Brain development of neonatal guinea pigs in vivo measured by Diffusion Tensor Imaging at 9.4 T

J. Kim[1], I-Y. Choi[1,2], Y. Dong[3], C. P. Weiner[3], and S-P. Lee[1,4]

[1]Hoglund Brain Imaging Center, University of Kansas Medical Center, Kansas city, KS, United States, [2]Department of Neurology, University of Kansas Medical Center, Kansas city, KS, United States, [3]Obstetrics and Gynecology, University of Kansas Medical Center, Kansas city, KS, United States, [4]Department of Molecular and integrative Physiology, University of Kansas Medical Center, Kansas city, KS, United States

Introduction

Guinea pigs are recognized as a good model for human pathology such as juvenile diabetes, or pregnancy complications such as chronic fetal hypoxia because of their precocious neurological development in contrast to other non-precocious rodents. Hypoxia is one of the pregnancy complications that would lead to fetal neuron-developmental brain damage [1]. Diffusion Tensor Imaging (DTI) provides distinctive endogenous contrast for brain tissue delineation and the contrast is consistent during the course of postnatal development. Most studies on brain development have relied on histology or ex vivo [2]. In this study, we use *in vivo* DTI to quantitatively measure brain development of white matter, especially corpus callosum, of guinea pig neonates.

Methods

Spin-echo DTI data were obtained at 9.4 T Varian system equipped with a 12 cm gradient coil (40 G/cm, 250 μs) and shim coil (Magnex Scientific, Abingdon, UK) with second-order shim strength up to 0.4 G/cm^2. The magnet was interfaced to a Varian INOVA console (Varian Inc., Palo Alto, CA). A quadrature surface RF coil consisting of two geometrically decoupled loops was placed on the animal head for transmitting and receiving at 400 MHz proton frequency.

Anesthesia was induced by 4% isoflurane mixed with 4L/min O_2 and 1L/min air and maintained by 1-1.5% isoflurane. Body temperature was maintained at 38˚C using hot water pad and monitored via rectal probe. Respiration, heart rate, and blood oxygen level were also monitored via respiration pillow and pulse oximeter. DTI data were acquired at 4 time-points (postnatal days: P1, P7, P28, and P42) for four guinea pig neonates. DTI parameters were FOV = 2.5x2.5cm^2 (for P1, P7, and P28) & 3x3cm^2 (for P42), matrix = 128x128, TR/TE = 1000/23ms, six diffusion directions: [0.707, 0.707, 0], [0.707, 0, 0.707], [0, 0.707, 0.707], [-0.707, 0.707, 0], [0.707, 0, -0.707], [0, -0.707, 0.707], b = 832 s/mm^2, NEX = 2, and the slice thk = 1mm. Image analysis was performed using FSL [3].

Results and Discussion

Development of guinea pig brains from day 1 (P1) to day 42 (P42) is shown in Fig 1 FSL processed RGB principle eigenvector of the diffusion tensor map modulated by fractional anisotropy (FA) map. DTI results showed good contrast for delineation of anatomical structures. White matter tracks appear bright (high tissue diffusion anisotropy) with diffusion orientation perpendicular to the axonal fibers' trajectories. At P1, corpus callosum is not fully formed and at P7, we can detect it is extended caudally with the growth of cortical hemisphere, shown mainly in green. An ROI is manually drawn around corpus callosum and average FA values are obtained from each time point (Fig 2). The average FA value increased from 0.518 ± 0.047 (mean ± SD) at P1 to 0.603 ± 0.042 at P42. FA value increases with time within ROI and this means more pronounced trajectories of axonal fibers, i.e., more axons are formed.

The results demonstrate the feasibility to quantitatively measure postnatal brain development of guinea pig neonates using DTI *in vivo*. In contrast to conventional MRI, DTI provides good and consistent delineation of brain structures. This method could provide an important way to quantitatively study abnormalities of brain development and to understand the underlying mechanisms of the most common cause of fetal brain damage such as chronic fetal hypoxemia.

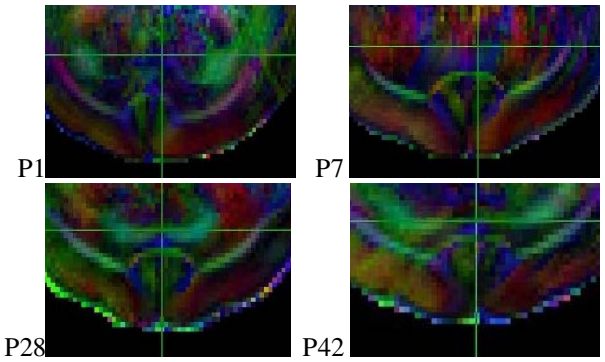

Fig 1. Principle eigenvector map at each time point

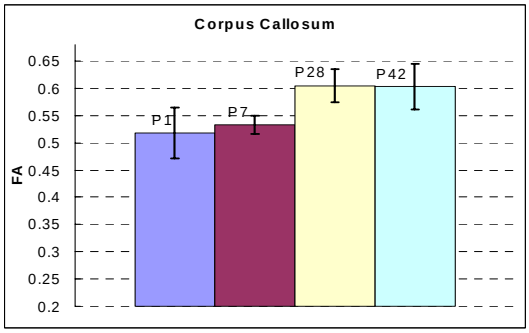

Fig 2. Group average FA value with error bar at each time point

References

1. Thompson et al. Am J Physiol Regulatory Integrative Comp Physiol 279:1813 (2000). 2. Zhang et al. NeuroImage 26:1042 (2005). 3. Smith et al NeuroImage 23(S1):208 (2004)