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Normal Postnatal Development of the Corpus Callosum as Demonstrated by MR Imaging

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Sixty-three patients, 3 days to 12 months old, were examined by MR imaging to evaluate the normal development of the corpus callosum in the first year of life. During the first month of life the corpus callosum is uniformly thin and of the same signal intensity as white matter throughout the brain. During the second month, a variable spurt of growth occurs in the genu, followed by a similar period of rapid growth in the splenium between 4–6 months of age. High signal intensity on T1-weighted images related to the myelination process begins to appear in the splenium by about 4 months and in the genu by about 6 months. The corpus callosum has an adult appearance on sagittal scans by about 8 months of age.

MR imaging has become a valuable tool in pediatric neuroimaging. The combination of multiplanar capability and increased contrast resolution (compared with CT) has resulted in high sensitivity in the detection of brain and spine lesions [1–3] and the capability to evaluate normal brain maturation [4, 5]. Although the corpus callosum has been shown to be a sensitive indicator of dysgenic and destructive processes in the brains of children [6], no normal standards have been established for the appearance and growth of the corpus callosum in the infant. The purpose of this study was to establish standards for normal development of the corpus callosum in the first year of life.

Materials and Methods

MR scans of 63 patients 3 days to 12 months old (mean, 5.2 months) were reviewed retrospectively to evaluate the corpus callosum. Clinical indications for MR were suspected or confirmed seizure disorders (31 patients), macrocephaly (20 patients), trauma (eight patients), suspected child abuse (three patients), and history of a twin with a brain anomaly (one patient). All subjects had achieved normal developmental milestones and had normal cerebral myelination for their age. All the MR scan findings were normal.

All patients were scanned on a 1.5-T unit.* Measurements were obtained from T1-weighted midline sagittal spin-echo images, 400–600/20/2 (TR/TE/excitations), with a 128 × 256 matrix and 5-mm sections. Required measurements were obtained from a single midline sagittal section and occasionally from adjacent sections if the head was skewed in the scanner. Measurements with calipers were made directly from the films to the nearest millimeter.

The thickness of the corpus callosum was measured as described by Rakic and Yakovlev [7] at the genu, splenium, and midbody immediately anterior to the columns of the fornix (Figs. 1 and 2). In 39 patients, the length of the corpus callosum was measured from the anteriormost aspect of the genu to the posteriormost aspect of the splenium. The greatest anteroposterior dimension of the brain was then measured from the inner table of the frontal bone to the inner table of the occipital bone, and the ratio of these numbers was calculated (Table 1).

The appearance and progression of changes in relative signal intensity in the corpus callosum (believed to be secondary to myelination) were also noted in each patient, as were changes in the callosal shape. The cingulate gyrus was evaluated on parasagittal images.

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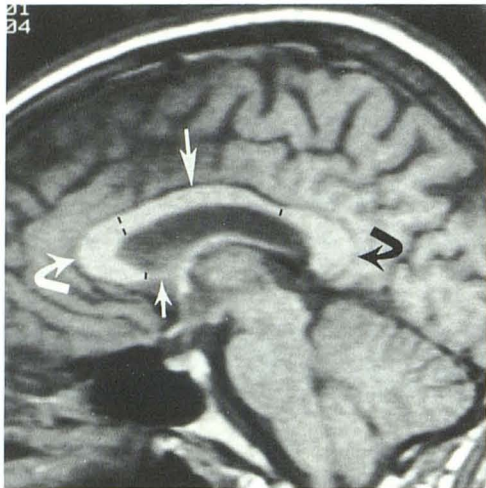


Fig. 1.—Spin-echo image, 600/20, of normal adult corpus callosum shows rostrum (short straight arrow), genu (white curved arrow), body (long straight arrow), and splenium (black curved arrow). There is focal thinning at junction of body and splenium. We have observed this narrowing in a substantial number of patients and believe it to be a normal variant.

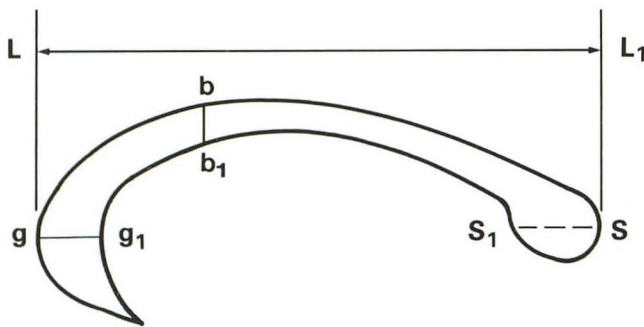


Fig. 2.—Method by which measurements were obtained. The width of the genu was measured as a line from g to g₁; body from b to b₁, and splenium from S to S₁. The length of the corpus callosum was measured from the anterior tip of the genu to the posterior tip of the splenium, shown here as the length from L to L₁.

Results

In the neonate, the corpus callosum was thin and flat, without the normal bulbous enlargements at the genu and splenium (Fig. 3). The body underwent a steady, gradual increase in thickness from 1.5–2 mm at 2 weeks old to 3–4 mm by 12 months. In four patients there was a narrowing of the posterior callosal body near the splenium.

At 2 weeks, the genu measured approximately 4 mm in diameter. At 6–12 weeks there was a variable enlargement; otherwise, the growth was gradual. By the twelfth month, the average thickness of the genu was 8–9 mm (Fig. 4). The genu was quite variable in thickness at all ages, as exemplified by the fact that it measured 8 mm in a 2.3-month-old infant, 5 mm in a 4.1-month-old infant, 10 mm in an 8.6-month-old infant, and 6 mm in an 11.4-month-old infant.

At 2 weeks of age, the splenium was intermediate in size between the genu and body with a thickness of about 3 mm. Thickness gradually increased with acceleration between 4 and 6 months (Fig. 4), and the shape of the splenium changed in appearance from a rectangular extension of the body to the more adult bulbous dorsal termination of the corpus callosum (Fig. 5). By 12 months of age, the splenium was 7–9 mm thick, approximately equal in size to the genu.

There was a slight trend toward an increase in length of the corpus callosum during the year, from approximately 5 cm in length at birth to approximately 6 cm by 12 months of age, but there was marked variation in length at all the ages studied (Fig. 4). The ratio of the corpus callosum length to the anteroposterior diameter of the brain, however, remained quite constant in the 0.35–0.45 range in all patients studied, with only statistical variation. Since the callosal length exhibited little change or variability in the assessment of this measurement, it was measured in only 43 patients.

At birth, the corpus callosum was isointense relative to the white matter of the centrum semiovale on all imaging sequences. Toward the end of the fourth month of life, the splenium and posterior body began to show increased intensity on T1-weighted images, thought to be related to the process of myelination. Gradually over the next 2 months, foci of high intensity developed and coalesced further rostrally in the corpus callosum. At the end of the sixth month, the

TABLE 1: Measurements of Corpus Callosum in Normal Postnatal Development

Age (months)	No. of Patients	Mean $\pm$ 1 SD (mm)				Callosum:Brain Ratio ^b
		Thickness			Length ^a	
		Genu	Midbody	Splenium		
0–2	12	5.1 $\pm$ 1.0	2.3 $\pm$ 0.5	3.7 $\pm$ 0.6	47.7 $\pm$ 2.8	0.395
2–4	18	5.0 $\pm$ 1.3	2.5 $\pm$ 0.5	4.5 $\pm$ 0.9	51.2 $\pm$ 4.5	0.398
4–6	7	7.0 $\pm$ 1.3	3.0 $\pm$ 0.8	5.8 $\pm$ 1.3	50.8 $\pm$ 3.4	0.394
6–8	7	6.3 $\pm$ 1.0	2.8 $\pm$ 0.4	6.6 $\pm$ 0.6	54.0 $\pm$ 0.8	0.400
8–10	8	7.7 $\pm$ 1.3	4.2 $\pm$ 1.0	7.6 $\pm$ 1.6	59.0 $\pm$ 8.2	0.388
10–12	11	7.8 $\pm$ 1.1	4.2 $\pm$ 0.8	8.3 $\pm$ 1.2	57.6 $\pm$ 4.9	0.392

^a Measured in 43 patients.

^b Determined by dividing length of the corpus callosum by anteroposterior diameter of the brain. This ratio was calculated in 39 patients.

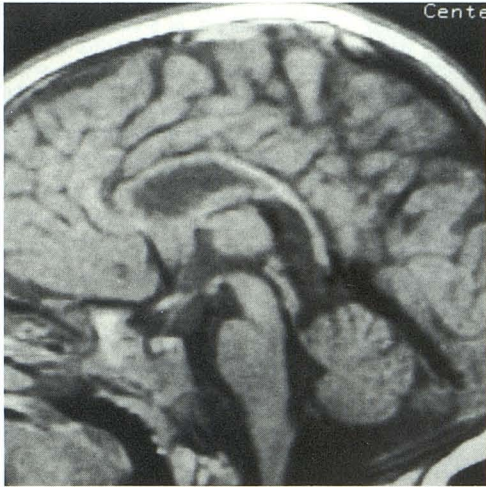


Fig. 3.—Midsagittal spin-echo image, 600/20, in 2-week-old neonate. At this age, the corpus callosum is thin and flat, without the normal bulbous enlargements at the genu and splenium.

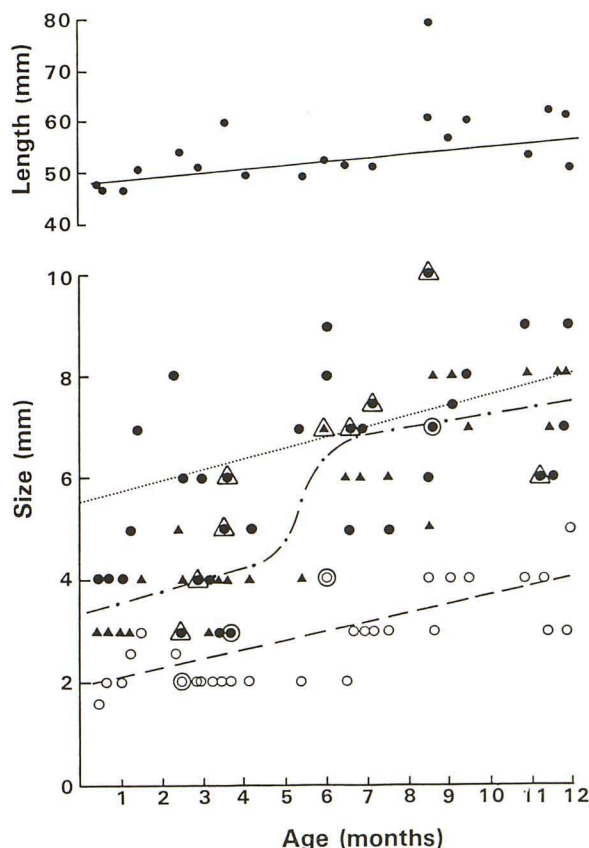


Fig. 4.—Lower scale: size of the splenium (triangles), body (open circles), and genu (solid circles) with respect to age in patients examined in this study. A least-squares line is drawn for the splenium (dot-dash), body (dashed line), and genu (dotted line). A steady, gradual enlargement of the callosal body occurs while the splenium undergoes a rapid increase in size between 4 and 6 months of life. The genu was extremely variable in size at all ages. In some patients, the genu rapidly enlarged in the second and third month of life.

Upper scale: circles depict the length of the corpus callosum at the various ages studied. The length gradually increased in size throughout the first year of life.

genu was of high signal intensity (Fig. 5). By the age of 8 months, all the examined patients had a corpus callosum essentially identical in configuration and intensity to that of an adult, except for size (Fig. 6).

Discussion

The corpus callosum forms between 8 and 20 weeks of gestation [6, 7]. The embryologic development is complex and will not be reviewed in detail here. Interested readers are referred to a companion article [6] or to the definitive work of Rakic and Yakovlev [7]. Briefly, the corpus callosum forms in an anterior to posterior direction with the genu forming first followed by the body, the splenium, and lastly the rostrum. The bed for ingrowth of the callosal fibers forms between approximately 8 and 16 weeks of gestation. The callosal fibers themselves begin to cross first at approximately 12 weeks in the genu; the fibers of the rostrum are the last to cross the midline, doing so at 18–20 weeks of gestation. Although all the components of the corpus callosum are present by 20 weeks, the structure is far from complete in terms of growth. From 20 weeks to term, the length increases by a factor of 2.5; the thickness of the body increases by 30% and the genu by 270% [7]. Although the size of the corpus callosum in utero has been established by pathologic studies, little is known about its development after birth. An understanding of normal callosal development has become particularly important in the light of results of a recent study that show the corpus callosum is useful as an indicator of both congenital and degenerative brain disorders in children [6]. The purpose of our present study was to establish those norms for the infant in the first year of life.

The appearance of the corpus callosum is quite different in the neonate when compared with the adult; an adult appearance slowly evolves over the first 8 months of life. The first postnatal change is a substantial, albeit variable, thickening of the genu, which frequently occurs as early as the second and third months (Fig. 4). De Lacoste et al. [8] have demonstrated that the fibers crossing through the genu come from the inferior frontal and anterior inferior parietal regions. The enlargement of the genu, therefore, presumably relates to the development of the interhemispheric connections of the precentral and postcentral gyri; these areas, which are involved with basic motor and sensory functions, develop early in life [9].

At birth, the splenium is intermediate in size between the genu and body of the corpus callosum. It slowly enlarges until the fifth and sixth months, when a rapid increase in size occurs, resulting in the bulbous splenium seen in the adult corpus callosum. By the end of the seventh month, the splenium is equal in size to the genu; it then gradually enlarges with the genu and the rest of the brain through the remainder of the first year. The fibers in the splenium arise from the visual and visual-association areas of the cortex [8]. The rapid development of the splenium, not surprisingly, corresponds temporally with increasing visual awareness at 4–6 months of age. It is during this period that the infant develops binocular vision and visual accommodation and begins to identify objects [10]. Both binocular vision and object identification are

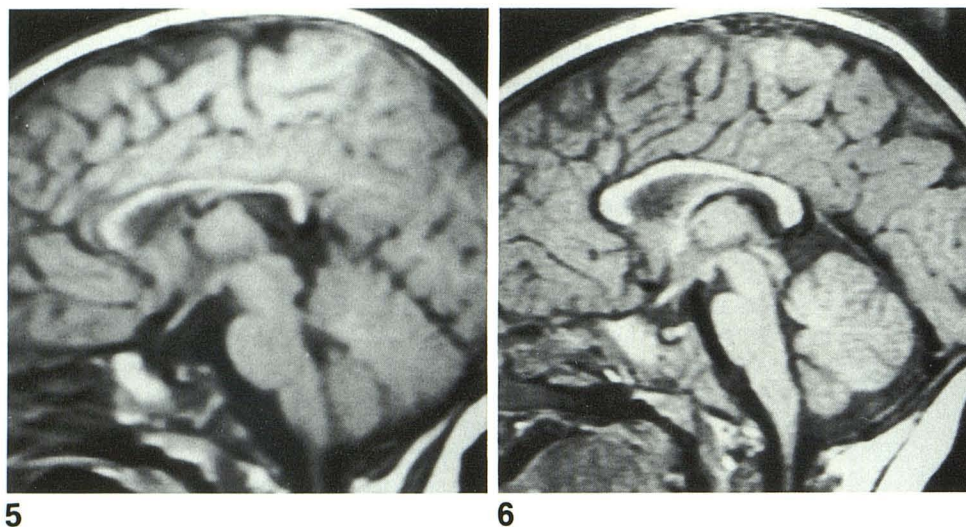


Fig. 5.—Midline sagittal spin-echo image, 600/20, in 6-month-old infant. By the end of 6 months, the splenium shows a bulbous enlargement, similar to but smaller than that in the adult. Moreover, by 6 months of age the entire corpus callosum is of high signal intensity, caused by the process of myelination.

Fig. 6.—Midline sagittal spin-echo image, 600/20, in 8-month-old infant. Corpus callosum has essentially an adult appearance by this age. Note marked uniform hyperintensity and bulbous enlargements of splenium and genu.

dependent on interhemispheric connections. Thus, the enlargement of the splenium presumably relates to the development of connections between the visual cortex and the association areas of the brain in the increasingly visually aware child.

The body of the corpus callosum enlarges slowly over the entire 12 months without any detectable growth spurts. The size of the body is relatively uniform, except that in four of our patients a focal thinning was seen at the junction of the body and splenium (Fig. 1). This narrowing has also been observed in a substantial number of adults and older children whose MR examinations were otherwise unremarkable or demonstrated unrelated lesions. McLeod et al. [11] found a narrowing at this location in 22% of 450 randomly selected patients. This narrowing is almost unquestionably a normal variant.

The absence of significant enlargement of the body compared with the genu and splenium probably reflects the anatomic origin of these fibers and the phylogenetic development of the brain. Sensory and visual function are important early in life for all animals. It is therefore not surprising that the areas of the brain serving these functions develop first (pathologic studies have shown that these areas myelinate first [9]) and that the association fibers involving these functions, which run through the corpus callosum, develop early as well. The more gradual growth of the body of the corpus callosum probably reflects the lesser importance of association areas in the temporal and parietal lobes (from which these fibers originate) in early life and in lower orders of animal life.

The relative increase in signal intensity that develops in the posterior corpus callosum at about 4 months of age and progresses toward the genu over the next 2 months is believed to result from the process of myelination. A similar signal intensity is associated with the white matter on axial T1-weighted images and corresponds to known myelination patterns [12]. We have observed this maturation of the corpus callosum on axial and sagittal T1-weighted MR images of

many patients and found a consistent temporal sequence. The splenium is of high signal intensity by the end of the fourth month. The maturation proceeds rostrally to the genu, which is of high signal intensity by the end of the sixth month. The corpus callosum is of a uniformly high signal intensity by the end of the eighth month. These findings are compatible with the known occipital to frontal pattern of myelination within the brain [9, 12]. This change is reflected in a decreasing of the signal intensity on T2-weighted images (spin-echo, 2500/70) at a slightly later time, appearing in the splenium at approximately 6 months of age and in the genu at approximately 8 months.

The relative lack of change in the length of the corpus callosum during the first year of life was somewhat surprising and contradicts results obtained in a previous study based on a small number of autopsies [7]. The large variation in head size and shape in the general population, as compared with the slow rate of callosal growth, is the probable cause of the apparent lack of change in callosal growth. Interestingly, the ratio of callosal length to anteroposterior brain diameter was quite constant throughout the population sampled, independent of head shape and size, reflecting the parallel growth of the brain and its components. Owing to the insensitivity of callosal length as a marker of normal growth, the change in callosal shape and signal intensity is the preferred means of judging normal maturation of the corpus callosum and thereby normal brain development.

Results obtained in our present study differ from those obtained pathologically [7] in that our measurements are uniformly somewhat larger. For example, in four infants up to 24 months of age, Rakic and Yakovlev [7] obtained an average callosal length of 44.8 mm; we obtained an average of 52.9 mm in 43 patients up to 12 months of age. Similar differences were obtained in measurements of the thickness of the genu, body, and splenium. The most likely cause of this discrepancy is that the cadaver brains shrank as a result of formalin fixation. Our measurements are probably more

accurate anatomically as well as statistically, because of the larger sample population.

It would be interesting to correlate our data with similar data obtained by sonography, which, in general, is the primary method used for neuroimaging in infants. We have been unable to find sonographic data relating to normal callosal development. It is doubtful whether our data would be applicable to sonograms, because in sonography the angle of the transducer with respect to the corpus callosum should distort the measurements.

In summary, the corpus callosum changes considerably in appearance during the first year of life; this evolution occurs in an ordered fashion. Awareness of the normal sequence of events in callosal maturation is important in the differentiation of normal from abnormal brain development.

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