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BIOMARKERS OF DEVELOPMENTAL BRAIN INJURY IN PRETERM INFANTS: REPORTING ON METABOLOMICS ACTIVITIES OF THE NEOBRAIN CONSORTIUM

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Background and aims: A novel component in the Neobrain consortium was the large scale quantification of metabolites and their implication/use for translational research. Here we report on the

1) adequacy of the metabolomics technology

2) characterisation of metabolic responses to several types of injury in plasma

3) identification of metabolic markers of brain injury in animal models and humans.

Methods: Study comprises animal models of hypoxia-ischemia, excitotoxic brain injury and intrauterine LPS exposure in fetal sheep and a human cohort of 41 preterm infants (28-32 weeks of gestation). Metabolite panel covering 230 compounds (acylcarnitines, lipids, prostanoids, amino acids and derivatives, oxidised products of cholesterol, small organic acids,sugars) was applied in plasma. In the sheep model and infants, extend of brain damage has been assessed by MRI, aEEG and histopathology in animals.

Results: Insults causing brain injury induced significant changes in the plasma metabolome in all animal models. In the sheep model we detected a significant correlation of metabolites with outcome at several time points. In the preterm infants ADMA/SDMA, specific acyl carnitines, lysoPCs and amino acids were significantly increased in infants with abnormal MRI at term, overlapping with metabolites detected in the animal models.

Conclusions: Hypothesized at the start at the project, metabolic changes associated with perinatal brain injury is demonstrated in several animal models and translated in humans. Metabolite profiling can effectively be applied to pediatric research to complete our fragmented knowledge. It enables identification of patterns of dysregulation (biomarker discovery) together with the elucidation of their underlying mechanism (biological plausibility).