

Co-ingestion of glutamine and leucine synergistically promotes mTORC1 activation.

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Abstract

Leucine (Leu) regulates protein synthesis and degradation via activation of mammalian target of rapamycin complex 1 (mTORC1). Glutamine (Gln) synergistically promotes mTORC1 activation with Leu via glutaminolysis and Leu absorption via an antiporter. However, Gln has also been shown to inhibit mTORC1 activity. To resolve this paradox, we aimed to elucidate the effects of Gln on Leu-mediated mTORC1 activation. We administered Leu, Gln, tryptophan, Leu + Gln, or Leu + tryptophan to mice after 24-h fasting. The mice were then administered puromycin to evaluate protein synthesis and the gastrocnemius muscle was harvested 30 min later. Phosphorylated eukaryotic initiation factor 4E-binding protein 1, 70-kDa ribosomal protein S6 kinase 1, and Unc-51 like kinase 1 levels were the highest in the Leu + Gln group and significantly increased compared with those in the control group; however, Gln alone did not increase the levels of phosphorylated proteins. No difference in glutamate dehydrogenase activity was observed between the groups. Leu concentrations in the gastrocnemius muscle were similar in the Leu-intake groups. Our study highlights a novel mechanism underlying the promotive effect of Gln on Leu-mediated mTORC1 activation, providing insights into the pathway through which amino acids regulate muscle protein metabolism.