Contrasting Perspectives in Exercise Science & Sports Medicine

Are Acute Post–Resistance Exercise Increases in Testosterone, Growth Hormone, and IGF-1 Necessary to Stimulate Skeletal Muscle Anabolism and Hypertrophy?

PREVAILING PERSPECTIVE

Acute post–resistance exercise (RE) increases in anabolic hormones may not be "necessary" to stimulate skeletal muscle anabolism and hypertrophy; however, as we will support in the following discussion, post-RE increases in these hormones are "optimal" for maximizing skeletal muscle anabolism and hypertrophy. For purposes of this presentation, increases in testosterone (T) and growth hormone (GH) will also imply increases in insulinlike growth factor 1 (IGF-1) (22,24). Furthermore, we will limit the discussion of these adaptations to men, while recognizing that training variables such as training history, mode, intensity, volume, and rest interval (RI) length in between sets will have compelling influence on the hormonal responses to RE.

DEFINING THE SCOPE

Studies examining the influence of acute RE-induced T and GH responses on skeletal muscle anabolism have included both trained and untrained young (18–30 yr) and older (60–80 yr) men. Regardless of trained state or age, substantial evidence indicates RE protocols and short-term resistance training (RT) using two to four sets, 8–15 repetition maximum (RM), ≤2-min RI, and RE that activates large muscle masses (i.e., multijoint movements) elicit the greatest acute elevations in T and GH (1,2,6,14,21,23,24,26,27,33,35,42). Further, recent evidence suggests strength RE protocols and short-term RT prescribed using 1) two to eight sets, 3–6 RM, ≤90-s RI, with multijoint movements (42); or 2) five sets, 3–5 RM, 3-min RI, followed by an additional set of a 25–35 RM, after a 30-s RI (13,14) elicit significant elevations in T and GH. Therefore, there is strong evidence that RE can result in substantial postexercise elevations in anabolic hormones. So the question posed is, "Do these acute RE-induced elevations in T and GH translate into skeletal muscle anabolism and hypertrophy?"

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Contrasting Perspectives

CHALLENGING PERSPECTIVE

A pervasive view in the area of endocrine responses to resistance exercise is that acute postexercise hormonal responses of testosterone, growth hormone (GH), and insulinlike growth factor 1 (IGF-1) are critical for subsequent skeletal muscle anabolism. If this is the case, then exercise regimes can be manipulated to enhance hormonal responses and thus enhance skeletal muscle adaptations such as strength and muscle mass gain. Despite this alluring prospect, we contend that postexercise increases in testosterone, GH, and IGF-1 are not necessary to stimulate skeletal muscle anabolism and hypertrophy and that measurement of the responses of these hormones yields little in the way of insight into longer-term resistance training-related adaptation.

Despite the prevalent view (25) that exercise-induced hormones regulate hypertrophy, there is a surprising lack of direct supporting evidence for this assertion. In fact, Wilkinson et al. (48) observed significant gains in strength and hypertrophy in the absence of any measurable changes in free testosterone and IGF-1. More recently, we conducted two studies (44,46) to directly examine whether exercise-induced elevations in testosterone, GH, and IGF-1 were necessary for or could enhance muscle anabolism. We used a study design in which the elbow flexors were exposed, postexercise, to either near-basal hormone concentrations or high hormone concentrations that were the result of an intense lower body exercise routine. We used this "low and high" hormone exposure model to examine the effects of postexercise hormone concentrations on muscle anabolism acutely (46) and chronically with resistance training (44). In both studies, whey protein was provided postexercise to provide substrate for any potential divergent anabolic responses initiated by the low and high hormone environments knowing that in the absence of postexercise nutrition, positive net protein balance does not occur. In the low hormone condition, myofibrillar protein synthesis was elevated acutely, and gains in strength and hypertrophy occurred after training, despite testosterone, GH, and IGF-1 concentrations that were similar to basal levels.

SUPPORTING STUDIES

The following investigations incorporated dissimilar methodologies but provide strong evidence in support of the prevailing perspective. Three studies were selected that used short-term RT interventions and examined the influence of physiologically elevated acute hormonal responses on human skeletal muscle (13,26). Two studies were selected examining the effects of physiologically elevated acute T on molecular mechanisms initiating skeletal muscle anabolism (35,49).

Kvorning et al. (26) investigated 22 recreationally active, untrained men, 20–30 yr. The endogenous production of T was suppressed by the use of a GnRH agonist (goserelin) compared with a placebo group (unaltered endogenous T levels). Both groups performed identical 8 wk of total body RT programs: 3 $d \cdot wk^{-1}$ training frequency, sessions 1–8 (3–4 × 10 RM, 2-min RI), sessions 9–16 (3–4 × 6 RM, 3-min RI), and sessions 17–24 (3–4 × 10 RM, 2-min RI). Two-thirds of the program was hypertrophy training, designed to elicit acute elevations in T and GH (24,27,42). Study participants in the placebo group experienced significant acute elevations in T and GH in response to at least 16 of the 24 total training sessions, whereas those in the goserelin group did not experience acute elevations of T in response to any of the training sessions. The lean mass increases in the legs were greater in the placebo group compared with the goserelin group ($P < 0.05$). Furthermore, the clinically important increases in total body lean mass revealed a strong trend ($P = 0.07$) toward statistically significant differences between the two groups. These findings demonstrate an implicit link between endogenous T, both resting levels and the magnitude of acute responses to RE, and the hypertrophic adaptation to short-term RT.

Goto et al. (13) evaluated 17 untrained men, 19–22 yr, performing leg press and leg extension exercises 2 $d \cdot wk^{-1}$ and compared the effects of a 4-wk periodized combination-type RT program (5 × 3–5 RM; 3-min RI; sixth set, 25–35 RM, after a 30-s RI after the fifth working set) to a 4-wk periodized strength RT program (5 × 3–5 RM; 3-min RI), after a 6-wk periodized hypertrophic RT program performed by all study participants (two rounds of 3 × 10–15 RM, 30-s RI, 3-min rest in between rounds, and 3- to 5-min rest in between exercises). Combination-type RE induced significantly greater acute increases in GH compared with strength RE (14). During the final 4-wk phase of training, CSA increased in response to combination-type RT and decreased in response to strength RT ($P = 0.08$ between groups). This evidence suggests that muscle CSA may be augmented by enhancing the acute GH response through performance of a single set of low-intensity, high-repetition exercise, immediately after repeated sets of high-intensity, low-repetition exercise, during short-term RT.

That is, postexercise increases in testosterone, GH, and IGF-1 were not necessary to stimulate anabolic processes (46), as we had reported previously (48). Furthermore, when testosterone, GH, and IGF-1 were elevated postexercise, there was no enhancement of myofibrillar protein synthesis acutely or gains in strength and hypertrophy with training. Thus, our acute mechanistic findings (46) mirrored what we observed in a chronic training study (44). It can be noted here that muscle protein synthesis is measured acutely because it is the primary determinant of enhanced muscle protein anabolism that occurs after resistance exercise and feeding (12). According to the proposed and validated models of protein accretion (29), the accumulation of repeated periods of enhanced protein balance after exercise and dietary amino acid consumption result in hypertrophy.

A study that was similar in design (31) to our previous work (44) reported contrasting findings that suggested that exercise-induced elevations in endogenous hormones underpinned superior adaptations in strength and some measures of hypertrophy. Notwithstanding methodological considerations (30), a proposed explanation for the disparate findings between studies (31,44) was that the exercise order in our study may have masked a "hormonal enhancement" effect. Specifically, because our participants trained their arms before their legs, it was suggested that the lower body exercised muscles may have "stolen" hormone-rich blood from the arm and therefore impaired adaptation (31). Therefore, we recently measured brachial artery blood flow and testosterone, GH, and determined IGF-1 concentrations to estimate hormone delivery to the elbow flexors when they were trained before or after leg exercise (45). We found no differences in the hormone delivery and thus no evidence that the ostensibly anabolic properties were compromised because of the lack of hormone delivery due to exercise order.

Other lines of evidence fail to support the thesis that exercise-induced testosterone, GH, and IGF-1 are important regulators of muscle anabolism. Our examination of associations of exercise-induced hormones and gains in strength and hypertrophy in a large cohort showed that hormone responses did not account for variance in training adaptations in strength or hypertrophy (47). Furthermore, divergent gains in strength and hypertrophy by high responders and low responders were not explained by their hormone response. In a proof-of-concept study (43), we demonstrated that women, who exhibited a 45-fold lower postexercise testosterone response (after accounting for ~20-fold lower baseline testosterone), elevated myofibrillar protein synthesis to a similar extent as men. That is, despite not having the "benefit" of postexercise testosterone, women were able to generate a robust elevation in rates of myofibrillar protein synthesis, which should have been compromised if exercise-induced

In the third study, our laboratory recently completed an investigation of 22 recreationally active men, 64–72 yr (unpublished results). Participants performed free weight– or machine-based total body RE protocols, with a 3 $d \cdot wk^{-1}$ training frequency. We compared the effects of an 8-wk periodized strength RT program using short RI (SS) (2–3 × 4–6 RM; 60-s RI) to the same 8-wk periodized strength RT program using extended RI (SL) (2–3 × 4–6 RM; 4-min RI), after a 4-wk periodized hypertrophic RT program performed by all study participants (2–4 × 8–15 RM; 60-s RI). Strength RE protocols with short RI induced significantly greater acute increases in T and GH compared with strength RE protocols with extended RI. Across the final 8-wk RT phase, total body lean mass increases were greater in response to SS compared with SL ($P < 0.05$). This finding suggests that lean mass gains are enhanced by acute elevations in T and GH through the use of short RI within short-term strength RT.

Willoughby and Taylor (49) examined the effects of acute increases in T across three sequential hypertrophic RE bouts, separated by 48 h, on skeletal muscle androgen receptor (AR) mRNA and protein expression as well as myofibrillar protein content in nine young men (17–21 yr). T was elevated after all three RE bouts ($P < 0.05$). AR mRNA and protein were elevated 48 h after bouts 2 and 3 ($P < 0.05$) and correlated with acute RE-induced increases in T immediately post-RE ($P < 0.05$). Lastly, myofibrillar protein content was elevated 48 h after bout 3 ($P < 0.05$). These findings suggest that repeated exposure to RE-induced increases in T mediates upregulation in acute AR expression and subsequent increases in myofibrillar protein, possibly because of enhanced ligand-binding capacity and via the T-AR signaling pathway.

Spiering et al. (35) investigated six men, 22–30 yr. All study participants performed a control RE protocol (bilateral knee extensions, 5 × 5 RM, 90–95% 1RM, 3-min RI) and a high-T RE protocol (upper body protocol [4 × 10 RM, 80% 1RM, 2-min RI], immediately preceding the same control RE protocol). Acute T responses were significantly greater with the high-T RE protocol compared with the control RE protocol. Muscle tissue analysis revealed only the high-T RE protocol potentiates AR responses to acute RE. RE-induced acute elevations in T prevented catabolism of muscle AR content post-RE, via enhanced AR mRNA translation and increased AR half-life. This evidence suggests RE prescription that maximally elevates T will likely optimize hypertrophic adaptations to RT via enhanced T–AR interactions.

STUDIES WITH OPPOSING PERSPECTIVE

Investigations in men with prostate cancer receiving androgen deprivation therapy (castrate T levels) and testosterone was truly necessary to the postexercise anabolic response. We view these data (29,43) as providing further support of a paradigm in which mechanisms that are intrinsic to the muscle itself and not dependent on systemic exercise-induced hormonal elevations, are responsible for contraction-mediated hypertrophy.

Doessing et al. (9) demonstrated that exogenous GH administration, which produces supraphysiological systemic GH and IGF-1 concentrations, does not stimulate myofibrillar protein synthesis but rather stimulates synthesis of collagen proteins. It is unknown whether exercise-induced GH/IGF-1 could also be stimulating collagen synthesis and thus strengthening connective tissue, which might be advantageous in supporting a bigger stronger muscle as the result of resistance training. From a practical standpoint, in our studies of elbow flexor hypertrophy, the high GH/IGF-1 condition did not result in any difference in morphological (fiber or muscle CSA) or functional measure (1 or 10 RM or isometric strength) that we measured versus a low (~basal) GH/IGF-1 condition. Therefore, if there was some unmeasured difference in the composition of the connective tissue between conditions, it had no benefit to strength or hypertrophy. We do know that exercise-induced GH does not describe the training-induced phenotype. For example, peak GH concentration and area under the curve (AUC) are greater after cycling at 70% $\dot{V}O_{2max}$ than after resistance exercise (11). On the basis of these observations and studies by Doessing et al. (9), it is difficult to envision a plausible mechanism by which transient exercise-induced increments in GH or IGF-1 concentration stimulates hypertrophy. In contrast to GH, exogenous testosterone is unequivocal in its ability to stimulate hypertrophy; however, in an exercise-induced environment, what is the real anabolic potency of testosterone?

The anabolic properties of exogenously administered testosterone (4) are frequently and broadly cited as a rationale for the measurement of postexercise hormonal profiles, which are interpreted as a proxy for the anabolic potential of skeletal muscle. However, a crucial point is that muscle mass accretion during exogenous testosterone analog administration is related to cumulative androgen exposure, which is the product of both dose and duration (4). Figure 1 illustrates this point and why the application from exogenous to endogenous testosterone is a flawed comparison. Basically, the transient (~30 min) nature of exercise-induced testosterone is inconsequential compared with the sustained increases in testosterone with exogenous dosing which represents a markedly higher cumulative androgen dose and that results in muscle hypertrophy (4). We do not claim to have tested all the nuances of the endocrine response to resistance exercise. For instance, the numerous isoforms of GH (25) alone may always captivate speculation until they are each investigated, but this is a straw argument if skeletal

participating in RT programs have demonstrated significant improvements in muscle mass and strength; however, these gains are modest at best (10). Wilkinson et al. (48) evaluated 10 men, 21–22 yr, performing an 8-wk RT program, 3 d·wk^{-1} training frequency, with unilateral leg press and knee extension (three sets, 6–10 RM, 80–90% 1RM, 3-min RI). The 8-wk RT program did not elicit significant acute changes in T, GH, or IGF-1. CT scans revealed significant increases in muscle CSA. These findings suggest unilateral RE that does not induce significant acute elevations in T, GH, or IGF-I may still stimulate muscle hypertrophy. However, it is difficult to determine whether this anabolic response is "optimal" because we know that both RE and T supplementation independently stimulate skeletal muscle hypertrophy and that the combination of RE and T supplementation results in an even greater anabolic response (3,26).

SUMMARY

Dismissal of the role of RE-induced elevations in anabolic hormones to maximally stimulate skeletal muscle anabolism and hypertrophy appreciably understates the importance of these hormones to the physiological mechanisms responsible for hypertrophic adaptations to RT. The aforementioned studies supporting the prevailing perspective demonstrate that acute endogenous increases in anabolic hormones, as well as their influence on skeletal muscle receptors and resulting hypertrophic response, are critical to optimizing RE-induced adaptations and, thus, health and performance across the lifespan.

REPLY TO CHALLENGING VIEW

Post-RE elevations in anabolic hormones may not be "necessary" to promote some degree of skeletal muscle anabolism after an RT program, and a review of recent literature suggests that the research is inconclusive as to whether or not the post-RE anabolic hormonal response plays a significant role in skeletal muscle hypertrophy (32). We maintain that these elevations are critical to optimizing hypertrophic and strength gains as part of an integrative response to well-designed and applicable RE stimuli, leading to chronic functional improvements in skeletal muscle mass and force production.

Phillips et al. have proposed a unique "low and high" hormone exposure model to study the influence of acute changes in T, GH, and IGF-1 after RE and chronically with RT (43,44); however, their model includes supplementation with whey protein before and/or after RE albeit in both the low and high hormone groups. We contend that the inclusion of a protein supplement in this study design is a major confounding factor because it is well known that amino acids are potent hormone secretagogues that inhibit muscle protein breakdown and

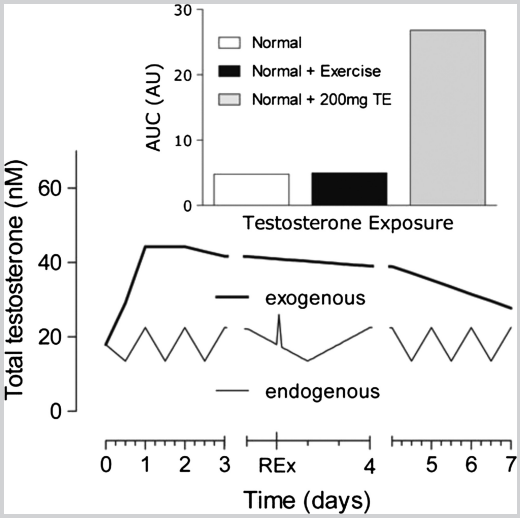

FIGURE 1—A comparison of the effect of exogenous testosterone (200 mg testosterone enanthate) (8) versus a schematic of the diurnal variation of testosterone throughout a given week, and the contribution of a "testosterone-spike" after a workout on day 4 to cumulative testosterone (inset shows testosterone area under the curve [AUC] on day 4 in arbitrary units [AU]).

muscle receptors for all these isoforms do not also exist. Similarly, although there are hundreds of resistance exercise program permutations, all of which could affect hormonal responses, we propose that the divergent hormone models that we used gave ample opportunity for the highly complex hormonally mediated "anabolic" responses to be manifest in phenotypically superior adaptations. What then are the implications of a theory that is not underpinned by exercise-induced hormones? From an applied standpoint, it means that exercise programs do not need to be designed based on hormonal nuances. It means that large muscle group exercises do not need to be paired with small exercises for the purpose of capturing "anabolic effects" derived from the hormonal response. From a basic sciences standpoint, hypertrophy that occurs with resistance training is mediated by intramuscular intrinsic processes which, as opposed to measuring systemic hormonal responses as being causative or influential in hypertrophy, are an area that we view as requiring further investigation.

REPLY TO PREVAILING PERSPECTIVE

We demur with Schroeder and Villanueva's assertion of evidence that greater hormonal responses provide an "optimal" anabolic environment; of course, we do not disagree with their initial concession that acute postresistance exercise increases in anabolic hormones may not be necessary to stimulate hypertrophy. This admission naturally means that other nonhormonal mechanisms can clearly dictate the entire hypertrophic response.

Schroeder and Villanueva begin by stating that "for purposes of this presentation, increases in testosterone

stimulate muscle protein synthesis, modulating skeletal muscle hypertrophy (20,28,41). The anabolic implications of protein supplementation are well documented (7,50). Dillion et al. (7) demonstrated that older women who have negligible circulating T and were not exposed to RE received amino acid supplementation for 3 months and had significant increases in basal muscle protein synthesis and increases in lean body mass, demonstrating the potent influence of amino acid supplementation on skeletal muscle anabolism, even in the absence of RE. In fact, Phillips et al. reported similar findings in young women with greater gains in muscle mass and strength when consuming fat-free milk post-RE compared with carbohydrates (19). Furthermore, the ingestion of casein and whey proteins 1 h after an RE bout results in greater muscle anabolism compared with the ingestion of a placebo after RE (40). Therefore, it could be argued that supplementation with protein in combination with an RE model may mask potential enhanced effects mediated by acute increases in anabolic hormones because of the powerful influence of amino acids on molecular transcription and translation processes involved in skeletal muscle protein synthesis.

Sex-based comparisons of myofibrillar protein synthesis after RE, with or without post-RE nutrient ingestion, emphasize two major concerns: 1) protein synthesis measured after an acute bout of RE (46) does not always occur in parallel with chronic upregulation of causative myogenic signals (5) and 2) it is not necessarily predictive of long-term hypertrophic responses to RT programs (39). In addition, circulating T levels are approximately 10-fold higher in men compared with women, and this is believed to be the primary rationale why men display substantially greater postpubescent muscle mass (18). Lastly, older women with low basal T levels display blunted increases in maximal strength and hypertrophy compared with those with higher T concentrations (15,16).

Phillips et al. previously reported that RE shortens the duration (<28 h), for which muscle protein synthesis is elevated after exercise (38). Yet they have designed an RT program (44) where participants trained once every 72 h for weeks 1–6 and once every 48 h for weeks 7–15, resulting in an average of less than two (1.87) RE sessions per week. From an applied perspective, this frequency of training stimuli is inadequate and likely related to the minimal growth experienced by both training groups. If the acute training stimulus for a hypertrophic adaptation is lacking because of an inadequate RE scheme design, it becomes difficult to justify the lack of RE-induced hypertrophy, let alone identify mechanisms contributing or not contributing to the chronic adaptive response.

Lastly, the selection of elbow flexor musculature should be challenged (44,46). How relevant is elbow flexor hypertrophy? How much additional growth can be

(T) and growth hormone (GH) will also imply increases in IGF-1" (22, 24). This is problematic because exercise-induced GH responses are robust and related to large muscle masses employed, whereas IGF-1 responses are equivocal. This problem is highlighted by merely examining the two studies (22,24) that the authors cite as justification for the "implied" IGF-1 response:

"SM-C [IGF-1] demonstrated random significant increases above rest in both males and females in response to both HREPs … The more anaerobic P-2 HREP produced a clear and sustained elevation of hGH…" (22).

"The pattern of SM-C did *not* consistently follow hGH changes … Furthermore, whereas an exercise protocol consisting of 10 repetitions and 1 min rest produced a greater GH AUC than other protocols, IGF-1 AUC was no different" (24).

Therefore, clearly changes in postexercise IGF-1 cannot be implied by changes in postexercise GH. More to the point, there is little evidence that exercise-induced GH mediates gains in strength and hypertrophy at all, through IGF-1 or otherwise as evidenced by numerous studies that are not citable here due to word limits; however, most notably, GH does not enhance myofibrillar protein synthesis (9) or hypertrophy (37).

The authors state, "Furthermore, we will limit the discussion of these adaptations to men…" This limitation is perplexing but we suspect that the reason that women are left out is that they do not conveniently fit the authors" "optimal hormonal" paradigm? For example, despite a 45-fold lower exercise-induced testosterone response than men (43), women show similar MPS (43) and hypertrophy (36) responses compared with men. Schroeder and Villanueva continue, "Three studies were selected that utilized short-term RT interventions and examined the influence of physiologically elevated acute hormonal responses on human skeletal muscle" (13,26). First, Schroeder and Villanueva overstate the original viewpoint of Goto et al. (13) who were far more cautious in concluding, "However, this interpretation [of a partial role in hypertrophy] of the circulating of GH *needs much precaution* [emphasis added]…" Second, reference 26 describes a study in which testosterone was pharmacologically ablated to concentrations that were *chronically* near castrate levels. We disagree with the viewpoint that this is an experimental paradigm that is reflective of the effect of *physiological* acute exercise-induced hormone responses on hypertrophy (discussed further in the following sections). Finally, the third study is an unpublished study by Schroeder and Villanueva's laboratory and thus cannot be scrutinized.

Schroeder and Villanueva rely on more research of questionable relevance to the exercise-induced question, citing a resistance training study in cancer patients undergoing ADT (again, this treatment reduces testosterone

experienced by such a small muscle mass in response to RT? We contend that the majority of RE protocols relevant to applied professions inevitably induce transient elevations in anabolic hormones, specifically training multiple compound movements before isolation movements within a single RE bout (at least 4–6 movements total), using moderate to high volumes, moderate to high training loads, and short rest interval lengths in between sets. We believe that investigations of adaptations elicited by RE protocols that are not of value to clinicians or strength and conditioning professionals considerably limits the meaningfulness, applicability, and clinical relevance of the findings.

CONCLUDING STATEMENT

The anabolic hormonal milieu is necessary to maximize functional adaptations to RT. Although post-RE elevations in anabolic hormones may not be necessary to acutely stimulate muscle protein synthesis or promote hypertrophy of small muscle masses, these elevations in anabolic hormones are ideal to optimize functional performance gains in whole body skeletal muscle mass and strength in men and women across the lifespan.

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to near castrate levels 24 h a day). Notwithstanding limited relevance, it is interesting (and encouraging for those undergoing ADT) that robust gains in strength and hypertrophy, that are similar to gains in healthy individuals, can still be achieved by using high intensity resistance exercise protocols even despite undergoing ADT (17). Further references cited by Schroeder and Villanueva continue to have limitations as to the insight they provide. For example, Willoughby and Taylor (49) compared resistance exercise to a nonexercised control. Spiering et al. (35) showed divergence in androgen receptor content at one of two time points postexercise but because androgen receptor content was the lone outcome measure in that study, it is impossible to determine whether these findings have implications for hypertrophy. To summarize, we view Schroeder and Villanueva's interpretation of the studies cited to be lacking in support for the original question posed in some cases and incorrectly interpreted as being supportive in others.

Schroeder and Villanueva draw their perspective to a close by citing two interesting studies (4,26). Although seminal, in our view, these studies (4,26) have little to do with whether or not physiological postexercise testosteronemia mediates hypertrophy with resistance exercise. That is, testosterone ablation to hypogonadal levels (26) or exogenous testosterone administration to create supraphysiological testosteronemia (4) are not models that come close to mimicking exercise-induced androgen exposure. There are several reasons

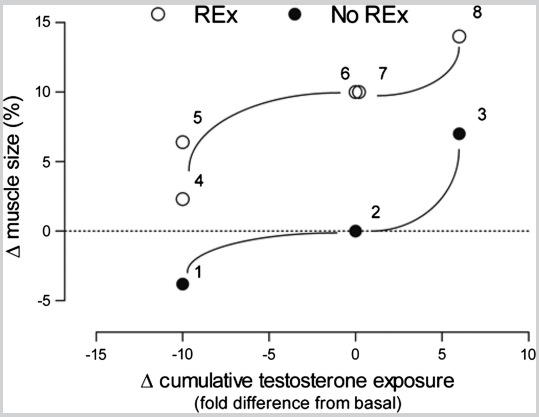

FIGURE 2—Fold changes in cumulative testosterone (from basal rested) versus hypertrophy curve. Data points 6 and 7 show postexercise testosterone (low vs high respectively) within a physiological range having a negligible effect on cumulative androgen exposure and therefore hypertrophy. REx, resistance exercise; ADT, androgen deprivation therapy; TE, testosterone enanthate. Points with No REx: 1, from Smith et al. (34); 2, Reference point at position (0,0) representing young men no resistance exercise (REx); 3, from Bhasin et al. (3). Points with REx: 4, from Kvorning et al. (26); 5, from Hanson et al. (17); 6, average of low hormone condition from West et al. (44) and Ronnestad (31); 7, average of high hormone condition from West et al. and Ronnestad; 8, Bhasin et al. (3). Further research is required to determine the exact shape of the curve between data points (estimated).

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why pharmacologic elevations or ablation of testosterone cannot be used to "imply" relevance to transient postexercise testosteronemia. First, elevations in postexercise hormonal concentrations are fleeting compared with the long-lasting hypo- or hyperandrogenemia seen in pharmacological interventions (see Fig. 1). Second, pharmacological-induced hormone concentrations are far greater than those that occur in normal diurnal variation and transiently postexercise. Finally, pharmacological hyperandrogenemia is accomplished by administering testosterone derivatives that have different chemical structures, excretion kinetics and half-lives, and receptor affinities versus endogenous androgens and so do not appropriately mimic normal transient hormonal changes occurring postexercise.

We constructed Figure 2, using published data, to illustrate how changes in cumulative androgen exposure impact hypertrophy. According to Figure 2, atrophy occurs during hypotestosteronemia, but resistance training can provoke partial (26) or potentially full (17) hypertrophy responses. At top center, elevations in testosterone postexercise have a negligible effect on cumulative androgen exposure (data points 6 and 7 are nearly overlaid) and hypertrophy. Exogenously induced hyperandrogenemia enhances muscle mass; resistance training further enhances the gain in muscle mass. In summary, hyper- or hypoandrogenemic states bear little resemblance to short-lived (~30 min) exercise-induced hormonal changes; therefore, we fail to see the relevance of arguments that invoke these states as being supportive of the original topical question that was posed. Overall, a hypothesis that is based on cumulative androgen exposure explains why transient exercise-induced elevations in testosterone do not have a significant effect on hypertrophy.

CONCLUDING STATEMENT

It is time to write the requiem for studies that measure only postexercise hormonal responses and infer a potential effect on hypertrophy. We find that the evidence for such an assertion lacking and causal interpretation unwarranted given the lack of evidence that exercise-induced hormones are important in regulating hypertrophy after resistance exercise. Moreover, pharmacologic ablation and exogenous androgen administration are not appropriate models from which to draw conclusions about the effect of exercised-induced changes in hormonal concentrations on hypertrophy.

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