JOURNAL CLUB

Growing collagen, not muscle, with weightlifting and 'growth' hormone

Nicholas A. Burd, Daniel W. D. West, Tyler A. Churchward-Venne and Cameron J. Mitchell
Exercise Metabolism Research Group, Department of Kinesiology, McMaster University, Hamilton, ON, Canada, L8S 4K1

Email: burdna@mcmaster.ca

Resistance exercise remains unchallenged as an extremely potent exercise perturbation to induce significant increases in skeletal muscle mass. In recent years, manipulation of acute exercise variables (intensity, volume, rest interval) and type (multi-joint or single joint) of exercise has been employed to induce a favourable 'anabolic' hormonal milieu (large systemic increases in growth hormone (GH), testosterone and insulin-like growth factor (IGF-1)) in which to bathe the muscle following the exercise bout has been a goal among resistance exercise enthusiasts.

Presumably, this recommendation has largely developed based on the observation that GH secretion is linear in growing children and thus must be growth promoting in adults also; however, human studies tell a different story in that no significant increases in muscle protein synthesis or lean body mass can be detected in healthy young adults when exogenous GH is administered (Yarasheski *et al.* 1992). What is more, physiological levels of exercise-induced increases in GH availability have no influence on myofibrillar protein synthesis or muscle hypertrophy in healthy young adult men (West *et al.* 2009*a*,*b*). Therefore, the exact physiological role of acute increases in GH following exercise in healthy adults is unknown.

Recent, very elegant, work by Doessing and colleagues (Doessing *et al.* 2010), published in *The Journal of Physiology*, gives us a clue as to the conundrum of what increments in systemic GH in response to exercise might be doing. These investigators performed a randomized, double-blinded, placebo-controlled crossover trial in which sedentary subjects were supplemented with recombinant human GH (rhGH) initially (1–7 days) at 33.3 μg kg^{-1} day^{-1} and at 50 μg kg^{-1} day^{-1} for the latter half (8–14 days) of the experimental period. Each supplementation period was separated by a 5 month wash-out period. After each period, participants performed a unilateral bout of leg extension exercise at 10 sets of 10 repetitions at 70% of their concentric best effort (1RM). It is worth highlighting that the unilateral model was an excellent exercise choice as this minimized the amount of active muscle mass and ultimately did not induce large systemic increases in GH during the placebo trial. Subjects returned to the laboratory and underwent a stable isotope infusion to determine fasted-state fractional synthetic rates of tendon and muscle collagen proteins and myofibrillar proteins at 24 h post exercise. Tendon and muscle tissue was also obtained to examine different IGF-1 splice variants mRNA (IGF-1Ea and IGF-1c) and collagen mRNA (collagen I and III). The researchers were successful in eliciting the desired effect in the supplementation group as shown by the increase in the concentration of circulating GH. Specifically, rhGH showed a linear increase with supplementation doses of 33.3 and 50 μg kg^{-1} day^{-1} at days 1–7 and 8–14, respectively. Unsurprisingly, a corresponding increase in systemic IGF-1 and IGFBP-3 also occurred with rhGH supplementation, whereas there were no changes in systemic GH or associated blood indices in the placebo condition.

The anabolic potency of resistance exercise was not demonstrated in collagen or myofibrillar protein synthesis in the study by Doessing and colleagues (Doessing *et al.* 2010). It was reasoned that the number of contractions performed (i.e. volume) during the exercise bout was sub-optimal in contractions. These data are in conflict with Miller *et al.* (2005) who utilized a unique, high exercise volume, one-legged kicking model to induce robust increases in fed-state myofibrillar and muscle collagen protein synthesis which persisted for up to 72 and 48 h post exercise, respectively. However, it is worth considering that a fundamental difference between the Miller *et al.* (2005) and Doessing *et al.* (2010) studies is the fact that the latter study was performed in the fasted state and therefore substrate (i.e. amino acids) may have become limiting and may provide the explanation for the observed lack of elevation in myofibrillar synthesis at 24 h post exercise.

The connective tissue component of skeletal muscle, which is predominantly composed of collagen, is important for transferring the force produced by the myofibrillar proteins out to the tendon and bone for movement. In contrast to myofibrillar protein synthesis, it appears that rhGH has profound effects on tendon and muscle collagen protein synthesis along with a corresponding increase in locally derived muscle IGF-1 mRNA and collagen mRNA. Furthermore, increases in GH not only increased systemic IGF-1 but also locally produced IGF-1Ea in tendon tissue. It is worth noting that these data may explain the adverse events that are commonly associated with rhGH supplementation such as soft tissue edema, joint pain and carpel tunnel syndrome with essentially no ergogenic effects on strength or muscle mass, which necessitates the accretion of myofibrillar proteins. While exogenous GH administration clearly elevates collagen synthesis, it remains to be seen whether the acute elevation of exercise-induced GH can confer any benefit to the integrity of the extracellular matrix and provide a more extensive external support lattice for skeletal muscle which could possibly enhance the ability to endure higher training loads with subsequent bouts. While this effect remains unreported, if this is the case, it would be of significance for strength-trained athletes whose primary goal is to lift progressively heavier loads; however, for body builders, recreationally active, or ageing individuals, physiological and transient elevations in GH are neither required nor do they enhance muscle hypertrophy (West *et al.* 2009*a*).

In summary, the authors are to be commended for their investigation providing further insight into the role of rhGH on the human muscle–tendon complex. They combined static measurements (i.e. mRNA expression) with a sensitive method of determining

DOI: 10.1113/jphysiol.2009.185306

the response of muscle and tendon to rhGH and exercise by utilizing stable isotope methodology to measure the rate of incorporation of amino acids into target tissues, enabling a more comprehensive understanding at both the transcriptional and translational level of the cell. As noted (Doessing *et al.* 2010), this information could prove to be useful in the clinical setting insofar as treating musculotendinous injuries are concerned and provide further evidence that rhGH supplementation is not anabolic toward contractile tissue in adult humans – a message that those taking GH in the hope of growing bigger muscles might not wish to hear!

References

Doessing S, Heinemeier KM, Holm L, Mackey AL, Schjerling P, Rennie MJ, Smith K, Reitelseder S, Kappelgaard AM, Rasmussen MH, Flyvbjerg A & Kjaer M (2010). Growth hormone stimulates the collagen synthesis in human tendon and skeletal muscle without affecting myofibrillar protein synthesis. *J Physiol* **588**, 341–351.

Miller BF, Olesen JL, Hansen M, Døssing S, Crameri RM, Welling RJ, Langberg H, Flyvbjerg A, Kjaer M, Babraj JA, Smith K & Rennie MJ (2005). Coordinated collagen and muscle protein synthesis in human patella tendon and quadriceps muscle after exercise. *J Physiol* **567**, 1021–1033.

West DW, Burd NA, Tang JE, Moore DR, Staples AW, Holwerda AM, Baker SK & Phillips SM (2009*a*). Elevations in ostensibly anabolic hormones with resistance exercise enhance neither training-induced muscle hypertrophy nor strength of the elbow flexors. *J Appl Physiol*; DOI:10.1152/japplphysiol.01147.2009.

West DW, Kujbida GW, Moore DR, Atherton P, Burd NA, Padzik JP, De Lisio M, Tang JE, Parise G, Rennie MJ, Baker SK & Phillips SM (2009*b*). Resistance exercise-induced increases in putative anabolic hormones do not enhance muscle protein synthesis or intracellular signalling in young men. *J Physiol* **587**, 5239–5247.

Yarasheski KE, Campbell JA, Smith K, Rennie MJ, Holloszy JO & Bier DM (1992). Effect of growth hormone and resistance exercise on muscle growth in young men. *Am J Physiol Endocrinol Metab* **262**, E261–E267.

Acknowledgements

We would like to thank Dr Stuart Phillips for his helpful editing of this manuscript.