REVIEW ARTICLE

MRI of the Fetal Brain

C. Weisstanner · G. Kasprian · G.M. Gruber · P.C. Brugger · D. Prayer

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Abstract The purpose of this article is to provide an overview of the possibilities for fetal magnetic resonance imaging (MRI) in the evaluation of the fetal brain. For brain pathologies, fetal MRI is usually performed when an abnormality is detected by previous prenatal ultrasound, and is, therefore, an important adjunct to ultrasound. The most commonly suspected brain pathologies referred to fetal MRI for further evaluation are ventriculomegaly, missing corpus callosum, and abnormalities of the posterior fossa. We will briefly discuss the most common indications for fetal brain MRI, as well as recent advances.

Keywords Fetal MRI · Fetal brain · 3T · Postmortem MRI

Introduction

Although ultrasound (US) remains the predominant modality for evaluating disorders related to pregnancy, fetal MRI has been increasingly used and is considered a complemen-

D. Prayer, MD (⊠) · C. Weisstanner · G. Kasprian Department of Radiology, Division of Neuro- and Musculoskeletal Radiology, Medical University of Vienna, Währinger Gürtel 18–20, 1090 Vienna, Austria e-mail: daniela.prayer@meduniwien.ac.at

C. Weisstanner University Institute for Diagnostic and Interventional Neuroradiology, Inselspital, University of Bern, Bern, Switzerland

G.M. Gruber · P.C. Brugger Center of Anatomy and Cell Biology, Integrative Morphology Group, Medical University of Vienna, Vienna, Austria tary technology. MRI of the fetus is not limited by fetal position, obesity, or oligohydramnios, and visualization of the brain is not restricted by the ossified skull. With its higher resolution, contrast abilities, as well as a large field of view, MRI facilitates the examination of fetuses with large or complex anomalies as well as visualization of lesions within the context of the entire fetal body. The purpose of this article is to provide an overview of fetal MRI of the brain.

History

Fetal MR was first described in 1983 [1]. Because of fetal motion, fetal MR was recommended in late pregnancy or in cases of oligohydramnios. To decrease fetal motion, benzodiazepines or curarization were used [2, 3]. Even with this limitation, fetal MRI was considered a valuable complement to US, especially for the further evaluation of problems first detected by US. One of the main advantages was that the whole brain could be visualized, even in late pregnancy. In addition, image quality is not impaired by the bony skull, and therefore, orthogonal sections can be acquired more easily. With the development of fast MR techniques and MRI software, here especially the half-Fourier acquisition single-shot turbo spin-echo (HASTE) sequence, fetal MR could be performed without sedation, which has led to an increased usage of this imaging tool.

Normal Development

For proper interpretation of fetal MRI, a radiologist should have a deep understanding of normal developmental anatomy. A familiarity with primary neurulation, ventral induction, commissuration, cortical formation, premyelination, transient structures of the cerebral hemispheres, and sulcation is necessary. There are also valuable resources that delineate the normal fetal brain in MR for comparison purposes [4, 5].

From T2-weighed Imaging to Functional Imaging

Single-shot fast spin-echo (SSFSE) sequences are the most widely used in fetal MR imaging. Because of single-slice acquisition, fetal motion will only affect those slices acquired while motion occurs [6]. Improved sequences enabled assessment of the brain tissue not only by T2-weighted imaging, but also by T1-, diffusion-weighted, and fluid-attenuation inversion recovery (FLAIR) sequences. Because of the high contrast between cerebrospinal fluid and brain tissue, T2-weighted imaging is primarily used to describe the surface of the fetal brain [7]. T1-weighted sequences allow the detection of hemorrhage and fat deposition, and can depict fetal organs selectively with T1-hyperintensity, such as the pituitary gland (Fig. 1) and liver. With echoplanar (EPI) sequences, fetal skeleton information, hemorrhage, and/or calcifications, for example, in CMV-infection (Fig. 2), can be gathered. Structural imaging is the mainstay of MR diagnosis, but other modalities, such as diffusion tensor imaging with tractography [8, 9], single-voxel spectroscopy for brain metabolism [10], and blood-oxygen-level dependent (BOLD) imaging for functional imaging studies [11] may improve diagnostic accuracy in CNS pathologies. Imaging parameters of most sequences are listed in Table 1.

Fetal CNS Anomalies

Malformations of the central nervous system are very difficult to characterize prenatally. In tertiary referral centers with expert neurosonographers, fetal MRI has been shown

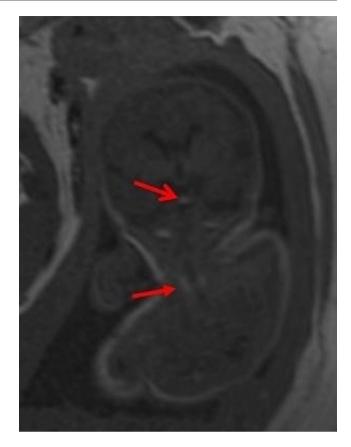
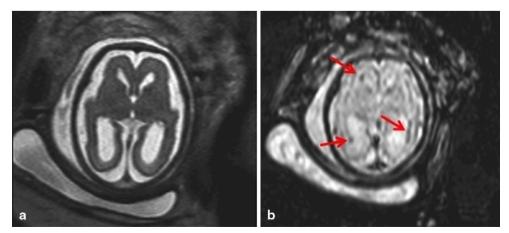


Fig. 1 Coronal T1-weighed image of a fetus at 35+3 GW. The hypophysis (*open arrow*) can be clearly discerned as a hyperintense focus. In addition to that, the lobes of the thyroid gland (*closed arrow*) can be seen as hyperintense foci

to be advantageous with respect to clinical counseling of cases with CNS malformations [12].

The most common referrals for fetal brain imaging will be briefly discussed below and include disorders of cortical malformation, commissural abnormalities, ventriculomegaly, infratentorial pathologies and acquired pathologies.

Fig. 2 a Axial T2-weighed image of a fetus at 27+5 GW with CMV-infection. In this image, no calcification can be detected. With the EPI sequence, **b** periventricular calcifications are seen as hypointense foci



Sequence	TR (ms)	TE (ms)	Slice thickness (mm)	Matrix	FOV (mm)	Flip angle
T2 (SSFSE)	shortest	100/140	4	256×153	200-230	90
SSFPE	shortest	shortest	5	192×219	260	80
T1 FFE	shortest	4.6	4	208×165	325	80
SSH GRE EPI	3000	53	4	160×95	230	90
DWI (b=700)	1470	125	5	128/81	250	90
DTI (b=1000)	1649	90	5	112×67	230	90

FOV field of view, TR relaxation time, TE echo time, ms milliseconds, DTI diffusion tensor imaging, DWI diffusion weighted imaging, EPI echo planar imaging, FFE fast field echo, SSFSE single-shot fast spin-echo, SSFPE steady-state free-precession, SSH single-shot, GRE gradient echo, mm millimeter.

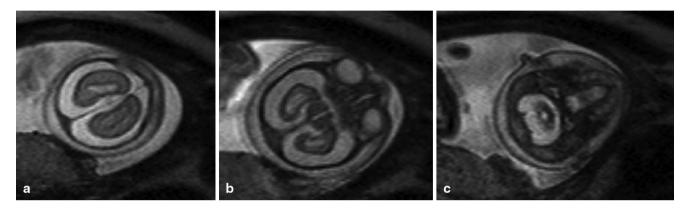


Fig. 3 SSFPE images of a fetus at 24+0 GW with (micro-)lissencephaly a and b and no visible sulcation. c Hypoplastic cerebellum

Disorders of Cortical Formation

Disorders of cortical formation are already present when fetal MRI is usually performed because cortical development starts in the eighth to ninth postconceptional week [13]. For example, lissencephalies (Fig. 3) may be suspected because of a disordered lamination of the fetal brain with a diminished discrimination of the subplate. Another hint about the presence of abnormal gyration may be atypical sulcation or the preterm appearance of gyri [14]. The detection of heterotopia, unless it involves larger parts of the brain, may be difficult before the third trimester.

Commissural Abnormalities

With an incidence of 0.5–70 in 10,000, agenesis of the corpus callosum is one of the most common congenital brain malformations [15]. Because the presence of associated intra- or extracranial anomalies determines the future neurodevelopmental outcome, the exclusion of associated abnormalities is crucial. With fetal MRI, important additional information can be gained [16]. With optimized sequence planning, such as strict use of orthogonal and midline sagittal slices to visualize the configuration of all commissures[17], the sensitivity of fetal MRI can be improved. In addition to that, associated cortical malformations, acquired pathologies [18], and brainstem and cerebellar abnormalities may be detected. Partial callo-

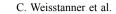
sal agenesis [19] and a sufficiently sized, but an abnormally formed, corpus callosum [20] are among the most frequently missed pathologies by fetal MRI. In these cases, advanced MR imaging techniques, such as DTI with tractography, may depict the commissures and misguided fiber tracts [21, 22] and may provide additional information (Fig. 4).

Ventriculomegaly

One main indication for fetal MR is ventriculomegaly diagnosed by ultrasound. It is defined as an atrial width more than 10 mm and can be further categorized as mild (atrial width between 10 and 12 mm), moderate (atrial with up to 15 mm), and severe ventriculomegaly (atrial width over 16 mm) [23]. Since the majority (85%) of cases with ventriculomegaly have an additional brain pathology [24], an exact search for such pathologies is indicated (Fig. 5). Signs of associated pathologies include pathologic shape/borders of the ventricle, obliteration of the 4th ventricle (Chiari II malformation), intraventricular material, commissural agenesis/dysgenesis, disorders of cortical formation, and malformation of the posterior fossa and/or midbrain.

Infratentorial Pathologies

Malformations of the posterior fossa are often suspected in fetal US. MRI is advantageous over US for the proper



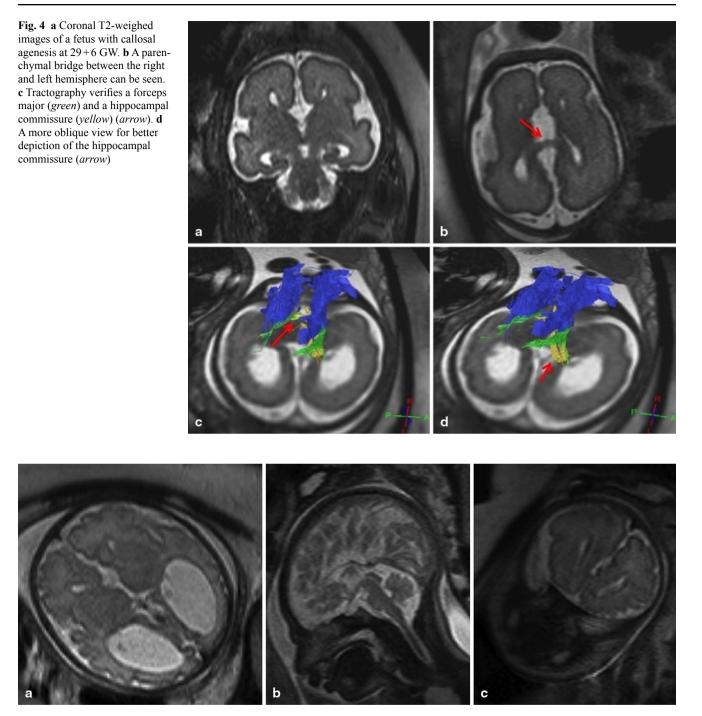


Fig. 5 a Axial SSFPE image of a fetus at 34+0 GW, with severe ventriculomegaly. b On this sagittal image, associated agenesis of the corpus callosum can be seen, with the typical steerhorn appearance of the frontal horns in (c)

evaluation and multidimensional analysis of the cerebellum, cerebellar parenchyma, vermis, and brainstem [25]. In pontocerebellar hypoplasia, the cerebellum is too small. An enlarged retrocerebellar fluid space can be seen with or without cerebellar pathology. Is the cerebellum involved with a dysplastic vermis, as in Dandy Walker malformation (Fig. 6)? Or is the cerebellum not involved, as in cisterna magna? The cerebellum might just be compressed because of a space-occupying arachnoid cyst, and a change in the normal signal intensity of the cerebellar parenchyma may be a result of hemorrhage or tumors [26].

Acquired Pathologies

The main acquired pathologies detected by fetal MRI are ischemic infarctions, hemorrhage, and brain tumors. Typi-

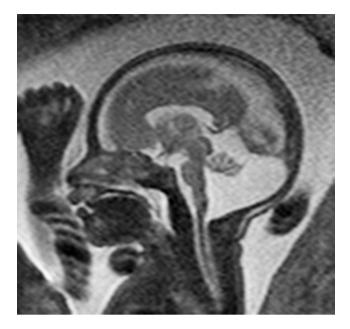


Fig. 6 Sagittal SSFPE image of a fetus at 28+3 GW with enlarged posterior fossa and dysplastic, upwardly rotated vermis, typical of a Dandy Walker malformation

cally, early-stage ischemic infarctions show restricted diffusion [27] at the beginning of the infarction to focal T2-weighted hyperintense lesions, and, in some cases, subsequently, to a reduction of brain tissue [28]. Because of changes in local susceptibility caused by blood breakdown products, echoplanar sequences are especially sensitive to hemorrhage [29], and can also be used to detect calcifications as a consequence of many acquired fetal or maternal diseases [30]. Brain tumors or vascular malformations lead to parenchymal changes [31], and, particularly in the case of vascular malformations, the demonstration of associated findings may direct therapeutic planning [32, 33] (Fig. 7).

Just CNS-Imaging? From CNS Imaging to "Whole Uterine-Imaging"

Especially in the case of complex malformations, a fetal MRI study should not be restricted to the brain. For example, in congenital muscular dystrophies caused by the fukutin-related protein gene (FKRP), mutations of a broad spectrum

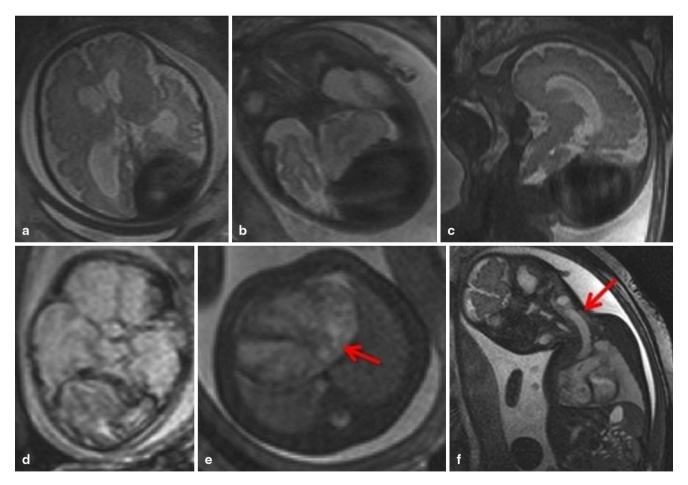


Fig. 7 Axial **a** and **b** sagittal **c** T2 weighed images of a fetus at 31+3 GW with a dural vascular malformation, enlarged torcular herophili and compression of the cerebellum. **d** On the EPI sequence, no hemorrhage can be detected. **e** Axial SSFPE through the thorax is depicted, as a consequence of the vascular malformation of a dilated heart (*arrow*) and engorged internal jugular vein (**f**: *arrow*)

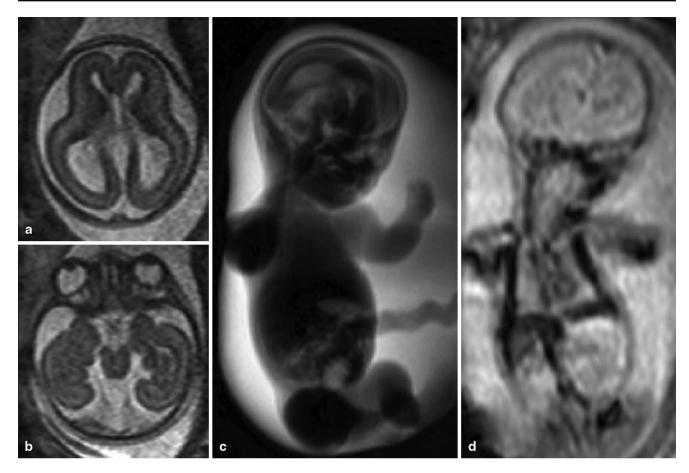


Fig. 8 a and b Axial SSFPE images of a fetus at 20+0 GW with thanatophoric dysplasia. In a mild ventriculomegaly can be seen and in b dysplasia of the mesial temporal lobes is evident. c Thick-slab heavy T2-weighed image demonstrates a narrow thorax and short extremities. d Coronal EPI sequence shows the bones as hypointense structures. The right humerus is bowed

of phenotypes, ranging from severe congenital muscular dystrophies to a much milder limb-girdle muscular dystrophy, in addition to eye and brain abnormalities, can be found [34]. Joubert syndrome, one of the axonal guidance disorders, can coexist with retinopathy, liver disease, kidney disease, polydactyly, obesity, and/or situs inversus [35]. Inferomesial temporal and occipital lobe abnormalities can be detected in hypochondroplasia [36], and of the temporal lobe in thanatophoric dysplasia [37] (Fig. 8). Congenital heart diseases lead to altered cerebral perfusion, which may lead to impaired brain growth [38], and congenital diaphragmatic hernias may also have an impact on brain development [39]. Thus, in any case, an examination of the brain by MRI should always include imaging of the whole fetus and placenta.

Pivotal Questions in Fetal Imaging

Indications

Indications for fetal MRI include the confirmation of inconclusive sonographic findings and the evaluation of sonographically occult diagnoses. Indications may vary widely, as a consequence of the different states of experience of the sonographers and the specialties of the respective perinatal center.

Safety Issues and Examination at 3 T

If the medical situation warrants fetal MRI, the ACR guidance document on MR safe practices 2013 declares, "pregnant patients can be accepted to undergo MR scans at any stage of pregnancy" [40]. At present, almost all fetal MRI are acquired on 1.5 T machines, but the desire for better anatomical delineation has led to imaging of the fetus at 3 T [41]. On the question of the maximum field strength that can be applied, the report of the Canadian Task Force on Preventive Health Care concludes "Fetal magnetic resonance imaging is safe at 3.0 T or less during the second and third trimesters" [42]. Gadolinium may be used when the benefits outweigh the potential risks, although the effects of gadolinium on the fetus are still unknown [40].

Postmortem MRI

Perinatal autopsy is essential to determine the cause of death, and also to provide additional information about disease processes [43]. Autopsy may also be used to evaluate modern imaging methods. But, despite this unquestionable role, autopsy rates have steadily declined over the last decade. Postmortem MRI is an acceptable alternative method to autopsy [44], and showed a diagnostic sensitivity of 100%, and a specificity of 92% with regard to fetal brain pathologies [45].

Conclusion

Fetal MRI allows excellent detailed visualization of the fetus *in utero*, as well as the extrafetal structures. With a systemic approach, and a thorough knowledge of the developing brain structures, fetal MRI is effective in the detection of subtle fetal brain abnormalities and in the assessment of complex lesions. Fetal MRI also helps in patient management and therapy decision-making.

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Conflict of Interest The authors declare that there are no actual or potential conflicts of interest in relation to this article.

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