Acute Hypoxia Rapidly Alters Myotube Size in vitro & Myostatin Signaling in vivo

Bradley Elliott¹, Derek Renshaw¹, Stephen Getting¹, Peter Watt² & Richard Mackenzie¹
1. Faculty of Science & Technology, University of Westminster & 2. Chelsea School, University of Brighton

Introduction
Skeletal muscle is the largest tissue in humans and is key in thermoregulation, locomotion, glycolysis and homeostasis. Muscle atrophy increases mortality to a variety of disorders. Myostatin is a powerful regulator of muscle mass¹ and acts via multiple pathways to induce atrophy².

In vitro – Does hypoxia directly increase myostatin & induce atrophy?
C2C12 myoblasts were either scratched and exposed to hypoxia or differentiated into myotubes and exposed to hypoxia.

Hypoxia is a poorly understood inducer of muscle atrophy. Atrophy is seen in mountaineering humans³ (figure 1). Rats exposed to hypoxia for 5 weeks show increased myostatin expression⁴, as do COPD patients who are chronically (at least 6 months) hypoxicemic. Both COPD patients and mountaineering individuals are difficult models to study, as they present with several confounding factors.

We therefore aimed to investigate the effect of hypoxia upon myostatin expression in vitro and in vivo in healthy humans, hypothesizing that hypoxia alone would be sufficient to induce increased myostatin expression and therefore be causative of muscle atrophy.

In vivo – Does hypoxia increase myostatin?
Participants (N = 8, 21%) were exposed to hypoxic (12% O₂) or control (21% O₂) conditions in a counter-balanced design.

Discussion
Hypoxia rapidly induces atrophy of myotubes in vitro, with decreased protein content and decreased size, in a time-dependent manner. Hypoxia decreased muscle myostatin content in vivo relative to resting control, suggesting myostatin was either degraded or left the muscle tissue to act in its endocrine role.

These results suggest hypoxia alone is sufficient to induce atrophy. This may in part explain hypoxic conditions or disorders where muscle atrophy is seen. Current work is examining the dose- and time-dependent effect of hypoxia in vivo (figures 7 & 8), before attempts to inhibit the effect of hypoxia upon muscle mass in vivo can be attempted in a similar manner to our in vitro work.


Financial support was provided by the Society for Endocrinology (UK), The Physiological Society & the University of Westminster.