Neuro-endocrinology BRIEFINGS

25

ANABOLIC STEROIDS: A FATAL ATTRACTION?

SUMMARY

Anabolic-androgenic steroids (AAS) are widely abused, but the potential for dependence and addiction remains unclear. Recent studies from our laboratory have shown that male and female hamsters will voluntarily self-administer testosterone and other AAS. Furthermore, we have observed fatal androgen overdose during self-administration. This suggests that AAS are potentially addictive, independent of their effects on muscle mass or athletic performance.

Stuck on steroids?

Anabolic-androgenic steroids (AAS) are drugs of abuse. Despite bans on steroid use, Olympic athletes, professional cyclists, American baseball players, and even racehorses have tested positive for AAS. However, AAS are no longer the exclusive province of elite athletes. Among high school seniors in the United States (18 years of age), the lifetime incidence for steroid use (4.0%) is comparable to that for crack cocaine (3.6%) or heroin (1.8%). Today, it is estimated that over 3 million people may have used AAS.

AAS users take steroids for their anabolic effects, particularly increased lean muscle mass which leads to improved athletic performance. However, AAS also have androgenic actions similar to testosterone, to enhance male secondary sexual characteristics. AAS users attempt to maximize the anabolic actions, while minimizing androgenic side-effects. Nonetheless, there is no purely anabolic steroid. AAS are derived from testosterone, and all have a combination of anabolic and androgenic actions.

Steroids in mind

AAS also affect brain and behavior. Neurons in the brain have androgen receptors to bind testosterone and other androgens. In animals, testosterone promotes social behaviors, including mating and aggression. In humans, excessive aggression ('roid rage) is widely recognized in the popular press (68,000 results on Google, 11/2005), and anecdotal reports suggest that AAS may heighten sexual desire. AAS abuse has also been associated with adverse behavioral and psychiatric effects, including euphoria, depression, anxiety, paranoia, and violent behavior. In fact, major mood disorders associated with AAS use often appear during AAS withdrawal.

Whether AAS cause dependence and addiction is controversial. Clearly, much of the motivation to initiate steroid use derives from anabolic effects on athletic performance and physique. In humans, it is difficult to separate the direct psychoactive effects of AAS from reinforcement due to their systemic anabolic effects. By contrast, animal studies can assess the reinforcing

effects of steroids in a context where athletic performance is irrelevant.

Got Roids? Testing times

In our laboratory, hamsters voluntarily self-administer testosterone and these studies suggest that the reinforcing effects of AAS are transduced in the brain. With this approach, we have shown that male and female hamsters self-administer testosterone across a 20-fold range of concentrations. However, females and castrated males are less sensitive than gonad-intact males to testosterone at low concentrations, suggesting that circulating androgens from the gonads enhance responsiveness to administered androgens. Testosterone is not the only steroid that is self-administered. Male hamsters will voluntarily self-administer highly androgenic steroids, including nandrolone, dihydrotestosterone and drostanolone and also androgen precursors such as androstenedione. However, weakly androgenic AAS (oxymetholone and stanozolol) are not reinforcing. Together, these results indicate that the most androgenic AAS are also the most reinforcing.

In time, we realized that some hamsters died during testosterone self-administration. Deaths occurred most often when animals abruptly increased their androgen intake in a "binge" of self-administration. Hamsters that binge on androgens are torpid, with depressed locomotion, body temperature and respiration. These symptoms are reminiscent of overdose with opioids (heroin, morphine). We determined that the opioid antagonist naloxone blocks both testosterone self-administration and the depressive symptoms of testosterone overdose. These data suggest that, at high doses, AAS cause death due to interactions with endogenous opioid systems in the brain.

"Are anabolic-androgenic steroids addictive? Probably. Are they as addictive as cocaine or heroin? Probably not."

Is testosterone actually addictive in animals? Addiction is characterized by loss of control over use, such that subjects continue to seek out the drug despite adverse consequences. Other criteria to establish addiction include tolerance, withdrawal and sensitization. Thus far, we have observed tolerance to the depressive symptoms of testosterone overdose, as well as conditioned avoidance to locations associated with androgen withdrawal. Tolerance, withdrawal and self-administration to the point of death do indeed suggest the potential for androgen addiction.

How dangerous are they?

Users have repeatedly assured us that AAS "aren't classically addictive" but the animal studies now suggest otherwise. Are AAS addictive? Probably. Are they as addictive as cocaine or heroin? Probably not. According to Dr. Leslie Henderson of Dartmouth Medical School, "most people who take AAS don't hole up in an apartment in Seattle listening to old Nirvana records and panhandling 24/7. Neither do most people who drink alcohol, and yet this drug is taken seriously." Addiction is not an all-or-none phenomenon. Many people can drink, smoke and bet on horses occasionally without developing dependence, yet we recognize the addictive potential of alcohol, nicotine and gambling. The potential for AAS addiction undoubtedly depends on use: the amount, frequency and types of steroids ingested, and on the individual user. It may be that AAS dependence develops only in susceptible individuals, similar to other mildly-reinforcing drugs. Nonetheless, it is time to cease pretending that the effects of AAS stop at the neck.

Author:
Ruth I Wood
Keck School of Medicine
University of Southern California
Los Angeles, CA, USA

Editor:
Dr R John Bicknell
The Babraham Institute
Babraham Research Campus
Cambridge CB2 4AT UK

john.bicknell@bbsrc.ac.uk

For further reading references, additional copies and general information, please contact the editor

The full Briefings series can be viewed at website http://www.neuroendo.org.uk