In Utero MRI Study of Fetal Baboon Brains at 3T

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INTRODUCTION

The development of the central nervous system (CNS) in primates during fetal and early postnatal life involves highly orchestrated changes in its structural and biochemical characteristics of the brain. Investigation of fetal brain development *in vivo* using MRI offers an attractive alternative to post-mortem studies for developmental studies, particularly for longitudinal studies of fetal brain across gestation in individual pregnancies. Our goal was to demonstrate the feasibility and utility of using MRI for longitudinal investigations of fetal brain development on baboons [1].

METHODS

A total of 7 pregnant baboons were studied. Two baboons were used to establish animal transport and care procedures within the MRI scanning environment. The other 5 pregnant baboons underwent repeated scans beginning at 56 days gestation (dg). In 2 pregnancies, fetuses were scanned 5 to 6 times from the 2nd trimester until term birth. In the other 3 pregnancies scanning studies were limited to the 2nd trimester because of other research protocols. The interval between scans was 2-3 weeks. All animal care and experimental procedures were reviewed and approved by the IACUC of Columbia University and the New York State Psychiatric Institute. For scanning, the animal was kept anesthetized and mechanically ventilated. Controlled ventilation minimized movement artifact from both mother and fetus for scanning of the fetal brain. Heart rate and percent saturation of blood with oxygen were monitored to maintain maternal stability.

MRI pulse sequences were implemented on a GE Signa EXCITE 3T whole-body scanner (GE Medical Systems, Milwaukee, WI). We used a quadrature head coil manufactured by GE for subsequent scans of the abdomen of the pregnant baboon. This GE head coil accommodated the pregnant baboon and provided an image quality superior to that of the other coils we tested. With both ends of the GE head coil open, a pregnant baboon at term, equipped with thermal wrapping, sensors to monitor vital signs, a bladder catheter, and ventilatory tubing for administration of anesthesia, fit comfortably within the coil. Pregnant baboons were placed in the coil feet first.

We used Fast Spin Echo (FSE) sequences to acquire T1W and T2W images of fetal brains. FSE allowed images with higher in-plane resolution (FOV of 12-14 cm with a matrix more than 128x128, up to 192x192, all zero-filled to 256x256) and better through-plane resolution (slice thicknesses of 2.0 - 3.0 mm, with 0 mm spacing).

We also used FSE for all T_1 and T_2 relaxometry measurements [2] with parameters: FOV = 12 cm, matrix size = 128 x 128, slice thickness = 3 mm, slice spacing = 0 mm, NEX = 1, echo train length (ETL) = 32. For T_2 relaxometry measurement by FSE, the images are acquired at effective TEs of around 10, 35, 70, 105, 140, 175, 210, and 245 ms, with TR = 3500 ms. For T_1 relaxometry measurement by IR-FSE, the images are acquired at TIs of 60, 300, 750, 1500, and 3000 ms, with TR = 10000 ms and Minimum TE. All the parameters are fixed during the longitudinal scans. Maps of T_1 and T_2 values in the fetal brain were obtained by curve-fitting on a pixel-by-pixel basis the series of T_1- and T_2-weighted images obtained at differing TIs or TEs. A single component for T_1 and T_2 was assumed for the calculation of T_1 and T_2 values.

We also attempted DTI sequence based on EPI: FOV = 12 cm, matrix size = 64x64, slice thickness = 2 mm, slice spacing = 0 mm, TE = 100 ms, TR = 8000 ms, NEX = 3, b-value = 1000 s/mm^2, and 11 directions of diffusion gradients

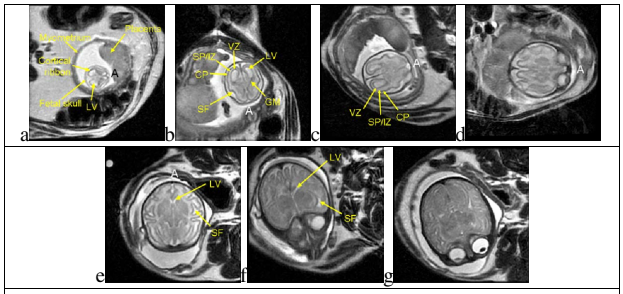

Figure 1 T2W images at various gestational ages: (a) 64 dg; (b) 90 dg; (c) 105 dg; (d) 132 dg; (e) 141 dg; (f) 162 dg; (g) 185 dg.

RESULTS AND DISCUSSIONS

High-resolution T2W images were used to evaluate structural development of the fetal brain. These structures included the cortical plate (CP), subplate (SP), ventricular zone (VZ), germinal matrix (GM), and Sylvian fissure (Fig. 1). Among other events, the initiation of cortical gyration and sulcation, and the appearance of the subplate, are noted before 90 dg.

We observed that both T_1 and T_2 values decreased in CGM and in WM as the brain matures (Fig.2). This decrease, however, occurred at differing rates across each tissue type. T_1 relaxation times eventually became comparable across GM and WM, as did T_2 relaxation times. In support of the validity of these techniques, relaxation times of CSF remained constant over gestation. The diminishing differences in relaxation times between GM and WM with advancing GA produce progressively poorer image contrast as the fetal brain matured (Fig.1).

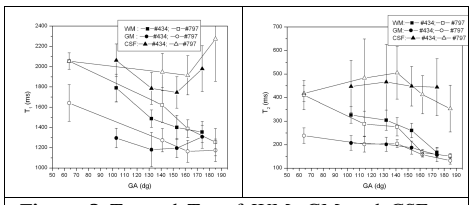

Figure 2 T_1s and T_2s of WM, GM and CSF at different GAs. Data are from three baboon fetuses (#415 and #797). T_1s and T_2s in both WM and GM decrease until the convergence near term.

We used a FACT-based algorithm for fiber tracking [3]. We assessed various parameters for tract termination. However, fiber tracking could not be carried out successfully because of insufficient SNR in the diffusion weighted images. DTI nevertheless did provide useful information about early development in the fetal baboon brain. For example, by approximately 110 dg, the corpus callosum was clearly visible (Fig.3). From 6 fetal DTI scans (mean gestational age 126 ± 26 dg, range: 90 to 162 dg), the mean ADC value was 1.81 ± 0.15 μm^2/ms in white matter and 1.30 ± 0.14 μm^2/ms in deep gray matter.

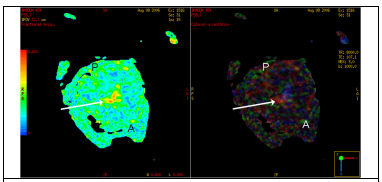

Figure 3 Maps of (Left) fractional anisotropy (FA) and (Right) orientation at 115 dg. Corpus callosum (arrows) is already visible. A: anterior; P: posterior.

We have developed a protocol for imaging the fetal brain in pregnant baboons at a field strength of 3T. This protocol will advance longitudinal studies of brain maturation by allowing investigators to acquire more detailed information about the fetal brain at specific stages of development.

REFERENCES

[1] Liu, et al. NeuroImage, under review. [2] Liu, et al. ISMRM 2007;15:2348. [3] Xu, et al. NeuroImage 2002;17:1131.