White matter changes in lipopolysaccharide (LPS) treated fetal sheep measured by high field diffusion tensor imaging (DTI)

Y. Van de Looij ^{1,2}, J.M. Dean³, G. Lodygensky⁴, F. Lazeyras⁵, I. Kjellmer⁶, R. Gruetter^{2,5,7}, C. Mallard³, P.S. Huppi¹, S.V. Sizonenko¹

¹Division of Child Development & Growth, Dept. of Pediatrics, University of Geneva, Switzerland. ²Laboratory of Functional and Metabolic Imaging (LIFMET), Ecole Polytechnique Fédérale de Lausanne Switzerland, ³Perinatal Center, Department of Neuroscience and Physiology, Sahlgrenska Academy, University of Gothenburg, Sweden. ⁴Department of Pediatrics, Washington University, St Louis, USA. ⁵Department of Radiology, University of Geneva, Switzerland. ⁶Department of Pediatrics, Sahlgrenska Academy, University of Gothenburg, Sweden and ⁷Department of Radiology, University of Lausanne, Switzerland.

LPS induces an inflammatory response and white matter (WM) injury in the developing brain. DTI measures the translational movement of water among the tissue in three-dimensional spatial directions. Fractional anisotropy (FA) a measure of the degree of preferential direction of water diffusivity is considered to reflect tissue microstructure organization.

The aim of this study was to measure changes in WM FA after fetal LPS exposure.

Fetal sheep received vehicle (control, n=7) or LPS (200ng; n=7) at 103d gestation (term = 145d). Fetal brains were collected after 10d recovery and formalin-fixed for subsequent MRI (9.4T magnet). FA was measured in corpus callosum (CC) and periventricular WM (PVWM) in the anterior, median and posterior brain levels.

FA values in the LPS group were significantly lower than controls in the CC and PVWM: $\underline{\text{CC}}$: anterior 0.67±0.08 and 0.86±0.06 p=0.0023, middle 0.55±0.08 and 0.66±0.04 p=0.0006 and posterior 0.76±0.05 and 0.85±0.04 p=0.0012 respectively; $\underline{\text{PVWM:}}$ posterior 0.61±0.11 and 0.78±0.08 p=0.01 respectively (Mann-Whitney test). FA levels in the PVWM anterior and middle slices showed a tendency to be lower in the LPS group (p=0.053).

These lower FA levels reveal alteration in the developing white matter tracts after fetal exposure to LPS prior to the onset of myelination.