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ABSTRACT

This review of the literature on the psychological and behavioral effects of anabolic-androgenic steroids (AS) first looks at aspects of the history and prevalence of AS use in competitive sports. Research suggests that one-quarter to one-half million adolescents in the United States have used, or are currently using AS. Some effects of androgens on the central and peripheral nervous systems are reported. Numerous studies have examined relationships between testosterone levels, mood and behavior. A pattern of association between plasma testosterone and both subjectively-perceived and observed aggressive behavior has been revealed. Results from studies examining the effects of androgen therapy in individuals with androgen deficiencies have been mixed. Some demonstrate significant, positive psychological changes with AS and others do not. Examination of the effects of mental health in athletes with AS shows that for the most part, individuals use AS to significantly improve appearance and/or performance beyond what would be expected from training alone. The effects of AS have been reported in relation to withdrawal symptoms. Withdrawal effects include mood swings, violent behavior, rage, and depression; possibly severe enough to lead to thoughts of suicide. Methodological shortcomings in the studies reviewed are discussed. A summary reviews the issues associated with AS use in light of the methodological limitations. Medical and legal concerns regarding the psychological and behavioral effects of AS are discussed. (LLL)

# PSYCHOLOGICAL AND BEHAVIORAL EFFECTS OF ANABOLIC-ANDROGENIC STEROIDS

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# PSYCHOLOGICAL AND BEHAVIORAL EFFECTS OF ANABOLIC-ANDROGENIC STEROIDS

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## INTRODUCTION

Most of us are aware of the current controversy surrounding the use of anabolic-androgenic steroids (AS) by athletes to enhance performance. AS are a group of synthetic derivatives of the male sex hormone, testosterone (T), which have been modified to prolong their presence in the bloodstream for maximal gains in muscular strength and size and to minimize their masculinizing (androgenic) effects. Male sex steroids were isolated, chemically characterized and the nature of their effects demonstrated over 50 years ago. AS can be broadly classified into those which are active when taken orally and those which are active when taken by intramuscular injection. AS are readily available through "black market" sources or from some medical professionals and are thought to speed recovery from exercise and allow gains in strength and lean body mass beyond that expected by training alone.

AS have been used by athletes to enhance performance for many years. The first reports of widespread use appeared in the 1950s among weight lifters and body builders. Since that time their use has permeated a myriad of sports. It is now evident that the use of steroids is not limited to elite

amateur athletes, but that it has trickled down through the colleges to the high school and junior high school levels, including recreational athletes and non-athletes. A nationwide study of AS use found that 6.6 percent of male high school seniors have used them.

The use of AS has also become a major health concern, prompting efforts to classify them as a controlled substance.

## PERSPECTIVE

The psychological and behavioral aspects of maleness were noted by Aristotle prior to 300 B.C. and were studied in numerous uncontrolled experiments up through the 1800s which sought to demonstrate that the testes contained substances which produced and maintained vitality, strength, energy, and youthfulness. The effects of purified sex hormones, including those on mood and mental disorders, began to be experimentally and clinically explored more intensively a half century ago when commercial preparations became available. Since that time, a number of literature reviews have reported on these and other effects.

For many years testosterone preparations were rather widely and successfully used in the treatment of involutional psychoses, melancholia, and depression. Recently, however, in contrast to these earlier findings, more focused clinical reports have suggested that affective and psychotic syndromes, some of violent proportions, may be associated with the use of AS in particular individuals. Several cases have recently been reported wherein presumed psychological and behavioral effects of AS are alleged by defendants to have significantly influenced the commission of criminal acts. This legal strategy has been identified in the popular press as the

"dumbbell defense."

The purposes of this presentation are to review: 1) selected aspects of the history and prevalence of AS use in competitive sports; 2) some effects of androgens on the central and peripheral nervous systems; 3) the relationship between endogenous plasma testosterone levels and mood and behavior in normal males and in prisoners; 4) the effects of the clinical use of AS on mood and behavior in hypogonadal males and depressed patients; 5) the relationship of AS use to aggression and mental health in athletes, including issues of psychological dependence and withdrawal; and 6) the major methodological issues involved in assessing the relationship between AS administration, mood and behavior.

## HISTORY AND PREVALENCE OF AS USE

The primary use of AS is in replacement therapy for male hypogonadism; other medical uses of AS include growth promotion in various forms of stunted growth, osteoporosis, mammary carcinoma, anemias, and hereditary angioneurotic edema. Observation and clinical trials indicate that adjuvant therapy with AS can be supportive in the treatment of conditions characterized by a negative nitrogen balance, e.g., major surgery, cahexia of various origins, burns, traumata, convalescence from illness, injuries and immobilizations, as well as during radiotherapy with cytoxic drugs. Unfortunately, research concerning additional legitimate applications of AS has most likely been impeded by the existing emotional polarization of AS supporters and opponents. The frequent and often hysterical references in the popular press to unsubstantiated adverse effects of AS has often resulted in the loss of both the media's and the medical and scientific

communities' credibility. This, in turn, deters research on beneficial and legitimate medical uses, and acts as a stimulus and encouragement for litigation against physicians.

Anabolic steroids have been used by athletes to enhance their appearance and performance for many years. Payne suggested that the use of AS was a significant problem at the 1964 Olympic Games. Ljungqvist reported that one-third of a sample of elite track and field athletes surveyed in Sweden admitted to systematic use by 1972. Silvester reported that 68 percent of a sample interviewed at the 1972 Olympic Games from seven countries competing in such diverse activities as throwing, jumping, vaulting, sprinting, and running, admitted having used AS. It is now evident that the use of AS is not limited to elite amateur and professional athletes. It has trickled down from the professional and college levels to the high schools and junior high schools. The survey by Buckley et al. suggests that one-quarter to one-half million adolescents in the United States have used, or are currently using, AS. A nation-wide survey of alcohol and drug use among college athletes indicated that AS were used in all men's sports, one women's sport, and that the overall use of AS by athletes in all sports was four percent.

The estimated prevalence of non-medical AS use, and the implications for society and public health, have prompted several scientific meetings, including a technical review at the National Institute on Drug Abuse in 1989, and both federal and state investigations and efforts to reclassify them (AS) as controlled substances despite nonconcurrence from the American Medical Association.

## EFFECTS OF AS ON THE NERVOUS SYSTEM

AS have been shown to have significant effects on both the development and function of the nervous system. Many years ago, androgens were shown to act directly on the brain. Data from animal studies indicate that both estrogens and androgens act on neural structures that are identical to, or closely associated with, sensory pathways and the ventricular recess organs of the hypothalamus. Androgens have been reported to selectively stimulate neurons of the somatomotor system and circuits associated with aggression. Researchers have demonstrated quantitatively the physiological correlates of certain previously reported behavioral effects of AS. These include an increase of mental alertness, mood elevation, improvement of memory and concentration, and reduction of sensations of fatigue, all of which can be partly related to the "stimulatory" effects of AS on the central nervous system. EEG profiles resulting from varying dosages of AS were found to be very similar to those seen with such psychostimulants as dextroamphetamine and the tricyclic anti-depressants. Others have concluded that the adrenergic-like effects of T on brain function are a result of an elevation of the brain's norepinephrine level, which might result from the inhibition of monoamine oxidase activity in the brain. Further speculation indicates that the "heightened" state of behavioral reactivity which facilitates the automatization of behavior may well be due to an increased level of epinephrine in the brain.

Inasmuch as improvements in muscle strength and power can, in part, be accounted for by neural factors, including neurotransmitter levels, findings that androgens may in some manner modify neural and neuromuscular functions support the concept of a significant role for these mechanisms in the production of ergogenic effects.

## ENDOGENOUS PLASMA TESTOSTERONE LEVELS AND MOOD AND BEHAVIOR

Numerous studies have documented relationships between T levels, dominance, and aggressive behavior in various species of animals including non-human primates. In general, these and other studies indicate that the level of T, particularly in the prenatal period, but also during puberty and even in adulthood, are important in establishing a biologic readiness for normal, aggressive behavior and in facilitating the expression of aggression in "appropriate" social settings in adult animals. They also indicate that both learning and social factors significantly influence the actual expression of aggression in adulthood. However, the extent to which exposure to T, or other AS, at any phase of the life cycle, and particularly during adulthood, is related to altered moods and feelings in humans, to the expressions of aggression in humans and even other primates, relative to animals lower in the evolutionary chain, is not well known.

Relative to the animal literature, fewer studies have assessed the relationship of endogenous or exogenous androgens to aggression or violent behavior in humans. In general, the relationship in human research is less clear than in animal research for a variety of reasons. First, it is difficult to demonstrate that animals, possibly excluding primates, experience emotional states that are qualitatively similar to human experiences such as euphoria, depression, anger, and others. Second, the effects of sex hormones vary considerably among individuals as well as species. Consequently, conclusions drawn from animal models must be applied cautiously to humans. Lastly, human subjects cannot be subjected to many of the stringent controls and manipulations used in animal

research. Nevertheless, aggressive behavior, and other feelings of hostility, have been demonstrated to be related to endogenous T levels in a number of studies using human subjects. These investigations, which correlate levels of T with aggressive behavior, have been conducted with normal and incarcerated males, and men with genetic differences in T production. They have also investigated the effects on behavior of administered T and anti-androgenic agents.

Several studies have examined the relationship between T levels and aggression in adolescents and young athletes. Some investigations have examined the relationship of T and mood in adult males, whereas several other investigations have examined T levels and aggression in prisoners. Additional studies have examined the relationship of T to moods other than aggression. In summary, a pattern of association between plasma T and both subjectively-perceived and observed aggressive behavior has been revealed in many studies. However, the relationships between plasma T and psychometric indices of aggression and hostility have been less consistent. Finally, the other side, and an important consideration, of the question of the relationship of T, mood, and behavior, is to what extent aggressive behavior, successful "expression" of aggression, or non-aggressive success, produce higher levels of T.

## EFFECT OF AS ON MOOD AND BEHAVIOR IN HYPOGONADAL AND DEPRESSED PATIENTS

Several studies have been conducted over the years examining the effects of androgen therapy in individuals with androgen deficiencies. Results from these studies are mixed. Some demonstrate significant, positive psychological changes with AS; others do not. However, no adverse or

undesired psychological or behavioral effects were observed in these studies. Interestingly, five of the six studies which administered oral androgens reported improved mood states following therapy; the results of the two using intramuscular injections of various T esters found no change. Finally, in a carefully controlled, double-blind cross-over comparison of biweekly injections of T esters or placebo in two groups of men with normal T levels, researchers found no significant change in mood ratings following twelve weeks of treatment.

Research and anecdotal information suggested some time ago that the use of steroids result in, along with their many side effects, various mental disturbances including schizophrenia and manic depression, even though estrone was used successfully in both males and females in the treatment of depression and other mental disturbances occurring with menopause and what would now probably be referred to as andropause beginning in the mid-1930s.

It is now well known that, in excess, glucocorticoids can produce emotional instability, ranging from euphoria to suicidal despondency. Mental disorders associated with corticosteroid (CS) administration have been documented since the early 1950s and several literature reviews have related the characteristics of CS-induced, psychiatric disorders. Considering the structural similarities of cortical and anabolic steroids, and their multiple additive and synergistic and competitive actions, it is not surprising that their administration would result in similar effects on mood and behavior.

Androgens have been used in the treatment of mental disorders for over 50 years. Results from published studies generally indicate positive, rather than negative, effects following androgen therapy in mental

(especially depressed) patients. However, it is unknown whether long-term use or use of pharmocological doses by otherwise healthy individuals, particularly adolescents, might result in similar outcomes.

## AS USE AND MENTAL HEALTH IN ATHLETES

Very few scientific studies are available on the personality and psychological characteristics or the changes that might be incurred as a result of heavy resistance training in competitive weight lifters and body builders. Further, there is little understanding of the extent to which resistance (or other) training may affect and/or facilitate the expression of aggression. Psychological and behavioral changes, such as increased aggressiveness and irritability, have been reported on an anecdotal basis by athletes using AS as well as their families and friends. It is possible, however, that, as occurs with the use of so many drugs, many of the subjectively-perceived psychological and behavioral changes reported by AS users are a direct result of expectancy, imitation, or role modeling. Observing the actions of other AS users and athletes may greatly influence the expectations and behaviors of those in the initial and early continuation of use. In addition, aggressive or even violent behavior that may be unacceptable outside the athletic environment may not only be fully acceptable but actually encouraged and even required within the weight room or on the playing field.

Several researchers have suggested that some, if not most, of the ergogenic benefits of AS may derive from their psychological effects. It is possible that AS use may elevate arousal, increase self-confidence and pain threshold, and facilitate expression of the "all-out" physical effort

demanded during training and competition in a variety of sports. In the absence of adequate external forces, internal discipline, or social coping skills, these phenomena could lead to expression of aggression at inappropriate times.

One researcher has reported that one value of taking AS, as expressed by some athletes, lay in the reduction of fatigue during the training season which allows for more training to be done. Other researchers provide anecdotal or self-reported information that athletes using AS generally are less easily fatigued, allowing for longer, more frequent, and/or more intense training sessions. This could be related to the fact that AS can block and reverse the anti-catabolic effects of glucocorticosteroids that are released during periods of stress including physical exertion. Another researcher has suggested that the increases in aggression and energy that the athlete feels may be the result of neurological changes previously mentioned. In cases where AS do improve physical or physiological capacities or performance, the improvement is likely due, to some extent, to increases in training per se as well as to any pharmacological effect. Despite these suggestions and self-reports, scientific data supporting the notion that psychological changes (enhanced arousal, confidence, aggression, motivation) play a primary role in mediating any ergogenic effects of AS is lacking.

Several studies have examined the side effects of AS. Currently, the most frequently quoted report concerning the psychological and behavioral effects of AS is that of Pope and Katz which appeared in the April, 1988 issue of the American Journal of Psychiatry. This report serves as an example of the problems typically encountered in examining the psychological and behavioral effects associated with AS use. Pope and Katz

interviewed forty-one steroid users using a structured diagnostic interview. Self-reports of various psychiatric syndromes during AS use were compared with periods of no AS use. Results indicate that according to DSM-III-R criteria, five subjects (12%) manifested psychotic symptoms, four others (10%) had "subthreshold" or equivocal psychotic symptoms, five subjects (12%) reported a manic episode, and 22 percent developed a full affective syndrome during AS use. It is unclear whether these groups were mutually exclusive. None of the 41 subjects recalled adverse effects of AS sufficient to require medical consultation and apparently none sought treatment for their mental health disturbances. Although Pope and Katz do not elaborate on their recruitment of participants, other than to report that they were volunteers obtained by advertisements at 38 gymnasia in the Boston and Santa Monica areas and paid $25 for a confidential interview, they do state that "...despite our considerable efforts at recruitment, only a minority of steroid users were willing to be interviewed." Unfortunately, their difficulty in obtaining subjects raises questions about the representativeness of their sample relative to the population of AS users. Given the vast pool of potential participants, their difficulty in obtaining volunteers could suggest a low incidence of psychiatric problems among AS users as well as a basic mistrust of the medical and scientific establishment. It is conceivable that those AS users who elected to participate in the study were individuals with the greatest severity and frequency of mental disturbance. It is also probably safe to assume that individuals willing to take AS and other drugs of questionable origin, content, and purity, and with serious legal as well as health effects differ from the population on a wide variety of characteristics, including mental health. Fifteen percent of Pope and Katz's subjects

reported past alcohol abuse or dependence and 32% reported other prior substance abuse or dependence, including cannibis (17%) and cocaine (12%). Interpretation of the reports of these subjects must be tempered by the lack of information regarding the extent to which their use occurred concurrently with AS and with psychiatric symptoms and by the absence of knowledge on the interaction of AS and such drugs of abuse. Seventeen percent had a first degree relative with a major affective disorder and two subjects reported symptoms of a full affective disorder when not taking steroids. Finally, while it is difficult to establish the extent to which AS may have contributed to the psychotic episodes reported by Pope and Katz, and while the media have sensationalized their findings somewhat, it seems likely that, with more widespread use of AS and increased efforts to document such reactions, additional cases will be forthcoming.

For the most part, individuals use AS to significantly improve appearance and/or performance beyond what would be expected from training alone. Also, individuals using AS appear to believe that higher doses and continued use result in greater gains. When individuals discontinue using AS, their size and strength diminish, often very dramatically, and this outcome, as well as any psychological effects of use which serve to create a new body image, improved self-esteem, heightened libido and general euphoria, are thought to motivate renewed use of AS.

As with CS, increasing attention and discussion is being focused on the withdrawal effects that athletes encounter when they cease use of AS. Interestingly, many of the same effects attributed to AS use are alleged to occur following AS cessation. Purported withdrawal effects include mood swings, violent behavior, rage, and depression, possibly severe enough to

lead to thoughts of suicide. However, these findings must be tempered by the fact that individual responses to different AS, doses, and lengths of administration likely vary somewhat unpredictably. Further, beyond these initial reports, no threshold dosage that may produce the effects (mood swings, violent behavior, rage, depression) or time-course concerning the onset or elimination of these effects once AS use has been initiated or terminated have been fully documented (which may depend, in part, on the length of AS use, particular desired as well as undesired effects experienced, dosage, and a host of other factors). Finally, weight training per se may be addictive in the sense of promoting compulsive, stereotypical, and repetitive behavior to include not only the strength training but dieting, drug use, and a host of other lifestyle variables as well.

The use of educational intervention programs for the prevention and treatment of AS abuse has been examined in several studies. One report has proposed that education is the most feasible alternative for curbing AS use by adolescents. Another study found that an educational program which emphasized alternatives to AS use such as nutrition principles and strength training techniques was more effective in improving attitudes towards potential AS use than either an education program in which no alternatives were discussed or no intervention program. Yet another report suggests that education alone may not be as effective as clinical assessment and consultation in the care of individuals abusing AS. Medication has also been suggested for amelioration of the symptoms of AS withdrawal.

## MAJOR METHODOLOGICAL PROBLEMS

As mentioned previously, any attempt to evaluate and summarize the psychological and behavioral effects associated with the use of AS is complicated by the numerous methodological shortcomings of many of the investigations including inappropriate sampling strategies, lack of adequate control groups, use of several types, doses, and length of administration of AS, and a variety of techniques used to assess the psychological and behavioral outcomes.

A significant number of studies did not control for or report family or previous personal history of mental illness and/or aggressive behavior, thereby resulting in a possible selection bias in the study population. In addition, selection of physically and/or mentally ill patients, persons, volunteers, etc. as subjects, raises the question of the generalizability of the findings to otherwise healthy individuals. Many of the studies reported on here were conducted with small sample sizes, thus reducing the statistical power available to detect significant differences. Furthermore, small sample sizes have precluded the examination of steroid effects in additional sub-groups such as age, race, gender, educational level, and social class. Small sample size makes it difficult to control for potential confounding variables using multivariate statistical techniques. Sampling of blood and urine was inconsistent among studies, with respect to timing, or often unreported. Often multiple samples were not obtained.

A number of studies failed to incorporate control groups. Many studies, for ethical and legal reasons, did not randomly assign subjects to treatment, use comparable reference groups, or take advantage of single- or double-blind designs.

All AS are not the same; significant variation among AS regarding acute physical effects has been noted and there is significant individual variation in response to the same androgen and dose. Caution must be exercised when attempts are made to generalize the psychological and behavioral effects (findings) from a study using one type of AS to a different steroid used in another study. There is also the possibility that adverse reactions may represent toxic responses in some individuals. Also, while reporting the average steroid dose used, some studies failed to examine or report any dose/response relationship. In addition, even when dosage was provided, estimating the bioavailable equivalence between oral and injectible AS is difficult. Moreover, in hypogonadal patients it appears that oral AS are the only type of AS that produce positive mood changes, although the doses of injectible steroids administered in these studies often tended to be below those required to restore and maintain normal plasma testosterone levels. In other users (athletes) it is the oral AS that are associated with the adverse psychological changes. Finally, because as much as 50-80 percent or more of the AS used by athletes may have been obtained from "black market" sources, case reports of individuals using these drugs must be evaluated accordingly given the absence of knowledge concerning their actual content.

Defining aggression and assessing aggressive behavior is itself difficult. Since a variety of psychological inventories were used across studies, comparability of findings between studies is difficult. In some cases, nonstandardized and/or unpublished inventories were used. As a result, some of the questionnaires may have been inadequate for detecting behavioral change.

Finally, an overriding concern is the accurate documentation of any

change in behavior with AS use. No studies of actual behavior while in athletic competition have been reported. Some studies were unclear regarding how changes in behavior associated with AS use were determined. It is possible that some of the behavioral differences reported resulted from some investigations relying upon self-reports and other self-defined measures of behavioral change, while others used observers and/or interviews to document behavioral changes. Consequently, aggressive feelings that failed to be manifested as aggressive actions may have either gone unrecognized or been over-reported.

## SUMMARY

Both prospective and retrospective methods have been used to evaluate the psychological and behavioral effects of AS. However, statements regarding this topic must remain tentative due to the diversity of study designs and results. Many of the reported behavioral effects have come primarily from studies using a small number of subjects in which patients were administered AS for a variety of clinical conditions. These studies have found positive or unchanged moods and behavior. Extremely small numbers of athletes have been studied, and the findings derived from patient populations can only be generalized to athletes with caution, particularly as athletes are known to use several drugs concurrently and to use "black market" drugs, the content of which may be suspect. And lastly, the interactive effects of AS and environmental factors, stress levels, and often drugs of various types (including analgesics, anti-inflammatories, alcohol and other psychoactive substances), on feelings and behavior remains unresolved in humans.

In summary, the few investigations conducted, primarily in prisoner populations, have shown a significant positive relationship between endogenous T levels and aggressive behavior. However, the questions of the extent of the relationship and of the interaction between T and aggression remain unanswered. Do elevated T levels result in more aggressive behavior or does more aggressive behavior cause T levels to increase? In addition, what does the interaction of physical activity and an emotionally charged environment have on T production and behavior? Future research will undoubtedly need to examine the positive psychological effects of AS use as has occurred in the majority of patient samples. There may be significant numbers of individuals whose mental health has been <u>improved</u> through AS use.

Both medical and legal concerns regarding the psychological and behavioral effects of AS have been raised. Unfortunately, objective evidence documenting the short-term psychological and behavioral changes accompanying and following AS use by athletes is extremely limited and inconclusive. As indicated, many of the studies in this area suffer from methodological inadequacies. As several researchers have pointed out, extremely little is known about the long-term health impact of AS and their interactions with other drugs, including drugs of abuse. Consequently, the need for much additional research is strongly indicated.

Although some athletes and coaches believe that AS exert a positive effect by enhancing performance through altered psychological states, others point out the potential negative effects of violent and aggressive behavior. With present estimates of a million or more AS users in the United States, an extremely small percent of AS-using athletes appear to experience mental disturbances which result in their seeking clinical

treatment, and of those who do, some may already suffer from existing mental health and/or other substance abuse problems. At this point a cause-effect relationship has yet to be established. Moreover, of the seemingly small population of individuals who do experience significant psychological and behavioral changes, most apparently recover without legal or other problems when the use of androgens is terminated.

References available upon request.

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