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INFLAMMATORY PRIMING OF THE FETAL SHEEP METABOLISM PREDICTS BRAIN DAMAGE

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Background and aims: Prenatal inflammation is currently being seen as one important factor of brain injury in preterm infants. Currently there is a lack of an early biomarker of brain injury. In addition it is not known how prenatal inflammation influences fetal metabolism in short and long-term.

Here, we

1) characterise the fetal metabolic response to intrauterine inflammation

2) identify metabolic markers of brain injury.

Methods: Fetuses were randomized to i.v. bolus infusion of either saline-vehicle (n=7) or 200ng E.coli LPS (n=9) at 102.5±0.5 days of gestation. Blood samples were collected at baseline 2h, 6h hours and daily up to 10 days for metabolite quantification. Metabolites were correlated to findings in MRI, EEG and histopathology.

Results: LPS induced a two-phase pattern in metabolite changes. Within the first 3 days, 121 metabolites were impacted (immune response, energy metabolism and tissue injury). Thereafter, a transient period (4-6days) without changes compared to baseline, was followed by a second phase marked by an opposite regulation of energy metabolites and inflammatory markers. At the multivariate level, the two-phase characteristics of the metabolite response to LPS was strongly associated with white/grey matter volumes and the number of oligo-2 positive cells at 2h-to 2days and at 6-9days.

Conclusions: In this first in-utero analysis we detected a significant impact of LPS on fetal metabolism in both the short and long-term. Thus we hypothesize that there is specific inflammatory priming of the fetal metabolism in the blood, as supported by the bi-phasic pattern of metabolites, which correlate with brain injury.