Acute hypoxia influences muscle protein turnover in human skeletal muscle.

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Introduction: Hypoxia is a state of reduced O2 tension in tissue, including skeletal muscle. It elicits various responses in the cell leading to preserving O2. One of these responses is decreasing protein turnover, as stated by in vitro studies (Pettersen et al., 1986). On the other hand, in vivo studies are not that conclusive due to higher variability (Mizuno et al. 2008). Therefore, this study aims to get more detail on pathways involved in anabolic and catabolic signaling in human skeletal muscle as a response to acute hypoxia.

Methods: According to a randomized cross-over study, 15 healthy men participated in 2 experimental sessions separated by a 4-week wash-out period. After a standardized breakfast, subjects were randomly assigned to a 4-h lasting seated experimental trial in normoxia (NOR) or hypoxia (11% O2¸ HYP). Three biopsies were taken at the start (T0), after 1-h (T60) and at the end of the trail (T240). Furthermore, arterial blood saturation (SpO2) and muscle tissue oxygenation (TOI) were measured by pulsoximetry and Near-infrared spectroscopy (NIRS). Western blot and qPCR were used to determine phosphorylation status or mRNA quantity of several components involved in the regulation of protein synthesis (i.e. protein kinase B and p70 ribosomal S6 kinase, Redd1), breakdown (i.e. 26s Proteasome β5) and hypoxic signaling (i.e. Hypoxia Inducible Factor-1α, VEGF-A).

Results: Despite a large decrease in SpO2 (HYP, 75.5 ± 2.02% vs NOR, 99.0 ± 0.18%, $p<0.05$), TOI was only slightly reduced (HYP, 65.8 ± 1.39% vs NOR, 68.5 ± 1.19%, $p<0.05$). Hypoxia delayed the return to basal state after feeding for both PKB and P70S6K phosphorylation ($p<0.05$), furthermore significant differences were found between NOR and HYP at T240 (p-PKB: NOR, 0.44±0.06 vs. HYP, 0.75±0.06 and p-P70S6K: NOR, 0.32±0.09 vs. HYP, 0.48±0.10, $p<0.05$). Redd1, increased ~2-fold at T240 in HYP compared to NOR at the same time ($p<0.05$). Activity of 26s proteasome β5 increased by 19 % in NOR at T240 compared to T0 ($p<0.05$). Conversely, no effect in time was present in HYP ($p>0.05$). HIF-1α mRNA was not changed throughout the experiment, whereas VEGF-A significantly increased in HYP compared to NOR at T240 (~1.5 fold, $p<0.05$).

Conclusion: Our results provide evidence that acute hypoxia slows down the return to basal state of several components of protein synthesis and protein breakdown after feeding. This impairment in the regulation of protein turnover could participate to the decrease in muscle mass observed after long-term exposure to hypoxia.

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