corpus Callosum*, Methuen, London, 1986, 255 pp.
- [14] Cowell, P.E., Allen, L.S., Zalatio, N.S. and Denenberg, V.H., A developmental study of sex and age interactions in the human corpus callosum, *Dev. Brain Res.*, 66 (1992) 187–192.
- [15] de Lacoste, M.C., Holloway, R.L. and Woodward, D.J., Sex differences in the fetal human corpus callosum, *Hum. Neurobiol.*, 5 (1986) 93–96.
- [16] de Lacoste, M.C., Kirkpatrick, J.B. and Ross, E.D., Topography of the human corpus callosum, *J. Neuropathol. Exp. Neurol.*, 44 (1985) 578–591.
- [17] De Lacoste-Utamsing, M.C. and Holloway, R.L., Sexual dimorphism in the human corpus callosum, *Science*, 216 (1982) 1431–1432.
- [18] Denckla, M.B., Revised physical and neurological examination for subtle signs, *Psychopharmac. Bull.*, 21 (1985) 773–800.
- [19] Fleischhauer, K. and Wartenberg, H., Elektronenmikroskopischen Untersuchungen über das Wachstum der Nervenfasern und über das Auftreten von Markscheiden im Corpus Callosum der Katze, *Z. Zellforsch.*, 83 (1967) 568–581.
- [20] Giedd, J.N., Castellanos, F.X., Casey, B.J., Kozuch, P.L., King, A.C., Hamburger, S.D. and Rapoport, J.L., Quantitative morphology of the corpus callosum in attention deficit hyperactivity disorder, *Am. J. Psychiatry*, 151 (1994) 665–669.
- [21] Giedd, J.N., Snell, J.W., Lange, N., Rajapakse, J.C., Kaysen, D., Vaituzis, A.C., Vauss, Y.C., Hamburger, S.D., Kozuch, P.L. and Rapoport, J.L., Quantitative magnetic resonance imaging of human brain development: ages 4–18, *Cereb. Cortex*, in press.
- [22] Goyette, C.H., Conners, C.K. and Ulrich, R.F., Normative data on the Revised Conner's Parent and Teacher Rating Scales, *J. Abnorm. Child Psychol.*, 6 (1978) 221–236.
- [23] Hellige, J.B., Cox, J.P. and Litvac, L., Information processing in the hemispheres: selective hemisphere activation and capacity limitations, *J. Exp. Psychol. Gen.*, 108 (1979) 251–259.
- [24] Holloway, R.L. and de Lacoste, M.C., Sexual dimorphism in the human corpus callosum: an extension and replication study, *Hum. Neurobiol.* 5 (1986) 87–91.
- [25] Hynd, G.W., Semrud-Clikeman, M., Lorys, A.R., Novey, E.S. and Eliopoulos, D., Brain morphology in developmental dyslexia and

- attention deficit disorder/hyperactivity, *Arch. Neurol.*, 47 (1990) 919–926.
- [26] Hynd, G.W., Semrud-Clikeman, M., Lorys, A.R., Novey, E.S., Eliopoulos, D. and Lyytinen, H., Corpus callosum morphology in attention deficit–hyperactivity disorder: morphometric analysis of MRI, *J. Learn. Disabil.*, 24 (1991) 141–146.
- [27] Innocenti, G.M., Growth and reshaping of axons in the establishment of visual callosal connections, *Science*, 218 (1981) 824–827.
- [28] Innocenti, G.M., The development of interhemispheric connections, *Trends Neurosci.*, 4 (1981) 142–144.
- [29] Innocenti, G.M. and Caminiti, R., Postnatal shaping of callosal connections from sensory areas, *Exp. Brain Res.*, 38 (1980) 381–394.
- [30] Jacobson, M., *Developmental Neurobiology*, Plenum Press, New York, 1991.
- [31] Jastak, S. and Wilkinson, G.S., *Wide Range Achievement Test, Revised Edition*, Jastak Assessment Systems, Wilmington, DE, 1984.
- [32] Joseph, R., Awareness, the origin of thought, and the role of conscious self-deception in resistance and repression, *Psychol. Rep.*, 46 (1980) 767–781.
- [33] Juraska, J.M. and Kopicik, J.R., Sex and environmental influences on the size and ultrastructure of the rat corpus callosum, *Brain Res.*, 450 (1988) 1–8.
- [34] Kappers, C.U.A., Huber, G.C. and Crosby, C.C., *The Comparative Anatomy of the Nervous System of Vertebrates Including Man*, Vol. 2, MacMillan, New York, 1936.
- [35] LaMantia, A.S. and Rakic, P., The number, size, myelination, and regional variation of axons in the corpus callosum and anterior commissure of the developing rhesus monkey, *Soc. Neurosci. Abstr.*, 10 (1984) 1081.
- [36] Levy, J., Interhemispheric collaboration: single mindedness in the asymmetric brain. In C.T. Best (Ed.) *Hemisphere Function and Collaboration in the Child*, Academic Press, New York, 1985, pp. 11–32.
- [37] Levy, J. and Trevarthen, C., Color-matching, color naming and color memory in split brain patients, *Neuropsychology*, 19 (1981) 523–541.
- [38] Mathalon, D.H., Sullivan, E.V., Rawles, J.M. and Pfefferbaum, A., Correction for head size in brain-imaging measurements, *Psychiatry Res.: Neuroimaging*, 50 (1993) 121–139.
- [39] Njokiktjen, C., *Pediatric Behavioral Neurology, Vol. 3, The Child's Corpus Callosum*, Suyi Publications, Amsterdam, 1991, pp. 22.
- [40] Oppenheim, J.S., Benjamin, A.B., Lee, C.P., Nass, R. and Gazzanga, M.S., No sex-related differences in human corpus callosum based on magnetic resonance imagery, *Ann. Neurol.*, 21 (1987) 604–606.
- [41] Oppenheim, J.S., Skerry, J.E., Tramo, M.J. and Gazzanga, M.S., Magnetic resonance imaging morphology of the corpus callosum in monozygotic twins, *Ann. Neurol.*, 16 (1989) 100–104.
- [42] Pandya, D.N. and Rosene, D.L., Some observations on trajectories and topography of commissural fibers. In A.G. Reeves (Ed.), *Epilepsy and the Corpus Callosum*, Plenum, New York, 1985, pp. 21–35.
- [43] Pujol, J., Vendrell, P., Junque, C., Marti-Vilalta, J.L. and Capdevila, A., When does human brain development end? Evidence of corpus callosum growth up to adulthood, *Ann. Neurol.*, 34 (1993) 71–75.
- [44] Rapoport, S.I., Integrated phylogeny of the primate brain, with special reference to humans and their diseases, *Brain Res. Rev.*, 15 (1990) 267–294.
- [45] Rasband, W., *Image (1.6)*, National Institutes of Health (Public Domain), Bethesda, MD, 1993.
- [46] Rauch, R.A. and Jinkins, J.R., Analysis of cross-sectional area measurements of the corpus callosum adjusted for brain size in male and female subjects from childhood to adulthood, *Behav. Brain Res.*, 64 (1994) 65–78.
- [47] Rosenthal, R. and Bigelow, L., Quantitative brain measurements in chronic schizophrenia, *Br. J. Psychiatry*, 121 (1972) 259–264.
- [48] Rumsey, J.M., Casanova, M.F., Mannheim, G.B., Patronas, N., DeVahgn, N., Hamburger, S.D. and Aquino, T., Corpus callosum morphology, as measured with MRI, in dyslexic men, *Biol. Psychiatry*, in press.
- [49] SAS Institute, *SAS, Version 6*, SAS Institutes, Inc, Cary, North Carolina, 1990.
- [50] Schulz, R. and Curnow, C., Peak performance and age among super-athletes: track and field, swimming, baseball, tennis and golf, *J. Geront.*, 43 (1988) 113–120.
- [51] Shanks, M.F., Rockel, A.J. and Powel, T.P.S., The commissural fiber connections of the primary somatic sensory cortex, *Brain Res.*, 98 (1975) 166–171.
- [52] Snell, J.W., Merickel, M.B., Ortega, J.M., Goble, J.C., Brookeman, J.R. and Kassell, N.F., Boundary estimation of complex objects using hierarchical active surface templates, *J. Patt. Recogn.*, in press.
- [53] Stuss, D.T., Biological and psychological development of executive functions, *Brain Cogn.*, 20 (1992) 8–23.
- [54] Szatmari, P., Offord, D.R. and Boyle, M.H., Correlates, associated impairments and patterns of service utilization of children with attention deficit disorder: findings from the Ontario child health study, *J. Child Psychol. Psychiatry*, 30 (1989) 205–217.
- [55] Tomasch, J., Size, distribution and number of fibers in the human corpus callosum, *Anat. Rec.*, 119 (1954) 119–135.
- [56] Waxman, S.G. and Swadlow, H.A., Ultrastructure of visual callosal axons in the rabbit, *Exp. Neurol.*, 53 (1976) 115–128.
- [57] Wechsler, D., *Wechsler Intelligence Scale For Children — Revised*, The Psychological Corporation, New York, 1974.
- [58] Wechsler, D., *Wechsler Adult Intelligence Scale — Revised*, The Psychological Corporation, 1981.
- [59] Weis, S., Weber, G., Wenger, E. and Kimbacher, M., The human corpus callosum and the controversy about sexual dimorphism, *Psychobiology*, 16 (1988) 411–415.
- [60] Weis, S., Weber, G., Wenger, E. and Kimbacher, M., The controversy about sexual dimorphism of the human corpus callosum, *Int. J. Neurosci.*, 47 (1989) 169–173.
- [61] Welner, Z., Reich, W., Herjanic, B., Jung, K. and Amado, H., Reliability, validity and child agreement studies of the diagnostic interview of children and adolescents (DICA), *J. Am. Acad. Child Adol. Psychiatry*, 26 (1987) 649–653.
- [62] Witelson, S.F., On hemisphere specialization and cerebral plasticity from birth. In C.T. Best (Ed.), *Hemisphere Function and Collaboration in the Child*, Academic Press, Orlando, 1985, pp. 33–85.
- [63] Witelson, S.F., The brain connection: the corpus callosum is larger in left-handers, *Science*, 229 (1985) 665–668.
- [64] Witelson, S.F., Hand and sex differences in the isthmus and genu of the human corpus callosum, *Brain*, 112 (1989) 799–835.
- [65] Witelson, S.F. and Kigar, D.L., Anatomical development of the corpus callosum in humans: a review with reference to sex and cognition. In D.L. Molfese and S.J. Segalowitz (Eds.), *Brain Lateralization in Children: Developmental Implications*, The Guildford Press, New York, 1988, pp. 35–57.
- [66] Woodcock, R.W. and Johnson, B.B., *Woodcock-Johnson Psychoeducational Battery*, DLM Teaching Resources, Allen, TX, 1977.
- [67] Yakovlev, P.I. and Lecours, A.R., The myelogenetic cycles of regional maturation of the brain. In A. Minkowski (Ed.) *Regional Development of the Brain in Early Life*, Blackwell Scientific, Oxford, 1967, pp. 3–70.
- [68] Zaidel, D. and Sperry, R.W., Memory impairment after commissurotomy in man, *Brain*, 97 (1974) 263–272.
- [69] Zaidel, D. and Sperry, R.W., Some long-term effects of cerebral commissurotomy in man, *Neuropsychology*, 15 (1977) 193–204.