Neuropsychiatric Effects of Anabolic Steroids in Male Normal Volunteers

Tung-Ping Su, MD; Michael Pagliaro, RN; Peter J. Schmidt, MD; David Pickar, MD; Owen Wolkowitz, MD; David R. Rubinow, MD

Objective.—To evaluate the acute effects of anabolic steroids on mood and behavior in male normal volunteers.

Design.—A 2-week, double-blind (subject and rater), fixed-order, placebo-controlled crossover trial of methyltestosterone.

Setting.—An inpatient research unit at the National Institutes of Health.

Subjects.—A volunteer sample of 20 men who were medication free, free of medical and psychiatric illness, not involved in athletic training, and had no prior history of anabolic steroid use.

Intervention.—A sequential trial for 3 days each of the following four drug conditions: placebo baseline, low-dose methyltestosterone (40 mg/d), high-dose methyltestosterone (240 mg/d), and placebo withdrawal.

Main Outcome Measures.—Mood and behavioral ratings were completed during each drug condition and included both subjective and objective measures.

Results.—Significant ($P<.05$) albeit subtle increases in symptom scores were observed during high-dose methyltestosterone administration compared with baseline in positive mood (euphoria, energy, and sexual arousal), negative mood (irritability, mood swings, violent feelings, and hostility), and cognitive impairment (distractibility, forgetfulness, and confusion). An acute manic episode was observed in one of the 20 subjects, representing a 5% incidence, even under these conservative conditions. An additional subject became hypomanic. Baseline characteristics including family psychiatric history or previous drug abuse did not predict symptom changes.

Conclusion.—This is the first placebo-controlled prospective study demonstrating the adverse and activating mood and behavioral effects of anabolic steroids.

(*JAMA*. 1993;269:2760-2764)

ANABOLIC steroids are synthetic androgens that, compared with testosterone, have greater anabolic (growth-promoting) activity relative to androgenic (masculinizing) activity. This group of steroids is indicated in the treatment of certain medical conditions: aplastic anemia, hereditary angioedema, hypogonadism in males, some forms of debilitating chronic illness, and breast cancer.[1] However, in contrast to their medical indications, over the past 30 years anabolic steroids have been used by members of the athletic community because of the belief that they increase lean body mass, physical strength, and aggressiveness and reduce recovery time between workouts.[2,3] It has been estimated that over a million persons in the United States abuse non–medically prescribed steroids in this fashion.[4]

In association with the increased nonmedical use of anabolic steroids, reports appeared describing steroid-precipitated mood and behavioral disturbances.[5] Case reports have observed the following: psychoses,[6] hypomania,[7] a delirium with the presence of choreiform movements,[8] and violent criminal acts.[9] In 1988, Pope and Katz[10] administered the Structured Clinical Interview for DSM-III-R (SCID) to 41 athletes who had previously abused anabolic steroids and asked them to answer questions for periods of both steroid use and nonuse. The SCID identified nine subjects (22%) who met diagnostic criteria for a manic or depressive episode during exposure to, or withdrawal from, anabolic steroids. Five subjects (12%) experienced a manic episode while using steroid and five subjects (12%) developed an episode of major depression during steroid withdrawal (one subject experienced both). These investigators also identified five additional athletes (12%) who experienced psychotic symptoms, such as hallucinations and/or delusions, during anabolic steroid exposure. Several studies[11-13] administering psychological inventories to groups of steroid users and nonusers also demonstrated significant increases in symptoms of aggression, hostility, anger, irritability, depression, and anxiety in anabolic steroid users, although increased aggression and/or hostility was not observed by Bahrke et al.[14]

Depression and suicidal ideas have also been reported as part of a putative withdrawal syndrome during the first 3 months after discontinuation of long-term anabolic steroids.[15-17] Conversely, anabolic steroids and/or testosterone have been observed in some but not all studies to improve both mood and sexual performance, particularly in hypogonadal or depressed men.[18-22] Finally, a paranoid reaction has been described to accompany the concurrent administration of anabolic steroids and antidepressants.[23]

In general, investigations of the neuropsychiatric effects of anabolic steroids have been hindered by a number of methodologic problems including the following: (1) the lack of a prospective experimental design; (2) the absence of a placebo control; (3) the failure to adequately characterize subjects with respect to baseline mood and behavioral symptoms, past personal psychiatric history, premorbid personality traits, and psychological functioning; (4) the inability to control for the coadministration of psychotropic drugs or other drugs of abuse, as well as for the multiplicity of preparations, dosages, and schedules of administration of anabolic steroids employed; and (5) the failure to exclude subjects with concurrent medical illness.

From the Section on Behavioral Endocrinology, Biological Psychiatry Branch (Drs Su, Schmidt, and Rubinow), and Experimental Therapeutics Branch (Drs Su, Pickar, and Wolkowitz), National Institute of Mental Health, Bethesda, Md; Mental Health Nursing Service, Nursing Department, Clinical Center, National Institutes of Health, Bethesda, Md (Mr Pagliaro); and Department of Psychiatry, University of California, San Francisco (Dr Wolkowitz).

Reprint requests to Section on Behavioral Endocrinology, National Institute of Mental Health/NIH, 9000 Rockville Pike, Bldg 10, Room 3N238, Bethesda, MD 20892 (Dr Su).

This study systematically evaluated the effects of anabolic steroids on mood, behavior, and cognition in a prospective, double-blind, placebo-controlled design in healthy normal volunteers who were screened for the absence of any past psychiatric history or concurrent psychotropic drug use. Additionally, this study attempted to identify changes in central nervous system biochemistry and neuroendocrine function that are associated with the administration of anabolic steroids in an attempt to further our understanding of possible mechanisms by which anabolic steroids may alter central nervous system function. These biological effects of anabolic steroids will be described in a subsequent report.

METHODS

Subject Selection

Twenty-three healthy male volunteers underwent a thorough medical evaluation including history, physical examination, and laboratory testing that included urine drug screening. Three subjects were excluded during the screening process: one with possible tuberculosis and two with positive urine screens for marijuana and phencyclidine (PCP). The remaining 20 subjects were administered a structured psychiatric diagnostic interview, the Schedule for Affective Disorders and Schizophrenia—Lifetime Version (SADS-L),[24] to confirm the absence of significant current or past psychiatric history or history of anabolic steroid abuse as well as current or recent (past 2 years) history of alcohol or other substance abuse. Subjects also completed a self-administered personality disorder questionnaire for DSM-III-R, Personality Diagnostic Questionnaire Revised (PDQR).[25,26] All subjects were medication free and gave written consent for the investigation. This protocol was reviewed and approved by the National Institute of Mental Health Institutional Review Board.

Type of Anabolic Steroid and Dosage Employed

Methyltestosterone, 17β-hydroxy-17α-methylandrost-4-en-3-one, is an oral androgenic anabolic steroid. The medically recommended dosages are 10 to 40 mg daily in adult males. Each capsule administered in this study contained either methyltestosterone (40 mg) or placebo.

Procedure/Protocol

Subjects were admitted to a National Institute of Mental Health inpatient research ward, to which they acclimated for the first 2 days. For the next 12 days, volunteers received in a double-blind fashion (both subjects and raters were unaware of medication status or study design) methyltestosterone or placebo under four 3-day drug conditions: placebo (baseline), followed by methyltestosterone at a dose of 40 mg per day (low-dose condition), then at a dose of 240 mg per day (high-dose condition), followed by placebo (withdrawal). All subjects received two capsules three times a day (10 AM, 2 PM, 6 PM). As noted above, the dose of 80 mg by mouth three times a day of methyltestosterone exceeded the recommended therapeutic dose of 40 mg and was at the low end of the range of doses reported to be used by athletes (six to 100 times recommended therapeutic doses).

Behavioral Evaluation and Symptom Ratings

All subjects completed daily at 10 AM, 6 PM, and 10 PM a visual analogue self-rating scale (VAS) that measured a variety of mood, behavioral, and cognitive symptoms reported in association with anabolic steroid exposure. Subjects were instructed to place a line through the scale at the point on the range of symptoms that best described their experience at the time they completed the ratings. In addition, subjects completed the following ratings three times per day on the same schedule as the VAS: the Beck Depression Inventory (BDI)[27] and the Spielberger State Trait Anxiety Inventory (STAI) State Form.[28] Further, 15 subjects completed the Symptom Checklist (SCL-90)[29] at the end of each of the four drug conditions. The ratings for the initial five subjects were not obtained, as the SCL-90 was not included in the early study design. Objective behavioral ratings, performed by nursing staff blind to medication status and experimental design, included the following: a modified 24-item Brief Psychiatric Rating Scale (BPRS),[30] the Hamilton Depression Rating Scale (HAM-D),[31] and the Mini-Mental State Examination (MMSE).[32] The interrater reliabilities for these rating scales among nursing staff were 0.87, 0.79, and 0.95 for the BPRS, HAM-D, and MMSE, respectively. Finally, subjects were asked to keep diaries of experiences throughout the study, and on completion of the experimental protocol they were asked to describe any distinct or noticeable behavioral changes that they experienced during the protocol.

In addition to the symptom rating scales described above, vital signs and daily records of activity were obtained during the study.

Statistical Analysis

Data were analyzed in the following ways. First, to detect robust medication-related effects, an analysis of variance with repeated measures (ANOVA-R) of the VAS symptoms was performed with drug condition (baseline, low dose, high dose, withdrawal) as the within-subjects factor. The ANOVA-R was also used to generate the error terms used in the planned post hoc comparisons described below. For each symptom, the highest rating (of the three obtained per day) was selected and averaged for the 3 days during each drug condition. Additionally, mean ratings were calculated during each drug condition for each symptom at each rating time (morning: 10 AM; evening: 6 PM; night: 10 PM). Second, to examine the main comparison of the study, symptom scores during the baseline and the high-dose conditions were compared with paired t tests and with Bonferroni t tests (to adjust for the number of comparisons performed). Symptoms analyzed in this fashion included the following: mean of the most symptomatic daily scores during each drug condition (as described above) for the analogue scales; mean of the three daily analogue scale rating scores for each rating time during each drug condition; mean of the daily highest score on the BDI and STAI; and mean of the daily score from the nurses' ratings on the BPRS, HAM-D, and MMSE during each drug condition. Third, to examine potential unique effects of the low-dose and withdrawal conditions, both were compared with baseline with post hoc t tests.

The SCL-90 self-rating scores at the end of each of the four drug conditions were analyzed for each subscale using ANOVA-Rs and paired t tests to identify drug effects (as described above). The nursing observations were also analyzed by comparisons identical to those used for the visual analogue behavioral measures. Activity monitor[33] recording of the amount of continuous overthreshold wrist movements during 15-minute intervals was performed in each subject continuously for the whole study period. Four 15-minute activity intervals in an hour were averaged to represent hourly activity. The daily activity was the mean of the 24 hourly measures.

Complete activity records were obtained for only 16 of the 20 subjects because of technical difficulties. The ANOVA-R of the means of the three daily activity measures during each drug condition was performed as well as Pearson correlation coefficients for the change in activity with the change in VAS energy self-ratings from baseline to high-dose condition. All values are reported as mean±SD.

Biological Measures/Plasma Anabolic Steroid Levels

Repeated blood and cerebrospinal fluid samples were collected for clinical and

Table 1.—Comparisons of Daily Highest Score in Visual Analogue Scale Self-ratings*

Symptom	Mean Scores (±SD)				ANOVA-R		
	B	LD	HD	W	F	P	df
Sexual arousal	27.3 (29.8)	31.9 (33.4)†	35.3 (31.1)†	36.0 (32.9)†	6.2	<.01	3,17
Headache	10.7 (11.0)	23.1 (22.0)†	13.7 (16.7)‡	16.6 (17.0)	3.8	<.05	3,13
Distractibility	4.6 (4.4)	6.7 (8.3)§	11.4 (9.8)†	6.7 (6.9)	2.6	<.1	3,17
Energy	37.5 (30.8)	38.0 (30.1)	42.0 (28.5)‖	39.9 (33.6)	2.6	<.1	3,17
Irritability	14.6 (17.7)	19.0 (16.3)	20.9 (19.8)‖	18.6 (17.3)	NS	...	...
Anger	5.5 (8.9)	5.4 (7.2)	7.4 (11.6)¶	5.2 (6.3)	NS	...	...
Violent feelings	23.9 (18.4)	22.8 (19.6)	27.1 (20.3)¶	24.6 (19.8)	NS	...	...
Fatigue	12.8 (12.1)	15.4 (13.3)	16.6 (16.6)¶	12.4 (13.9)	NS	...	...
Insomnia	9.5 (11.4)	14.6 (15.8)	17.2 (16.8)¶	11.5 (15.2)	NS	...	...
Appetite	33.7 (16.3)	37.2 (16.4)‖	33.1 (18.8)	35.9 (16.1)	NS	...	...

*All paired *t* test *P* values represent comparisons with baseline means, except as otherwise noted. B indicates baseline; LD, low dose; HD, high dose; W, withdrawal; ANOVA-R analysis of variance with repeated measures; and NS, nonsignificant for all four treatment conditions.
†$P<.01$ (Bonferroni *t*, $P<.05$).
‡$P<.05$ (the comparisons are between low-dose and high-dose means).
§$P<.1$ (the comparisons are between low-dose and high-dose means).
‖$P<.05$.
¶$P<.1$.

research purposes. The results of these measures will be reported elsewhere. Free methyltestosterone levels were obtained at baseline, during high-dose steroid administration, and during withdrawal. Levels were measured by gas chromatography/mass spectroscopy.[34] The relationship between symptom development (high-dose–baseline values) and methyltestosterone levels was assessed with Pearson product moment correlation coefficients.

RESULTS

Subject Characteristics

Twenty male volunteers (11 white and nine African American; 10 high school and 10 college graduates) ranged in age from 18 to 42 years (mean±SD, 27.5±5.7 years). None of the subjects were conditioned athletes or had been previously exposed to anabolic steroids. Four subjects had a brief past history of substance abuse but had been abstinent for 3 to 20 years and were included in the study. On the PDQR five subjects scored above the customary cutoff of 15, but all were below 40, a score reported to be associated with a significant personality disturbance.

Side Effects and Laboratory Tests

Vital signs were normal throughout the study. Decreased urine output (<700 mL/d) (n=3), acne (n=3), and itching (n=2) occurred during the high-dose condition, and urinary frequency (n=3) and headaches (n=6) occurred during the low-dose condition. Headaches were difficult to attribute to the methyltestosterone because of the emergence of possible post–lumbar puncture headaches. Results of laboratory tests including liver function, kidney function, glucose level, electrolytes, complete blood cell count, sedimentation rate, prothrombin time and partial thromboplastin time, urinalysis, and cerebrospinal fluid biochemistry were all within normal limits during, and 7 to 10 days after finishing, the study.

Behavioral Evaluation and Symptom Ratings

Visual Analogue Scale Measures.—*Four Drug Condition Comparisons (Baseline, Low Dose, High Dose, Withdrawal).*—ANOVA-R identified significant effects of drug condition for the symptoms of sexual arousal and headache (Table 1) as well as trends for distractibility and increased energy (Table 1) and morning forgetfulness and nighttime mood swings (Table 2).

High-Dose vs Baseline Comparisons.—Significant increases were found in the high-dose condition for the symptoms of distractibility, level of energy, irritability, and sexual arousal and a trend in the symptoms of insomnia, anger, violent feelings, and fatigue (Table 1). Additionally, significant increases for each rating time were identified during the high-dose condition on distractibility (evening), mood swings (nighttime), violent feelings (nighttime), euphoria (morning), forgetfulness (morning), and confusion (nighttime) (Table 2).

Baseline vs Low-Dose and Withdrawal Comparisons.—While almost all symptom ratings during the low-dose condition were intermediate between those at baseline and during the high-dose condition, headache ratings during the low-dose condition were significantly greater than both baseline and high-dose ratings. Low-dose ratings for sexual arousal and appetite were also significantly greater than baseline. Only ratings of sexual arousal were significantly greater during withdrawal compared with baseline.

BDI and STAI Self-ratings and HAM-D, BPRS, and MMSE Objective Ratings.—Significant increases during the high-dose condition compared with baseline were observed in the mean of the daily BDI, BPRS, and HAM-D scores (Table 3). Compared with baseline, BPRS and HAM-D scores during withdrawal and HAM-D scores during the low-dose condition were also elevated. There were no significant drug effects on the STAI or the MMSE ratings.

SCL-90.—ANOVA-R identified significant effects of drug condition on the following subscale scores for four drug conditions: somatization, depression, anxiety, and hostility (Table 3). Compared with baseline ratings, scores of hostility, anxiety, and somatization were significantly higher during the high-dose condition and scores of depression, anxiety, obsessive-compulsion, and somatization were significantly higher during the low-dose condition. There were no changes in the scores of other subscales.

Activity Monitor.—ANOVA-R identified no significant effects of drug condition on mean daily activity units. However, the changes in activity observed between the baseline and the high-dose condition were significantly correlated with the changes in VAS energy self-ratings (Pearson $r=.71$, $P<.005$).

Nursing Assessments and Observations.—Based on clinical observations (consisting of the subjects' diaries and the nurses' reports), three subjects met DSM-III-R criteria (except the duration criterion for depression) for affective disorders (one, mania; one, hypomania; one, major depression) during methyltestosterone administration. The subject who developed a major depression also concomitantly experienced a severe post–lumbar puncture headache. No psychotic symptoms were observed in any subject.

The subject who developed mania was a 34-year-old white man with no past personal or family psychiatric history (including substance abuse). He was ob-

Table 2.—Comparisons of Visual Analogue Scale Self-ratings at Each of Three Daily Rating Times*

Symptom	Time Point	Mean Score (±SD) B	LD	HD	W	ANOVA-R F	P	df
Self-confidence	Evening	58.9 (11.3)	62.9 (13.5)†	62.5 (12.3)	60.7 (14.1)	4.0	<.05	3,17
Forgetfulness	Morning	2.4 (2.1)	3.7 (4.3)	4.2 (3.6)‡	3.4 (4.2)	2.6	<.1	3,17
Distractibility	Evening	2.8 (2.2)	3.9 (4.7)	7.1 (7.1)§	4.3 (4.2)	2.8	<.1	3,17
Mood swings	Night	19.4 (19.3)	23.3 (18.9)	26.4 (21.7)§	24.8 (21.3)	3.1	<.1	3,15
Violent feelings	Night	16.8 (16.9)	18.4 (18.4)	21.9 (19.4)§	19.1 (19.7)	NS	...	...
Euphoria	Morning	55.7 (10.3)	55.6 (11.3)	59.3 (12.8)‡	56.7 (12.5)	NS	...	...
Sexual arousal	Evening	55.2 (6.8)	58.5 (12.6)	59.5 (10.0)‡	59.4 (12.6)	NS	...	...
Confusion	Night	3.4 (6.4)	3.6 (6.1)	6.1 (8.9)‡	2.9 (3.2)	NS	...	...

*All paired *t* test *P* values represent comparisons with baseline means. B indicates baseline; LD, low dose; HD, high dose; W, withdrawal; ANOVA-R, analysis of variance with repeated measures; and NS, nonsignificant for all four treatment conditions.
†$P<.1$.
‡$P<.05$.
§$P<.01$ (Bonferroni *t*, $P<.05$).

Table 3.—Comparisons of Daily Behavioral Rating Scale Scores*

Behavioral Measures	Mean Scores (±SD) B	LD	HD	W	ANOVA-R F	P	df
BPRS	25.7 (1.6)	26.2 (2.4)	27.5 (4.3)†	26.9 (2.4)†	3.0	<.1	3,17
HAM-D	1.6 (1.7)	2.8 (2.2)†	3.6 (4.2)†	2.9 (2.5)†	2.9	<.1	3,17
BDI	1.0 (1.8)	2.0 (2.7)	2.1 (2.9)†	2.1 (3.0)‡	NS	NS	...
SCL-90 Subscales					NS	NS	...
Somatization	0.7 (0.9)	2.3 (1.9)†	2.0 (2.4)†	1.1 (1.4)	5.1	<.05	3,12
Depression	0.9 (1.1)	2.3 (2.2)†	1.7 (2.4)	0.7 (1.4)	4.7	<.05	3,12
Anxiety	0.3 (0.6)	1.3 (1.9)†	1.2 (1.9)†	0.7 (1.2)	3.8	<.05	3,12
Hostility	0.2 (0.6)	0.8 (0.9)	1.7 (2.9)†	0.3 (0.7)	4.8	<.05	3,12
Obsessive-compulsive	0.7 (1.2)	2.0 (2.1)†	2.1 (2.3)‡	0.6 (1.1)	NS	NS	...

*The SCL-90 was administered at the end of each drug condition. All of the other scales were administered daily. All paired *t* test *P* values represent comparisons with baseline means. BPRS indicates Brief Psychiatric Rating Scale; HAM-D, Hamilton Depression Rating Scale; BDI, Beck Depression Inventory; SCL-90, Symptom Checklist 90; B, baseline; LD, low dose; HD, high dose; W, withdrawal; ANOVA-R, analysis of variance with repeated measures; and NS, nonsignificant for all four treatment conditions.
†$P<.05$.
‡$P<.1$.

served to exhibit intrusive behavior and giddiness and reported an increased libido and energy level on the last day of the low-dose condition. He developed manic symptoms including mixed euphoria and dysphoria, irritability, alternating feelings of high energy and fatigue, pressured speech, racing thoughts, sleep disturbance, and increased libido at the end of the high-dose condition. His negative mood symptoms increasingly became predominant. He felt extremely angry, violent, and aggressive. He also reported being severely distractible and confused. On the first day of the withdrawal period, his violence and impulsivity led to his request to be placed in open seclusion. Symptoms gradually subsided and completely disappeared over the next 3 days, and he was discharged at the end of the withdrawal period.

Anabolic Steroid Blood Levels

The mean plasma level of free methyltestosterone 13 hours after the last dose administered was 63.4±73.5 nmol/L. Steroid levels were undetectable at baseline and following withdrawal (3 days). No significant correlations were observed between anabolic steroid levels and body weight or the change in morning behavioral symptoms (either individual symptoms or groups of symptoms reflecting positive mood, negative mood, or cognitive impairment) from baseline to the high-dose condition.

COMMENT

This is the first study to examine the behavioral effects of anabolic steroids in a placebo-controlled, prospective fashion. On the basis of case studies, retrospective reports, and psychological inventory surveys of anabolic steroid users, we anticipated discovering increased mood and behavioral symptoms during anabolic steroid administration compared with baseline. Consistent with these expectations, we found significant increases during the high-dose condition of mean daily highest VAS ratings of distractibility, irritability, and energy level, with trends for an increase in anger, violent feelings, insomnia, and fatigue. Additionally, significant increases were seen during high-dose methyltestosterone administration at one of the three daily rating times for mood swings, violent feelings, forgetfulness, confusion, and euphoria. These VAS data were paralleled by increases during the high-dose condition of the mean daily BDI, HAM-D, and BPRS scores as well as the hostility, anxiety, and somatization scales of the SCL-90. These latter findings appear to confirm the report by Perry et al[19] that anabolic steroid users showed increased hostility, anxiety, somatization, and depression on the SCL-90 during drug use. Our findings also parallel those of Hannan et al,[35] who observed significant treatment-related increases on the hostility and resentment/aggression subscales of the Minnesota Multiphasic Personality Inventory after 6 weeks of treatment with testosterone or the anabolic steroid, nandrolone.

The increased symptoms that we observed during anabolic steroid administration, while significant, were subtle, reflecting several factors. First, the response to anabolic steroids across members of the subject group was highly variable, ranging from negligible to dramatic. A marked increase in symptoms during steroid administration in only four or five subjects was sufficient to enable relatively small differences in means to reach statistical significance. Symptomatic differences did not, however, reflect differences in plasma anabolic steroid levels. Second, compared with anabolic steroid self-administration in the naturalistic setting, our subjects received only a low dose of a single anabolic steroid for a very short period of time, therefore biasing against identification of the dra-

matic behavioral effects that, by anecdote, occur after high doses (up to a hundred times the therapeutic dose) of multiple anabolic steroids for lengthy periods (weeks to months). Third, several subjects stated that, while still blind, they recognized the changes that occurred during the third phase (high dose) of the study only from the vantage point of the last drug condition (withdrawal), therefore suggesting that the self-ratings may, in some cases, have been relatively insensitive. While many of the symptom comparisons did not reach significance when a Bonferroni correction was applied, the mood and behavioral changes seen were, in general, consistent with retrospective and concurrent reports describing irritability, mood lability, aggressiveness, confusion, and hypomania[7-10] in association with anabolic steroid administration. As the changes we observed were in the predicted direction, we believed that a two-tailed t test was conservative and that the symptom increases were not simply a reflection of multiple comparisons.

While symptom ratings during the low-dose condition were, in general, intermediate between those at baseline and those during the high-dose condition, significant increases in ratings were seen for three symptoms during the low-dose but not the high-dose condition: headache, appetite, and depression (SCL-90). Interpretation of these few exceptions is complicated by the appearance of possible post–lumbar puncture headaches during the low-dose condition in six of the 20 subjects, consistent with a post–lumbar puncture headache rate of approximately one third in normal volunteers.[36]

It has been suggested that the ostensible salutary effects of anabolic steroids on athletic performance derive, in part, from an enhanced sense of well-being and increased enthusiasm for training. Although self-ratings appeared to move, in general, in a negative direction during high-dose anabolic steroid administration, we did observe (consistent with earlier reports) a significant increase in sexual arousal, energy, and, during the morning, euphoria. Evening self-confidence ratings also increased during anabolic steroid administration compared with baseline. While these changes were, again, subtle, their accuracy is suggested by the confirmation of self-ratings of energy by activity monitor records. Subjects' energy self-ratings were highly correlated with activity monitor readings during the high-dose condition.

In conclusion, although the results of this prospective, placebo-controlled study in a hospital setting may not generalize well to unregulated use in a naturalistic setting, we nonetheless have demonstrated that anabolic steroids have a significant impact on mood and behavior in normal male volunteers even during short-term, relatively low-dose administration. High-dose anabolic steroids in our sample were associated with significant albeit subtle increases in the following: (1) positive mood: euphoria, energy, and sexual arousal; (2) negative mood: irritability, mood swings, violent feelings, anger, and hostility; and (3) "cognitive" symptoms: distractibility, forgetfulness, and confusion. Profound "psychoactive effects" (mania) were seen in one of the 20 subjects, representing a 5% incidence, even under the conservative conditions of this trial. No predictors at baseline, including presence of personal past histories of substance abuse or family history of mental illness or substance abuse, were related to the symptom changes. This study confirms, therefore, earlier studies suggesting both the activating and adverse mood and behavioral effects of anabolic steroids and further suggests that identification of the possible mechanisms of these effects may significantly advance our understanding of behavioral regulation in humans.

The authors are grateful to the 4 East patient care unit nursing staff at the clinical center, National Institutes of Health, for their help with behavioral measures, data collection, and clinical care; to John Bartko, PhD, for statistical consultation; and to Christine Ayotte, PhD, for methyltestosterone assay performance.

References

1. *Physicians' Desk Reference*. 43rd ed. Oradell, NJ: Medical Economics Co Inc; 1989:851-852.
2. Cowart VS. National Institute on Drug Abuse may join in anabolic steroid research. *JAMA*. 1989; 261:1855-1857.
3. Council on Scientific Affairs, American Medical Association. Drug abuse in athletes: anabolic steroids and human growth hormone. *JAMA*. 1988;259: 1703-1705.
4. Kashkin KB, Kleber HD. Hooked on hormones? an anabolic steroid addiction hypothesis. *JAMA*. 1989; 262:3166-3170.
5. Williamson DJ, Young AH. Psychiatric effects of androgenic and anabolic-androgenic steroid abuse in men: a brief review of the literature. *J Psychopharmacol*. 1992;6:20-26.
6. Annitto WJ, Layman WA. Anabolic steroids and acute schizophrenic episode: case reports. *J Clin Psychiatry*. 1980;41:143-144.
7. Freinhar JP, Alverez W. Androgen-induced hypomania. *J Clin Psychiatry*. 1985;46:354-355.
8. Tilzey A, Heptonstall J, Hamblin T. Toxic confusional state and choreiform movements after treatment with anabolic steroids. *BMJ*. 1981;285:349-350.
9. Barker S. Oxymethalone and aggression. *Br J Psychiatry*. 1987;151:564.
10. Pope HG Jr, Katz DL. Affective and psychotic symptoms associated with anabolic steroid use. *Am J Psychiatry*. 1988;145:487-490.
11. Choi PYL, Parrott AC, Cowan D. High-dose anabolic steroids in strength athletes: effects upon hostility and aggression. *Hum Psychopharmacol*. 1990;5:349-356.
12. Lefavi RG, Reeve TG, Newland MC. Relationship between anabolic steroid use and selected psychological parameters in male bodybuilders. *J Sport Behav*. 1990;13:157-166.
13. Perry PJ, Yates WR, Andersen KH. Psychiatric symptoms associated with anabolic steroids: a controlled, retrospective study. *Ann Clin Psychiatry*. 1990;2:11-17.
14. Bahrke MS, Wright JE, O'Connor JS, Strauss RH, Catlin DH. Selected psychological characteristics of anabolic-androgenic steroid users. *N Engl J Med*. 1990;323:834-835.
15. Brower KJ, Blow FC, Eliopulos GA, Beresford TP. Anabolic androgenic steroids and suicide. *Am J Psychiatry*. 1989;146:1075.
16. Brower KJ, Blow FC, Beresford TP, Fuelling C. Anabolic-androgenic steroid dependence. *J Clin Psychiatry*. 1989;50:31-33.
17. Tennant F, Black DL, Voy RO. Anabolic steroid dependence with opioid-type features. *N Engl J Med*. 1988;319:578.
18. Vogel W, Klaiber EL, Broverman DM. A comparison of the antidepressant effects of a synthetic androgen (mesterolone) and amitriptyline in depressed men. *J Clin Psychiatry*. 1985;46:6-8.
19. Itil TM, Michael ST, Soldatos C. Androgens as antidepressants. *Psychopharmacol Bull*. 1979;15: 31-35.
20. Itil TM, Cora R, Akpinar S, Herrmann WM, Patterson CJ. 'Psychotropic' action of sex hormones: computerized EEG in establishing the immediate CNS effects of steroid hormones. *Curr Ther Res*. 1974;16:1147-1167.
21. Beumont PJV, Bancroft JHJ, Beardwood CJ. Behavioural changes after treatment with testosterone: a case report. *Psychol Med*. 1972;2:70-72.
22. Itil TM, Michael ST, Shapiro DM, Itil KZ. The effects of mesterolone, a male sex hormone, in depressed patients (a double blind controlled study). *Methods Find Exp Clin Pharmacol*. 1984;6:331-337.
23. Wilson I, Prange A, Lara P. Methyltestosterone with imipramine in men: conversion of depression to paranoid reactions. *Am J Psychiatry*. 1974; 131:21-24.
24. Spitzer RL, Endicott J. *Schedule for Affective Disorders and Schizophrenia—Lifetime Version*. New York, NY: New York State Psychiatric Institute, Biometrics Research; 1975.
25. Hyler SE, Rieder RO, Williams JBW, Spitzer RL, Lyons M, Hendler J. A comparison of clinical and self-report diagnoses of DSM-III personality disorders in 552 patients. *Compr Psychiatry*. 1989; 30:170-178.
26. Hyler SE, Rieder RO. *Personality Diagnostic Questionnaire (PDQ)—Revised (PDQ-R)*. New York, NY: New York State Psychiatric Institute; 1987.
27. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. *Arch Gen Psychiatry*. 1961;4:561-571.
28. Spielberger CB, Gorsuch RL, Luschene RE. *STAI Manual for the State-Trait Anxiety Inventory*. Palo Alto, Calif: Consulting Psychologists Press; 1970.
29. Derogatis LR, Lipman RS, Covi L. The SCL-90: an outpatient psychiatric rating scale. *Psychopharmacol Bull*. 1973;9:13-28.
30. Overall JE, Gorham DR. The Brief Psychiatric Rating Scale. *Psychol Rep*. 1962;10:799-812.
31. Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry*. 1960;12:56-62.
32. Folstein MF, Folstein SE, McHugh PR. 'Mini-Mental State,' a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975;12:189-198.
33. Colburn TR, Smith BM, Guarini JJ, Simmons NN. An ambulatory activity monitor with solid state memory. *Instrument Soc Am Trans*. 1976;15:149-154.
34. Lal S, Vasavan Nair NP, Thavundayil JX, Tawar V, Guyda H, Ayotte C. The effect of methyltestosterone on the growth hormone response to the dopamine receptor agonist, apomorphine. *Prog Neuropsychopharmacol Biol Psychiatry*. 1991;15:263-268.
35. Hannan CJ Jr, Friedl KE, Zold A, Kettler TM, Plymate SR. Psychological and serum homovanillic acid changes in men administered androgenic steroids. *Psychoneuroendocrinology*. 1991;16:335-343.
36. Tourtellotte WW, Haerer AF, Heller GL, Somers JE. *Post–Lumbar Puncture Headaches*. Springfield, Ill: Charles C Thomas Publisher; 1964.