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Limbic Lobe Embryology and Anatomy: Dissection and MR of the Medial Surface of the Fetal Cerebral Hemisphere

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PURPOSE: To facilitate understanding of limbic lobe anatomy by showing embryologic transformations of the medial surface of the cerebral hemisphere. **METHODS:** Brains from fetal specimens ranging from 13 to 24 weeks of gestational age were dissected. Photographs were made of the medial surface of the cerebral hemisphere. MR images of different fetal specimens of similar age were made for comparison of MR anatomy with dissected material. **RESULTS:** At 13 weeks, the entire inner limbic arch of the hippocampal formation is visible on the medial surface of the cerebral hemisphere. The hippocampal sulcus extends from frontal lobe to temporal lobe. At 16 weeks, the outer neocortical limbic arch of the subcallosal area, cingulate gyrus, and parahippocampus gyrus is present. Growth of the corpus callosum is associated with reduction in size of the hippocampal formation in the frontal lobe. The sulcus of the corpus callosum is the remnant of the anterior part of the hippocampal sulcus. At 18 weeks, growth of the parahippocampal gyrus begins to conceal the hippocampal formation. The supracallosal gyrus (indusium griseum), hidden from view by the corpus callosum, and the paraterminal gyrus are remnants of the previously larger hippocampal formation. **CONCLUSIONS:** Analysis of fetal specimens in different developmental stages with dissection and MR provides insight into embryologic transformations responsible for the complex anatomy of the limbic lobe.

Index terms: Brain, anatomy; Fetus, magnetic resonance

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The intricate anatomy of the limbic lobe as seen on magnetic resonance (MR) has been described by several investigators (1–6). This anatomic complexity results, in part, from developmental changes in the relationship of the phylogenetically older components of the limbic lobe with the neocortex. Because knowledge of embryology can elucidate anatomic relationships in the adult brain, we decided to examine limbic lobe development in fetal specimens using techniques of dissection and MR imaging. Our purpose was to demonstrate embryologic transformations occurring on the medial surface of the cerebral hemisphere to help explain limbic lobe anatomy in adults. Anatomic studies by Marchand (7), Blumenau (8), Retzius (9), and Streeter (10) have used drawings, casts, or models to show the early developmental changes of the limbic lobe on the medial surface of the cerebral hemisphere.

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Materials and Methods

Sixteen human fetal specimens were examined, 10 with dissection and 6 with MR imaging. All specimens were normal in appearance. The specimens, preserved in 10% formaldehyde, ranged from 13 to 24 weeks of gestational age. Fetal age was assessed by comparing occipitofrontal diameter and the crown-rump length to atlas standards (11, 12).

Dissection of 10 specimens was performed in the following manner. The leptomeninges were removed. The medial surface of the brain was examined after brain transection in the midsagittal plane. No abnormalities were seen. To see the temporal lobe, the cerebellum and brain stem were removed, and the hypothalamus and thalamus were partially resected. Initial stages of the dissections were performed using a 3-diopter magnifier. A dissecting microscope was used to examine the medial surface of the hemispheres. The specimens were photographed with a 35-mm camera and a macro lens. Depending on specimen size, 12-, 20-, and 36-mm extension rings for magnification were added separately or in combination between the lens and the camera body.

To identify limbic lobe structures, previous studies of human embryology and anatomy were used (7–9, 13–19). It was useful to consider the limbic system as two arches—outer and inner—extending from the frontal lobe to the temporal lobe. The outer arch includes the subcallosal area, cingulate gyrus, isthmus cinguli, and parahippocampal gyrus. The inner arch consists of the paraterminal gyrus, indusium grisium (supracallosal gyrus), fasciolar gyrus, and the hippocampal formation. Separating the outer and inner arches is the hippocampal sulcus.

Dissection of younger fetal specimens was difficult. The partially myelinated brain with its high water content does not fix well, even after being preserved in 10% formaldehyde for 20 years. The pia mater and blood vessels help maintain the shape of the fetal brain after it is removed from the cranial cavity. Once the pia mater and blood vessels are removed, the underlying brain will frequently disintegrate. Because specimens can dry quickly and lose their features, effort was taken to keep them moist with water during dissection and photography. This step also prevented artificial fissures that can develop after removal of the pia mater (13). Of the 10 specimens (20 cerebral hemispheres), useful dissections were obtained on 5 hemispheres younger than 15 weeks, 4 hemispheres between 15 and 18 weeks old, and 4 hemispheres between 18 and 24 weeks old.

To correlate dissections with MR imaging, six fetuses that were not dissected were imaged in a General Electric (Milwaukee, Wis) Signa 1.5-T system. These specimens ranged in age from 13 to 24 weeks. Images in the sagittal and coronal planes were acquired using a three-dimensional spoiled gradient-echo sequence that accentuates T1 weighting. The parameters were 45/7/2 (repetition time/echo time/excitations), flip angle of 45°, matrix size of 256×192, field of view of 8 cm, and section thickness of 0.8 mm. A wrist coil with a 10-cm diameter was used. An ISG workstation (ISG Technologies Inc, Toronto, Canada) was used to reformat images in oblique sagittal planes. Of these six fetuses, MR images from two were suboptimal because of poor tissue contrast. The remaining four specimens with preserved MR anatomy had gestational ages of 13, 14, 18, and 24 weeks, respectively.

Results

Photographs of dissected specimens aged 13 weeks, 16 weeks, and 18 weeks are shown in Figures 1 through 3. MR images of 13- and 18-week specimens are shown in Figures 4 and 5.

At 13 weeks, before formation of the corpus callosum, the entire hippocampal formation is visible on the medial surface of the cerebral hemisphere (Figs 1 and 4). The inner limbic arch, consisting of the hippocampal formation, extends from olfactory tract to the temporal lobe. The hippocampal sulcus extends from frontal lobe to the temporal pole; it is wide and visible on the medial surface of the hemisphere. The neocortex of the temporal lobe and the uncus are small.

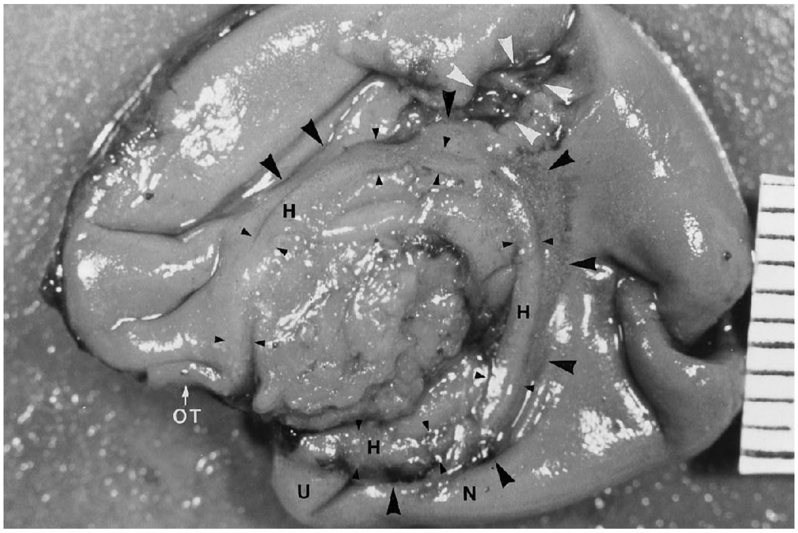
At 16 weeks, the neocortical outer limbic arch consisting of the cingulate gyrus and parahippocampal gyrus can now be identified (Fig 2). In the temporal region, the fornix and hippocampal formation are seen as separate structures, and the hippocampal sulcus is still large and visible. In frontal and parietal regions, however, the supracallosal hippocampus has decreased in size and becomes the indusium griseum. The corpus callosum is present and hides the indusium griseum from view. Associated with development of the corpus callosum, the hippocampal sulcus in the frontal and parietal regions becomes the sulcus of the corpus callosum.

At 18 weeks, the neocortical outer limbic arch consisting of the subcallosal area, cingulate gyrus, and parahippocampus gyrus is more prominent (Figs 3 and 5). As a result of marked expansion of the neocortex in the region of the parahippocampal gyrus and uncus, the hippocampal formation is found deep to the medial surface of the hemisphere and begins to disappear from view. After 18 weeks, the hippocampal formation and hippocampal sulcus are further hidden from view by continued growth of temporal lobe neocortex.

Discussion

This correlative study of fetal specimens with dissection and MR imaging illustrates anatomic transformations of the medial surface of the fetal human cerebral hemisphere (Figs 1–5). Knowledge of these transformations helps explain complex anatomic relationships in the adult limbic lobe.

The limbic lobe in the adult human brain consists of arches or curved bands of structures that surround the diencephalon and basal ganglia (1, 6, 17, 20). The outer arch includes the subcallosal area, cingulate gyrus, parahippocampal gyrus, and uncus. The inner arch consists of the paraterminal gyrus, supracallosal gyrus (in-



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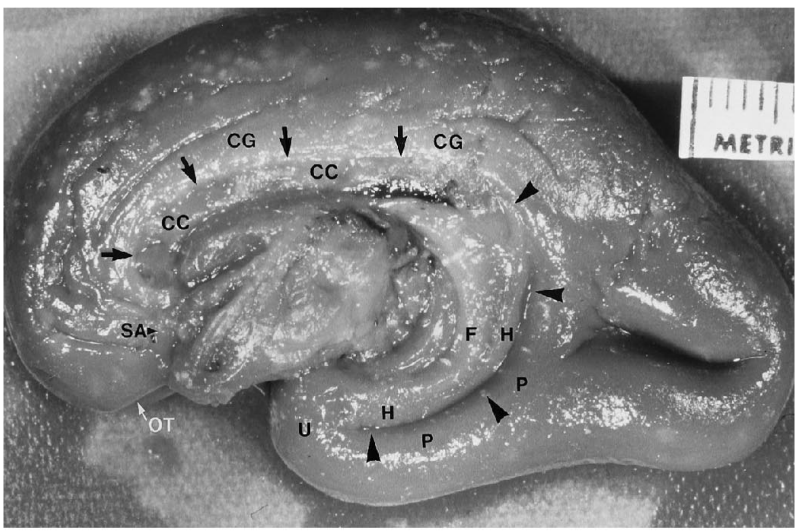

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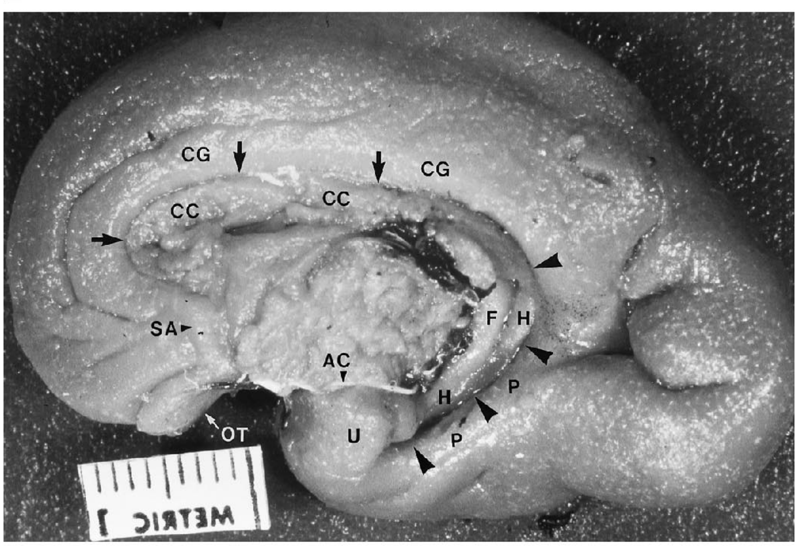

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Fig 1. Photograph of the medial surface of a cerebral hemisphere in a 13-week-old fetal specimen. The corpus callosum has not yet formed. The hippocampal sulcus (*large arrowheads*) is wide and visible throughout the medial surface of the hemisphere. In the parietal region, the hippocampal sulcus and neocortex are disrupted as a result of the dissection (*white arrowheads*). The uncus (*U*) and neocortex (*N*) of the temporal lobe are small. The inner limbic arch of the hippocampal formation (*H,* between *small arrowheads*) extends from the olfactory tract (*OT*) to the temporal lobe. It is approximately 1 mm in width and is visible in its entirety on the medial surface of the cerebral hemisphere. The distance between two adjacent ruler lines is 1 mm.

Fig 2. Photograph of the medial surface of the cerebral hemisphere in a 16-week-old specimen. The neocortical outer limbic arch can now be identified, consisting of the subcallosal area (*SA*), cingulate gyrus (*CG*), and parahippocampal gyrus (*P*). In the frontal and parietal regions, the corpus callosum (*CC*) is present, and the supracallosal hippocampus (indusium griseum) is hidden from view. The narrow sulcus of the corpus callosum (*arrows*) is the remnant of the larger hippocampal sulcus of the younger fetus. In the temporal region, the hippocampal sulcus (*large arrowheads*) is still large and visible. The fornix (*F*) and hippocampal formation (*H*) can be identified. The olfactory tubercle (*OT*) is visible near the subcallosal area (*SA*).

Fig 3. Photograph of the medial surface of the cerebral hemisphere of an 18-week-old specimen. The outer neocortical limbic arch of the subcallosal area (*SA*), cingulate gyrus (*CG*), and parahippocampus gyrus (*P*) is separated from the inner limbic arch by the sulcus of the corpus callosum (*arrows*) and hippocampal sulcus (*large arrowheads*). The olfactory tract (*OT*) is adjacent to the subcallosal area (*SA*). As a result of marked expansion of the neocortex in region of the parahippocampal gyrus (*P*) and uncus (*U*), the hippocampal sulcus (*large arrowheads*), fornix (*F*), and hippocampal formation (*H*) are located deep in the medial surface of the hemisphere and are beginning to disappear from view. The anterior choroidal artery (*AC*), injected with barium gelatin, was left in place.

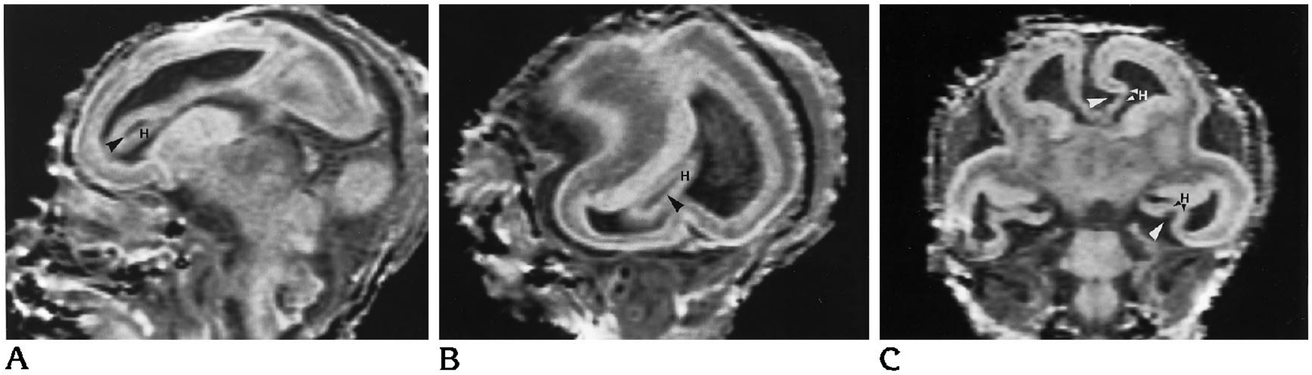
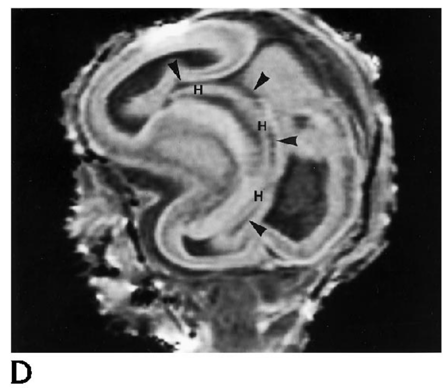


Fig 4. T1-weighted MR images of a 13-week-old fetus. *A,* Midsagittal, *B,* parasagittal, and *C,* coronal images show segments of the hippocampal formation (*H*) and the arched hippocampal sulcus (*large arrowheads*). *D,* A reformatted sagittal oblique image was created to view the medial aspect of the limbic lobe in its entirety, similar to dissected specimen in Figure 1. This reformatted image combines midsagittal frontal and parietal lobe structures seen in A with parasagittal temporal lobe structures seen in B and demonstrates that hippocampal formation and the hippocampal sulcus (*large arrowheads*) extend continuously from the frontal lobe to the temporal lobe.



dusium griseum), fasciolar gyrus, dentate gyrus, and cornu ammonis. These two limbic arches are separated by a third arch consisting of the sulcus of the corpus callosum and the hippocampal sulcus. The sulcus of the corpus callosum is between the cingulate gyrus and the supracallosal gyrus and is a remnant of the embryonic hippocampal sulcus. The hippocampal sulcus proper is bounded on one side by the subicular segment of the parahippocampal gyrus and on the other side by the dentate gyrus.

The hippocampal formation is the first cortical area to differentiate (15, 22, 23). Consisting of the dentate gyrus and cornu ammonis, the hippocampal formation first appears at 10 weeks of gestational age in the dorsomedial wall of the cerebral hemisphere adjacent to the lamina terminalis. The anterior part of the lamina

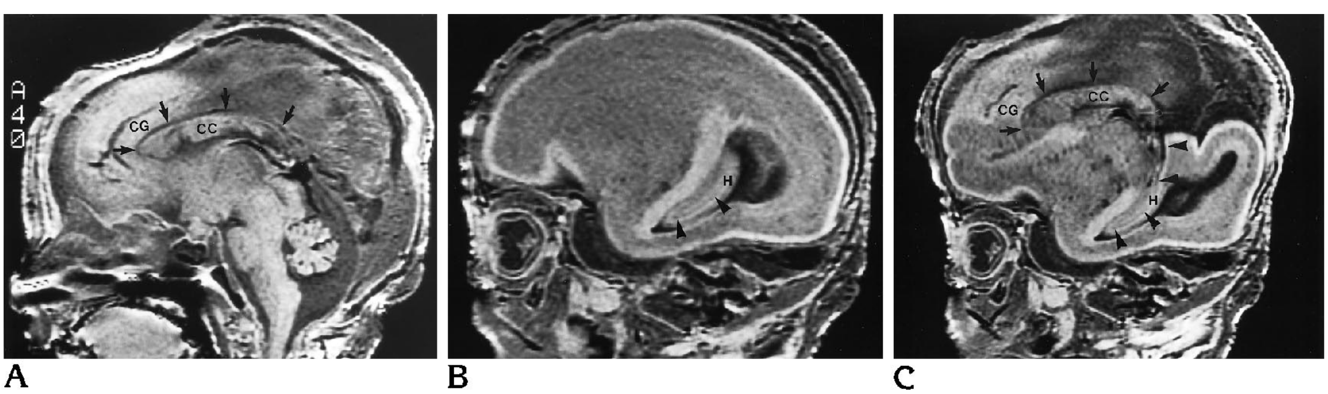


Fig 5. T1-weighted MR images of an 18-week-old fetus. *A,* midsagittal, *B,* parasagittal, and *C,* reformatted oblique sagittal views. The sulcus of the corpus callosum (*arrows*), between the corpus callosum (*CC*) and cingulate gyrus (*CG*), is the remnant of the anterosuperior aspect of the hippocampal sulcus (*arrowheads*). The reformatted oblique sagittal image (*C*), acquired as described in Figure 4, confirms continuity of the sulcus of the corpus callosum (*arrows*) and the hippocampal sulcus (*arrowheads*). The hippocampal formation (*H*) is visible in the temporal lobe region.

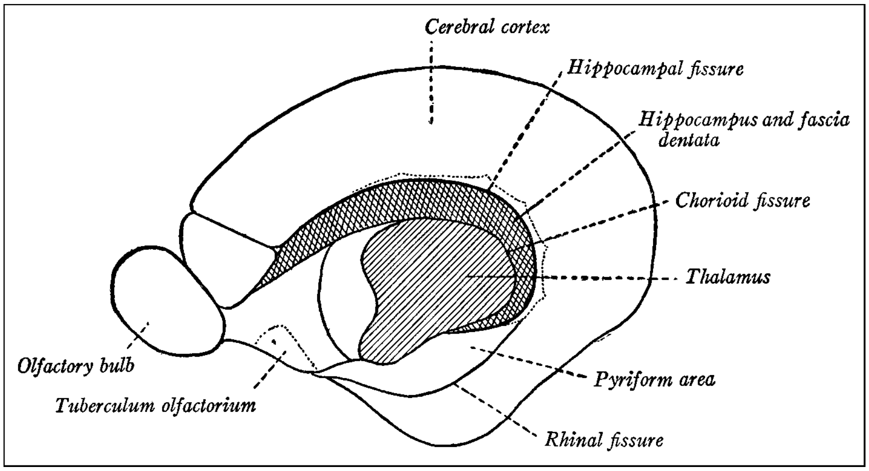


Fig 6. Diagram of a lateral view of the medial surface of the cerebral hemisphere of a monotreme, an egg-laying mammal without a corpus callosum. The inner limbic arch of the hippocampal formation extends from the frontal pole into the temporal lobe. The hippocampus and dentate nucleus are separated from the neocortex by the hippocampal fissure. In the human fetus, before corpus callosal development, the hippocampal formation and hippocampal sulcus have a similar appearance (from Ranson and Clark [30]).

terminalis near the chiasmatic ridge remains thin. The thicker dorsal part represents the lamina reuniens of His, a region of active cellular proliferation (24). The hippocampal primordium arises within the dorsal part of the lamina reuniens. The hippocampal formation undergoes a complex sequence of embryologic changes as it extends in a crescentic fashion, from the medial side of the olfactory evagination to the posterior end of the hemisphere, and later when the temporal lobe forms, anteroventrally into the temporal tip (23, 25). At 10 weeks, the hippocampal formation, which Macchi (25) names the *arcuate gyrus*, occupies a large part of the medial hemispheric wall. At this stage, the structure of the hippocampal formation is uniform throughout. Dorsally, it is separated from the neopallium by the hippocampal sulcus. On its concave aspect, the hippocampal formation is bordered by the choroidal fissure. At approximately the 14-week stage, coincident with the development of the corpus callosum, the dorsal (supracallosal) hippocampus starts to manifest regressive changes. The supracallosal indusium griseum and the paraterminal gyrus are remnants of the earlier large dorsal hippocampus. By the 17th week, the most developed region of the hippocampal formation is not over the diencephalon, but in the temporal lobe.

The hippocampal sulcus first appears at the 10-week stage as a result of differential growth of the dentate gyrus and the cornu ammonis (14, 22). The increasing thickness of the dentate gyrus rotates the hippocampal sulcus toward the cornu ammonis, making the sulcus deeper and sharply defined. By 15.5 weeks, the hippocampal sulcus is best developed in the temporal portion of the hippocampal formation. At 20.5 weeks, the relationship of the hippocampal sulcus with the surrounding structures is becoming similar to that of the adult brain. Anteriorly in the temporal lobe, a deep sulcus is still present. More caudally, where the dentate gyrus is infolded to a greater degree, the deep part of the sulcus is closed. Its walls are fused, and there is a remaining shallow indentation between the dentate gyrus and the presubiculum. Both pia mater and blood vessels may be included between the walls of the hippocampal fissure as they fuse. By 30 weeks, the well-developed hippocampal formation has acquired most of the its adult characteristics. The sulcus appears as a shallow groove on the surface with almost no indications of the earlier fusion of its walls. In some regions remnants of the leptomeninges can be identified deep to the groove. At times, a residual cavity of the hippocampal sulcus may remain, appearing on MR like a cystic structure of cerebrospinal fluid signal intensity within the hippocampus (3, 26).

Blumenau (8) discusses the transformation of the hippocampal sulcus into the sulcus of the corpus callosum. He refers to *Bogenfurche,* which in German means “arched sulcus” (27), stating, “The frontal part of the Bogenfurche corresponds to the sulcus of the corpus callosum which separates the corpus callosum from the gyrus corpus callosum. The back part of the Bogenfurche corresponds to the hippocampal fissure.” The gyrus corpus callosum most likely refers to the cingulate gyrus. Other German anatomists in the late 19th century also used the term *Bogenfurche* for the hippocampal sulcus (7, 9). Hines (13) and Macchi (25) mention Bogenfurche when discussing the hippocampal sulcus. Carpenter and Sutin (20) also state that the anterior portion of the hippocampal sulcus ultimately becomes the sulcus of the corpus callosum.

The extensive focus on the temporal lobe in MR imaging may lead to the notion that the hippocampal formation is strictly a temporal lobe structure. In many vertebrates without a corpus callosum, the hippocampus and dentate gyrus occupy a large portion of the medial surface of the cerebral hemisphere, extending from the frontal lobe to the temporal lobe. For example, monotremes (Fig 6) and marsupials have a well-developed hippocampal formation in the frontal lobes (28, 29). The hippocampal formation in the human fetus, before the formation of the corpus callosum, demonstrates to some extent a similar configuration (Figs 1 and 4). In primates, including adult humans, the hippocampal formation in the frontal and parietal lobes is reduced to a slender vestige consisting of the supracallosal gyrus (indusium griseum), a structure that cannot be seen on routine MR imaging. The frontal lobe remnant is the paraterminal gyrus, which is anterior to the rostrum and posterior to the posterior paraolfactory sulcus.

Conclusions

In the young human fetus that has not yet formed a corpus callosum, the hippocampal formation and hippocampal sulcus extend from frontal lobe to temporal lobe. The hippocampal sulcus can be considered a middle arch between inner and outer limbic lobe arches. With formation of the corpus callosum, there is marked reduction in the size of the hippocampal formation in the frontal and parietal lobes, and the anterior part of the hippocampal sulcus becomes the sulcus of the corpus callosum. The supracallosal gyrus (indusium griseum) and the paraterminal gyrus are remnants of a larger hippocampal formation present in the fetal frontal lobe before formation of the corpus callosum. The hippocampal formation and hippocampal sulcus in the young human fetus have a certain similarity to these structures in mammals not possessing a corpus callosum. Knowledge of embryologic modifications provides a foundation for understanding MR anatomy.

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