

Steroid use and human performance: Lessons for integrative biologists

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Synopsis While recent studies have begun to address how hormones mediate whole-animal performance traits, the field conspicuously lags behind research conducted on humans. Recent studies of human steroid use have revealed that steroid use increases muscle cross-sectional area and mass, largely due to increases in protein synthesis, and muscle fiber hypertrophy attributable to an increased number of satellite cells and myonuclei per unit area. These biochemical and cellular effects on skeletal muscle morphology translate into increased power and work during weight-lifting and enhanced performance in burst, sprinting activities. However, there are no unequivocal data that human steroid use enhances endurance performance or muscle fatigability or recovery. The effects of steroids on human morphology and performance are in general consistent with results found for nonhuman animals, though there are notable discrepancies. However, some of the discrepancies may be due to a paucity of comparative data on how testosterone affects muscle physiology and subsequent performance across different regions of the body and across vertebrate taxa. Therefore, we advocate more research on the basic relationships among hormones, morphology, and performance. Based on results from human studies, we recommend that integrative biologists interested in studying hormone regulation of performance should take into account training, timing of administration, and dosage administered when designing experiments or field studies. We also argue that more information is needed on the long-term effects of hormone manipulation on performance and fitness.

Introduction

One of the most widely discussed and controversial arenas of human performance concerns the use of steroid supplements to enhance athletic ability for a variety of sports, ranging from bicycling to baseball. There is strong evidence that human athletes have attempted to enhance their athletic performance using steroids since the 1950s, but whether, and in which sports, steroids are actually effective remains controversial (reviewed by Ryan 1981; George 2003; Hartgens and Kuipers 2004). In general, steroids used by athletes encompass a wide variety of forms of the androgen testosterone (George 2003), and most seem to have the classical androgenic and anabolic effects on men, although steroid use by women cannot be ignored (Malarkey et al. 1991; Gruber and Pope 2000). Alternative forms of testosterone (e.g., testosterone enanthate, methandrostenolone) are typically used by those desiring enhanced performance because ingested or injected testosterone is quickly metabolized into inactive forms (Wilson 1988). Thus, studies of humans that we

cite involve testosterone derivatives. Early studies of the effects of steroids on human performance, however, had major flaws in design, such as lack of control groups and a double-blind procedure, the presence of confounding factors (e.g., differences in level of exercise and in motivation), and inappropriate statistical techniques (reviewed by Bhasin et al. 2001; George 2003). These problems left open for many years the question of whether, and in what capacity, steroids actually enhance athletic performance, until more recent studies conclusively showed significant effects of steroids.

The topic of steroid effects on human athletic performance is germane to an emerging field of research investigating hormonal effects on animals' performance (e.g., sprint speed, endurance capacity, bite-force capacity) (Husak et al. 2009a), as testosterone may exert general effects on performance across widely divergent vertebrate taxa. Our goal in this review is to interpret the effects of steroids on human performance in this broader context of hormonal effects across a wider range of taxa.

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We are particularly interested in drawing lessons and potential avenues of research for animal biologists from published research on humans. We have performed a selective review of studies examining how humans' use of steroids affects skeletal muscle physiology and subsequent athletic performance. While studies of performance on nonhumans have dealt extensively with the effects of morphological traits on performance and the impact of performance on individual fitness (Arnold 1983; Garland and Losos 1994; Irschick and Garland 2001; Irschick et al. 2007, 2008; Husak et al. 2009a), there has been relatively little synthetic discussion of how hormones affect performance in non-human animals. We also point the reader towards several recent reviews of steroid use and performance by humans for details not discussed in our review (Bhasin et al. 2001; George 2003; Hartgens and Kuipers 2004).

General effects of testosterone on the phenotype of males

The development of primary and secondary sexual characteristics is stimulated by testosterone in vertebrate males, and these effects can be either organizational or activational in nature (Norris 1997; Hadley 2000). Organizational effects tend to occur early in development, and during a critical window of time, thereby resulting in permanent effects. On the other hand, activational effects occur in adults, and the effects are typically temporary (Arnold and Breedlove 1985). The hypothalamus stimulates production of gonadotropin-releasing hormone, which in turn stimulates production of luteinizing hormone in the anterior pituitary. Luteinizing hormone then stimulates production of testosterone in the Leydig cells of the testes. Testosterone then circulates throughout the body where it exerts effects on multiple target tissues that have the appropriate receptors or appropriate enzymes (e.g., aromatase or 5α -reductase) to convert testosterone for binding to other types of receptors (Kicman 2008). The widespread effects of circulating levels of testosterone on aggression, secondary sexual traits, and growth of skeletal muscle in males of many vertebrate species are well-documented (Marler and Moore 1988; Wingfield et al. 1990; Ketterson and Nolan 1999; Sinervo et al. 2000; Ketterson et al. 2001; Oliveira 2004; Adkins-Regan 2005; Hau 2007; contributions in this issue). In particular, production of testosterone by males has been linked with the expression of color and behavioral display signals, as well as aggression (Marler and Moore 1988; Kimball and

Ligon 1999; Hews and Quinn 2003; Adkins-Regan 2005; Cox et al. 2008) and increased growth (Fennell and Scanes 1992; Borski et al. 1996; Cox and John-Alder 2005), although this latter effect may depend on specific selective pressures on males (Cox and John-Alder 2005).

Effects of testosterone on the physiology of human skeletal muscle

Testosterone has multiple effects on skeletal muscle at the biochemical and cellular levels, but the direct cause-and-effect relationships among these effects are still unclear (Sinha-Hikim 2002; Hartgens and Kuipers 2004). The studies that we discuss here, and throughout the paper are from experiments or correlative studies conducted on adult individuals such that the effects seen are activational in nature, causing rather rapid changes to the phenotype. Increased testosterone causes increased protein synthesis by muscle cells (Griggs et al. 1989; Kadi et al. 1999; Hartgens and Kuipers 2004), which is necessary for anabolic effects and an increase in lean muscle mass. Sinha-Hikim et al. (2002) found a dose-dependent increase in the mean number of myonuclei found in skeletal muscle fibers (*vastus lateralis* muscle) with testosterone supplementation, as well as in the number of myonuclei per fiber (see also Eriksson et al. 2005). This increase was also associated with an increase in the number of satellite cells in the muscle tissue (but see Eriksson et al. 2005). Satellite cells are progenitor cells found external to muscle fibers that are incorporated into fibers and promote repair and growth of the muscle (Kadi and Thornell 2000; Reimann et al. 2000). However, the mechanism by which testosterone causes an increase in the number of satellite cells is unknown and could be due to testosterone (1) promoting cell division of satellite cells, (2) inhibiting apoptosis of satellite cells, or (3) causing differentiation of stem cells into satellite cells (Sinha-Hikim 2002). In any case, the functional implications for these findings are clear. More satellite cells likely result in more myonuclei per fiber, which, combined with increased protein synthesis, contribute to increases in muscle growth via an increased number and hypertrophy of muscle fibers (Kadi 2000; Kadi and Thornell 2000).

Testosterone also appears to cause a dose-dependent increase in the cross-sectional area of muscle fibers, although details about which types of fibers are affected and where in the body this occurs remains equivocal. Testosterone may increase the cross-sectional area of both type I

(oxidative “slow twitch”) and type II (glycolytic “fast twitch”) fibers simultaneously after administration (Sinha-Hikim 2002; Eriksson et al. 2005), but other studies have shown greater increases in type I than in type II fibers (Hartgens et al. 1996; Kadi et al. 1999; also in growing rats, Ustunel et al. 2003), increased size in only type I fibers (Alén et al. 1984; Kuipers et al. 1991, 1993), or increased size in only type II fibers (Hartgens et al. 2002). These mixed results are intriguing, because they suggest that different parts of the body, and, hence, different performance traits, may be affected differently by elevated testosterone levels. The likely mechanism for these differences is variation in density of receptors within the myonuclei of muscle fibers in different regions of the body (Kadi 2000; Kadi et al. 2000). An alternative hypothesis is that different types of fiber have differing relationships between the number of internal myonuclei and muscle cross-sectional area during hypertrophy (Bruusgaard et al. 2003). That is, some types of fibers may have internal myonuclei that can serve larger “nuclear domains” than can other types of fibers (reviewed by Gundersen and Bruusgaard 2008). If either of these hypothesized mechanisms is correct, then circulating levels of testosterone may only explain a portion of inter-individual (or interspecific) variation in performance. Testosterone may also stimulate changes in the proportions of types of fibers in muscles (Holmang et al. 1990; Pette and Staron 1997), although evidence for this effect in humans is mixed. For example, Sinha-Hikim et al. (2002) did not observe a change in the proportions of type I and type II fibers after administration of testosterone.

Changes in lower-level traits (e.g., protein synthesis, number of satellite cells, cross sectional area of muscle fibers) after testosterone supplementation, as described above, thus, result in changes at the whole-muscle level and explain many of the classic effects of testosterone that are desired by humans using steroids. That is, increasing testosterone via steroid use increases body weight, lean body mass, as well as cross-sectional area, circumference, and mass of individual muscles (i.e., “body dimensions”); however, there are numerous studies with contradictory results, finding no change in one, or all, of these traits, depending on the drug used, the dose taken, and the duration of use (reviewed by Bhasin et al. 2001; Hartgens and Kuipers 2004). The finding that testosterone can change muscle physiology and increase whole-muscle size and/or body mass is consistent with results in nonhuman animals. For example, testosterone implants increased size and

number of fibers in the sonic muscles of male plainfin midshipman fish (*Porichthys notatus*) (Brantley et al. 1993). Similarly, testosterone supplementation increased muscle mass and changed contractile properties of trunk muscles of male grey treefrogs (*Hyla chrysoscelis*) (Girgenrath and Marsh 2003) and of forelimb muscles of male frogs (*Xenopus laevis*, Regnier and Herrera 1993; *Rana pipiens*, Sidor and Blackburn 1998).

Effects of testosterone on humans’ performance

Whether steroids actually enhance performance of athletes was a subject of great controversy throughout the 1980s and 1990s (Ryan 1981; Haupt and Rovere 1984; Cowart 1987; Wilson 1988; Elashoff et al. 1991; Strauss and Yesalis 1991; Hartgens and Kuipers 2004), largely due to flaws in design of early studies (see above). However, the past decade has seen a surge in more carefully designed studies that have convincingly tested whether, all else equal, steroids increase performance. Hartgens and Kuipers (2004) found that 21 out of 29 studies they reviewed found an increase in humans’ strength after steroid use, with improvements in strength ranging from 5% to 20%. Storer et al. (2003) found that testosterone caused a dose-dependent increase in maximal voluntary strength of the leg (i.e., amount of weight lifted in a leg press), as well as in leg power (i.e., the rate of force generation). They further tested whether increased muscle strength was due simply to increased muscle mass or to changes in the contractile quality of muscle affected by testosterone, but they found no change in specific tension, or in the amount of force generated per unit volume of muscle. This latter result suggests that, at least for leg-press performance, testosterone increases strength by increasing muscle mass and not by changing contractile properties. Rogerson et al. (2007) found that supraphysiological doses of testosterone increased maximal voluntary strength during bench presses (see also Giorgi et al. 1999) and increased output of work and output of power during cycle sprinting compared to placebo control subjects. Thus, “burst” or “sprint” performance traits appear to be enhanced by increased testosterone, and this is in general agreement with studies of nonhuman animals (John-Alder et al. 1996, 1997; Klukowski et al. 1998; Husak et al. 2007). For example, experimentally elevated levels of testosterone caused increased sprint speed, relative to sham-implanted individuals, in northern fence lizards (*Sceloporus undulatus*) (Klukowski et al. 1998). These findings contrast with results for

endurance events, in which no increase in performance has been detected experimentally in humans (reviewed in George 2003; Hartgens and Kuipers 2004). The finding that endurance by humans is not enhanced by testosterone is unexpected since testosterone may increase hemoglobin concentrations and hematocrit (Alén 1985, but see Hartgens and Kuipers 2004) and exogenous testosterone increases endurance in rats (Tamaki et al. 2001) and male side-blotched lizards (*Uta stansburiana*) (Sinervo et al. 2000). More studies of the effects of increased testosterone on endurance would help to better clarify these seemingly paradoxical findings. One possibility that might explain species' differences in endurance is the relative proportion of type I fibers available for enhancement, which likely varies across species (Bonine et al. 2005), although this hypothesis needs explicit testing. Steroid use does not seem to consistently enhance recovery time after strenuous exercise (reviewed in Hartgens and Kuipers 2004), although it may in non-human animals (Tamaki et al. 2001). Storer et al. (2003) also found no change in fatigability (i.e., the ability of a muscle to persist in performing a task) of muscle during exercise, which is consistent with other studies (George 2003).

One of the problems in early studies of steroid effects was that the participants' history of training and exercise while taking steroids was not taken into account or controlled (Bhasin et al. 2001; George 2003; Hartgens and Kuipers 2004). Recent studies have shown that the presence or absence of exercise training during testosterone supplementation can have a marked impact on how much performance is enhanced, thus complicating results when training is not controlled. Bhasin et al. (2001) reviewed several examples of such results. They pointed out that testosterone supplementation alone may increase strength from baseline levels, but so will exercise alone with a placebo, such that strength levels with exercise alone are comparable to those with testosterone addition alone (Bhasin et al. 1996). Testosterone supplementation while undergoing exercise training typically has the greatest increase in strength compared to exercise only or testosterone only (Bhasin et al. 1996, 2001). These findings are consistent with those of others (reviewed by George 2003). Indeed, George (2003) suggested that steroids will only consistently enhance strength if three conditions are met: (1) steroids are given to individuals who have been training and who continue to train while taking steroids, (2) the experimental subjects have a high protein diet throughout the experiment, and (3) changes in performance are measured by the

technique with which the individuals were training while taking steroids. That is, one may, or may not, find a change in bench-press performance if individuals trained with leg presses, and not bench presses, while taking steroids. We note that the confounding effect of training is a rather intuitive finding, but it does point out potential problems in studies of non-human animals, specifically laboratory studies, which we address below.

Implications of studies of humans for studies of nonhuman animals

Given the effects of steroids on physiology and performance of human muscle, what can integrative biologists take away from these findings? We suggest that they can provide some valuable insights into the mechanisms of how hormones might regulate whole-animal performance traits in nonhuman animals. The most obvious lesson is that manipulating the circulating levels of testosterone, or its derivatives, increases overall strength, which has apparent benefits for performance in bursts, such as sprint speed. In contrast, there is little evidence from studies on humans for a positive effect on capacity for endurance, which is counter-intuitive, given the known effect of testosterone on hemoglobin concentrations and hematocrit. However, these same studies of humans also raise a host of issues that merit special consideration by researchers interested in hormonal effects on nonhuman animals, including effect of training, timing of administration, and dosage administered. We also argue that more information is needed on the long-term effects of hormonal manipulation on performance and fitness. Although recent studies suggest that increasing testosterone levels can enhance certain types of performance, we are not advocating or justifying the use of steroids by humans. There are numerous side effects of prolonged steroid use in humans, including cardiovascular problems, impaired reproductive function, altered behavior, increased risk of certain tumors and cancers, and decreased immune function, among others (reviewed by Pärssinen and Seppälä 2002; George 2003). These "side-effects" are in accordance with studies of nonhuman animals where higher testosterone levels are associated with such detrimental effects as increased loads of parasites, reduced immunocompetence, decreased body condition, reduced growth, and increased use of energy, ultimately resulting in reduced survival (Marler and Moore 1988; Folstad and Karter 1992; Salvador et al. 1996; Wikelski et al. 1999, 2004; Moore et al. 2000; Peters 2000; Klukowski and

Nelson 2001; Wingfield et al. 2001; Hau et al. 2004). Indeed, it is the presence of these very “side-effects” that has driven a great deal of research on behavioral and life-history tradeoffs mediated by testosterone (Ketterson and Nolan 1999; Ketterson et al. 2001). Higher levels of testosterone may enhance performance and increase success at some tasks, but its widespread “pleiotropic” effects on other aspects of the phenotype may result in a net detriment to fitness (Raouf et al. 1997; Reed et al. 2006; Ketterson et al. 2009).

We encourage researchers to complete more detailed studies of the interactions among hormones, morphology, and performance, especially across different types of performance traits (dynamic versus regulatory, see Husak et al. 2009a). Comparative data on whether the same, or different, hormones affect the same performance traits in different taxa (e.g., burst speed in fish, sprint speed in lizards) would be useful for understanding how different species have evolved unique, or conserved, endocrine control of morphology and function. A comparative approach is important, as other studies have shown different effects of testosterone on performance in different taxa (e.g., an increase in endurance for rats and lizards, but none for humans), and more research is needed to determine whether such differences are valid or purely methodological. Even though testosterone is confined to vertebrates, it is possible that studies with invertebrates may reveal similar effects on performance via different hormones, e.g., recent work showing a seemingly similar role of juvenile hormone for invertebrates as testosterone has for vertebrates (Contreras-Garduno et al. 2009; see also Zera 2006; Zera et al. 2007; Lorenz and Gäde 2009).

Correlative studies relating endogenous circulating hormone levels to natural variation in performance traits can provide valuable insight into potential mechanistic regulators of performance, but manipulations allow a more detailed examination of cause-and-effect relationships. Whether performance can be manipulated by reduction (castration) or supplementation (implants) of testosterone in non-human animals will depend on the type of performance and how it is affected by circulating levels of the androgen. Many dynamic performance traits, especially maximal performance, may show different responses to exogenous hormone in the laboratory versus field, compared to coloration or “behavioral” traits. For example, supplementation with testosterone may rapidly increase display behavior or aggression in the laboratory (Lovern et al. 2001; Hews and Quinn 2003) compared to control

animals, or corticosterone supplementation may decrease sexually selected color patterns (reviewed by Husak and Moore 2008). These examples are in contrast to supplementing testosterone in the laboratory and testing for an effect on performance. Aggression and coloration will not likely require training of the target trait to reveal an observed effect, whereas some performance traits may require training. Furthermore, regulatory performance traits (e.g., regulation of ions in seawater), on the other hand, may respond more directly to hormonal manipulation (see McCormick 2009), and will likely not require any training, but more empirical data are necessary to make generalizations.

It is also important to more closely inspect those traits that show no significant effect of testosterone on dynamic performance after manipulation in the laboratory. Such a “noneffect” may be due to numerous possibilities, the most obvious of which is that testosterone simply has no effect on a particular type of performance. However, a second possibility is that muscles involved in performance were not adequately trained during administration of supplemental testosterone, or there was no control of exercise during the period of testosterone administration. As an hypothetical example, one might not expect to see a large increase in the maximal flight speed of birds that were never allowed to fly following administration of exogenous testosterone. Indeed, *Gallotia galloti* lizards given exogenous testosterone were compared to lizards given sham implants and there was no difference in maximal bite force at the end of the experiment (K. Huyghe, J.F. Husak, R. Van Damme, M. Molina-Borja, A. Herrel, in review), despite increases in mass of the jaw muscles in testosterone-supplemented males. One possible explanation for this result is that these lizards did not “train” their jaw muscles enough while in captivity to increase muscle mass sufficiently to result in a measurable enhancement of performance. It is also possible that receptor density is very low or becomes low in trained muscles. Nevertheless, while training in animals seems straightforward in principle, in practice it is far trickier, and there also appear to be striking differences among species in the effects of training. Whereas some studies of mammals have successfully increased performance through training in a laboratory (Brooks and Fahey 1984; Astrand and Rodahl 1986), similar studies with lizards have found no effect (Gleeson 1979; Garland et al. 1987). In addition, while training might be successful with animals acclimated to a laboratory setting, inducement of stress, with a concomitant effect on corticosterone (Moore and Jessop 2003), and potentially

circulating testosterone levels, is a significant confounding factor. Another complementary option is to use field studies, where experimental groups are released into the wild to “train” themselves while accomplishing their day-to-day tasks and performing naturally. Of course, this approach also cannot take into account variation in “training” within experimental groups, as individuals will likely use their performance traits in different ways when left to their own devices. Consequently, this approach could result in unpredictable results in how hormones impact performance, unless one accepts the unlikely assumption that all experimental animals are performing in the same ways. Further, a field approach also does not take into account other “pleiotropic” effects of increased (or decreased) testosterone on the phenotype (e.g., increased activity or conspicuousness to predators), which can eliminate potential benefits to fitness from enhanced performance due to testosterone supplementation.

Studies seeking to manipulate performance with testosterone supplementation should also consider the timing of experiments. For example, testosterone should ideally be increased or decreased during times when the hypothalamic–pituitary–gonad (HPG) axis is responsive and receptors are expressed in the appropriate target tissues. Seasonal sensitivity of the male HPG axis is well documented (Fusani et al. 2000; Jawor et al. 2006; Ball and Ketterson 2008), and such effects should be considered. For example, male green anoles (*Anolis carolinensis*) given exogenous testosterone after the end of the breeding season in a laboratory setting did not increase head size or bite-force performance (J. Henningsen, J. Husak, D. Irschick, and I. Moore, unpublished data), presumably because some or all of the relevant target tissues were no longer sensitive to androgens. On the other hand, male brown anoles (*Anolis sagrei*) did show enhanced maximal bite force when testosterone was supplemented at the beginning of the breeding season when the target tissues are presumably sensitive to androgens (Cox et al., in press). Timing of experimentation is thus critical for designing studies examining hormonal effects, and the interaction between timing and training should also be considered, as training effects may be relevant for some seasonal periods, but not for others.

A related issue concerns how much hormone to administer to experimental subjects. Studies of human steroid use typically involve supraphysiological doses of testosterone, as this is the typical regimen for steroid-abusing athletes (George 2003; Hartgens and Kuipers 2004). Indeed, many studies

of steroid use by humans have been criticized for having experimental groups using physiological doses of testosterone. However, such criticism of seemingly unrealistic dosages highlights the differing goals of studies on human and non-human animals. Whereas studies of humans are focused on the role of supraphysiological doses on performance, those of nonhuman animals are more broadly interested in whether circulating testosterone affects performance within more natural bounds of variation (reviewed by Fusani et al. 2005; Fusani 2008). Supraphysiological doses can result in unexpected, or even counterintuitive, effects because endocrine systems tend to be homeostatic and compensatory after disruption via up- or down-regulation of various components within the system (Brown and Follett 1977).

There are few data on how testosterone affects dynamic performance during different stages of development, either in humans or in non-human animals. Practically all studies examining the effects of exogenous testosterone on humans have been on adults (reviewed by Hartgens and Kuipers 2004), but an increasing area of concern is steroid use by teenagers (Johnston et al. 2005). Because they are still developing physically, steroids may have dramatically different effects on dynamic performance in developing juveniles versus older adults. For example, steroid use is known to cause closure of growth plates of long bones (George 2003), potentially preventing growth to full height. Any manipulative hormone study examining effects on dynamic performance should also take baseline circulating levels into account, as there may be striking differences among age groups. For example, among sexually mature male green anole lizards in a well-studied New Orleans, Louisiana (USA) population, smaller “light-weight” males have lower circulating testosterone levels (Husak et al. 2007, 2009b), relatively smaller heads, and lower bite forces than do larger “heavy-weight” males (see Lailvaux et al., 2004; Vanhooydonck et al., 2005a), with the difference apparently due to age (Irschick and Lailvaux 2006). Smaller males with low testosterone levels seem unable to produce higher levels (Husak et al. 2009b), suggesting that testosterone levels are likely suppressed until a critical body size when the individuals become competitive with larger males. At this body size, elevated testosterone levels may accelerate growth of the head and increase bite force, although more data are needed to test this hypothesis. This ontogenetic increase in testosterone levels suggests that exogenous administration will have quite different effects on different age groups. For example, many hormones exert threshold effects

(reviewed in Hews and Moore 1997) in which increased amounts above a threshold level produce little noticeable effect, suggesting that exogenous administration may accomplish little for larger lizards already with high testosterone levels, but may have substantial effects on smaller lizards with low testosterone levels.

In this context, long-term studies in animal species that focus on younger individuals (see Cox and John-Alder 2005 and references therein) might be useful for understanding the potential costs and benefits of hormones in improving or decreasing dynamic performance. Scientists are well-aware of some of the short-term activational effects of testosterone in humans and nonhuman animals, but while some long-term effects of supraphysiological doses on human health are recognized (see Hartgens and Kuipers 2004), we know far less about long-term effects of elevated (but not supraphysiological) testosterone levels on longevity and lifetime reproductive success of nonhuman animals. Ethical considerations may preclude long-term hormone implantation in humans and nonhuman animals, but correlating natural variation in testosterone levels both with performance traits and with other demographic features, such as longevity and lifetime reproductive success, would be useful for understanding chronic effects. Elegant studies with the dark-eyed junco (*Junco hyemalis*) (Ketterson et al. 2001; Reed et al. 2006) show complex trade-offs between different components of reproductive success (e.g., investment in extra-pair fertilizations versus parental care) as a result of testosterone supplementation; other similar trade-offs might be occurring over longer time spans in other animal species.

Conclusions

Despite popular interest in steroids and their effects on human athletic performance, we still lack a broad understanding of the effects of testosterone on performance in different animal species.

Our review of the literature on human steroids highlights several issues that could prove useful for integrative biologists interested in determining links among hormones, morphology, performance, and fitness in nonhuman animal species. First, studies of steroid use by humans reveal many caveats related to experimental design and interpretation that should be considered by those studying nonhuman animals (e.g., training, diet, dosage effects). Second, because of conflicting results of testosterone on

different performance traits (e.g., burst performance versus endurance), more data are needed for such biomechanically opposing performance traits; testosterone may enhance multiple kinds of performance in some species, and only one kind in another. Third, while testosterone may have some general effects on dynamic performance in vertebrates, are there other hormones (e.g., juvenile hormone) that play a similar role in invertebrates? Finally, human steroid abusers often use various systems of “stacking”, where multiple drugs are taken in a specific order (George 2003), and such regimens are believed, by those who use them, to markedly increase dynamic performance. However, few studies have specifically examined how these regimes affect performance, or how the different regimes may be more, or less, effective in enhancing performance, either in humans or in non-human animal species. Furthermore, such practices are not restricted to multiple androgens, but may also include other hormones, such as growth hormone and insulin-like growth factor-I, which may, when taken exogenously, also enhance athletic performance and other aspects of the phenotype (Gibney et al. 2007). In this manner, the interactive effects of different hormone regimens for increasing animal performance are highly understudied. In conclusion, we have advocated an integrative approach for studying the evolution of morphology, function, and endocrine systems, and increased collaboration between researchers interested in human and in other animal systems may prove fruitful for both groups.

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