

LEUCINE ADMINISTRATION IN CONJUNCTION WITH CONTINUOUS FEEDING IMPROVES LEAN GROWTH IN A PRETERM PIGLET MODEL

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Background: Extrauterine growth restriction is a common adverse outcome in preterm infants and is associated with reduced lean growth and long-term morbidities. Previous work in our lab showed that continuous feeding blunts muscle protein synthesis compared to intermittent bolus feeding in neonatal pigs born at term (a highly translatable model for the human neonate). However, continuous feeding is still indicated in some infants due to feeding intolerance. Our lab has demonstrated that leucine acts as a nutrient signal to stimulate protein synthesis and that intermittent parenteral leucine (Leu) pulses during continuous orogastric feeding increases skeletal muscle mTORC1 signaling and protein synthesis in neonatal pigs born at term. We hypothesized that leucine pulsing during continuous feeding enhances mTORC1 signaling to protein synthesis and lean growth in a preterm piglet model.

Materials/Methods: Pigs delivered by cesarean section at 105 d gestation were gradually transitioned from parenteral to enteral feeding via an orogastric tube over 7 d and continuously fed a protein and energy balanced milk-replacer diet throughout the remainder of the study (24 d). Pigs were randomly assigned to either: 1) Leu (1600 μmol Leu/kg bodyweight/4 h; n = 4) or Alanine (1600 μmol Ala/kg bodyweight/4 h; isonitrogenous control; n = 4) groups. The assigned amino acid solutions were administered intravenously as a "pulse" for 1 h, every 4 h from Day 3 to Day 24 of study. Body composition was determined via dual x-ray absorptiometry on Day 22 and indices of amino acid signaling and mTORC1 activation were determined 60 min after initiation of the last pulse of Day 24.

Results: Leu-treated pigs had a higher average daily gain (ADG) ($P < 0.05$) and 13% higher final body weight than Ala-treated control pigs ($P < 0.05$). Total lean mass tended to be higher (+13%; $P < 0.06$) in Leu-treated compared to controls, while body fat percentage remained unchanged. Longissimus dorsi (LD) muscle weight was heavier in Leu-treated than control pigs ($P = 0.01$). Indices of mTORC1 activation, i.e., phosphorylation of S6K1 and 4EBP1 and abundance of the eIF4E-eIF4G complex, were increased in LD ($P < 0.01$) and gastrocnemius ($P < 0.05$) muscles of Leu-treated compared to control pigs.

Conclusions: These results show that leucine supplementation during continuous feeding enhances mTORC1 activated translation initiation in skeletal muscle leading to an increase in lean growth and weight gain in a preterm piglet model.

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