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Perinatal Neuroradiology



From the Fetus to
the Newborn



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Preface

This book originates from a very simple observation: for neuroradiologists which take care of neonatal brain, knowledge of what happens to the fetal brain, regarding both physiology and pathology, is essential to better understanding brain neonatal diseases. Nonetheless it is virtually impossible to assess the fetal brain by means of MRI without an appropriate knowledge of neonatal brain diseases.

Therefore, “prenatal and neonatal worlds” cannot be separated from both conceptual and practical point of view, but they should be studied together as a natural continuum regarding normal and pathological brain development.

From these considerations arises the subtitle: “from the fetus to the newborn”. This is not a classical and exhaustive textbook, but more properly a collection of cases organized in a systematic way, so as to follow, from midgestation until birth, the fate of brain anomalies, highlighting how they may change during the course of gestation and how it may be difficult to predict how a lesion will eventually appear.

The cases are organized in a systematic index covering the most important prenatal and postnatal brain diseases from the congenital genetic based to the acquired ones. Some conditions are not treated, because still predominantly better assessed by ultrasound, such as malformations of the spine or, extremely rare, such as prenatal metabolic or neoplastic brain diseases. Together with fetal and neonatal MR cases, high-resolution images of fetal MR autopsy cases are presented, either as a reference for normal anatomy or as a gross pathologic confirmation of a previous fetal MR.

Milan, Italy

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We are grateful to our MRI technicians which strongly collaborated to guarantee the high quality of MR studies and showed an enormous patience and empathy with small patients, expectant mothers and parents.

Thanks to the parents and to the families for allowing the publication of the images, understanding the meaning and the importance of scientific divulgation.

Finally thanks to everyone who we could not mention but who are in our hearts as a source of inspiration and motivation.

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Contents

1 Normal Development	1
Fabio Triulzi, Elisa Scola, and Sabrina Avignone	
1.1 Fetal MR Autopsy Technique	1
1.2 Fetal Anatomy on MR Autopsy	1
1.3 From the Fetus to the Newborn: In Vivo Anatomy	2
References	77
2 Normal and Abnormal Forebrain Commissures	79
Fabio Triulzi, Cristina Baldoli, Cecilia Parazzini, and Andrea Righini	
2.1 Commissure Development	79
2.1.1 Anterior Commissure	80
2.1.2 Hippocampal Commissure	80
2.1.3 Corpus Callosum	81
2.1.4 Corpus Callosum Development on Fetal MR and Fetal MR Autopsy	83
2.2 Commissure Malformations	83
2.2.1 Complete Commissural Agenesis	83
2.2.2 Partial Commissural Agenesis	84
2.2.3 Lipomas of the Corpus Callosum and Interhemispheric Cysts	84
2.3 Septum Pellucidum Anomalies	86
2.4 Holoprosencephaly	88
References	107
3 Posterior Fossa Malformations	109
Fabio Triulzi, Cristina Baldoli, Cecilia Parazzini, Özgür Öztekin, and Andrea Righini	
3.1 Fetal Cerebellar Anatomy and Development	109
3.2 Classification of Posterior Fossa Malformations	110
3.2.1 Anomalies of CSF Spaces	111
3.2.2 Predominantly Cerebellar Malformations	118
3.2.3 Cerebellar and Brainstem Malformations	125
3.2.4 Predominantly Brainstem/Midbrain Malformations?	127
References	138
4 Malformations of Cortical Development	141
Cecilia Parazzini and Fabio Triulzi	
4.1 Classification	141
4.2 Malformations Secondary to Abnormal Neuronal and Glial Proliferation or Apoptosis	141
4.2.1 Congenital Microcephaly	141

4.2.2	Megalencephaly	142
4.2.3	Cortical Dysgenesis with Abnormal Cell Proliferation (Without Neoplasia).	142
4.3	Malformations due to Abnormal Cortical Migration.	145
4.3.1	MCD with Neuroependymal Abnormalities: Periventricular Heterotopia	145
4.3.2	MCD due to Generalized Abnormal Transmantle Migration Lissencephaly/Subcortical Band Heterotopia (LIS/SBH)	148
4.3.3	MCD Presumably due to Localized Abnormal Late Radial or Tangential Transmantle Migration–Subcortical Heterotopia	150
4.3.4	MCD due to Abnormal Terminal Migration and Defects in Pial Limiting Membrane: Cobblestone Malformations.	151
4.4	Malformations due to Abnormal Postmigrational Development.	153
4.4.1	MCD with Polymicrogyria (PMG) or Cortical Malformations Resembling PMG.	153
4.4.2	Cortical Dysgenesis Secondary to Inborn Error of Metabolism	156
4.4.3	Focal Cortical Dysplasia due to Late Developmental Disturbances	156
	References.	163
5	Malformations of the Eye and Orbit.	165
	Chiara Doneda and Fabio Triulzi	
5.1	Embryology	165
5.2	Biometric/Morphometric Assessment	165
5.3	Hypotelorism and Hypertelorism.	167
5.4	Anophthalmia.	167
5.5	Microphthalmia	170
5.6	Buphthalmos	172
5.7	Optic Nerve Head Coloboma.	172
5.8	Microphthalmos with Cyst.	173
5.9	Congenital Cystic Eye	175
5.10	Persistent Hyperplastic Primary Vitreous	175
5.11	Optic Nerve Aplasia and Hypoplasia.	178
5.12	Dacryocystocele.	179
5.13	Congenital Nonvascular Tumors of the Orbit	180
5.14	Capillary Hemangioma	180
	References.	187
6	Vascular Malformations	189
	Cristina Baldoli, Silvia Pontesilli, Roberta Scotti, and Fabio Triulzi	
6.1	Dural Sinus Malformations	189
6.2	Vein of Galen Aneurysmal Malformation	191
	References.	198
7	Ventriculomegaly.	201
	Elisa Scola and Fabio Triulzi	
7.1	Diagnosis of Fetal Ventriculomegaly with Ultrasound and Magnetic Resonance Imaging.	201
7.2	Etiology-Based Classification	202
7.3	Ventriculomegaly and Associated Structural Abnormalities	206

7.4	Role of MRI in Ventriculomegaly Assessment	208
7.5	When to Perform MR Examination	209
7.6	Outcome of Fetal Ventriculomegaly	210
	References	219
8	Congenital Infections	221
	Fabio Triulzi, Chiara Doneda, Cecilia Parazzini, and Andrea Righini	
8.1	Cytomegalovirus Infection	221
8.2	Toxoplasmosis	228
8.3	Rubella Infection	229
8.4	HIV Infection and Parvovirus	230
8.5	Herpes Virus Infection	230
	References	235
9	Focal and Multifocal Ischemic/Hemorrhagic Lesions	237
	Andrea Righini and Fabio Triulzi	
9.1	Ischemic Lesions	237
9.1.1	Focal Ischemic Lesions on Arterial Basis	237
9.1.2	Focal Ischemic and Ischemic–Hemorrhagic Lesions on Venous Side Basis	239
9.2	Hemorrhagic Lesions	239
9.2.1	Focal Cerebral Hemorrhagic Lesions	239
9.2.2	Focal Cerebellar Hemorrhagic Lesions	242
	References	252
10	Twin to Twin Transfusion Syndrome	255
	Claudia Cinnante, Fabio Triulzi, and Andrea Righini	
10.1	Clinical and Pathophysiological Background	255
10.2	Fetal and Postnatal MRI	256
	References	261

Fabio Triulzi, Elisa Scola, and Sabrina Avignone

Fetal MR imaging covers a relatively long period of the fetal brain development: from approximately 18–19 gestational weeks (GW) until birth. Therefore, at present, it is possible to study more than a half of the entire gestational period by this technique.

Different authors and most of all, Catherine Garel, have reviewed systematically the normal development of the fetal brain as it appears on the MR images and reported normal biometrics curves as measured by MRI; gyration and myelination process has been extensively reported as well [1–6].

Here we present the fetal brain normal anatomy by means of MRI, with particular focus on the crucial period between 19 and 22 GW, taking into account the high-resolution images of MR autopsy (Fig. 1.1) as reference guideline to interpret the low-resolution fetal MR images.

1.1 Fetal MR Autopsy Technique

In order to prevent postmortem tissue autolysis, fetal MR autopsy studies were carried out within 24 h from death, without any fixation, in an intact fetus conserved in a refrigerator at 4–5°C prior to MR examination. The fetuses with spontaneous death in utero were not considered due to their long permanence at body temperature that accelerates the autolysis.

To obtain comparable images with the *in vivo* study, it is important to preserve the natural tissue contrast on T1 and T2-weighted images. The standard fixation with formalin causes a marked tissue dehydration and a modification of T1 and T2 contrast [7, 8]. On the contrary, an MR study performed within approximately 24–28 h from death without any fixation and with the fetal brain *in situ*, allows to maintain the normal contrast differences between tissues. It should

however be noted that even though cooling may preserve fetal brain from autolysis, it nevertheless decreases the T1 and T2 contrast between tissues [9], and of course postmortem imaging cannot be considered the same as clinical imaging in a living being. The absence of blood pressure can change the shape of vessels and of the brain, resulting for example in a kinking of the brainstem. The vaginal delivery may cause deformation of skull and brain as well. Blood elements sediment and intravascular clots may finally occur [10].

To obtain a reasonable compromise between acquisition time in a clinical setting and spatial resolution, the total acquisition time of a fetal MR autopsy is approximately 80 min by using a 3.0 T magnet. The T2-weighted images shown in this chapter are obtained applying a turbo spin-echo sequence (TR 6500 ms; TE 120 ms; FA 90°; NEX 4, acquisition time 20 min.); the voxel size was $0.3 \times 0.3 \times 1.2$ mm, equal to a true spatial resolution of 0.10 mm^3 (100 nl).

1.2 Fetal Anatomy on MR Autopsy

On the T2-weighted images of the fetal MR autopsy with spatial resolution of 100 nl, not only the three layers usually recognizable on *in vivo* fetal MR are visible, but also layer number 1, the marginal layer (Fig. 1.2), and, at least between 19 and 28 GW, a thin hypointense layer in the most external part of the subplate (Fig. 1.3). According to Kostovic et al., this thin layer could represent thalamocortical axons in the superficial layer of subplate that are waiting to enter the cortical plate [11], but at present, no correlation between these images and corresponding pathological specimens is available.

If we compare the single-shot T2-weighted images of the *in vivo* fetal MR (Fig. 1.4) with the turbo spin-echo T2-weighted images of the fetal MR autopsy (Fig. 1.5), we can highlight some changes in tissue contrast in the period between 19 and 22 GW that are barely visible on *in vivo* studies. Between 19 and 20 GW, the internal capsule and in particular the posterior limb of the internal capsule (PLIC) is clearly more hypointense than surrounding lentiform nuclei

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and thalami (Figs. 1.5, 1.6, 1.7, 1.8, 1.9, 1.10, 1.11, 1.12, 1.13, and 1.14); this is of course not due to the presence of myelin, it develops later in the last phase of gestation, but probably to the differences in contrast between the relatively compacted unmyelinated fibers and the relatively poor synapse density of the basal ganglia and thalami. Starting from 21 to 22 GW, the anterolateral aspect of the thalami before and the mesial part of the lentiform nuclei shortly after, begin to decrease their signal intensity on T2-weighted images and consequently PLIC becomes scarcely visible (Figs. 1.15, 1.16, 1.17, 1.18, 1.19, 1.20, 1.21, 1.22, 1.23, 1.24, 1.25, 1.26, 1.27, 1.28, and 1.29).

The posterior part of the thalami is particularly hyperintense on T2-weighted images at 19–21 GW; sometimes, this aspect can be misinterpreted as a lesion on the *in vivo* fetal images (Figs. 1.8h and 1.10f).

The maximum contrast between the intermediate zone and the subplate is reached at 19–20 GW (Figs. 1.8, 1.10, 1.12, and 1.14) and then rapidly decreases. At 28 GW the periventricular areas, and notably in the peritrigonal regions, are clearly more hyperintense on T2-weighted images than the surrounding parenchyma. At this stage, the classical three-layers aspect is no more detectable, and the subplate seems to be formed by thin different layers (Figs. 1.30, 1.31, and 1.32).

1.3 From the Fetus to the Newborn: In Vivo Anatomy

As previously reported, the fetal *in vivo* development was extensively reviewed in different articles and books; it should however be noted that the obstacle to an accurate and reliable brain MR imaging *in vivo* during fetal life is not only related to the poor spatial resolution but also to the poor contrast resolution. The T2-weighted sequences typically used in

fetal MR imaging are single-shot fast spin-echo or steady-state free precession 2D or 3D acquisitions both with a significant decrease of contrast resolution if compared with a turbo spin-echo sequence. This concept appears clear in the direct comparison between *in vivo* and *ex vivo* fetal MR images and also looking at the fetal MR *in vivo* imaging of the late gestation period (Figs. 1.33, 1.34, 1.35, and 1.36). In the case of Figs. 1.35 and 1.36, the spatial resolution is proportionally better than in the midgestation cases, but if we compare the contrast resolution of the single-shot fast spin-echo sequence of this fetal case with the T2-weighted image obtained with the traditional turbo or fast spin echosequence in the normal newborn (Fig. 1.37), the differences in contrast are quite obvious.

Modern MR imaging in newborns can at present take more advantage by the progressive widespread use of 3.0 T. Without relevant reduction of contrast resolution, the increase of signal-to-noise ratio of 3.0 T allows to significantly increase spatial resolution in a affordable acquisition time. The increase in tissue border definition and the overall better anatomical depiction in comparison with the 1.5 T magnet are well appreciable in Figs. 1.37 and 1.38.

It is well known how T1 relaxation time is influenced by the magnetic field and how tissues differences can be reduced at high field strength [12]; however, at 3.0 T, it has been demonstrated how the 3D T1-weighted sequence can maintain an optimal contrast resolution even in neonatal brain imaging [13]. Moreover, the increase in signal-to-contrast ratio can further reduce the size of the isotropic voxel even under the cubic millimeter, allowing extremely detailed reformatted images (Figs. 1.39, 1.40, 1.41, and 1.42). Normal anatomy and myelination obtained by *in vivo* MR in the newborns have been also extensively reviewed in different articles [14–16] and book chapters [17, 18], please refer to the figure legends for a detailed description.

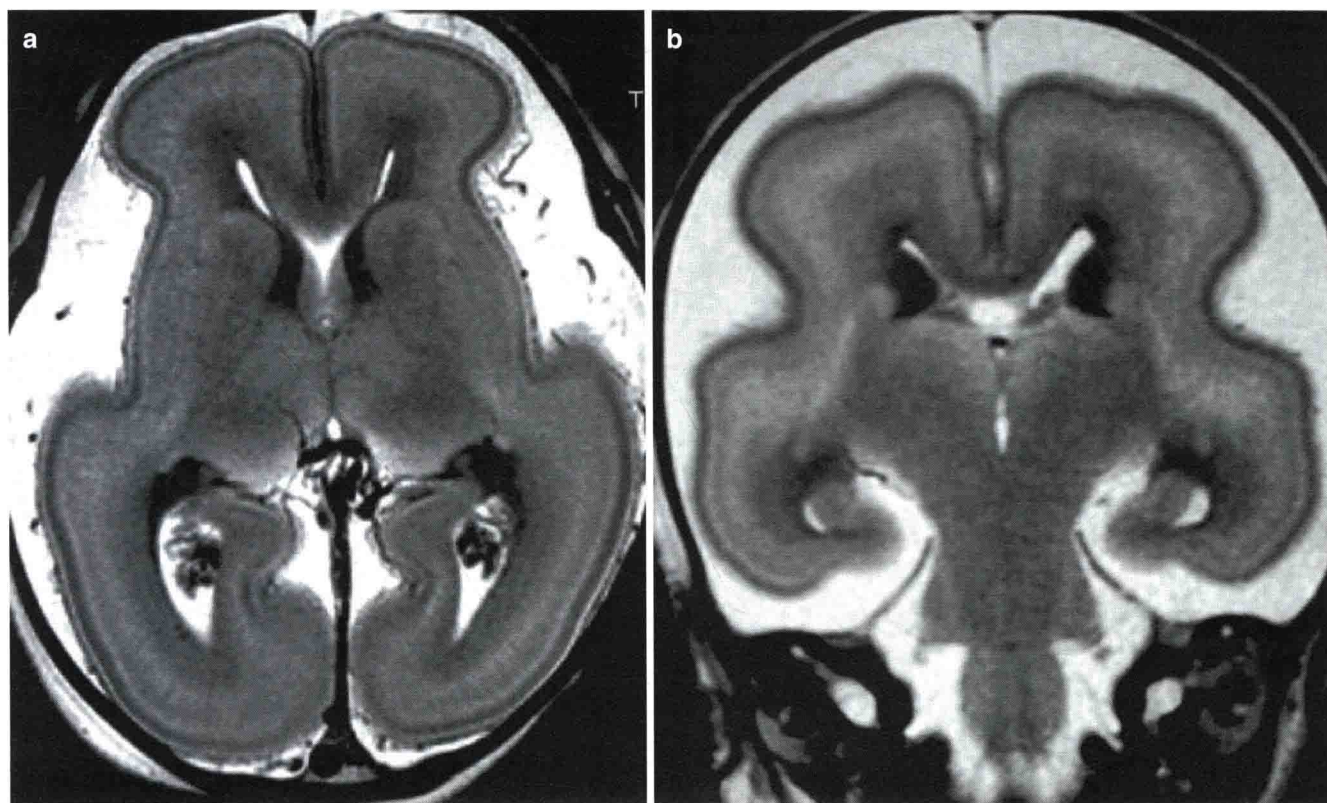


Fig. 1.1 Fetal MR autopsy. Normal brain at 22 gestational weeks (GW) (a) and 21 GW (b) on T2-weighted images. Voxel size 100 nl.

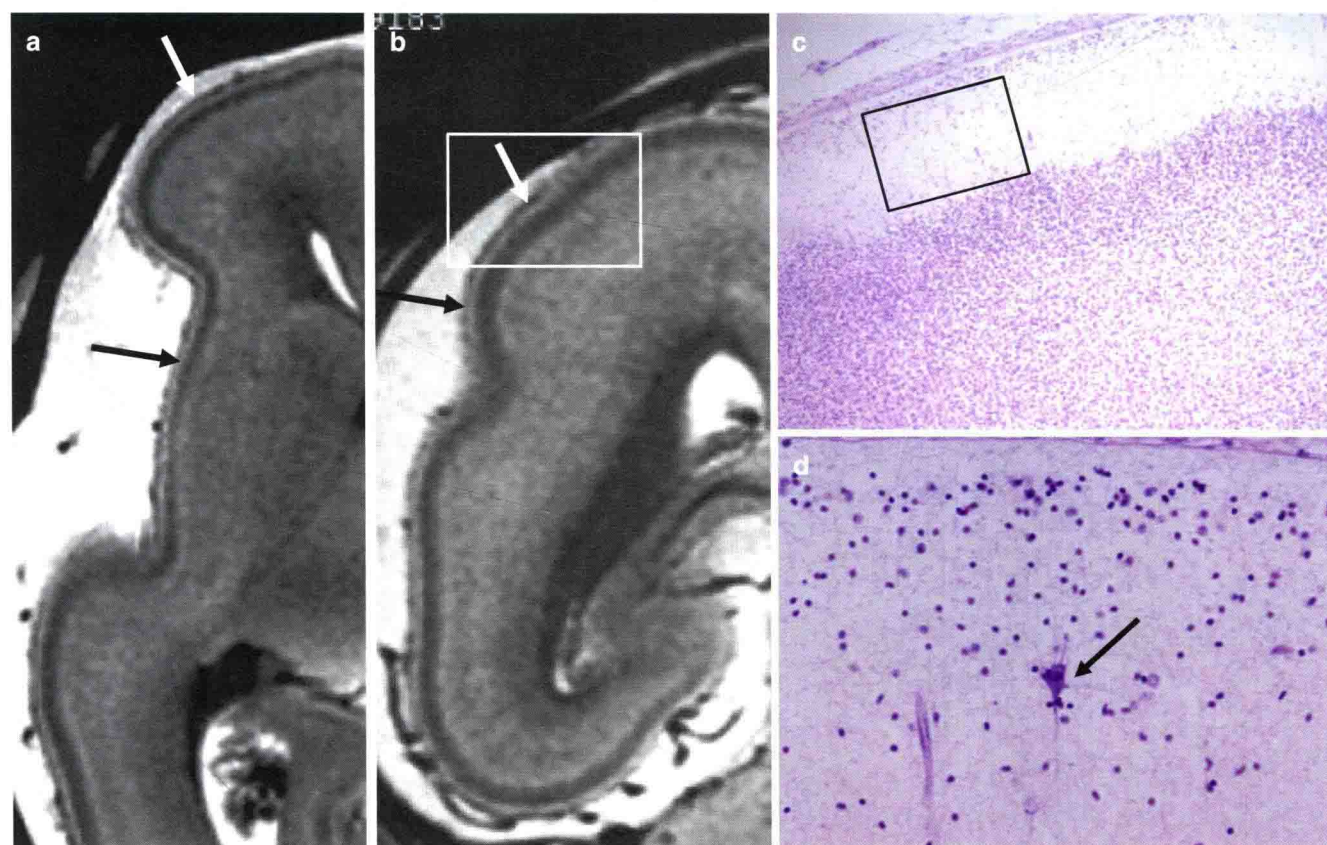


Fig. 1.2 Marginal zone on fetal MR autopsy (22GW). Layer I or marginal zone is detectable on fetal MR autopsy with a voxel size of 100 nl (arrows a, b). Correspondent histologic section stained with hematoxy-

lin-eosin (c) and closeup view on marginal zone shows a large Cajal-Retzius cell (black arrow) (d) (courtesy C. Frassoni, Neurological Institute C. Besta, Milan)

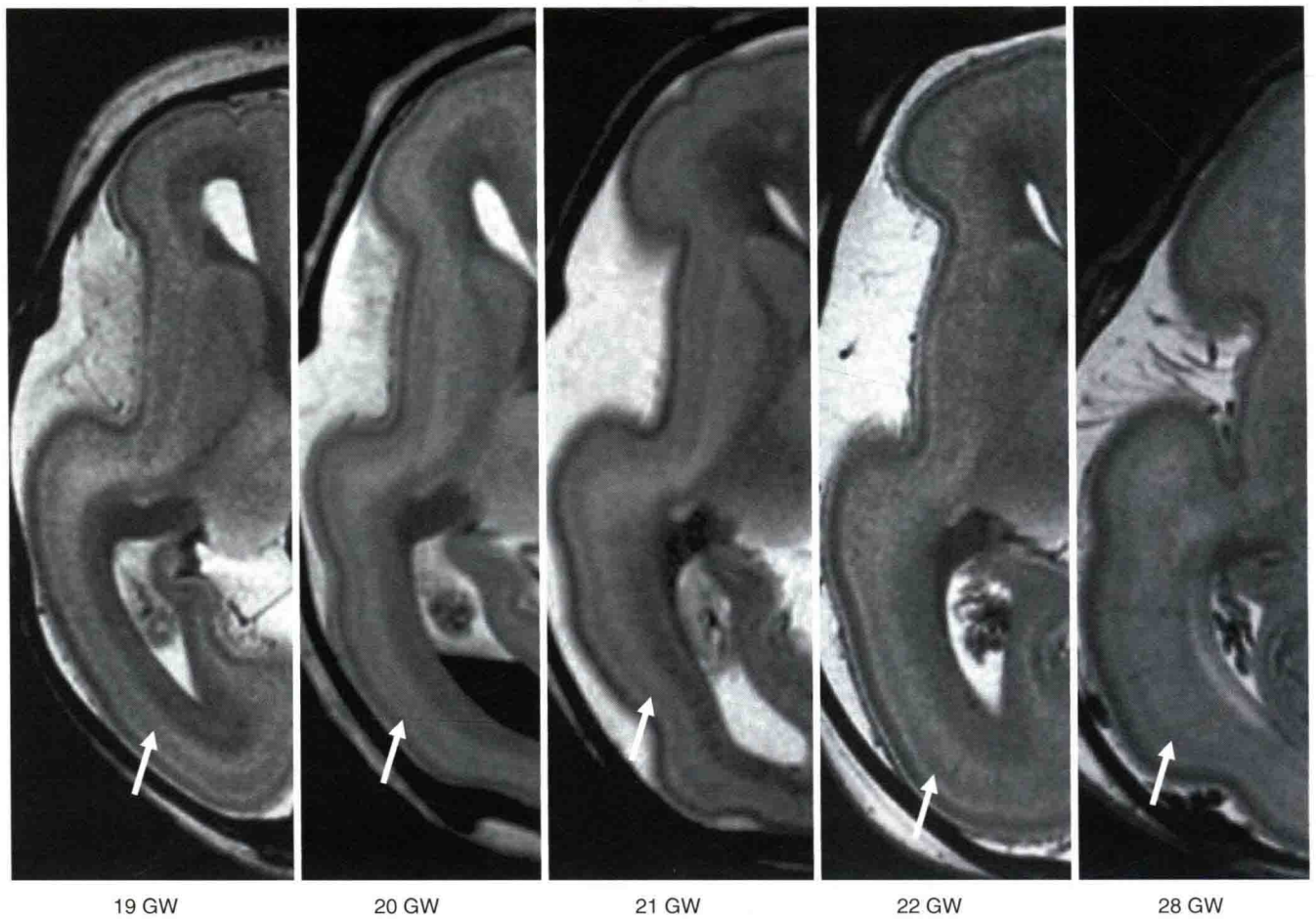


Fig. 1.3 A diffuse T2 hypointense layer on the more external part of subplate is recognizable on fetal MR autopsy between 19 and 28 GW (arrows). According to Kostovic et al., it could represent thalamocortical axons in the superficial layer of subplate that are waiting to enter the cortical plate

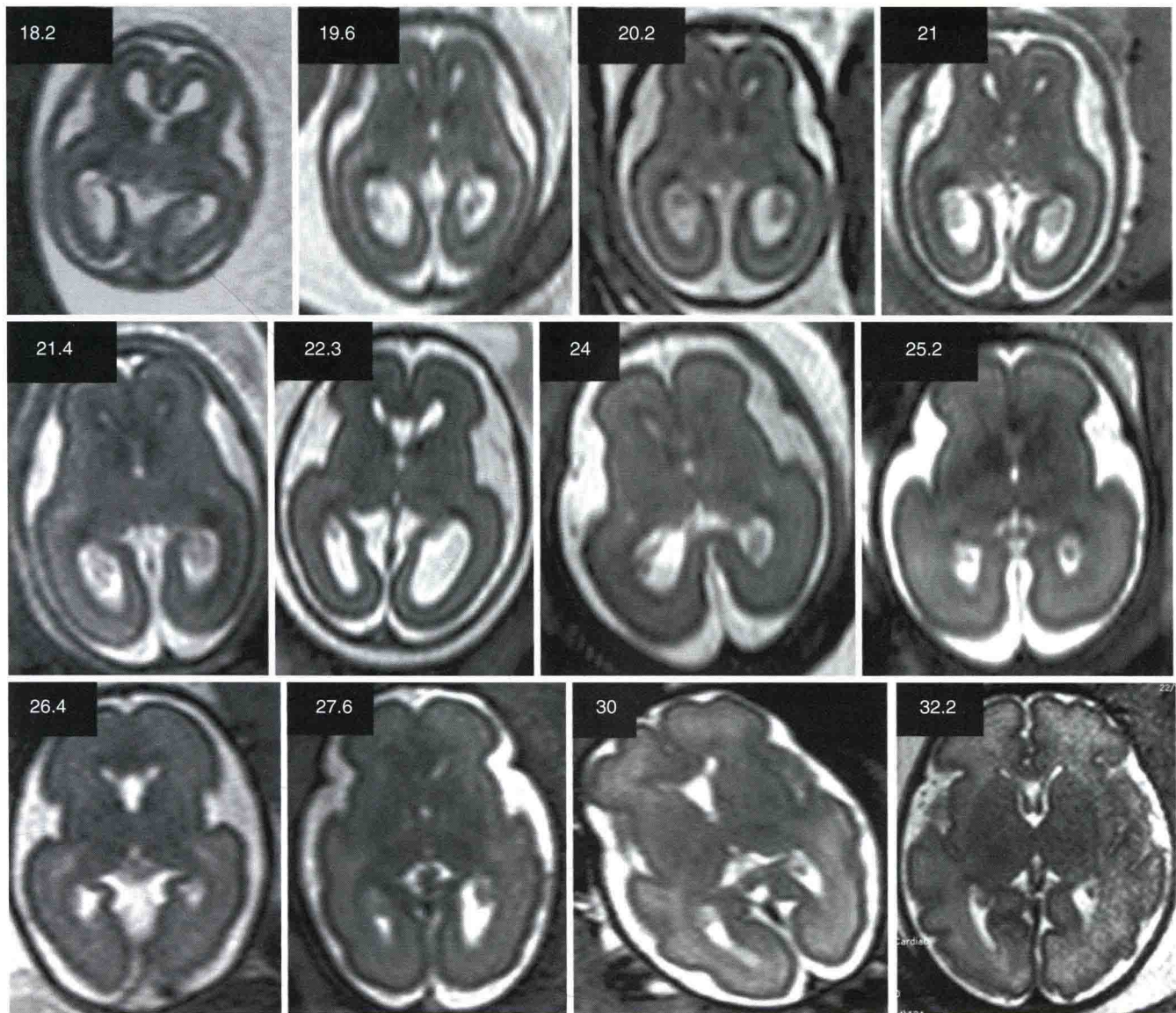


Fig. 1.4 Normal fetal brain development according to fetal MR. Twelve selected cases from 18.2 to 32.2 GW, axial T2-weighted images passing approximately through the thalamus. For the acquisition technique, see the text

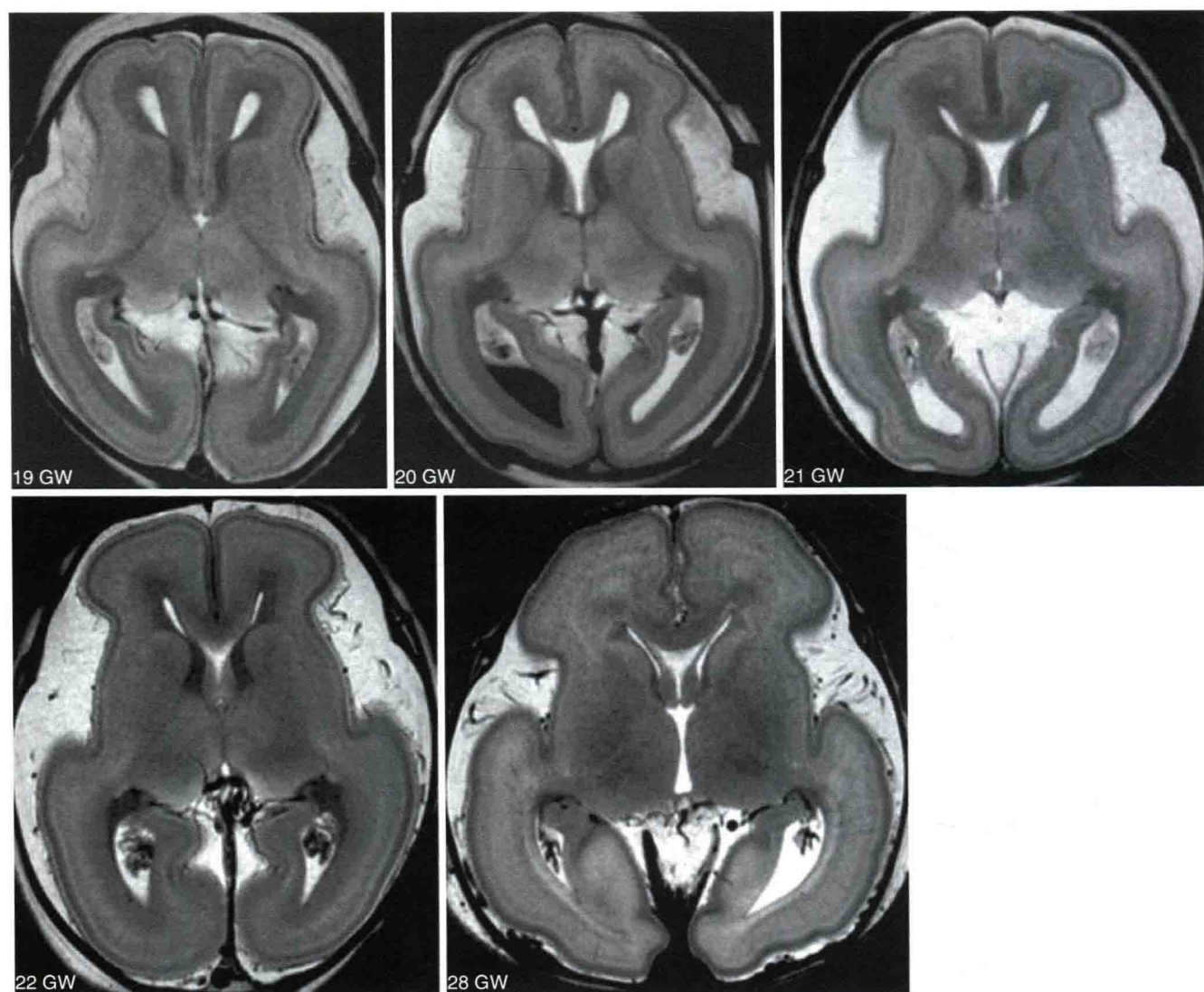


Fig. 1.5 Fetal MR autopsy. Normal cases at 19, 20, 21, 22, and 28 GW, representative axial T2-weighted images passing through the thalamus. Voxel size 100 nl. For the acquisition technique, see the text; all the cases are studied within 24 hours from termination of pregnancy (*TOP*)

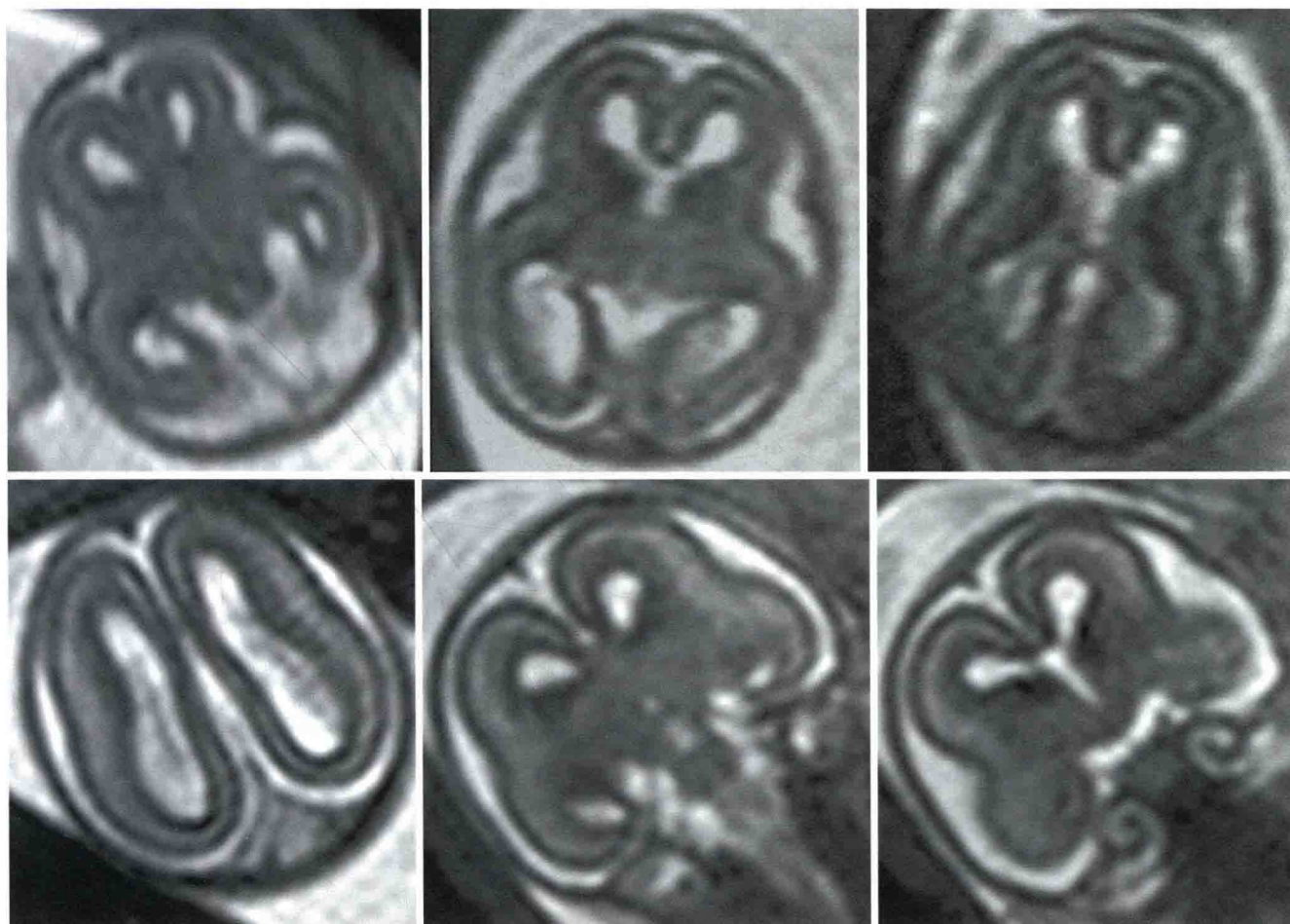


Fig. 1.6 Fetal MR, normal brain at 18.2 GW. Fetal MR is usually not performed before 19 GW. The fetal brain size is too small and the fetal movement is more pronounced. In this case, the parenchymal thickness

is still relatively thin in comparison to the ventricular size (*top row*). T2 signal contrast differences between cortical plate, subplate, and intermediate zone are however already appreciable (*bottom row*)

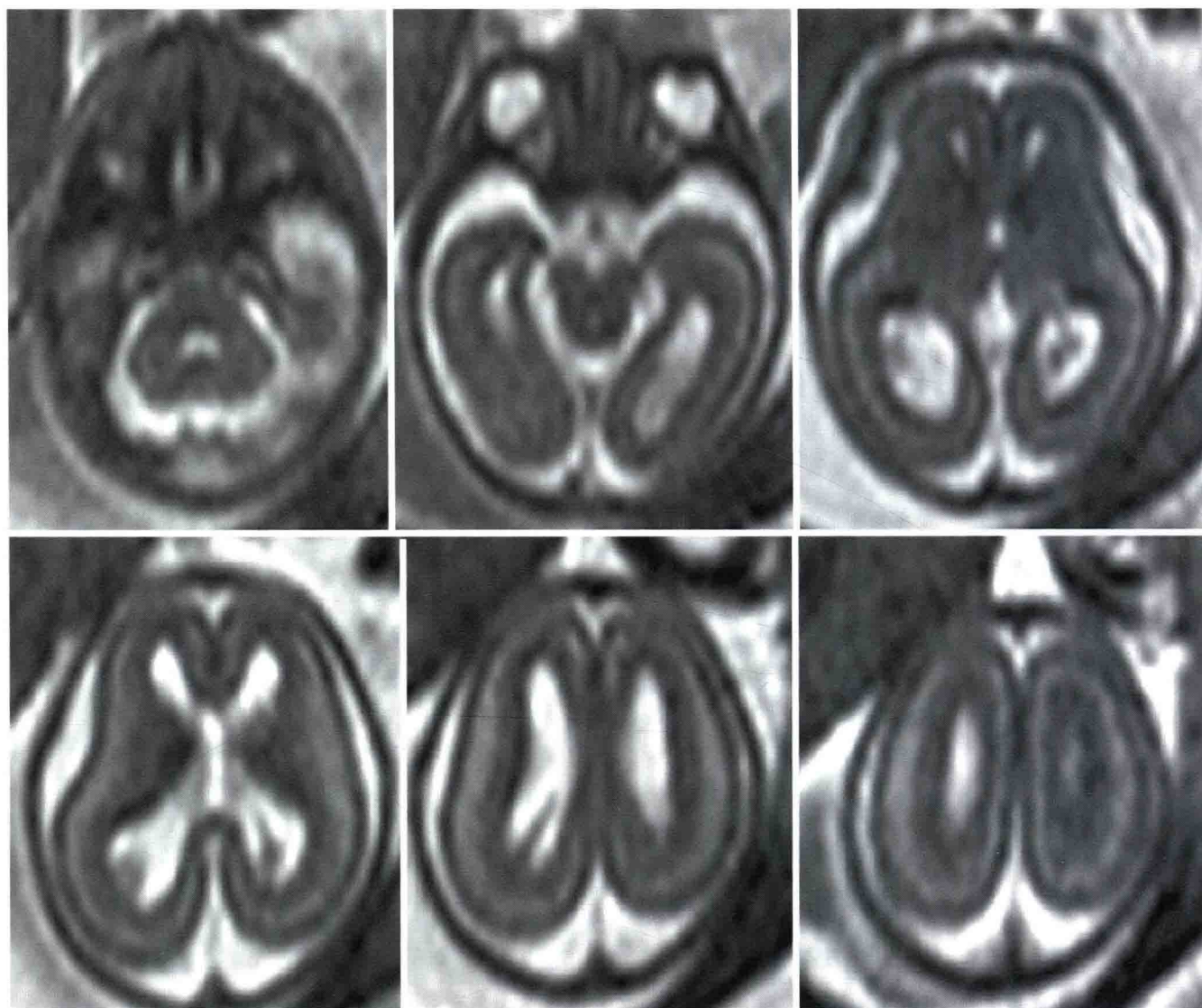


Fig. 1.7 Fetal MR, normal brain at 19.6 GW, axial sections. At this age, the main brain mantle layers, including germinal matrix, are usually well documented. Brain opercularization is going to become evident even though the surface of the brain is still substantially smooth