Anabolic-Androgenic Steroids and Psychiatric Effects

Illicit use of anabolic-androgenic steroids (AAS) has been associated with a variety of adverse psychiatric effects. Adverse psychiatric effects are defined for this testimony as disturbances in mood, thinking, behavior, and perception.

The most frequently described adverse psychiatric effects of AAS are extreme mood swings ranging from mania to depression, suicidal thoughts and behaviors, marked aggression including homicidal thoughts and behavior ("roid rage"), grandiose and paranoid delusions, and addiction (11, 20). Mania (or its less severe form known as hypomania), violent aggression, and delusions typically begin during a course of AAS use, whereas depressive episodes and suicide attempts are most likely to occur within three months of stopping AAS use, i.e., during AAS withdrawal (7). Fortunately, most psychiatric effects such as mood swings are reversible with medically monitored cessation of AAS use, but suicides and homicides are obviously irreversible.

Psychiatric effects of illicit AAS use among adolescents are not well-studied, but this age group may be particularly vulnerable. Adolescents are already subject to the normal surges of sex hormones during puberty, which are associated with expected, albeit sometimes problematic, changes in mood and behavior (16). Thus, taking additional sex hormones in the form of AAS could potentially exacerbate the usual degree of expected psychological turmoil normally observed during adolescence. *Suicide*, a grave indicator of vulnerability, *is the third leading cause of death among young people 15 to 24 years of age*, following unintentional injuries and homicide (5). *The association between illicit AAS and suicide, therefore, is especially troubling in adolescents.*

The true rate of adverse psychiatric effects among AAS users is unknown. Studies of illicit AAS users typically include small numbers of subjects who may not be representative of all AAS users; and the studies rely on self-report of past events which may not always be accurate (10, 14, 15). Another concern is that the amount of AAS consumed by illicit users is not easily measured or verified. Nevertheless, such *studies find higher rates of psychiatric effects in AAS users than in comparable nonusers* (14, 15), and one controlled study of 160 athletes reported that 23% of 88 AAS users were diagnosed with major mood disorders (i.e., mania, hypomania, or depression) in association with their AAS use, including 11% diagnosed with major depression (14). That study also suggested that psychiatric effects are dose-related: none of the AAS users taking low doses had major depression whereas medium-dose and high-dose users had rates of 6% and 28%, respectively. Another study (7) found that rates of depression were higher during AAS withdrawal than when actively taking AAS (6.5% vs. 1.3%). That study also found that 3.9% of 77 illicit AAS users had made suicide attempts during the withdrawal period (7). Rates of completed suicides, however, are especially hard to estimate. In a series of 34 forensically evaluated deaths among male AAS users, 11 users committed suicide, 9 were victims of homicide, 12 deaths were judged as accidental, and 2 were indeterminate (21).

Many methodological weaknesses of the above-cited studies are circumvented by conducting trials in which known amounts of AAS or placebo are administered in a randomized double-blind fashion to subjects without a past psychiatric history. (Double-blind means that neither subjects nor investigators knew who got placebo and who got AAS until after the study was completed). Such placebo-controlled, double-blind, randomized controlled studies represent the

gold standard in clinical drug trials. There are at least four such studies that employed relatively high doses of AAS (13, 19, 22, 24). *Three of these studies indicate that some individuals will experience severe, adverse psychiatric effects after high doses of AAS are administered* (13, 19, 24), although one study found no evidence of psychiatric effects (22). Averaging across studies, *recent reviews have concluded that the incidence of prominent irritability or hypomania attributable to steroids during controlled trials is 5%* (13, 18). These gold standard studies, however, are likely to underestimate the incidence and severity of psychiatric effects, because ethical considerations limit the maximum doses of AAS that can be administered to human subjects (13). Illicit AAS users typically consume 10 to 100 times the therapeutic doses prescribed legitimately by physicians to restore testosterone levels in patients who cannot make their own. By contrast, the maximum doses administered in the cited controlled trials were 5-6 times the therapeutic dose (13, 19, 22, 24). Nevertheless, even relatively lower-dose studies (2-3 times the therapeutic dose) have reported psychiatric effects such as increased feelings of anger and hostility without aggressive behavior (9). Other lower-dose studies, however, have not shown psychiatric effects (1, 20), emphasizing the importance of dose when making comparisons to patterns of illicit AAS use.

There are many factors that can influence the development of adverse psychiatric effects to drugs. Such factors include genetic vulnerability, social context, stress, personality characteristics, a past history of psychiatric problems, use of other substances, and expectancies. Expectancy theory suggests that if people expect to become violent on a drug, then they will – but to no greater extent than if they took a placebo or sugar pill. Controlled human studies attempt to exclude the influence of these other factors and to focus strictly on the pharmacologic effects of AAS. Animal studies provide another way to exclude non-pharmacologic influences. Based on reviews of these studies, *there is general consensus that AAS are psychoactive drugs that can contribute to and cause psychiatric effects* (17, 20, 25).

In contrast to undesirable psychiatric effects, AAS may also have some positive psychiatric effects. For example, testosterone was first used medically to treat depression in the 1930s. The antidepressant effects of AAS at generally low doses continue to be investigated and some encouraging findings were recently reported (12). For better or worse, therefore, AAS can have potent psychiatric effects.

At least 165 cases of addiction or dependence on AAS have been documented in the medical literature (2). Similar to other psychiatric effects, dependence typically occurs in individuals who chronically consume high doses and combinations of AAS taken as pills and/or injections for nonmedical purposes. *No cases of dependence have been associated with legitimate prescriptions of AAS used at therapeutic doses for medical purposes.* Moreover, there is good evidence from laboratory studies (23) that the addictive potential of AAS is less than that of drugs such as heroin (a Schedule I controlled substance) or cocaine (a Schedule II controlled substance). Therefore, AAS are considered to be correctly classified as Schedule III controlled substances, but any further restrictions on legitimate medical prescribing would be unjustified at this time.

The mechanisms by which AAS produce addiction and other psychiatric effects are unknown, but accumulating scientific evidence implicates AAS-induced changes in neurochemistry and

neurobiological functioning. AAS can alter the functioning of chemical systems in the brain including dopamine, serotonin, and endorphins (2, 3, 23) that are also affected by other abused drugs (e.g., alcohol and cocaine). In addition, AAS can induce brain wave patterns similar to those seen with stimulant drugs (6). More sophisticated brain imaging studies using magnetic resonance imaging (MRI) or positron emission tomography (PET) scanning would add greatly to our knowledge of AAS effects and mechanisms, but such studies have yet to be performed. Abnormally high or low levels of hormones are also important. Depressive symptoms during AAS withdrawal, for example, appear correlated with lowered levels of testosterone. A recent well-controlled study of drug-induced testosterone withdrawal in 31 men found that 10% developed clinically relevant depressive symptoms, including one man (3.2% of sample) who met full criteria for major depression (18).

Professional Athletes and Adolescents

How teenagers and student athletes regard the use of AAS use by professional athletes has not been investigated. Studies of adolescent use of other drugs, however, suggest the following: First, the adolescent's peer group is probably a more important influence than are adults and their warnings about drug use, although adult examples and role models can be important. Second, adolescents' use of a drug is strongly influenced by their perception of how harmful that drug is (8). In other words, the more harmful they perceive a drug especially to themselves personally, the less likely they will take it. Unfortunately, use of steroids by famous athletes who appear well in the media probably contributes to the perception that AAS are not harmful.

Educating America's Youth

Even though perceiving drugs as harmful reduces their use to some extent, simply educating youth about the dangers of AAS is not sufficient. In fact, education alone may increase the desire and intention of adolescents to use steroids. Alternatively, there is a comprehensive prevention program called ATLAS, which stands for "Adolescents Training and Learning to Avoid Steroids" that has been tested and found to be effective (4). No large-scale, mass media campaigns against the nonmedical use of AAS have been launched or evaluated.

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Adverse Psychiatric Effects

- Mood swings from mania to depression
- Suicidal thoughts and behaviors
- Marked or violent aggression ("roid rage")
- Homicidal thoughts and behaviors
- Grandiose or paranoid delusions
- Addiction

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When do symptoms begin?

During use

- Mania
- Aggression
- Homicidal behavior
- Delusions

During withdrawal (within 3 months)

- Depression
- Suicidal behavior

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Adolescents

- May be particularly vulnerable
- Already subject to the normal surge of sex hormones with expected mood changes
- Suicide is the 3rd leading cause of death in 15-24 year olds
- Steroids can increase suicide risk in age group already at risk

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How Common?

Estimated occurrence with illicit use

• Mania or hypomania	• 5%
• Major depression	• 3-11%
• Suicide attempts	• 4%

Malone et al (1995)
Pope & Katz (1994)
Schmidt et al (2004)
Thiblen & Petersson (2005)

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Fortunately

- Most users do not have psychiatric effects
- Most psychiatric effects are reversible with proper monitoring and treatment

Unfortunately

- Suicides & homicides are obvious exceptions

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Psychiatric effects influenced by:

- **Patterns of illicit use including dose**
- Genetics
- Social context
- Stress
- Personality characteristics
- Past psychiatric history
- Expectations

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Addiction

- At least 165 cases in nonmedical users reported in medical literature
- No cases reported with medical use at therapeutic doses

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How do they work?

- Alter hormone levels
- Alter brain chemistry and functioning
  - e.g., dopamine, serotonin, endorphins

Summary

- Steroids alter brain chemistry causing profound psychiatric effects
- Adolescents especially vulnerable
- True rates of adverse psychiatric effects influenced by drug and non-drug factors
- Addiction occurs with high-dose nonmedical use only

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