Diffusion MRI of *in utero* mouse embryos

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Introduction The mouse embryo is a widespread animal model for human development disorders. MRI offers a unique, noninvasive approach for imaging normal and abnormal mouse embryo development in later gestational stages. One of the difficulties of imaging *in utero* mouse embryos is the lack of tissue contrast exhibited by the embryo at high magnet field strengths. This project explores the use of diffusion-weighted MR microscopy to improve embryonic CNS tissue contrast while simultaneously addressing the major technical challenges of acquiring diffusion-weighted images in the presence of maternal respiratory motion. We report results using respiratory-gated, volumetric *in utero* diffusion-weighted images with an isotropic spatial resolution of 250 microns which allowed clear differentiation of CNS tissue boundaries in the murine embryonic brain.

Materials and methods C57BL/6 mice were arranged for timed mating. The pregnant mouse was anesthetized with isoflurane and placed in a cradle, the head of the mouse was restrained with a stereotactic jig and the body of the mouse was positioned in a 3-cm-ID volume RF coil. The whole setup was positioned in a vertical bore 11.7T magnet. A rectal thermocouple temperature probe was used to monitor the mouse temperature, which was maintained at 37^{o}C with a thermostatically controlled airflow. Diffusion-weighted axial images were acquired using a pulsed-field-gradient spin echo pulse sequence with fat suppression. Respiratory gating was used for all image acquisitions. Key imaging parameters were as follows: TE/TR = 16.7 ms /2000 ms, slice-thickness: 250 um, in-plane resolution: 234 um x 234 um, FOV: 30 mm x 30 mm, number of slices: 50, Δ = 8.5 ms, δ = 3 ms, nominal b value: 600 s/mm^2, number of averages: 4, total acquisition time: 20~30 min.

Results and Discussion Figure 1 is a schematic that shows the approximate slice position of the acquired axial diffusion-weighted images. Figure 2 shows the diffusion-weighted axial images acquired an individual stage E17.5 *in utero* mouse embryo with corresponding microhistological images from the Atlas of the Prenatal Mouse Brain (1). As expected the CSF within the aqueduct and the lateral ventricles is hypointense, allowing accurate identification of the cortical and periventricular margins. The brain parenchyma has a significantly lower diffusion coefficient because water diffusion is restricted by the microstructure of cells such as cell membranes, and appears hyperintense.

Conclusions Diffusion-weighted MRI, although technically difficult to acquire with high spatial resolution and minimal motion artifacts from *in utero* mouse embryos, can differentiate larger anatomical structures in later-stage mouse embryos *in utero*. This technique is noninvasive, requires no exogenous contrast agent and has potential for screening of developmental models of neurodevelopmental disorder models, particularly at mid- to late gestational ages. 3D anatomical maps of mouse embryos with congenital defects may be acquired.

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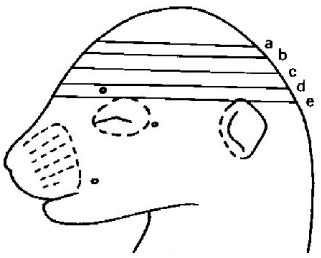

Fig.1 a schematic of axial slices of a mouse embryo. Schematic slice b corresponds to the image in Fig. 2a and schematic slice d corresponds to the image in Fig. 2b.

References: (1) Schambra U., Lauder J., Silver J.; Atlas of the Prenatal Mouse Brain.

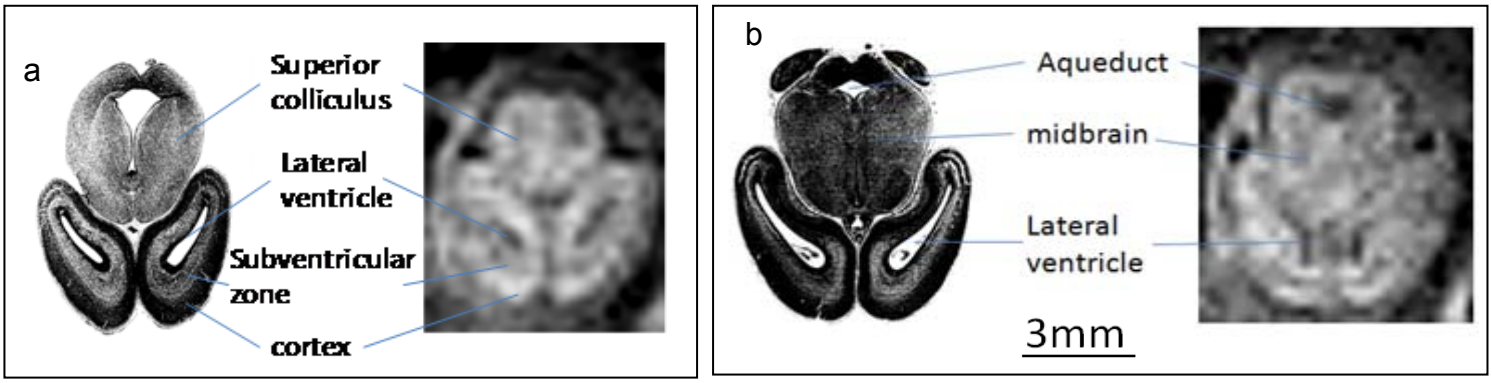

Fig.2 Diffusion-weighted axial slices of in utero mouse embryo brain. (a) and (b) approximately correspond to the slice position of b and d in Fig 1. The structures in the diffusion-weighted images are tentatively labeled according to the histology images from reference (1). Both images are shown to the same scale (scale bar in b = 3mm).