The impact of dietary methyl donors on whole-body methionine partitioning in the neonatal piglet

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Background

• Methyl groups are used in "Transmethylation" to synthesize critical metabolites and regulate gene expression through DNA methylation
• Demethylated methionine (homocysteine) can either form cysteine by "Transsulfuration" or be reformed by "Remethylation"
• As a result the methionine requirement is changed in the presence or absence of dietary cysteine
• Remethylation occurs by the dietary methyl donors folate and choline (via betaine)

Study Protocol

- 3-8 day old Yucatan mini piglets were anaesthetised and surgically implanted with gastric and venous catheters
- Diet was chronically infused using TPN pumps into the gastric catheter for the duration of the experiment
- Animals were divided into two groups based on diet (Table 1)
- All animals received two enteral isotope infusions: breath and blood samples were taken for MS analyses

Table 1: Piglets were randomised to a methyl-deficient (MD- or methyl-replete (MS+) diet

We aimed to quantify the potential for dietary methyl donors to affect the methionine requirement for protein and transmethylation
- To do this we restricted dietary methionine in neonatal piglets and compared in vivo methionine metabolism in individuals with- and without dietary methyl donors
- It was hypothesized that methyl donors would affect protein synthesis, remethylation and transmethylation

Results

• Phenylalanine and methionine infusions reached plateau in blood and breath in 4-, and 6-hours respectively (Figure 2)
• Stochastic measures of the phenylalanine infusion resulted in a number of differences based on dietary methyl donors (Figure 3)
- Phenylalanine flux was greater with methyl donors (MD- 425.7 ± 46.5 μmol Phe/hr/hr vs. MS+ 488.8 ± 32.6 μmol Phe/hr/hr); p=0.01
- Protein Synthesis was significantly higher with methyl donors (MD- 424.6 ± 46.7 μmol Phe/hr/hr vs. MS+ 480.7 ± 36.8 Phe/ hr/hr); p=0.02
- Protein Breakdown was lower during methyl deficiency (MD- 221.7 ± 44.4 μmol Phe/hr/hr vs. MS+ 282.8 ± 34.81 Phe/ hr/hr); p=0.01
• The flux of methionine through remethylation, transsulfuration and transmethylation are depicted in Figure 4:
  - Remethylation was higher in the MS+ piglets (MD- 5.1 ± 5.0 μmol Met/hr/hr vs. MS+ 12.8 ± 6 μmol Met/hr/hr); p<0.03
  - Transsulfuration was unchanged between the two groups and was highly variable during methyl deficiency
  - Overall Transmethylation was enhanced in the presence of methyl donors (MD- 5.4 ± 5.0 μmol Met/hr/hr vs. MS+ 14.6 ± 5.0 μmol Met/hr/hr); p=0.01

Discussion

Dietary methyl donors had a significant impact on whole-body protein dynamics in neonatal piglets
- Whole-body protein synthesis and breakdown were enhanced by dietary methyl donors by a similar amount, although protein synthesis was quantitatively greater overall
- The enteral flux of dietary phenylalanine was impacted significantly in the presence of methyl donors
- Through an increase in remethylation, methyl donors “spared” methionine for transmethylation and protein metabolism
- No conclusion dietary methyl donors should be considered when determining the methionine requirement in the neonate