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Morphometric Analysis of the Corpus Callosum Using MR: Correlation of Measurements with Aging in Healthy Individuals

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PURPOSE: To analyze changes of the human corpus callosum and MR midsagittal brain structures during normal aging. **METHODS:** A morphometric evaluation strategy for quantification of these brain structures on MR scans was developed. This computerized measuring program did allow the acquisition of more than 100 one- and two-dimensional parameters. **RESULTS:** During normal aging, the anterior parts of the corpus callosum (genu and anterior parts of the trunk) were significantly decreased, suggesting alterations of frontal and temporal interhemispheric fiber systems. Further changes were seen in callosal thickness and callosal width of the anterior parts of the corpus callosum. The profile area of the telencephalon was significantly reduced during normal aging. The size of the mesencephalon showed age-specific changes. **CONCLUSIONS:** The proposed computer program proved to be a powerful and reliable tool to get objective and reproducible quantitative data of corpus callosum and midsagittal brain structures. Specific age changes were found in the corpus callosum, indicating alteration of the frontotemporal interhemispheric fiber systems.

Index terms: Brain, measurements; Age and aging; Corpus callosum, magnetic resonance; Corpus callosum, anatomy

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The human corpus callosum is the largest commissural fiber system connecting both cerebral hemispheres. Four parts may be distinguished from rostral to caudal: rostrum, genu, trunk, and splenium (see Fig. 1, structure 1, a–d). In recent years, the human corpus callosum has attracted the interest of many investigators from diverse research areas.

In 1982, a sexual dimorphism of the human corpus callosum was described (1). The authors found the female splenium to be more bulbous than its male counterpart. They postulated a morphologic substrate for previously described

differences in visuospatial skills between males and females. However, their results could not be replicated by other research groups, either on autopsy brains (2, 3) or on magnetic resonance (MR) scans (4–9).

It has been shown that the corpus callosum is larger in left-handed and ambidextrous people than in right-handed people (10). The author concluded that the greater bihemispheric representation of cognitive functions in left- and mixed-handers may be associated with greater anatomical connection between the hemispheres. Using the Wada test to determine the side of cerebral speech dominance, a research group found that the midsagittal profile area of the corpus callosum was significantly greater in patients with right-hemispheric cerebral speech dominance (11).

Several papers have reported changes of the corpus callosum in schizophrenia. An increase in the average width of the callosal trunk in chronic schizophrenics compared with a healthy group has been described (12). In a replication study (13), it was shown that mean corpus callosum midsection of 21 early-onset, chronic schizophrenic brains had a significantly greater thick-

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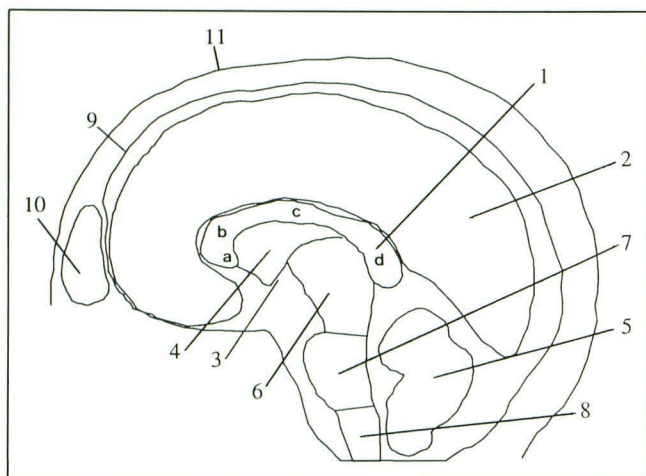


Fig. 1. Graphic plot showing the digitized structures to be measured. 1 = corpus callosum with: a = rostrum, b = genu, c = trunk, d = splenium; 2 = telencephalon; 3 = fornix; 4 = septum pellucidum; 5 = cerebellum; 6 = mesencephalon; 7 = pons; 8 = medulla oblongata; 9 = inner cranial cavity; 10 = sinus frontalis; and 11 = outer skull contour.

ness when compared with subjects with late-onset schizophrenia and patients with neurologic or other psychiatric diagnoses. In a further replication study (14), a significant increase in mean callosal thickness in middle and anterior, but not in posterior, parts of the callosal body was measured. Additionally, this group found that increased callosal thickness in schizophrenia was related to gender; schizophrenic women were found to have a highly significant increase in middle and anterior callosal thickness compared with control women. However, another group (15) found that schizophrenic patients had significantly longer corpora callosa, but they could not detect changes in the midsagittal profile area of the corpus callosum.

A vivid interest in the corpus callosum has also been incited by the growing number of partial or total callosotomies to manage medically intractable epilepsy (16–20).

Atrophic changes of the corpus callosum occur in multiple sclerosis (21–23). The degree of callosal atrophy is highly correlated with the estimated relative volume of periventricular multiple sclerosis lesions (21); callosal atrophy was more pronounced in demented than in nondemented multiple sclerosis patients (22).

The cited examples show the need for an accurate quantification protocol that allows detection and localization of changes within the corpus callosum occurring under various pathologic conditions. However, there is a striking lack

of a simple, objective, and reproducible evaluation procedure. Therefore, we implemented a morphometric evaluation strategy to quantify the human corpus callosum. This quantification method was applied to evaluate changes of the corpus callosum and midsagittal brain structures that occur with normal human aging.

Materials and Methods

In our retrospective study of the corpora callosa of a living population who have been imaged by nuclear MR, the sample consisted of 46 persons (20 men, 26 women) ranging in age from 20 to 80 years. The subjects were selected from a sample who had undergone MR imaging because of neurologic disturbances (ie, headache), but whose neuroradiologic reports were free of neuropathologic signs. Thus, persons with disease states involving the corpus callosum, such as multiple sclerosis (21–23) and demented states (24), and those with brain tumors and hydrocephalus were not included in the subject sample. Because a retrospective analysis was performed using material obtained from routine MR imaging, no information on hand preference could be obtained. Differences between men and women were tested and the results, showing no differences between the sexes, were reported earlier (8, 9).

Median-sagittal images were obtained with the 0.5-T superconductivity unit (Philips Gyroscan S5, Philips Electronic Instruments, Mahwah, NJ) with a conventional spin-echo technique providing a T1-weighted image, 350/30/2 (TR/TE/excitations). The image had a section thickness of 7 mm and a section gap of 1.6 mm. The imaging matrix was 256 × 256 and the field of view was 250 mm. The position of the median-sagittal scan was along the longitudinal fissure in order to obtain a scan on which no callosal or brain structure deviated from the midline.

The MR scans were entered by a black-and-white video camera (Panasonic) into the digital image analysis configuration microcomputer μ VaxII, Impuls 2300 graphics controller with digitizer GTCO Digi-pad. The metric scale, the most inferior points of rostrum and splenium, and the most inferior point of the frontal orbital cortex were entered into the system. The contours of the corpus callosum, septum pellucidum, fornix, telencephalon, midbrain, pons, medulla oblongata, inner cranial cavity, and outer skull were traced with the digitizer. The digitized structures are shown in the plot of Figure 1. The subsequent evaluation was generated automatically by software.

Three evaluation levels (level 1 to level 3) were considered. For each level, one- and two-dimensional data were obtained. One-dimensional data are given by the parameters length, height, width, and thickness. Profile area (or cross-sectional area) of the analyzed structures represents a two-dimensional parameter.

Level 1

Because the corpus callosum shows a high topographical variability it was analyzed at level 1 disregarding the surrounding brain structures.

The most inferior points of rostrum and splenium were connected by a tangent, the "horizontal inferior 1," HI-1 (Fig. 2). This line served as a reference line for the subsequent steps. The "vertical anterior 1" (VA-1) was constructed perpendicular to HI-1 and tangent to the genu; the "vertical posterior 1" (VP-1) was constructed perpendicular to HI-1 and tangent to the splenium, and the "horizontal superior 1" (HS-1) was constructed perpendicular to VA-1 and VP-1, parallel to HI-1, and tangent to the superior part of the trunk (Fig. 2). The callosal height (CH), defined as the distance between HI-1 and HS-1, and the callosal length (CL), defined as the distance between VA-1 and VP-1, were measured (Fig. 2). The profile area of the total corpus callosum (CPA) was evaluated.

The corpus callosum was divided into two, three, four, and five parts by equidistant vertical lines and the profile areas of these parts were consecutively evaluated (Fig. 2). We defined the first fifth to correspond to the genu; the second, third, and fourth fifths to correspond to the trunk; and the fifth fifth to correspond to the splenium. The width of the genu (C5T1) was defined as the maximum extension of the genu parallel to HI-1. To measure the height of the trunk, the lengths of the vertical lines within the trunk were evaluated (C5T2, C5T3, C5T4, C5T5). Second, the mean height of the trunk was determined by measuring and averaging the height of the trunk for each of the three fifths at 10 equidistant positions between two vertical lines (C5MT2, C5MT3, C5MT4) (Fig. 3).

The maximum splenial width was previously defined as the maximum distance between two parallel lines drawn at tangents to the dorsal and ventral splenial surfaces (1). However, this definition is vague; many tangents parallel to the dorsal and ventral splenial surfaces exist. In order to make the evaluation reproducible, the width of the posterior fifth of the corpus callosum was measured as follows: the maximum diameter of splenium parallel to HI-1 and the maximum diameter of splenium parallel to VP-1 were evaluated. The crossing point of these two lines served as a reference point for the following "rotatory diameter measurement" (8). Starting from the maximal vertical diameter (=D1), at regular intervals of 10°, chords connecting the splenial outlines and passing through the crossing point were built. The lengths of these 10 chords (D1 to D10) were evaluated (Fig. 4).

The length of the corpus callosum was defined above as the distance between VA-1 and VP-1. This length represents the maximum distance between the most anterior and posterior callosal parts. However, the callosal curvature was not taken into account. Therefore, a bisector line was defined to be the curved line from the tip of the rostrum to the tip of the splenium, where any point of the bisector line was equidistant from the dorsal and ventral surfaces of the callosum (25). In our opinion, the above-mentioned method (25) to construct the bisector line does not follow

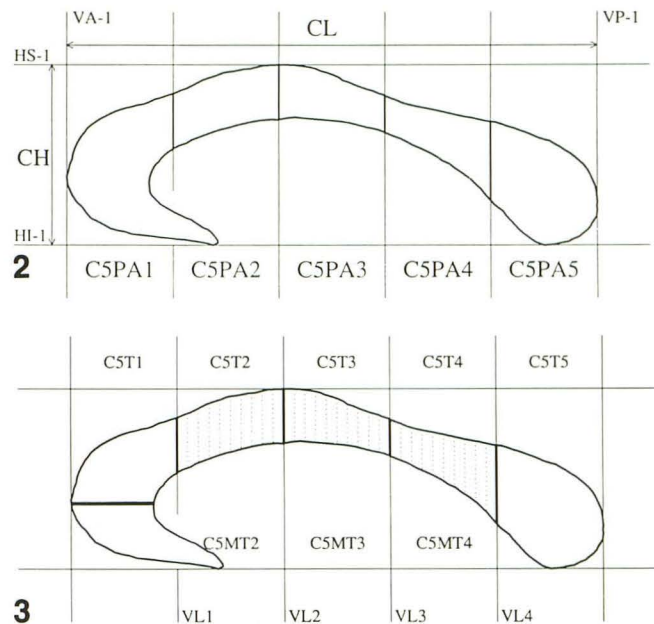


Fig. 2. Morphometric evaluation of the human corpus callosum. Level 1: horizontal standardization, evaluation of callosal height (CH), callosal length (CL), and of profile area of five equidistant callosal part with rostrum and genu (C5PA1), trunk (C5PA2, C5PA3, C5PA4), and splenium (C5PA5).

Fig. 3. Morphometric evaluation of the human corpus callosum. Level 1: evaluation of width of genu (C5T1), height of trunk (C5T2, C5T3, C5T4, C5T5), and mean height of trunk (C5MT2, C5MT3, C5MT4).

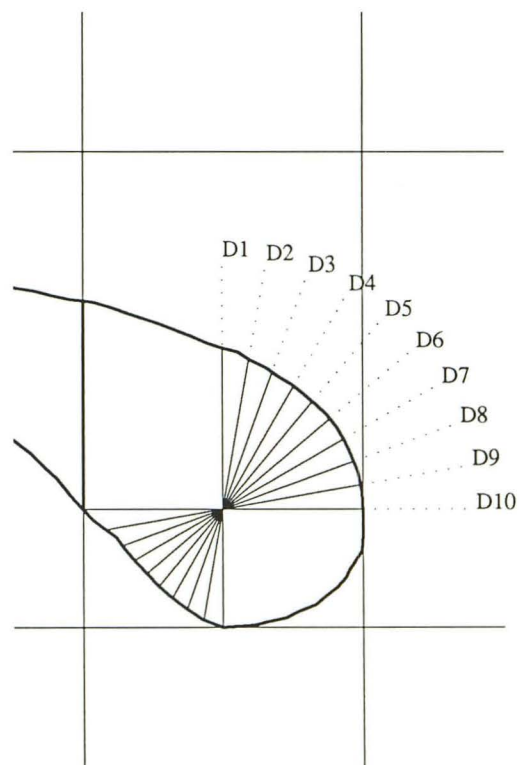


Fig. 4. Morphometric evaluation of the human corpus callosum. Level 1: rotatory diameter measurement of the splenium.

reproducible lines. It is not at all clear with which procedure the points, equidistant from dorsal and ventral surfaces, were constructed. Therefore, we introduce a bisector line that is constructed in the following way: the midpoint (PM) of the distance between the most inferior part of the rostrum and of the splenium served as the source for 250 radial chords originating from this point. The midpoints of these chords inside the corpus callosum were determined and connected by a median line. Thus, we defined bisector line 1 and measured its length (BIS1) (Fig. 5).

Level 2

At level 2, the structures surrounding the corpus callosum were evaluated. In analogy to level 1, a bounding box for the telencephalon was constructed as shown in Figure 6. In addition, a second "horizontal inferior 2" (HI-2') was constructed because the lowest point of the occipital lobe can extend lower than HI-2.

The height of the frontal telencephalon (BRHF) was defined as the distance between HI-2 and HS-2, and that of the occipital telencephalon (BRHO) as the distance between HI-2' and HS-2. The length of telencephalon (BRL) was defined as the distance between VA-2 and VP-2 (Fig. 6). Profile areas of the following brain parts were measured: telencephalon (BRPA), septum pellucidum (SPPA), mesencephalon (MEPA), pons (POPA), medulla oblongata (MOPA), and cerebellum (CERPA) (Figs. 6 and 7).

In addition, the following encephalometric parameters were determined. BCXDA: distance between VA-2 and the most anterior point of the genu corporis callosi, parallel to HI-2; BCXDP: distance between VP-2 and the most posterior point of the splenium corporis callosi, parallel to HI-2'; BCYDS: distance between HS-2 and the most superior point of the callosal trunk, parallel to VA-2.

Level 3

In addition to level 2, the inner and outer skull contours were digitized (see Fig. 1 and Fig. 7). The midsagittal profile area of the cranial cavity, defined by tracing the contour of the inner skull (SKIPA), was evaluated. An approximation of cerebrospinal fluid space was obtained by SKIPA—(CPA + BRPA + SPPA + BRSTPA + CERPA) (Fig. 7).

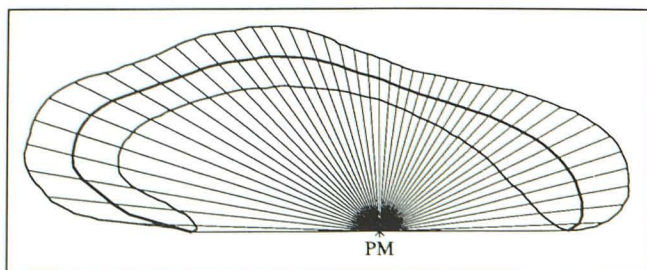


Fig. 5. Morphometric evaluation of the human corpus callosum. Level 1: tracing of bisector line 1. PM is the midpoint of the distance between the most inferior points of rostrum and splenium.

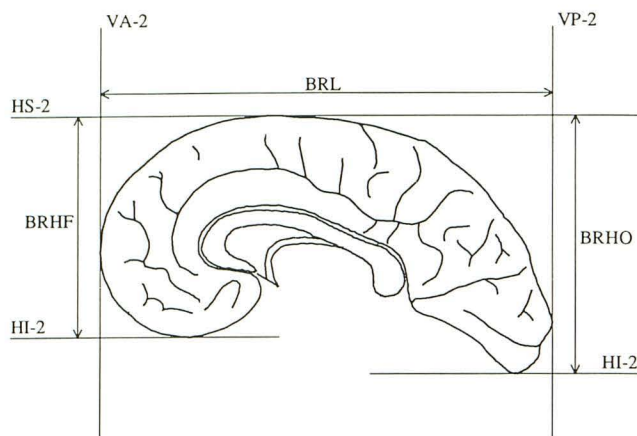


Fig. 6. Morphometric evaluation of midsagittal brain structures. Level 2: construction of the bounding for the evaluation of the telencephalon. Evaluation of brain length (BRL), and of frontal (BRHF) and occipital (BRHQ) brain height.

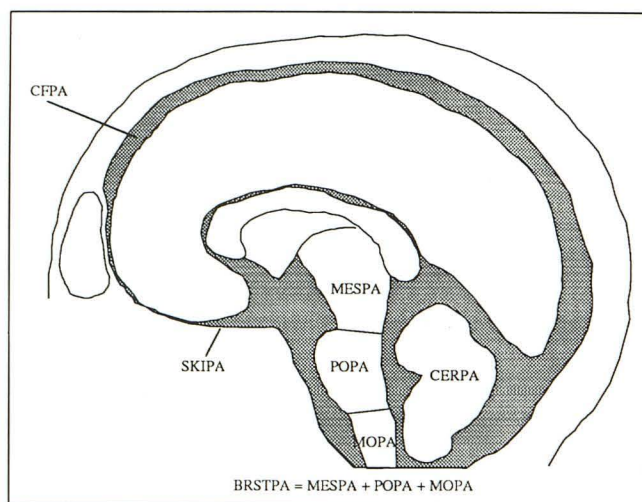


Fig. 7. Morphometric evaluation of midsagittal brain structures. Level 3: Evaluation of profile area of mesencephalon (MESPA), pons (POPA), medulla oblongata (MOPA), cerebellum (CERPA), inner cranial cavity (SKIPA), and cerebrospinal fluid space (CFPA).

Statistics

Changes occurring in the various brain structures during normal aging were analyzed by linear regression analysis.

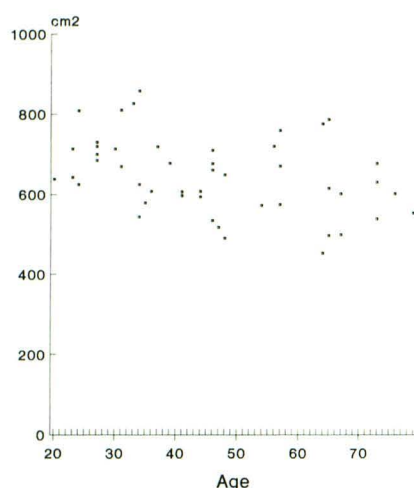
Results

During normal aging a significant decrease of the total callosal profile area (CPA) was found (Table 1, Fig. 8). A constant pattern of changes of the different callosal parts could be detected during normal aging. Indeed, the anterior parts of the corpus callosum (ie, rostrum, genu, and anterior parts of trunk) showed significant age changes (Table 1, Fig. 9). However, the posterior

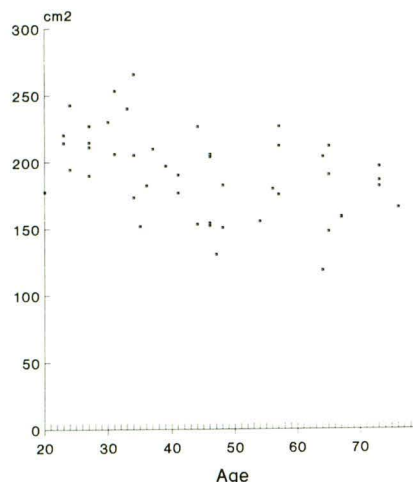
TABLE 1: Results of regression analysis of the morphometric evaluation of the human corpus callosum and surrounding midsagittal brain structures in normal aging

Parameters		<i>r</i>	<i>P</i>
Level 1			
CPA	Profile area of corpus callosum	-.53	.001
CL	Length of corpus callosum	+.04	.74
CH	Height of corpus callosum	+.08	.54
C2PA1	Profile area of the first half	-.32	.01
C2PA2	Profile area of the second half	-.02	.87
C3PA1	Profile area of the first third	-.32	.01
C3PA2	Profile area of the second third	-.20	.13
C3PA3	Profile area of the third third	-.01	.92
C4PA1	Profile area of the first fourth	-.31	.02
C4PA2	Profile area of the second fourth	-.30	.02
C4PA3	Profile area of the third fourth	-.14	.27
C4PA4	Profile area of the fourth fourth	-.06	.66
C5PA1	Profile area of the first fifth	-.29	.03
C5PA2	Profile area of the second fifth	-.33	.01
C5PA3	Profile area of the third fifth	-.19	.16
C5PA4	Profile area of the fourth fifth	-.15	.25
C5PA5	Profile area of the fifth fifth	-.11	.43
C5T1	Width of the genu	-.07	.60
C5T2	Width of the trunk at VL1	-.33	.01
C5T3	Width of the trunk at VL2	-.31	.02
C5T4	Width of the trunk at VL3	-.12	.37
C5T5	Width of the trunk at VL4	-.10	.46
C5MT2	Mean callosal height of second fifth	-.37	.005
C5MT3	Mean callosal height of third fifth	-.22	.10
C5MT4	Mean callosal height of fourth fifth	-.16	.24
D1	Maximal vertical diameter	-.09	.50
D2	Diameter at 10° from D1	+.01	.91
D3	Diameter at 20° from D1	+.05	.69
D4	Diameter at 30° from D1	+.08	.54
D5	Diameter at 40° from D1	+.11	.39
D6	Diameter at 50° from D1	+.13	.32
D7	Diameter at 60° from D1	+.16	.24
D8	Diameter at 70° from D1	+.19	.15
D9	Diameter at 80° from D1	+.24	.07
D10	Maximal horizontal diameter	+.24	.07
BIS1	Length of bisector line 1	+.10	.44
Level 2			
BRPA	Profile area of telencephalon	-.44	.0007
BRL	Length of telencephalon	-.39	.003
BRHF	Height of telencephalon at the frontal pole	-.39	.003
BRHO	Height of telencephalon at the occipital pole	-.08	.56
BCXDA	Distance between genu and frontal pole	-.59	.0000
BCXDP	Distance between splenium and occipital pole	-.27	.04
BCYDS	Distance between trunk and superior margin	-.37	.004
SPPA	Profile area of septum pellucidum	+.33	.01
Level 2			
BRSTPA	Profile area of brain stem	-.25	.06
MESPA	Profile area of mesencephalon	-.45	.0006
POPA	Profile area of pons	-.06	.67
MOPA	Profile area of medulla oblongata	+.09	.46
CERPA	Profile area of cerebellum	-.28	.03

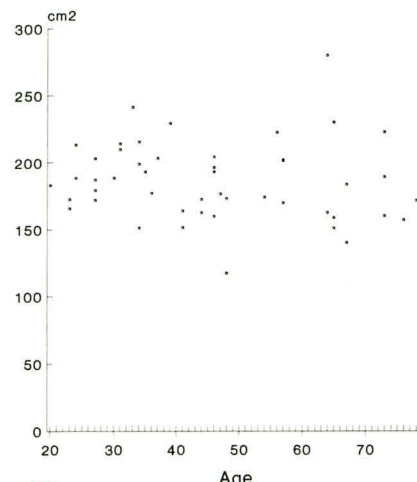
Note.—*r* = correlation coefficient; *P* = level of probability.



8



9



10

Fig. 8. Scatterplot displaying the values of the profile area of the total corpus callosum ($r = -.53$, $P = .001$).

Fig. 9. Scatterplot displaying the values of the profile area of the first fifth (1/5) of the human corpus callosum ($r = -.29$, $P = .03$).

Fig. 10. Scatterplot displaying the values of the profile area of the fifth fifth (5/5) of the human corpus callosum ($r = -.11$, $P = .43$).

callosal parts (ie, posterior parts of trunk and splenium) did not show significant age changes (Table 1, Fig. 10).

The width of the genu (C5T1) showed no age-specific changes, whereas the height of the anterior trunk (C5T2, C5T3) was significantly decreased. The other linear parameters of callosal height (C5T4, C5T5) did not show significant differences (Table 1). The mean height of the second fifth (2/5) of the corpus callosum (C5MT2) was significantly decreased during aging, whereas mean heights of the third (3/5) and fourth (4/5) fifth of the corpus callosum (C5MT3, C5MT4) remained unchanged (Table 1). When measuring the splenial width by the "rotatory diameter measurement," no significantly decreased diameters could be found (Table 1). The length of the bisector line 1 (BIS1) showed no significant age change (Table 1).

The profile area of the surrounding telencephalon (BRPA) was decreased with normal aging (Table 1). The frontal (BRHF), but not the occipital (BRHO), heights showed significant age change (Table 1). The profile area of the septum pellucidum (SPPA) was significantly increased with age. The encephalometric parameters describing the distance between the genu, trunk, and splenium of the corpus callosum and the frontal pole, superior margin, and occipital pole of the telencephalon (BCXDA, BCYDS, BCXDP), respectively, were decreased in normal aging (Table 1). The profile area of the brain stem (BRSTPA) was not changed during normal aging (Table 1). How-

ever, the different parts of the brain stem (ie, mesencephalon, pons, medulla oblongata) were differently altered by the aging process. The profile area of the mesencephalon (MSEPA) was significantly decreased with aging, whereas pons and medulla oblongata were unchanged. The profile area of the cerebellum (CERPA) measured at the level of the vermis was reduced in normal aging (Table 1).

Discussion

Method

The great variability of callosal size and location requires careful quantification procedures. A clear strategy for evaluation of the corpus callosum is necessary to obtain objective and reproducible results. In many papers dealing with quantification of the corpus callosum these basic scientific requirements have not been fulfilled. Exact definitions of the measuring steps, which would allow reproducibility of the results, were missing in many cases. So far, it is difficult to compare the results of different research groups.

Several authors used no quantification but applied rating scales to determine changes in callosal size (22, 23). However, the use of rating scales is questionable because the results are influenced by the subjectivity of the examiner. Other authors did not describe clearly their evaluation procedure (26–28). Exact information on the subdivision of the corpus callosum into parts is lacking (1, 7, 10, 11, 15, 28, 29); the authors

of these papers state only that the corpus callosum has been divided into 4 or 5 parts. An exact definition of callosal length is lacking. As we showed, callosal length can be interpreted in different ways. There exist many possibilities to divide the corpus callosum if one does not take into account the callosal curvature and use the proposed horizontal standardization. Clear descriptions of the quantification of measurements of callosal thickness and of splenium width were lacking (1, 5, 7, 10, 11, 15, 25, 28). As we showed, one-dimensional, or linear, measurements of callosal height, thickness, width, and length give restricted information because these measurements constitute a "snapshot" quantification. Thus, besides one-dimensional linear measurements, two-dimensional measurements (ie, profile area, or cross-sectional area) have to be taken. The human brain and the corpus callosum are three-dimensional structures, so three-dimensional evaluation (volume estimation) of the corpus callosum should not be omitted. Quantification of callosal volume is not possible on the median-sagittal plane; parallel frontal sections are required. This is possible with MR and with frontal sections of autopsy brain material. However, the exact boundaries of the corpus callosum with respect to the laterally located centrum semiovale is very difficult. Reference points that should allow such a bordering are highly variable in form and size. If the volume of the corpus callosum is estimated, the obtained data must be carefully interpreted.

Several attempts have been made to correlate morphologic defects and their localization in the corpus callosum with functional deficits (ie, disconnection syndromes). Anterior callosal hemorrhagic lesions have been localized on computed tomography scans (30). However, this task is very tedious and does not allow exact localization. The results of callosotomies have been checked on MR scans (31–33). The authors tried to establish a correlation between functional deficits and those callosal parts that have been separated upon surgery. However, an exact method that allows localization and quantification of the bisected callosal parts has so far not been used. In addition, it would have been interesting to know the size of those callosal parts that remained intact after surgery.

A simple and reproducible measuring strategy is required to estimate quantitatively normal and pathologic processes (ie, normal and pathologic aging, multiple sclerosis, schizophrenia) in the

human corpus callosum. Our measuring procedure fulfills these requirements and allows exact localization of pathologic processes in the corpus callosum. Thus, sequential studies with reliable quantification of time effects and/or therapy effects can be undertaken.

Normal Aging

It could be clearly demonstrated on MR scans that frontal callosal parts (ie, rostrum, genu, anterior parts of the trunk) are involved in normal aging. However, posterior callosal parts (ie, posterior parts of the trunk and splenium) did not show age-specific changes. The macroscopical finding of the corpus callosum shows that frontal and parts of the temporal interhemispheric fiber systems are altered in normal aging. Some results that support this hypothesis already exist. Using stereologic procedures, a decrease in the volume of the frontal lobe could be demonstrated macroscopically (34). A more exact evaluation of these macroscopic data revealed that mainly the orbital parts of the frontal lobe are changed (Weis and Haug, unpublished data). Histologic correlates for these macroscopic findings exist. Using variance analysis we showed that in area 11 (after Brodmann) of the frontoorbital cortex, neurons of layer 3 and 5 are lost during biologic aging (Weis and Haug, unpublished data). These two layers are the main origin of commissural fibers.

The thickness of the cerebral cortex previously has been estimated (35), and the following changes during normal aging shown. The thickness of the midfrontal cortex was significantly decreased with age. In the temporal superior cortex, this decrease was less significant than in the frontal cortex, whereas no significant decrement with age was found in the inferior parietal cortex (35). Thus, quantifiable anterograde changes of the corpus callosum reflect changes that occur in the cerebral cortex.

Aging and White Matter

There exist only a few papers dealing with white-matter changes in the central nervous system during aging. Several research groups have focused their interest on the development of the corpus callosum and its axons. We will briefly report some results of the effect of experimental conditions on the corpus callosum, since they involve some important aspects of the neurobiology of human postnatal development.

Postnatal development of the corpus callosum and callosal axons in rats raised under hypoxic conditions has been analyzed (36). The authors describe changes in the number of myelinated axons, their cross-sectional area, myelin sheet thickness, and number and thickness of myelin lamellae. The effects of undernutrition on the myelination process has been studied (37, 38). The percentage of myelinated axons is significantly reduced in undernourished rats. The number of myelin lamellae was reduced only in early postnatal days, whereas later no difference was found between control and treated rats (37). In another experiment, changes of the corpus callosum seen in nutritionally rehabilitated rats were investigated (38). In rats nutritionally rehabilitated for two weeks, only small axons did not show changes. The authors show that relatively large-sized axons do not produce in the ensheating oligodendroglia any compensatory increase in the layers of myelin.

The effects of external stimuli on the size and form of the corpus callosum have been investigated (39, 40). Macroscopic changes in callosal size in rats that were provided handling stimulation in early postnatal days were shown. Callosal size was larger in male than in female rats. The authors describe region-specific changes and suggest that certain callosal fiber populations were involved. They speculate that in their experimental system, increased callosal size is associated with greater hemispheric specialization (39). However, the authors did not provide data on axonal size and axonal number. Thus, it is questionable to correlate callosal size with the effect of early experience. Another research group found no macroscopic changes of callosal size in rats raised under similar environmental conditions (40). The ultrastructural analysis of the splenium corporis callosi revealed differences that were not apparent from gross-size measurement. Sex differences existed in axonal number and size, and the environment influenced these differences.

The normal postnatal development of the corpus callosum and its axons has been investigated several times in cats (41–43). At birth, the corpus callosum is made up of very small, densely packed, nonmyelinated fibers. Myelination starts at the 4th postnatal week. The corpus callosum is made up of 60% myelinated axons which display a diameter of 0.6 to 0.7 μm (41). Results of Looney and Elberger (42) indicate that myelination begins and ends earlier in the anterior region of the corpus callosum. Axons are contin-

uously lost between the 4th and 150th postnatal day (43).

In 1954, the number and size of axons in the corpus callosum was estimated in three human brains by light microscopy (44); a total of 174 to 193 million axons displaying a mean diameter of 1.5 μm was calculated.

Further investigations are directed towards the quantification of MR brain sections in order to get reliable and reproducible data on normal aging of the different brain structures. We will be able to state reliably when and where significant age changes occur. These data are needed to compare with similar evaluations of pathologic aging. Hence, the corpus callosum is a very good and sensitive indicator of the cerebral cortical state. Correlations between changes of the corpus callosum as well as of white matter with changes of the cerebral cortex will prove or disprove this hypothesis.

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