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Effects of Endogenous Testosterone and Estradiol on Sexual Behavior in Normal Young Men*

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ABSTRACT

The importance of androgens in establishing and maintaining sexual function in males of most species is well recognized. Estrogens also stimulate male sexual function in some species. In men, most studies of androgen effects on behavior have used hypogonadal men as an experimental model; much less is known about the role of endogenous testosterone (T) or estradiol (E_2) in the regulation of behavior in healthy, eugonadal men. In a randomized, double-blind study, we used a GnRH antagonist, Nal-Glu, without T replacement, to induce acute, profound, reversible gonadal steroid deficiency in 9 normal men for 6 weeks (Nal-Glu alone). We also studied the effects of partial androgen replacement by administering Nal-Glu together with T enanthate, 50 mg im weekly, to 10 other men. A third group of 10 men received Nal-Glu plus T, 100 mg im weekly. We studied the role of endogenous E_2 by administering Nal-Glu plus T, 100 mg im weekly, plus an aromatase inhibitor, testolactone (Teslac), 250 mg po qid, to 10 additional men (Nal-Glu+T+Teslac). Nine men received placebo injections and tablets. All subjects completed a behavioral questionnaire during the pretreatment period, at weeks 2, 4, and 6 of treatment, and at 3 weeks posttreatment.

Men who received Nal-Glu alone became profoundly hypogonadal within 1 week after treatment began. Serum T levels did not change significantly in the controls and in the men who received full T replacement but decreased to approximately half the baseline level in men who received partial T replacement. E_2 levels decreased profoundly in men who received Nal-Glu alone or Nal-Glu+T+Teslac and to a lesser degree in men who received partial T replacement. In men who received Nal-Glu alone, there were clinically and statistically significant decreases in the frequency of sexual desire, sexual fantasies, and intercourse at 4–6 weeks. These men also showed a strong trend ($P = 0.55$) towards decreased spontaneous erections after 4 and 6 weeks of treatment. A significant decrease in the frequency of masturbation was evident after 6 weeks. All measures returned to normal by posttreatment week 3. There was a trend toward increased aggression in the hypogonadal men, but this did not reach statistical significance. No changes in satisfaction or happiness with their partners were observed. There were no significant changes in any behavioral parameter during the study in men who received any of the other regimens.

Our data confirm the importance of physiological levels of T in maintaining sexual behavior in normal men. They also demonstrate that the effects of acute hypogonadism are not manifested immediately, but they become clinically and statistically significant after 4–6 weeks of androgen deficiency. Sexual function is restored at approximately the same time that serum T returns to normal levels. Our data also show that in experimentally hypogonadal men, replacement of androgens at a dose of 50 mg/week is adequate to maintain normal sexual function and behavior, and that circulating levels of E_2 have a limited role in the regulation of sexual behavior in normal men. The model of acute, reversible hypogonadism induced by GnRH antagonists plus varying amounts of androgen replacement offers an excellent *in vivo* bioassay for assessing androgen effects in men. (*J Clin Endocrinol Metab* **78**: 711–716, 1994)

IN MOST species, including human beings, male sexual function is at least partially dependent on the presence of androgens, particularly, testosterone (T) (1, 2). Men who are androgen deficient often manifest impaired libido and erectile function; these men generally show increased interest in sexual activity and improvement in several measures of sexual behavior during T replacement (1–7). Erectile function is frequently not improved by androgens, however (1, 5, 7), and the amount of androgen replacement required to preserve various aspects of sexual function and behavior is not clearly defined. In nonhuman primates, aggressive behavior is directly correlated with T levels (8), but in men, self-assessments of aggression do not correlate reliably with circulating T levels (9).

Most previous studies of androgens and sexual behavior in men have examined the effects of androgen replacement in the setting of testicular or pituitary disease leading to hypogonadism; in one recent report the effects of administration of supraphysiological doses of T to normal men were studied (10). However, little is known about the effects of acute androgen suppression on behavior in healthy young men, nor is the level of circulating T required to maintain sexual function in men known. Use of the GnRH antagonist, Nal-Glu, ([Ac-D2Nal[1],D4ClPhe[2],D3Pal[3],Arg[5],DGlu[6](AA), DAla[10]] GnRH) now allows for the experimental induction of acute, profound, and reversible hypogonadism in normal subjects (11–13). We hypothesized that daily administration of Nal-Glu without T replacement to normal men would

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have measurable effects on sexual and aggressive behavior within 6 weeks. We also questioned whether administration of Nal-Glu to men together with replacement of T at a dosage of 50 mg/week would maintain sexual function. Finally, since aromatization of T to estradiol (E_2) is important in maintaining sexual behavior in some species (14), we assessed whether suppression of E_2 in normal men while maintaining normal T levels would affect sexual or aggressive behavior. In this way we were able to evaluate the effects of physiological levels of T and E_2 on behavior in healthy, eugonadal young men.

Materials and Methods

Subjects

Fifty healthy men, ages 20–40, were recruited by advertisement in the local community to participate in a study of androgen effects on lipids and behavior. All were of normal body weight and had normal blood chemistries and fasting lipid profiles. None of the men took regular medications, smoked, or abused alcohol. All men signed a consent form approved by the University of Washington Human Subjects Committee.

One man who was assigned to the Nal-Glu alone group developed painful local reactions and therefore discontinued treatment after 3 weeks. Data from this subject were not included in the analysis. One man in the placebo group gained 7 kg despite a stable dietary intake; this subject's results were not included in the data analysis.

Study protocol

The study consisted of a 4-week pretreatment phase, a 6-week treatment period, and a 4-week recovery period. During the treatment period, each man was randomly assigned to one of the following experimental regimens (n = 10 in each group).

Nal-Glu alone. Nal-Glu, 75 μg/kg sc daily, plus T enanthate (Schoen Pharmaceuticals, Port Washington, NY), 100 mg in 1 mL sesame oil im weekly, 1 mL im weekly, plus placebo testolactone (Teslac, Bristol-Meyers-Squibb, Inc., New Brunswick, NJ), four times daily. These men were both T and E_2 deficient during the treatment period.

Nal-Glu+T(50 mg/week). Nal-Glu, 75 μg/kg sc daily plus T enanthate, 50 mg in 1 mL sesame oil im weekly, plus placebo Teslac capsules four times daily. These men had serum levels of T and E_2 that were approximately half the baseline values at the end of each week of the treatment period.

Nal-Glu+T(100 mg/week). Nal-Glu, 75 μg/kg sc daily plus T enanthate, 100 mg in 1 mL sesame oil im weekly, plus placebo Teslac capsules four times daily. These men had normal serum levels of T and E_2 at the end of each week of the treatment period.

Nal-Glu+T+Teslac. Nal-Glu, 75 μg/kg sc daily, plus T enanthate, 100 mg in 1 mL sesame oil im weekly, 1 mL im weekly, plus Teslac, 250 mg pO four times daily. These men were selectively E_2 deficient during the treatment period.

Placebo control. NaCl vehicle (0.9 mL, 150 mmol/L) sc daily, plus sesame oil placebo, 1 mL im weekly, plus placebo Teslac capsules four times daily.

Intramuscular injections were administered by nursing staff at the University of Washington Clinical Research Center. Each subject self-administered his sc injection daily. Teslac capsules were dispensed weekly during the treatment period; to ensure compliance, empty bottles were returned at each weekly visit.

The study was double-blind. Hormone levels were measured twice during the pretreatment period and weekly thereafter. Blood sampling was performed immediately before the next T injection; the values reported are therefore nadir values. Subjects were interviewed by one of the investigators weekly during the course of the study. Behavioral questionnaires were completed once during the pretreatment period, at weeks 2, 4, and 6 of the treatment period, and during week 3 of the posttreatment period. For each question, subjects were asked to choose the degree of frequency that most nearly matched their experience over the preceding 2 weeks.

Hormone analysis

Serum T levels were measured by RIA using reagents from the World Health Organization matched Reagent Program by methods previously described (15, 16). T was separated from serum by ether extraction; bound and free hormone were separated by dextran-coated charcoal. The assay sensitivity was 0.35 nmol/L; the inter- and intraassay variabilities were 4.1% and 8.1%, respectively. E_2 was measured by RIA using a kit purchased from ICN Biomedicals, Inc., Diagnostics Division (Carson, CA). The interassay variability was 15%, and the intraassay variability was 6%. In our laboratory, the limit of detectability of the assay is 18.3 pmol/L. Serum levels of LH and FSH were measured by an immunoradiometric method (MAIA clone, Serono Laboratories, Geneva, Switzerland). The limits of detectability of each assay was 0.5 IU/L. The interassay variabilities for LH and FSH were 10% and 11%, respectively. The intraassay variabilities were 4.8% and 7.0% for LH and FSH, respectively.

Behavioral questionnaires

The behavioral questionnaire consisted of 12 questions concerning sexual function, 2 questions regarding satisfaction with an ongoing relationship, and 6 questions assessing aggressive behavior. We included questions from several sources, including the Spanier Dyadic Adjustment Scale (17), Personality Research Form E (18), and standard sexual history forms (19). Each of these forms has been widely used in prior research and on clinical and nonclinical samples, as well as to measure the results of clinical interventions (20). Their psychometric reliability and validity properties have been shown to be adequate. We selected questions from each document to ensure a workable questionnaire length for the study. Subjects were also given an opportunity to comment on any aspect of their physical or emotional well being not addressed by the questionnaire.

Statistical analysis

All analyses were performed using nonparametric methods. For each parameter, between group differences were assessed using the Kruskal Wallace test. Within each treatment group, differences over time were analyzed using the Friedman test. A P value of less than 0.05 was considered significant.

Results

Serum hormone levels (Table 1)

Serum T and E_2 levels were similar in all of the groups before treatment. Men who received Nal-Glu alone became profoundly hypogonadal within a week after antagonist injections began and remained so for the duration of the treatment period. After 2 weeks of recovery, serum T and E_2 had returned to baseline, and gonadal steroid levels during the last 2 weeks of the recovery period were slightly above the baseline level. Men who received Nal-Glu+T (50 mg/week) had serum T and E_2 levels that were approximately half the baseline levels ($P < 0.05$ compared to baseline for each hormone). In men who received Nal-Glu+T (100 mg/week) or placebo, mean hormone levels did not change significantly during the study. In men who received Nal-Glu+T+Teslac, serum T levels remained unchanged,

TABLE 1. Mean serum levels of E_2 and T (mean ± SE) during the baseline, treatment, and posttreatment periods

	Baseline	Treatment	Posttreatment
T (nmol/L)			
Nal-Glu alone (n = 9)	20.0 ± 1.1	1.9 ± 0.9[a]	25.5 ± 1.3
Nal-Glu + T (50 mg/week) (n = 10)	17.3 ± 0.9	8.9 ± 0.6[a]	16.9 ± 1.5
Nal-Glu + T (100 mg/week) (n = 10)	20.3 ± 1.5	16.7 ± 1.4	18.6 ± 2.0
Nal-Glu + T (100 mg/week) + Teslac (n = 10)	18.7 ± 1.3	16.3 ± 1.7	17.2 ± 1.4
Placebo (n = 9)	19.2 ± 1.1	19.5 ± 1.0	20.1 ± 1.6
E_2 (pmol/L)			
Nal-Glu alone (n = 9)	155 ± 10	53 ± 6[a]	232 ± 21
Nal-Glu + T (50 mg/week) (n = 10)	149 ± 14	89 ± 7[a]	135 ± 14
Nal-Glu + T (100 mg/week) (n = 10)	134 ± 19	107 ± 11	116 ± 18
Nal-Glu + T (100 mg/week) + Teslac (n = 10)	125 ± 21	43 ± 13[a]	122 ± 21
Placebo (n = 9)	128 ± 24	126 ± 22	125 ± 22

[a] $P < 0.05$ compared with baseline and end-of-treatment values.

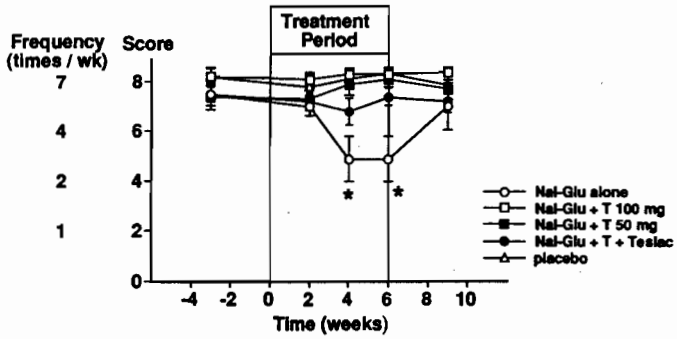

FIG. 1. Mean (±SE) frequency of sexual desire among subjects in each treatment group during the study. *, Significant difference compared to baseline ($P < 0.05$).

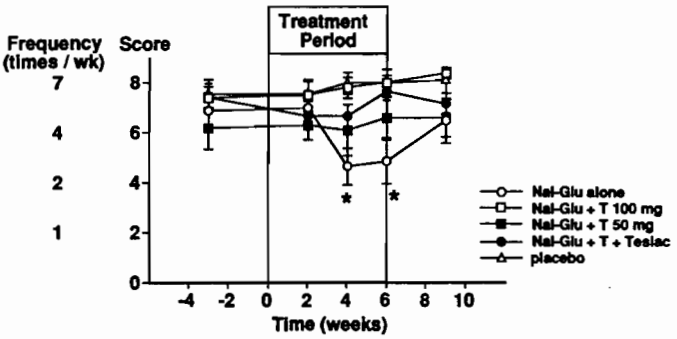

FIG. 2. Mean (±SE) frequency of sexual fantasies among subjects in each treatment group during the study. *, Significant difference compared to baseline ($P < 0.05$).

whereas serum E_2 levels fell to the castrate range during treatment ($P < 0.05$ compared to baseline) and normalized after treatment ended.

Sexual and aggressive behavior (Figs. 1–5, Tables 2–3)

In men who received Nal-Glu alone there were significant decreases in frequency of sexual desire and fantasies during

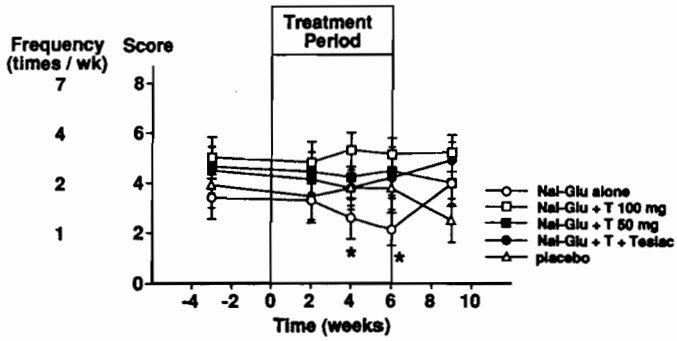

FIG. 3. Mean (±SE) frequency of sexual intercourse among subjects in each treatment group during the study. *, Significant difference compared to baseline ($P < 0.05$).

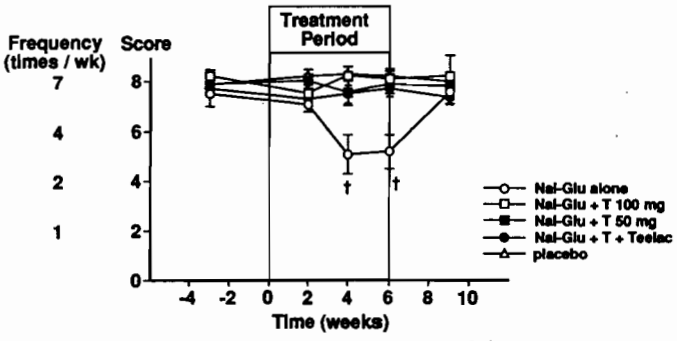

FIG. 4. Mean (±SE) frequency of sexual arousal (spontaneous erections) among subjects in each treatment group during the study. †, Significant difference ($P < 0.05$) compared to post treatment; $P = 0.55$ compared to baseline.

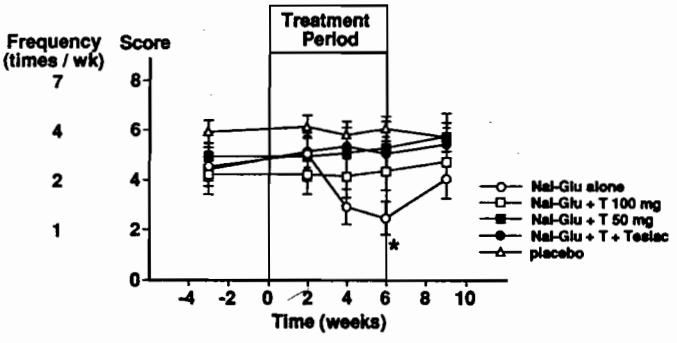

FIG. 5. Mean (±SE) frequency of masturbation in subjects in each treatment group during the study. *, Significant difference compared to baseline ($P < 0.05$).

the treatment period (Figs. 1 and 2), along with decreased frequency of intercourse (Fig. 3), kissing and fondling (data not shown). Frequency of intercourse decreased in all seven of the men with sexual partners (two men in this group did not have sexual partners during the study); frequency of desire and fantasies decreased in six of the men and did not change in three men (including both men who did not have sexual partners). Slight decreases in these measures occurred after 2 weeks; after 4, and 6 weeks, these decreases became clinically and statistically evident. These men reported a marked decrease in frequency of spontaneous erections after 4 and 6 weeks of treatment (Fig. 4; $P = 0.55$ compared to

TABLE 2. Mean (±SEM) degree of subject satisfaction with their sexual relationships with their mates (*top*) and degree of subjects' happiness in their relationship (*bottom*) during the study

	Baseline	Week 2	Week 4	Week 6	Post-tx
Nal-Glu alone (n = 9)	4.1 ± 0.74	3.4 ± 0.7	3.8 ± 0.7	4.0 ± 0.6	3.3 ± 0.7
Nal-Glu + T (50 mg/week) (n = 10)	4.5 ± 0.4	4.2 ± 0.7	4.0 ± 0.7	3.6 ± 0.7	3.8 ± 0.7
Nal-Glu + T (100 mg/week) (n = 10)	5.0 ± 0.4	4.7 ± 0.5	5.2 ± 0.6	4.9 ± 0.5	4.7 ± 0.6
Nal-Glu + T (100 mg/week) + Teslac (n = 10)	4.5 ± 0.7	4.5 ± 0.7	4.7 ± 0.6	4.4 ± 0.6	4.9 ± 0.4
Placebo (n = 9)	5.3 ± 0.5	4.7 ± 0.3	4.6 ± 0.5	4.7 ± 0.4	4.2 ± 0.9

Satisfaction with sexual relationship: Scores ranged from 1–6; 1 signifies extremely unsatisfactory, 6 signifies extremely satisfactory.

	Baseline	Week 2	Week 4	Week 6	Post-tx
Nal-Glu alone (n = 9)	3.1 ± 0.7	3.0 ± 0.6	3.0 ± 0.6	3.1 ± 0.7	3.3 ± 0.7
Nal-Glu + T (50 mg/week) (n = 10)	3.9 ± 0.4	3.6 ± 0.5	3.6 ± 0.5	3.7 ± 0.4	3.2 ± 0.5
Nal-Glu + T (100 mg/week) (n = 10)	3.9 ± 0.3	3.5 ± 0.5	3.5 ± 0.4	3.6 ± 0.5	3.1 ± 0.4
Nal-Glu + T (100 mg/week) + Teslac (n = 10)	4.0 ± 0.4	3.7 ± 0.4	3.9 ± 0.5	3.9 ± 0.6	3.7 ± 0.6
Placebo (n = 9)	3.8 ± 0.5	3.7 ± 0.6	3.6 ± 0.6	437 ± 0.6	3.5 ± 0.8

Happiness with relationship: Scores range from 0–6. A score of 0 signifies extremely unhappy; 3 signifies happy; 6 signifies extremely happy.

TABLE 3. Mean (±SEM) frequency of anger with self or with others (*top*) and frequency of desire to "smash things" (*bottom*) during the study

	Baseline	Week 2	Week 4	Week 6	Post-tx
Anger					
Nal-Glu alone (n = 9)	2.5 ± 0.4	2.6 ± 0.2	2.6 ± 0.2	2.0 ± 0.2	1.8 ± 0.2
Nal-Glu + T (50 mg/week) (n = 10)	2.4 ± 0.3	2.6 ± 0.4	2.4 ± 0.5	2.3 ± 0.3	1.8 ± 0.2
Nal-Glu + T (100 mg/week) (n = 10)	2.5 ± 0.5	2.9 ± 0.4	2.3 ± 0.2	2.8 ± 0.4	2.4 ± 0.2
Nal-Glu + T (100 mg/week) + Teslac (n = 10)	2.4 ± 0.2	2.4 ± 0.3	2.3 ± 0.2	2.2 ± 0.3	2.2 ± 0.2
Placebo (n = 9)	2.6 ± 0.2	2.8 ± 0.4	2.1 ± 0.2	2.1 ± 0.2	2.5 ± 0.3
Desire to smash things					
Nal-Glu alone (n = 9)	1.2 ± 0.2	1.6 ± 0.3	1.9 ± 0.4	1.4 ± 0.2	1.2 ± 0.2
Nal-Glu + T (50 mg/week) (n = 10)	1.3 ± 0.2	1.5 ± 0.2	1.4 ± 0.2	1.2 ± 0.1	1.4 ± 0.2
Nal-Glu + T (100 mg/week) (n = 10)	1.3 ± 0.2	1.7 ± 0.3	1.4 ± 0.2	1.7 ± 0.2	1.2 ± 0.1
Nal-Glu + T (100 mg/week) + Teslac (n = 10)	1.5 ± 0.3	1.7 ± 0.3	1.7 ± 0.3	1.4 ± 0.3	1.4 ± 0.2
Placebo (n = 9)	1.4 ± 0.3	1.9 ± 0.3	1.1 ± 0.1	1.1 ± 0.1	1.2 ± 0.2

Scores ranged from 1 (not at all)–6 (daily or more than once a day).

baseline, $P < 0.05$ compared to posttreatment). There was also a strong trend towards decreased ability to maintain an erection during intercourse, although this trend did not achieve statistical significance (data not shown). Frequency of masturbation decreased significantly by week 6 (Fig. 5); ability to achieve orgasm through masturbation was not impaired. By 3 weeks posttreatment, the baseline levels of all aspects of sexual activity had been resumed; although subjects were not questioned formally, some subjects commented spontaneously that they noted restoration of their pretreatment behaviors after 2 weeks of recovery. There were no significant changes in any parameter of sexual behavior in any of the other treatment groups.

Subjects were asked to describe their levels of satisfaction with their sexual relationships with their mates (ranging from extremely unsatisfactory to extremely satisfactory) and to describe their degree of happiness with their relationships (from extremely unhappy to extremely happy). There were no changes in mean levels of sexual satisfaction or overall happiness in any of the treatment groups throughout the course of the study (Table 2).

Aggression and irritability were evaluated by questions which included the subjects' frequency of anger with themselves or others, frequency of desire to smash objects, and frequency of desire to start a fight. Although there was a trend toward increased anger and aggression during the treatment period in men who received Nal-Glu alone, these trends did not achieve significance (Table 3). However, several men who received Nal-Glu alone reported in their written comments that they felt more irritable during the treatment period. There were no changes in measures of irritability or aggression in any of the other treatment groups.

Side effects

All men were able to self-administer the daily injections without difficulty. Most of the men receiving Nal-Glu experienced some local irritation and/or erythema at the site of injection; these effects disappeared within a few hours. A nontender, sc nodule developed at the injection site in most of these men and was most apparent in the leaner men. These nodules regressed within 2 weeks after injection. These effects did not hinder the daily activities of any of the men who completed the 6-week treatment period.

Discussion

We studied the effects of physiological levels of T and E_2 in normal men by administering the GnRH antagonist, Nal-Glu, daily for 6 weeks, with and without concurrent androgen replacement. Our results confirm that physiological levels of T play a critical role in maintaining sexual behavior in normal men. In men who received Nal-Glu alone, severe T

deficiency was induced after 1 week of treatment, whereas significant behavioral changes were manifested in 4–6 weeks. Our data also show that serum T levels need not be maintained consistently at a "normal" male level in order to maintain normal sexual function and behavior, and they demonstrate that in contrast to males of other species peripheral, physiological levels of serum E_2 appear to play little role in the regulation of sexual and aggressive behavior in normal men.

Several groups of investigators have demonstrated the ability of androgen replacement to increase the frequency of sexual thoughts, fantasies, and activities in men with varying degrees of chronic androgen deficiency due to testicular or hypothalamo-pituitary disease (1–7, 9). Kwan *et al.* (1) found that hypogonadal men had similar erectile responses to erotic films and self-generated fantasies whether they were T deficient or T replaced. We did not test erectile responses to defined stimuli, but our finding of no significant decrease in the ability of the experimentally hypogonadal men to maintain erections during intercourse is in agreement with the data of Kwan *et al.* (1) and with reports of some degree of preservation of sexual function in castrated men (2). Our data are also consistent with the hypothesis of those authors that the "major impact of testosterone may be on behaviors related directly to libido" (1). However, we tested only relatively acute responses to experimental hypogonadism; we cannot predict whether or not the behaviors we report would have been maintained over a longer time period.

We found that administration of Nal-Glu together with T, 50 mg weekly, maintained sexual function in our subjects. The blood sampling in our study occurred immediately before the next T injection (*i.e.* the measured levels were nadir levels), and serum levels during the few days after each injection were most likely within the normal male range. Serum T levels were clearly below the normal range for at least part of each week, yet, subjects did not report a varying degree of sexual interest or potency during the course of the week. Although our subjects did not keep daily behavior logs, and it is possible that some men may have forgotten transient decreases in desire, erections, *etc.*, these findings suggest that completely normal T levels are not required for maintenance of a usual level of sexual function. Buena *et al.* (21) have also found that sexual function was preserved in normal men who received a GnRH agonist together with a dose of sustained-release T that produced T levels at the lower end of the normal range. Gooren (22) and Salmimies *et al.* (23) have also reported that some men with moderately low T levels retain normal erectile function, with no changes observed during treatment with exogenous T. Thus, in many men, the threshold for impairment of sexual function appears to fall below the lower limit of normal circulating T levels in adult males.

In the male rat and in males of other species, E_2 is required for the full manifestation of normal sexual behavior (14). In hypogonadal males, Luisi and Franchi (24) found that androgen substitution with T undecanoate (an androgen which is aromatized to E_2) more effectively stimulated libido and erections than did mesterolone, a nonaromatizable androgen, and they suggested that E_2 might play a role in stimulating sexual behaviors in men. In contrast, Gooren (25) found that sexual function in normal men was unaffected by administration of Teslac or the E_2 antagonist, tamoxifen. Our results demonstrate that when circulating E_2 is selectively depleted, and at the same time T levels are maintained, sexual and aggressive activities in human males are unaffected. However, many of the effects of gonadal hormones on sexual behavior are thought to result from their effects on the central nervous system (CNS) (2). It is not known whether Teslac enters the CNS, and therefore it is not clear whether Teslac administration decreases E_2 levels in the CNS. Because of this uncertainty, we may conclude only that peripheral E_2 is not required for the maintenance of sexual functioning the human male.

In animals, T levels have been correlated with social status and with aggressive behavior (8, 26). In humans, the association of these factors is much less clear. In some settings, an increase in social status is accompanied by an increase in serum T (27), but in other settings, it is not (27). A very recent study by Su *et al.* (28) demonstrated that acute administration of the anabolic steroid, methyltestosterone, to normal men resulted in increases in hostility, violent feelings, and irritability. However, Anderson *et al.* (10) have shown that administration of supraphysiological doses of T enanthate to healthy male volunteers for 6 months does not cause any increase in aggressive behaviors or in irritability, and popular notions of endogenous T causing aggressive behaviors in males are not well supported by experimental studies (9, 29–31). Our data also suggest that there is no direct relationship between serum T levels and aggression or irritability; in fact, there was a suggestion of increased irritability in the hypogonadal men. It is important to note that we monitored only acute responses to experimental, rapidly induced androgen deficiency. It is impossible to be certain whether the effects of chronic androgen deficiency in a previously normal man would be similar to the acute responses. However, O'Carroll *et al.* (7) found that irritability decreased in chronically hypogonadal men receiving androgen replacement. These investigators also found increases in cheerfulness, relaxation, tension, and anxiety in the subjects. Thus the effects of physiological doses of androgens on human emotional traits and behavioral characteristics are quite complex.

In addition to their use in hypogonadal men, androgens are also being studied as hormonal male contraceptive agents, alone or in combination with GnRH antagonists and/or progestational agents. High dose T administration (alone or in combination with GnRH antagonists) induces azoospermia in only 50–70% of men (32, 33) and may also have undesirable effects on body weight and on plasma lipids (34). For these reasons, GnRH antagonists or progestins, together with lower replacement doses of T, may offer a useful approach for future contraceptive trials. Our results suggest that in the design of hormonal male contraceptive regimens, partial T replacement may be adequate to preserve sexual function. Of course, it will be essential to monitor the behavioral effects of any specific test paradigm.

In summary, we evaluated the role of physiological levels of T and E_2 on sexual and aggressive behavior in normal men. We found that acute, profound androgen deficiency resulted in decreased function of several aspects of sexual behavior, without marked changes in aggressive behaviors. The impairment of sexual behavior was apparent within 4 weeks after the induction of T deficiency; behavior returned to the baseline state within 3 weeks after treatment ended. Partial androgen deficiency or selective E_2 deficiency did not affect sexual or aggressive behaviors significantly. Our data confirm the importance of androgens in maintaining sexual function in men, and they also suggest that sexual function can be retained when serum T levels fall below the normal male range.

Acknowledgments

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