

Cerebral Protein Synthesis in the Ovine Fetus Near-term with Induced Hyper and Hypo-Aminoacidemia

"Jeremy McCallum" <mccallumjeremy@hotmail.com>

James N MacLachlan¹, Jeremy D McCallum¹, Norman B Smith², Brad Matuszewski¹, Bryan S Richardson¹.

Departments of Obstetrics and Gynecology¹, Physiology and Pharmacology¹, and Biochemistry², the Canadian Institutes of Health Research Group in Fetal and Neonatal Health and Development, Children's Health Research Institute, The University of Western Ontario, London, Canada.

Objectives: The precursor availability of amino acids within the developing brain may impact on protein synthesis and cerebral metabolism, thereby impacting growth processes. We have therefore utilized a mixed amino acid infusate and an insulin euglycemic clamp technique in the ovine fetus near term with moderate increases and decreases in circulating amino acid levels, respectively, and determined the impact on cerebral protein synthesis using [¹³C]-leucine tracer methodology, and on cerebral substrate flux.

Methods: Chronically instrumented pregnant sheep near term received a 6 hour infusion of Primene® 10%, Hyper amino acid (AA) group (n=10), or a co-infusion of insulin and 10% dextrose, Hypo AA group (n=8), together with a continuous infusion of L-[1-¹³C]-leucine to the fetus. Measurements were obtained for fetal plasma leucine enrichment at steady-state and brain tissue intracellular free and protein bound leucine enrichment at necropsy, followed by the determination of cerebral protein fractional synthetic rates (FSR). Cerebral substrate fractional extraction was measured at baseline and during the hyper and hypo amino acidemia experimented periods.

Results: Protein FSR for the cerebral cortex averaged ~57%/day and ~41%/day when using the intracellular free and plasma enrichment values for the precursor pool measurements, respectively, providing for maximal and minimal FSR values, and with little difference between the Hyper and Hypo AA groups, although significantly higher than respective values for the cerebellum, and higher than those previously reported for animals at this gestational age. Cerebral fractional extraction values for oxygen, glucose, leucine and leucine enrichment as measures of substrate flux were little changed between the baseline and experimental period.

Conclusions: Accordingly, there was no evidence for a differential effect of modest increases versus decreases in circulating amino acids on cerebral protein synthesis as studied. However, it is possible that the associated increase in fetal insulin with the amino acid and insulin/dextrose infusions reported by others, has similarly increased cerebral protein synthesis, thereby implicating a role for insulin in growth and developmental processes within the brain.