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PERSPECTIVES

Persistent physiological benefits from doping? Ethical implications for sports integrity

Pedro L. Valenzuela,[1,2] Sebastian Sitko,[3] and Yannis Pitsiladis[4,5]

[1]*Physical Activity and Health Research Group ('PaHerg'), Research Institute of Hospital 12 de Octubre ('imas12'), Madrid, Spain;* [2]*Department of Systems Biology, University of Alcalá, Madrid, Spain;* [3]*Department of Physiatry and Nursery, University of Zaragoza, Zaragoza, Spain;* [4]*International Federation of Sports Medicine (FIMS), Lausanne, Switzerland; and* [5]*Department of Sport, Physical Education, and Health, Hong Kong Baptist University, Kowloon Tong, Hong Kong*

Abstract

The effects of some widely abused doping substances such as anabolic androgenic steroids (AAS) on performance are well documented, particularly in the short term, and the use of these substances is banned by various sporting authorities, with athletes sanctioned from competing for up to 4 years. However, controversy exists on whether residual physiological effects of some doping practices could persist even years after discontinuation, granting unfair advantages to athletes long after sanctions have been served. Particularly, in support of the so-called muscle memory theory, growing evidence in both animals and humans suggests that AAS administration could exert long-term effects at the muscle level, notably a higher number of myonuclei. This effect could enhance retraining/muscle remodeling capacity long after AAS cessation, thus supposing an advantage for doped athletes even +4 years after doping practices have been discontinued. If confirmed, the persistence of physiological improvements resulting from past doping practices raises serious ethical concerns in the sports field and opens the door to lifelong sanctions.

anabolic steroids; doping; muscle memory; performance

Doping in sport remains a pervasive issue, with some athletes seeking illicit means to enhance their performance. The effects of some widely abused doping substances such as anabolic androgenic steroids (AAS) on performance are well documented, particularly in the short term (1), and the use of these substances is usually banned by various sporting authorities, with athletes sanctioned from competing for up to 4 years (although duration might depend on several factors). However, controversy exists on whether residual physiological effects of some doping practices could persist even years after discontinuation, granting unfair advantages to athletes long after sanctions have been served.

Despite their associated adverse health effects, AAS are abused by athletes mainly due to their short-term benefits on muscle strength and body composition (e.g., increased muscle mass), with potential—albeit still not consistently confirmed—effects also observed in endurance and exercise recovery (2). Growing evidence suggests, however, that some beneficial effects could also be obtained in the long term. This hypothesis would be particularly supported by the so-called muscle memory theory, which suggests that previously untrained fibers recruit myonuclei from activated satellite cells before hypertrophic growth, and then this higher number of myonuclei is retained in the long term even after processes of detraining or atrophy (3, 4).

Confirming the abovementioned theory, seminal studies by Kadi et al. and Eriksson et al. reported that high-level powerlifters who admitted having taken AAS for ~10 years had not only a larger muscle fiber size than their peers who had never taken these substances but also a greater number of myonuclei per fiber (5, 6). Years later, a study in mice confirmed that short-term treatment with AAS (testosterone propionate) induced a large increase in fiber size and in the number of myonuclei (7). Interestingly, 3 wk after discontinuation of AAS treatment, muscle fiber size decreased to the values observed in a sham group, but the number of nuclei remained elevated for at least 3 months (>10% of the mouse lifespan, equivalent to 8–10 yr in humans' age) (7). Moreover, this persistent increase in myonuclei maximized training-induced adaptations compared with the sham group when mice were again submitted to overload exercise, thus supporting the so-called "muscle memory" concept (7). The abovementioned findings in rodents argue strongly that AAS could exert long-lasting increases in the number of myonuclei, which might facilitate training adaptations even years after doping practices have been discontinued (Fig. 1).

More research is needed to confirm the muscle memory concept in general, particularly in humans (8), and the long-term effects of AAS in particular. However, recent studies seem to support this notion. A study has recently shown that

Correspondence: P. L. Valenzuela (pedrol.valenzuela@uah.es).
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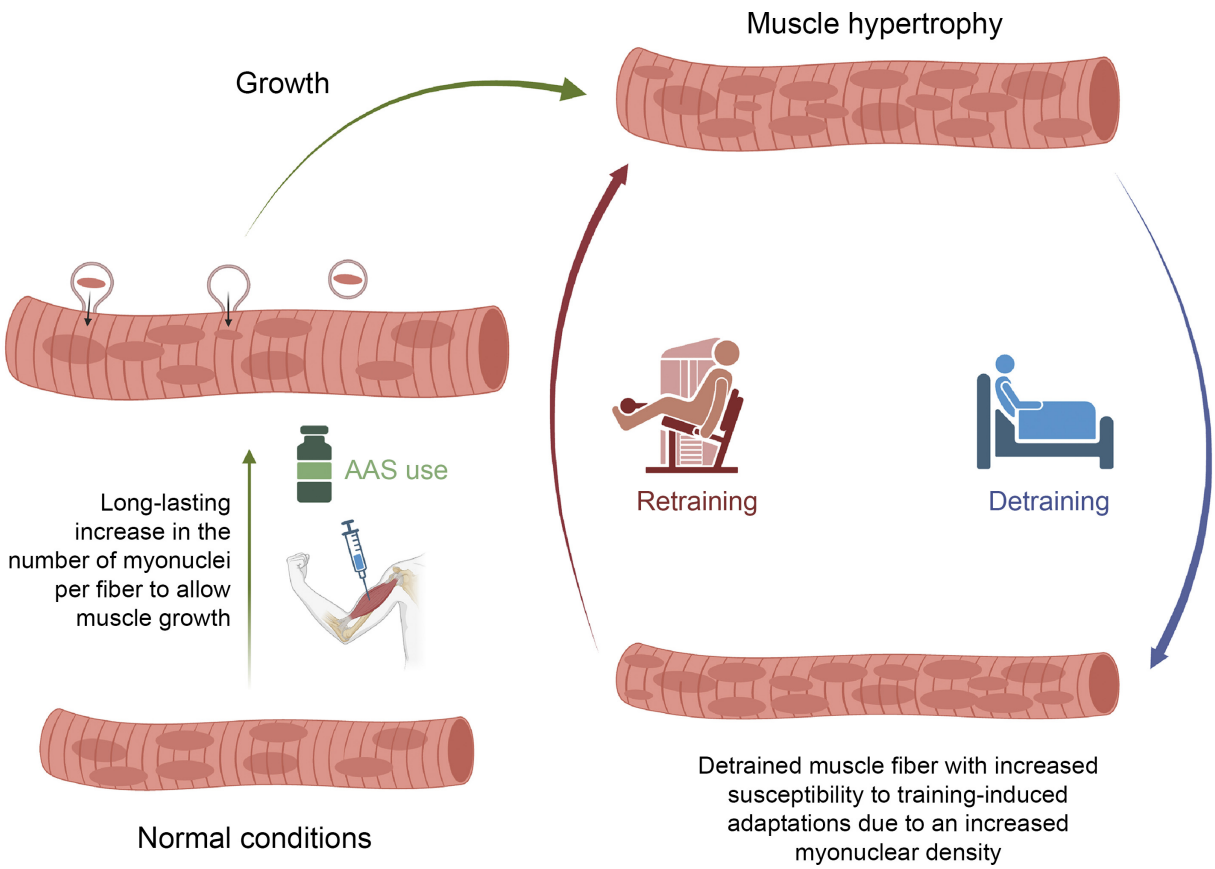

Figure 1. Potential long-term effects of anabolic androgen steroids (AAS) exposure.

old mice that had been treated with AAS during youth show higher rates of muscle protein synthesis compared with age-matched animals who had received a sham condition (9). In humans, Nielsen et al. (10) found a higher myonuclear density and DNA to cytoplasm ratio in former users of AAS (mean time since remission of 4 years, range 1–13) compared with a control group, with myonuclear density positively correlated with the time of AAS administration (10). Moreover, despite similar strength training frequency, former AAS users had greater lean body mass and maximal strength than controls (10). These findings suggest that AAS administration could enhance retraining/muscle remodeling capacity +4 years after AAS cessation, thus supposing a long-term advantage for doped athletes. More recently, we conducted a cross-sectional/longitudinal study involving 56 men aged 20 to 42 yr separated into 4 groups: nonresistance-trained, resistance-trained with no history of AAS, resistance-trained who had previously used AAS, or resistance-trained who were using AAS (11). Moreover, a subsample of the latter group was resampled after a cessation of AAS for ≥18 wk. As expected, fiber cross-sectional area decreased after cessation of AAS usage. However, the number of myonuclei per fiber remained similar or even increased between visits in one subject (11). The finding of a comparable number of myonuclei per fiber despite decrements in fiber cross-sectional area post AAS exposure is consistent with previous studies and the existence of the muscle memory mechanism in humans.

Although most evidence comes from the effects of AAS at the skeletal muscle level in relation to the muscle memory concept, the potential long-term benefits of other doping practices should not be disregarded. For instance, the higher training loads that can be sustained after other doping practices (e.g., erythropoietin administration) could maximize some cardiovascular adaptations, notably left ventricle remodeling in endurance athletes, which seems to occur in a dose-dependent manner with training load (12), although these adaptations are likely lost after a detraining process (13). Similarly, the muscle memory concept could also have implications in other contexts such as the transgender athletes, who seek eligibility in the female category but have been exposed to high levels of androgens during puberty (14). Indeed, transwomen still have an increased performance compared with cisgender women even after a 1 year period of testosterone suppression, which might be in part due to the muscle memory concept (15).

If confirmed, the muscle memory concept and particularly the persistence of physiological improvements resulting from past AAS exposure raise serious ethical concerns in sports, especially considering that success in elite sports usually depends on an advantage that can be less than 1%. Athletes who have engaged in doping practices may continue to benefit from their illicit actions long after any sanctions have been served, compromising the principles of fair play and equal opportunity. Further research is therefore urgently needed to confirm the long-term effects of doping practices and to develop strategies for detecting and mitigating these effects. Although a perfect randomized controlled trial in elite athletes might not be feasible, relevant bioplausible insights can be obtained from animal models, case

reports, and cohort studies. The ultimate prize for clean sport and fairness of such a development will be the strongest deterrent to date of doping: lifetime bans for users.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

P.L.V. and S.S. conceived and designed research; P.L.V. and S.S. drafted manuscript; P.L.V., S.S., and Y.P. edited and revised manuscript; P.L.V., S.S., and Y.P. approved final version of manuscript.

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