International Journal of Radiology and Diagnostic Imaging

E-ISSN: 2664-4444
P-ISSN: 2664-4436
IJRDI 2018; 1(2): 39-42
Received: 02-12-2018
Accepted: 22-12-2018

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Development of fetal cerebral sulci: A study using fetal MRI

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Abstract
Background: Fetal brain development, specifically the emergence of cerebral sulci, plays a crucial role in understanding fetal neurodevelopment. This study aimed to assess the normal development of fetal cerebral sulci using fetal MRI and to determine the gestational age at which various sulci become detectable.
Materials and Methods: A prospective descriptive anatomical study was conducted at the Department of Radiology, S.S. Institute of Medical Sciences, Davangere, from November 2017 to October 2018. The study included 50 antenatal mothers with singleton pregnancies, aged between 22 and 36 weeks of gestation. Participants underwent fetal MRI using a 1.5 Tesla Siemens Symphony SyngoMR machine, with HASTE T2-weighted imaging. The cerebral sulci were classified into three categories: present, absent, or partially developed, and evaluated by two blinded radiologists.
Results: The study observed the emergence of different cerebral sulci at distinct gestational weeks. Early sulci such as the cingulate and calcarine were detected by 24-25 weeks, while more complex sulci like the precentral, postcentral, and superior temporal sulcus became identifiable by 26-27 weeks. Full detection of these sulci occurred by 30-31 weeks, with the insular and occipito-temporal sulci appearing later. Statistical analysis showed significant correlations between sulcus detection and gestational age.
Conclusion: This study demonstrates the sequential development of fetal cerebral sulci and provides an important timeline for fetal brain maturation, with detectable sulci appearing progressively as gestation advances. The findings validate the use of fetal MRI in monitoring neurodevelopment and can serve as a reference for future studies on fetal brain abnormalities.

Keywords: Fetal MRI, cerebral sulci, fetal brain development, gestational age, neurodevelopment, prenatal imaging

Introduction
The assessment of normal cerebral sulcal development in the fetus using magnetic resonance imaging (MRI) has become an essential technique in the field of prenatal diagnostics, offering detailed insight into neurodevelopmental processes. In the human brain, sulcation is a key marker of cortical development and involves the formation of grooves or sulci on the brain's surface, which begins in early fetal life and continues through childhood. MRI, due to its superior resolution and ability to provide non-invasive, high-quality imaging, is increasingly used to monitor this process in utero, allowing for early identification of abnormal patterns that could indicate developmental disorders. The fetal brain undergoes significant changes during the second and third trimesters, where sulcal formation accelerates, making this period crucial for studying normal and abnormal cortical development. MRI techniques, including both conventional and advanced imaging sequences, have enabled the detection of subtle variations in the appearance of the cerebral sulci, offering a window into the fetus's neurological status. Studies have demonstrated that a clear understanding of the normal trajectory of sulcal development is essential for distinguishing between normal variants and pathological conditions, such as congenital malformations or neurogenetic disorders, which might not be immediately apparent through other imaging methods [1]. Moreover, research suggests that certain deviations in sulcal patterns may be indicative of underlying structural brain abnormalities, such as lissencephaly, polymicrogyria, or schizencephaly, providing valuable prognostic information for clinicians [2]. Additionally, fetal MRI has been shown to enhance the evaluation of brain maturity in fetuses at risk for neurodevelopmental conditions, offering a means for timely intervention and management [3]. As our understanding of fetal neurodevelopment grows, the role of MRI in assessing cerebral sulcal development continues to evolve, positioning it as a

critical tool in prenatal care. The ability to monitor this developmental process non-invasively has greatly impacted prenatal medicine, providing insights that were previously difficult to obtain, and allowing for a better understanding of the normal and abnormal development of the fetal brain [4]. Recent studies have highlighted the growing importance of early neuroimaging in predicting the future cognitive and motor outcomes of children, suggesting that fetal MRI could play a pivotal role in shaping early diagnostic approaches [5]. The aim of this study is to establish reference standards for assessing normal fetal sulcation in utero using fetal MRI, with objectives to determine the usefulness of antenatal MRI in identifying normal sulcal development and to evaluate its utility in creating a normogram for sulcal development to estimate the correct gestational age in antenatal fetuses.

Materials and Methodology

This was a prospective descriptive anatomical study conducted at the Department of Radiology, S.S. Institute of Medical Sciences, Davangere, from November 2017 to October 2018. The study aimed to assess the normal development of fetal cerebral sulci using fetal MRI. A total of 50 antenatal mothers, aged between 22 to 36 weeks of gestation, were included in the study. The gestational age of the fetuses was determined by the first-trimester dating scan, using the crown-rump length to establish accurate gestational age, rather than relying on the last menstrual period. The study participants were selected from the outpatient population, including those who underwent routine ultrasound examination or MRI for maternal indications. Prior to inclusion, each subject underwent a screening ultrasound to rule out any other fetal anomalies or gross neurological abnormalities. All participants provided informed consent after being fully informed about the study in their preferred language.

The inclusion criteria consisted of antenatal mothers with a singleton pregnancy and a gestational age between 22 and 36 weeks, whose ultrasound examination showed apparently normal fetal findings. The mothers were required to have had a first-trimester dating scan and to have given consent for fetal MRI. Exclusion criteria included mothers with a history of epilepsy, congenital malformations, or neurodevelopmental disorders in previous pregnancies, as well as those with high-risk pregnancies such as pregnancy-induced hypertension, gestational diabetes, or obesity. Twin pregnancies were also excluded.

Fetal MRI was performed in the early morning after an overnight fasting period, with instructions for mothers to empty their bladder before the procedure to minimize fetal movement. No sedation or medication was administered. MRI was conducted using a 1.5 Tesla SIEMENS SYMPHONY SYNGOMR machine with a phased-array torso surface coil. The primary sequence used was the half Fourier acquired single-shot turbo spin echo (HASTE) sequence, a T2-weighted imaging method that helps minimize movement artifacts and improve image quality.

Scans were performed with the fetus in an optimal position, as determined by localizer images. Based on the position of the fetal head, serial images in three orthogonal planes were acquired, with slice thickness set to 4-6 mm and a matrix size of 169x256. About 9 to 19 slices were obtained for each subject, with an interslice thickness of less than 2 mm. A careful evaluation of the fetal cerebral sulci was done, categorizing them into three categories: present, absent, or partially developed. The evaluation was performed by two experienced radiologists who were blinded to the gestational age of the fetuses. The identified sulci were examined in an ordered manner, starting from the medial cerebral surface and progressing to the ventral and vertex areas, ensuring that all sulci were assessed comprehensively.

Results

The study included 50 antenatal mothers. The mothers in the study were relatively young, with ages ranging from 19 to 35 years. The mean maternal age was 23.49 years, and the median age was 24 years, indicating that the majority of the participants were in their early twenties.

Table 1 provides a breakdown of the gestational age and gravida status of the study participants, showing the distribution of pregnancies across different gestational age groups. The data indicates a predominance of primigravida (first-time mothers) across all gestational age categories, with 50 participants in total. The number of multigravida (women with previous pregnancies) was smaller, making up 42% of the sample.

Table 1: Gestational Age and Gravida

Gestational age (in weeks)		Primigravida	Multigravida
22-23 weeks	7 (14%)	4 (8%)	3 (6%)
24-25 weeks	7 (14%)	5 (10%)	2 (4%)
26-27 weeks	6 (12%)	3 (6%)	3 (6%)
28-29 weeks	7 (14%)	3 (6%)	4 (8%)
30-31 weeks	7 (14%)	3 (6%)	4 (8%)
32-33 weeks	7 (14%)	6 (12%)	1 (2%)
≥34 weeks	9 (18%)	5 (10%)	4 (8%)
Total	50 (100%)	29 (58%)	21 (42%)

The study on the development of fetal sulci provides valuable insights into the timing and progression of brain development during gestation. It highlights the sequential emergence of different sulci and their correlation with gestational age. Early in the gestation period, at 22-23 weeks, only a few sulci, such as the cingulate and calcarine sulci, are detectable. However, by 24-25 weeks, a significant number of sulci, including the marginal, collateral, and central sulci, start to become visible. These findings suggest that during the early stages of fetal development, the brain undergoes rapid structural changes, with sulci becoming distinguishable in a predictable sequence.

By 26-27 weeks, sulci such as the precentral, postcentral, and superior temporal sulcus (Posterior part) become detectable, with full detection occurring by 30-31 weeks. This period marks the transition from the appearance of basic sulci to more complex brain regions, indicating a refinement of brain architecture. In this phase, the brain's functional areas begin to take shape, corresponding to increasing neurological maturation.

Notably, the insular and inferior temporal sulci emerge slightly later, becoming fully detectable only around 30-31 weeks and 32-33 weeks, respectively. The late detection of these sulci emphasizes the continued development and specialization of the fetal brain in the later stages of gestation. The occipito-temporal sulcus, which becomes fully detectable by 34 weeks, is another example of a structure that matures towards the end of pregnancy, reflecting the final stages of cortical development.

Table 2: Correlation between gestational age and presence of sulci

	22-23 weeks	24-25 weeks	26-27 weeks	28-29 weeks	30-31 weeks	32-33 weeks	34 weeks and above
Cingulate sulcus	40%	100%	100%	100%	100%	100%	100%
Calcarine sulcus	60%	100%	100%	100%	100%	100%	100%
Marginal sulcus	0	100%	100%	100%	100%	100%	100%
Collateral sulcus	0	100%	100%	100%	100%	100%	100%
Central sulcus	0	100%	100%	100%	100%	100%	100%
Pre-central sulcus	0	100%	100%	100%	100%	100%	100%
Post-central sulcus	0	100%	100%	100%	100%	100%	100%
Superior or temporal sulcus	0	100%	100%	100%	100%	100%	100%
Inferior temporal sulcus	0	100%	100%	100%	100%	100%	100%
Insular sulcus	0	100%	100%	100%	100%	100%	100%
Intra-parietal sulcus	0	100%	100%	100%	100%	100%	100%
Occipito-temporal sulcus	0	100%	100%	100%	100%	100%	100%

Statistical analysis further supports the consistency and significance of these findings, with p-values below 0.01 across all sulci. The comparison between gestational age and sulcus development is highly significant, reinforcing the temporal patterns observed. Additionally, while the study's participant pool included both primigravida and multigravida women, the primary focus remains on fetal brain maturation, demonstrating a reliable pattern of sulcus development across gestational weeks. This comprehensive analysis underscores the relationship between gestational age and fetal brain maturation, with clear milestones marking the appearance of key sulci.

Table 3: Sequence of sulci detection and its correlation

Name of sulci	First Detection	100% Detection	Latest Detection	P value
Cingulate Sulcus	24-25 weeks	24-25 weeks	34 weeks	0.0005
Calcarine Sulcus	24-25 weeks	24-25 weeks	34 weeks	0.0005
Marginal Sulcus	24-25 weeks	26-27 weeks	34 weeks	0.0005
Collateral Sulcus	26-27 weeks	30-31 weeks	34 weeks	0.0005
Central Sulcus	26-27 weeks	30-31 weeks	34 weeks	0.0005
Precentral Sulcus	26-27 weeks	30-31 weeks	34 weeks	0.0005
Postcentral Sulcus	26-27 weeks	30-31 weeks	34 weeks	0.0005
Superior Temporal Sulcus (Post)	26-27 weeks	30-31 weeks	34 weeks	0.0005
Inferior Temporal Sulcus	28-29 weeks	32-33 weeks	34 weeks	0.0005
Insular Sulcus	30-31 weeks	34 weeks	34 weeks	0.0005
Intraparietal Sulcus	28-29 weeks	30-31 weeks	34 weeks	0.0005
Occipitotemporal Sulcus	30-31 weeks	34 weeks	34 weeks	0.0005

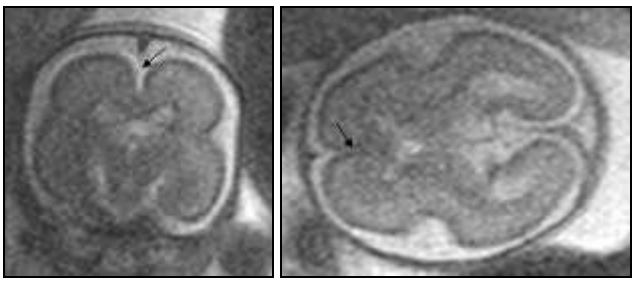

Fig 1: Arrows showing inter-spheric fissure

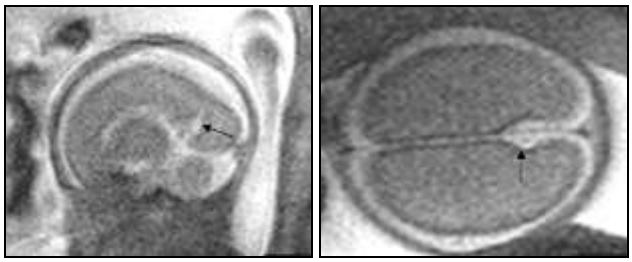

Fig 2: Arrows showing Parieto-occipital fissure

Discussion

This study was undertaken to investigate the sequential emergence of fetal sulci and their correlation with gestational age. The identification of sulci during fetal development provides valuable insight into the maturation of the brain and can serve as a marker for neurodevelopmental progress. Previous studies have demonstrated that cortical sulci emerge at distinct points during gestation, reflecting the growing complexity of the brain's organization. The goal of this study was to examine the specific gestational weeks at which various sulci become detectable, with the intention of adding clarity to the timeline of brain maturation.

The results of this study are consistent with the findings of other fetal brain development research. For example, studies by Benders *et al.* [6] and Gao *et al.* [7] also observed that sulci like the cingulate and calcarine become detectable around 24-25 weeks, corroborating the current study's identification of these sulci during early gestation. The gradual appearance of more complex sulci, such as the precentral and postcentral sulci by 26-27 weeks, aligns with findings from Poupon *et al.* [8] and others, suggesting that fetal brain development proceeds in a predictable and orderly fashion.

However, there are some differences in the timeline of sulcus detection. For instance, the current study detected the insular sulcus at 30-31 weeks, while similar studies such as those by Horsch *et al.* [9] and Toh *et al.* [10] have reported this sulcus becoming identifiable slightly earlier, at around 28-29 weeks. These variations may be attributed to differences in imaging techniques or the sample populations studied. Additionally, the full detection of the occipitotemporal sulcus by 34 weeks observed in this study is in line with earlier research by Dubois *et al.* [11], further supporting the idea of a standard timeline for sulcus

formation in utero.

Conclusion

This study provides valuable insights into the timing and sequential development of fetal cerebral sulci using fetal MRI. The results indicate a predictable pattern of sulcus emergence, with early detection of basic sulci such as the cingulate and calcarine sulci by 24-25 weeks. As gestation progresses, more complex sulci, including the precentral and postcentral sulci, become detectable by 26-27 weeks, while others such as the insular and occipito-temporal sulci appear later in gestation. These findings underscore the importance of fetal MRI as a tool for understanding fetal brain maturation and provide a foundation for further research into prenatal brain development.

Acknowledgement

The authors would like to thank all the participants in this study for their invaluable contribution and also to the staff at Department of Radiology for providing the necessary infrastructure and support for conducting this study.

Conflicts of Interest

The authors declare that there are no conflicts of interest related to this study.

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