ISMRM 2009: Rise and Fall of the Brain 1: Developing Brain

MRI of Normal Fetal Brain Development

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Fetal MRI is a powerful neuroimaging tool that is increasingly used in both the clinical and research milieu. The advent of single-shot-fast-acquisition techniques allow excellent anatomical definition, which has resulted in improved characterization of developmental processes of the normally developing fetal brain. A comprehensive understanding of normal fetal brain development is essential in order to be able to recognize developmental and acquired brain abnormalities. Fetal MRI is usually performed after the 16-18th week of gestation when the critical stages of organogenesis are complete. Therefore, normal fetal brain maturation can be studied by in vivo MRI from 18 weeks gestational age to term.

- Normal developmental processes
    - MRI signal changes in the fetal brain is influenced by regional developmental changes in high water content of the extracellular matrix in the immature unmyelinated brain, as well as shifting patterns of brain cellular density.
    - These brain tissue changes result from highly regulated sequential processes of cellular proliferation, migration, organization, and myelination.
    - Normative brain biometric data are available for assessing growth of brain structures, as well as for the schedule of gyral formation, the appearance and disappearance of transient brain structures (e.g., subplate), and myelination. Although myelination of cerebral hemispheres occurs mostly postnatally, MR signal changes can be seen in the white matter as early as 20 weeks' gestation and is considered another important indicator of fetal cerebral maturation.

- Understanding signal changes associated with maturation
    - To date, fetal MRI has relied primarily on T2-weighted ultrafast spin-echo sequences, given the longer acquisition times of T1-weighted MRI. However, T1-weighted gradient-echo sequences and steady-state free precession sequences are also used.
    - The developmental decrease in brain water content and increase in brain cell density are associated with shortening of T1 and T2 relaxation times, with increased T1 and decreased T2 intensity.
    - Surface features of the fetal brain are best distinguished by T2-weighted MRI, while differences in cell density are best distinguished by T1-weighted MRI.

- Newer Fetal MRI techniques
    - Diffusion-weighted imaging (DWI)/Diffusion tensor imaging (DTI): The progressive increase in density of premyelinating oligodendrocytes and later myelination in the immature white matter, results in a progressive decrease in brain water and increase in brain lipids leading to a decrease in apparent

diffusion coefficient (DWI). The increasing organization of developing axonal tracts increases the directionality of diffusion, resulting in increased fractional anisotropy (DTI).

- Proton magnetic resonance imaging (MRS) detects the shift in resonance frequency associated with different chemical environments providing insights into cerebral metabolism. With normal fetal brain maturation there is a progressive third trimester increase in the neuro-axonal marker, N-acetyl aspartate. Lactate a marker of anaerobic metabolism has been detected in the abnormal fetal brain, the brain of premature infants, and in the term newborn following perinatal asphyxia, but has not been detected in the otherwise normal fetal brain.
- Quantitative 3-D volumetric MR can provide important insights into the rate and progression of *in utero* brain development including the growth of different brain structures (e.g., cerebrum, cerebellum) as well as brain tissue types (e.g. cortical grey matter, unmyelinated and myelinated white matter, cerebrospinal fluid).
- Functional MRI: Preliminary studies have demonstrated neurovascular coupling in response to spontaneous or elicited brain activation (using vibroacoustic and visual stimuli). Because of required fetal immobility studies to date have been confined to fetuses over 36 weeks, when the fetal head begins to stabilize in the maternal pelvis.

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