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The Effects of Supraphysiological Doses of Testosterone on Angry Behavior in Healthy Eugonadal Men—A Clinical Research Center Study*

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ABSTRACT

Anecdotal reports of "roid rage" and violent crimes by androgenic steroid users have brought attention to the relationship between anabolic steroid use and angry outbursts. However, testosterone effects on human aggression remain controversial. Previous studies have been criticized because of the low androgen doses, lack of placebo control or blinding, and inclusion of competitive athletes and those with preexisting psychopathology. To overcome these pitfalls, we used a double-blind, placebo-controlled design, excluded competitive athletes and those with psychiatric disorders, and used 600 mg testosterone enanthate (TE)/week. Forty-three eugonadal men, 19–40 yr, were randomized to 1 of 4 groups: Group I, placebo, no exercise; Group II, TE, no exercise; Group III, placebo, exercise; Group IV, TE plus exercise. Exercise consisted of thrice weekly strength training sessions. The Multi-Dimensional Anger Inventory (MAI), which includes 5 different dimensions of anger (inward anger, outward anger, anger-arousal, hostile outlook, and anger eliciting situations), and a Mood Inventory (MI), which includes items related to mood and behavior, were administered to subjects before, during, and after the 10 week intervention. The subject's significant other (spouse, live-in partner, or parent) also answered the same questions about the subject's mood and behavior (Observer Mood Inventory, OMI). No differences were observed between exercising and nonexercising and between placebo and TE treated subjects for any of the 5 subdomains of MAI. Overall there were no significant changes in MI or OMI during the treatment period in any group. Conclusion: Supraphysiological doses of testosterone, when administered to normal men in a controlled setting, do not increase angry behavior. These data do not exclude the possibility that still higher doses of multiple steroids might provoke angry behavior in men with preexisting psychopathology. (*J Clin Endocrinol Metab* **81:** 3754–3758, 1996)

THE EFFECTS of androgenic/anabolic steroids on aggression remain controversial (1–2). Testosterone promotes aggressive behavior among male animals (3–8), particularly, at the time of mate selection, but its effects on human aggression remain unclear (1–2). There is a significant, though not a strong, correlation between serum testosterone levels and some aspects of aggressive behavior in men (9–15). A significant proportion of steroid users report mood disorders, manic and hypomanic syndromes characterized by aggressiveness, and other psychiatric problems (18, 22–24). Steroid users have higher scores than nonusers on the anger arousal and hostile outlook dimensions of the Multi-Dimensional Anger Inventory (MAI, 19), and show higher levels of aggression, hostility, irritability and hyperactivity than non-users (25). Several studies (25–26) have reported increased aggression, irritability, euphoria, and psychiatric effects among athletes given moderate doses of methyl testosterone. Administration of high doses of testosterone cypionate results in increased aggressive responding in men compared to placebo (27). These observations and case reports (16–21) of violent crimes committed by individuals taking anabolic steroids have brought attention to the relationship of anabolic steroid use to angry outbursts.

Most of the published studies have suffered from significant flaws in study design that have been discussed in excellent reviews (1–2, 28). Some of the studies are case reports, while many others are correlational studies (29). Controlled studies on the behavioral and psychiatric effects of androgenic steroids have been limited (30). In most experimental studies, the doses of androgenic steroid used have been small (31–37). Many of the studies have included competitive athletes whose motivation to win may override the need to comply with the research protocol. Moreover, most of the studies are based on self reports of athletes or body builders (15–16, 18). It is possible that the subjects themselves may not be cognizant of the change in their behavior, although others in close contact with the subject may discern a significant change. None of the previous studies (15–18) has verified the subject's behavior by questioning the significant other. Only a few studies have examined the change in behavior during androgen treatment (25–27). Finally, some of the studies have

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included individuals with earlier psychiatric problems or behavior disorders; their inclusion can confound the data.

We used a double-blind, placebo-controlled study design. Competitive athletes and men with psychiatric illness, behavior disorders, or drug use were excluded. The exercise stimulus and the nutritional intake were standardized. The dose of testosterone enanthate used, 600 mg/week, was the highest dose ever used in a controlled study. In addition to the subject, a significant other (spouse, live-in partner, or a live-in parent) was asked to independently respond to the questionnaire at the same time. Standardized and validated instruments (38) were used to assess angry behaviors. Because many of the publicized cases of "roid rage" had involved athletes, we also examined the interaction between testosterone and resistance exercise with respect to their effects on mood and angry behavior.

Materials and Methods

Methods

All subjects provided a written, informed consent approved by the Institutional Review Boards of the Research and Education Institute and Charles R. Drew University of Medicine and Science. These subjects were part of a larger study; details of the overall experimental design have been described in a previous publication (39).

Subjects. Healthy, eugonadal, nonobese (less than 15% of ideal body weight) men, 19–40 yr of age, who had earlier experience with weight lifting but were not currently engaged in competitive sports were recruited. Men with systemic illness, disabilities that interfered with the subject's ability to exercise, psychiatric or behavior disorders, and those unable to comprehend the protocol were excluded.

Study design. Of the 50 men who were recruited, 7 dropped out during the control phase because of scheduling difficulties or compliance problems. Forty-three subjects were randomized to one of the following four groups: group I, placebo and no exercise; group II, testosterone, but no exercise; group III, placebo, exercise; and group IV, testosterone plus exercise.

The study was divided into a 4-week control period, a 10-week treatment period, and a 16-week recovery period. Three of the 43 men dropped out during the treatment phase because of compliance problems (one subject), use of illicit drugs detected on routine drug screen (one subject), and an automobile accident (one subject). Ten subjects in group I, 10 in group II, 9 in group III, and 11 in group IV completed the study.

Treatment. Subjects received either 600 mg testosterone enanthate in 3 mL sesame oil or placebo (3 mL sesame oil alone) by intramuscular injection in the gluteal region every week in the Clinical Research Center (CRC) to assure compliance.

Standardization of protein and energy intake, and exercise stimulus. Two weeks before treatment day 1, the men were instructed to take a standardized daily 36 kcals/kg diet containing 1.5 g/kg protein and 100% RDA intake of vitamins, minerals, and trace elements. Compliance was verified every four weeks by 3-day food records.

Groups III and IV completed 10 weeks of controlled and supervised strength training using a 3-day per week regimen, as previously described (39). All subjects trained at intensities calculated from their initial 1-repetition maximum values.

Instruments:

The three instruments used, the Multidimensional Anger Inventory (MAI), the Mood Inventory (MI), and the Observer Mood Inventory (OMI), were administered at baseline and during treatment weeks 6 and 10, 7 days after the previous injection to coincide with the nadir testosterone levels. The subjects answered the questions in the privacy of a Clinical Research Center room. The OMI was given to a significant other at approximately the same times.

The multidimensional anger inventory (38) was selected as a standardized and previously validated instrument that has been used in previous studies related to steroid use and aggressive behavior (18). The instrument was administered and scored in the same manner as the original measure. This instrument contains 38 items that measure the following dimensions of anger: frequency, duration, magnitude, range of anger eliciting situations, and hostile outlook. The number of items included to assess the dimensions of anger were 5 for frequency (*e.g.* I tend to get angry more frequently than most people); 2 for duration (*e.g.* I get angry and stay angry for hours); 4 for magnitude (*e.g.* People seem to get angrier than I do in similar circumstances-reverse scored); 12 for mode of expression; 6 for hostile outlook (*e.g.* people talk about me behind my back); and 9 for range of anger eliciting situations (*e.g.* I get angry when someone lets me down). Each of the 38 statements were rated in terms of how self-destructive they were. Responses to the questions ranged from 1 (completely false) to 5 (completely true).

Mood inventory (MI) and the observer mood inventory (OMI). Both of these instruments included 39 items that were identical and selected on the basis of face validity. Some items were adapted from existing inventories and were rephrased and duplicated as necessary to provide a consistent format for the OMI and MI; others were written specifically for this study. The purpose of the OMI was to obtain data that were based upon observations of a significant other (*i.e.* spouse, a live-in-partner, or a live-in parent) over time, with the intention of providing an independent check on the responses of the study subjects.

The MI and OMI were organized into three sections and contained 1) 20 items related to general mood (*e.g.* OMI: During the past two weeks how would you describe his mood toward his family? MI: During the past two weeks how would you describe your mood toward your family?); 2) 9 items related to emotional stability (*e.g.* OMI: During the past two weeks has he seemed like he would strike someone? MI: During the past two weeks have you felt like striking someone? Responses to these questions were 1-yes, 2-no.), and 3) 10 items related to angry behavior (*e.g.* OMI: During the past two weeks has he used bad language more than usual? MI: During the past two weeks have you used bad language more than usual? Responses for these questions ranged from 1-rarely to 10-frequently). The instruments were developed primarily by the investigators to supplement the information contained in the MAI pertaining to work, personal life, and exercise habits of subjects, activities that could be verified by a third party observer.

The reliability of the instrument was tested using the test-retest (7-day time elapse) procedures in 41 college students. Reliability coefficients for the three subsections ranged from 0.78 for the 20-item section on mood, 0.99 for the 9-item section on emotional stability, and 0.70 for the 10-item section on angry behavior. The overall reliability coefficient for the MI was 0.81. Face validity was established by a review panel whose members had experience in the field of measurement and health and exercise science. Panel members were asked to rate each item as "not useful", "useful", and "very useful". Items deemed "not useful" by more than 33% of the panel were removed, and others were reworded for clarity and balance based on the feedback from the panel.

Hormone measurements. Serum total and free testosterone, LH, FSH, and sex-hormone binding globulin (SHBG) levels were measured on three occasions during the control period and on days 2, 3, 7, 14, 28, 42, 56, and 70. Hormone assays have been previously described (39).

Statistical analysis. Scores were tallied for each of the three sections in the OMI and MI (general mood, emotional stability, and angry behavior) and the five subdomains in the MAI (anger-in, anger-out, hostility, anger eliciting situations, and anger arousal), and means and standard deviations were computed. Time-by-treatment interactions were examined using repeated measures analysis of variance and Maulchy's test to test sphericity. In no case was the null hypothesis of sphericity rejected at the 0.05 level of significance. Also, no significant treatment/exercise interactions were observed at the 0.05 level. Therefore, for the purpose of increasing group size, the following results are based upon analyses of two groups; the subjects receiving the placebo with or without exercise, and the subjects receiving testosterone enanthate with or without exercise.

Results

At baseline, the four treatment groups did not differ significantly from one another in age, ethnic background, height, weight, or body mass index. Mean serum testosterone, LH, and FSH levels were also not significantly different between these four groups. Details of these data have been presented in a separate manuscript (39).

Hormone levels. Mean serum total and free testosterone levels significantly increased in the testosterone treated men (16.1 + 1.3 to 76.9 + 5.6 nmol/L, mean + SEM, baseline *vs* nadir levels during treatment) but did not change significantly in the placebo-treated men (18.6 + 1.3 to 19.4 + 1.3 nmol/L, mean + SEM, baseline *vs* nadir levels during treatment, 39). Serum LH and FSH levels decreased significantly in the testosterone treated men (LH, 3.49 + 0.36 *vs* 0.42 + 0.13 U/L, mean + SEM baseline *vs* treatment, 39), but not in the placebo treated men (3.62 + 0.39 *vs* 4.58 + 0.47 U/L, mean + SEM, baseline *vs* treatment levels). Significant suppression of serum LH and FSH levels in the testosterone treated subjects, but not in the placebo treated subjects, provides further evidence that the subjects adhered to the treatment regimens.

Multidimensional anger inventory (MAI)

No significant differences were observed in any of the subdomains of the MAI scores at the baseline (before administration of the drug), between the subjects who received testosterone and the subjects who received the placebo (Table 1). Analysis of variance with repeated measures revealed no significant differences in the interaction between treatment and time for any of the five subdomains of anger-in ($P > 0.905$), anger-out ($P > 0.071$), hostile outlook ($P > 0.553$), anger arousal ($P > 0.612$), and the range of anger eliciting situations ($P > 0.343$).

Mood Inventory

There were no significant group differences between the testosterone or placebo treated subjects on any of the items related to general mood either before or at the end of the 10-week treatment period (Table 2). There was also no significant time-by-treatment interaction. Similarly, there were no significant differences in group scores related to emotional stability or angry behavior between the subjects receiving testosterone and the subjects receiving the placebo either before or after the treatment period; there were also no significant time-by-treatment interactions (Table 2).

Observer Mood Inventory (OMI)

There were no significant changes in the OMI scores for any of the subdomains between groups or within each treatment group (Table 3). We were unable to detect any significance within or between group differences for any of the subdomains of the mood inventory. However, to assess whether there were any subjects in the testosterone group who had high scores, we carefully scrutinized responses of individual subjects and their significant others. Considering that 1 = "rarely occurring" and 10 = "frequently occurring", any number approaching 10, say 7 or above, would be worthy of closer attention because this would indicate that some abnormal behavior patterns were beginning to emerge. We found that five men on testosterone and/or their significant others had reported high scores (>7) on the mood inventory. For example, a significant other of subject 29 reported that the subject had "lost temper more than usual (10)", been angrier than usual with those who disagreed with him (8), been "told frequently that he had a problem with his aggressive temper (9)." However, an equal number (five) of subjects in the placebo treated group also had scores of 7 or more.

Discussion

Our study failed to detect any significant effects of testosterone treatment on mood or the subsets of angry behavior examined. Several previous reports that have linked hostility and aggressive behavior to anabolic steroid use have had significant problems of study design and instrumentation; consequently, this issue has continued to be controversial. The subjects in this blinded study were men with no history of previous behavioral or psychiatric problems or drug use. Although those evaluating the outcomes were blinded, we can not be entirely sure whether the subjects were completely unaware of the treatment; some men who developed acne or experienced weight and strength gains may have assumed themselves to be receiving testosterone. High degree of compliance was achieved. The relative lack of significant effects of testosterone on angry behaviors indicates that there is not a simple, direct, causal relationship between steroid use and aggressive behavior in normal men.

The steroid used in this study (testosterone enanthate) was selected for use based on its safety record established in male contraceptive studies (42) and clinical experience. The dose of testosterone enanthate used in this study was the highest dose used in any clinical trial designed to examine the effect of testosterone on body composition or behavior. We rec-

TABLE 1. Effect of testosterone treatment on multidimensional anger inventory scores

Treatment group	Placebo treated men			Testosterone treated men			F	P
	Baseline	Week 6	Week 10	Baseline	Week 6	Week 10		
Anger arousal	1.83 ± 0.45	2.18 ± 0.72	2.00 ± 0.62	1.88 ± 0.66	2.20 ± 0.61	2.13 ± 0.70	0.26	0.621
Range of anger eliciting situations	2.83 ± 0.67	2.96 ± 0.60	2.76 ± 0.57	2.79 ± 0.54	2.84 ± 0.54	2.96 ± 0.58	0.93	0.342
Hostile situations								
Hostile outlook	2.50 ± 0.54	2.64 ± 0.71	2.44 ± 0.52	2.59 ± 0.89	2.43 ± 0.72	2.57 ± 0.62	0.36	0.553
Anger-in	2.16 ± 0.64	2.14 ± 0.42	2.12 ± 0.53	2.07 ± 0.78	2.01 ± 0.59	2.15 ± 0.58	0.01	0.905
Anger-out	3.50 ± 0.79	3.42 ± 0.70	3.25 ± 0.80	4.02 ± 0.65	3.91 ± 0.75	3.88 ± 0.57	3.51	0.070

Baseline = MAI scores on day 0. Week 6 = MAI scores during the treatment week 6. Week 10 = MAI scores during treatment week 10. Data are mean ± SD. Placebo treated men = Men treated with placebo injections with or without resistance exercise. Testosterone treated men = Men treated with 600 mg testosterone enanthate/week with or without resistance exercise. F, F statistic for repeated measures analysis of variance; P, probability value associated with the F statistic.

TABLE 2. Effects of testosterone treatment on mood inventory scores

Treatment groups	Placebo treated men			Testosterone treated men			F	P
	Pre	Week 6	Post	Pre	Week 6	Post		
General mood	7.46 ± 1.12	7.06 ± 0.96	7.17 ± 0.91	7.02 ± 0.96	6.85 ± 0.96	6.28 ± 2.67	0.35	0.56
Emotional stability	1.94 ± 0.07	1.87 ± 0.16	1.91 ± 0.13	1.86 ± 0.18	1.83 ± 0.17	1.87 ± 0.16	0.64	0.42
Angry behavior	2.19 ± 1.29	2.93 ± 1.36	2.85 ± 1.43	3.08 ± 2.03	3.30 ± 1.57	3.14 ± 1.83	0.01	0.90

Data are mean ± SD. Baseline = Pre-test Mood Inventory scores on day 0. Week 6 = Mood Inventory scores during treatment week 6. Week 10 = Mood Inventory scores during treatment week 10. Placebo treated men = Men treated with placebo injections with or without resistance exercise. Testosterone treated men = Men treated with 600 mg testosterone enanthate/week with or without resistance exercise. F, F statistic for repeated measures analysis of variance; P, probability value associated with the F statistic.

TABLE 3. Observer Mood Inventory (OMI) scores for the placebo and testosterone treated subjects

Treatment Groups	Placebo Treated Men			Testosterone Treated Men			F	P
	Baseline	Week 6	Week 10	Baseline	Week 6	Week 10		
General mood	7.04 ± 0.9	6.62 ± 1.04	6.44 ± 1.41	6.57 ± 1.24	5.41 ± 2.93	5.93 ± 2.85	1.0	0.50
Emotional stability	1.94 ± 0.08	1.89 ± 0.14	1.90 ± 0.09	1.87 ± 0.13	1.82 ± 0.17	1.85 ± 0.16	1.83	0.14
Angry behavior	2.65 ± 1.60	2.96 ± 1.87	2.96 ± 1.78	2.92 ± 1.78	3.86 ± 2.60	3.32 ± 1.77	0.87	0.59

Baseline = Pretreatment scores on day 0. Week 6 = OMI scores during week 6 of treatment. Week 10 = OMI scores during week 10 of treatment. Placebo treated men = Men treated with placebo injections with or without resistance exercise. Testosterone treated men = Men treated with 600 mg testosterone enanthate/week with or without resistance exercise. Data are mean ± SD. F, F statistic for repeated measures analysis of variance; P, probability value associated with the F statistic.

ognize that some competitive and recreational athletes and body builders use even higher doses of androgenic steroids or "stack" multiple steroids (31–37). This study did not address the issue of whether still higher doses of multiple steroids might affect some aspects of aggressive behavior.

Dabbs *et al.* (9, 29, 41) have reported a significant relationship between serum testosterone levels and violence of crime among prison inmates. Mean testosterone levels were higher in delinquent subjects, males and females, than in the control group of college students. In a study of Vietnam veterans (11, 41), testosterone at adolescence predicted later difficulties, including problems at school. Men with lower testosterone levels appear to be more docile and develop more stable communal relationships. However, the reported correlations between serum testosterone levels and antisocial behavior are not very high ($r = 0.15$ to $r = 0.20$, 28), and serum testosterone levels may be affected by agonistic or social encounters.

The effects of testosterone in promoting aggression among male animals at the time of mate selection are established. Testosterone has been shown to affect scent marking behavior, one measure of territoriality among male animals (8). The competition among new born male hyenas is a testosterone dependent phenomenon (3). In contrast to animals, human behavior is quite complex and modified by social forces and learned restraints. It is conceivable that the behavioral effects of testosterone may be greatly attenuated in carefully recruited individuals with relatively high education level, such as the ones selected for this study. Indeed, testosterone levels predict delinquency more strongly in men with low education and socioeconomic status than in those with high socioeconomic status (29).

These data and published information still do not adequately explain why some steroid users become excessively antisocial (20–23) and experience increased aggressiveness (33) while others use steroids and continue to behave in accordance with normal social expectations. Further explanations will need to come from research that focuses more comprehensively on a broader spectrum of variables including the psychological make-up of the user, the nature, potency, and dosage of the steroid, history of use, and routes of administration. It is conceivable that the previously reported psychological effects of steroids originate from the disposition of individuals who already have an existing psychopathology, rather than from effects that are directly attributable to the steroid. It is also not clear whether steroids used in combination with other steroids or chemical substances increase the likelihood of eventual aggressive behavior. The relationship, if any, of previous steroid abuse, or the type, dose, and route of steroid to the subsequent angry outburst remains to be defined.

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