particularly in comparison to the total amount of *l*-NE found in the hypothalamus (about 0.1 μg). It is possible to suppress or stimulate feeding behavior with doses of *l*-NE as low as 5-μg. Quantities below 5 μg fail to affect feeding behavior. Possibly, these quantities are too small to influence sufficient postsynaptic receptor sites. Uptake mechanisms on the surface of vascular, glial, and neuronal cells remove *l*-NE from the extracellular hypothalamic space. These mechanisms, in conjunction with intracellular monoamine oxidase, may reduce substantially the amount of exogenous *l*-NE that penetrates to the synaptic receptor sites.

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Plasma Testosterone Levels in the Male Rhesus: Influences of Sexual and Social Stimuli

Abstract. *Four adult male rhesus monkeys were provided access individually to a group of receptive females. Each male assumed dominance and engaged in frequent copulations. Plasma testosterone levels increased two- to threefold during this period. Next, each male was subjected to sudden and decisive defeat by a large all-male group, and plasma testosterone fell following this experience. Two males were later reintroduced to the females, and plasma testosterone rose rapidly to the previous elevated levels.*

It has been reported that plasma testosterone in male rhesus monkeys living in social groups is correlated with dominance rank and frequency of aggressive behavior (*1*). It was not clear whether the increased levels of testosterone observed in more dominant or aggressive males preceded the differences observed in social behavior, or whether the differences in testosterone were a reflection of the effect of the social environment. Did subordinate animals with lower frequency of aggressive behavior have lower testosterone levels because of their rank and relationship to the other animals, or was testosterone secretion relatively stable and thus functioning in some way to influence the animal's behavior and social rank? The present study was undertaken to see if alterations in the animal's social environment would affect plasma testosterone levels.

By systematically manipulating the social environment for four adult male rhesus monkeys over a 4-month period, we observed both elevations and depressions in plasma testosterone. When males were provided access to sexually receptive females, testosterone levels increased, and when they were briefly exposed to a large group of males, resulting in sudden and profound defeat, testosterone levels fell.

The studies took place in large outdoor compounds, approximately a third of an acre (about 0.13 ha) in area. Plasma testosterone was measured by a modification of the protein-binding technique of Mayes and Nugent (*2*), and social interactions were scored with the use of a standard behavioral inventory. The first study was on the effect of access to sexually receptive females. This occurred in three phases, each lasting 2 weeks: (i) individual cage; (ii) access as the only male to a group of adult females ($N = 13$), some in estrous; and (iii) return to cage.

Access to a group of females provided a mixed stimulus. Males became the alpha, or dominant, animal, along with engaging in frequent sexual behavior (for example, sex present, hip-touch, mount). The social interactions during the first hour after the males were placed with the females are shown in Table 1. Throughout the hour, males displayed frequent noncontact aggression, usually in the form of threat or chase (26 to 29 percent of all behaviors observed). They received frequent submissive behavior (for example, avoidance, grimace, squeal, crouch) from the females (48 to 55 percent), and by the end of the hour received no aggression (contact or noncontact) from the females. Contact aggression (for example, bite, hit, slap, pull) was relatively infrequent and was rare throughout the period with the females. Receiving frequent submissive responses and no threats from the females reflected the males' assumption of dominance status following their introduction to this new group. In the first 20 minutes, sex behavior accounted for 23 percent of all social interactions, and rose to 46 percent by the end of the hour. Grooming and sex behavior continued to be the most frequent forms of social interaction between the males and the females during the following 2 weeks.

Plasma was drawn for testosterone analysis from 0900 to 1000 hours to minimize the effects of diurnal varia-

Table 1. Behavior responses scored during the first and last 20 minutes of the hour after male monkeys were introduced to the female group and the male group. The values represent the various behaviors as a percentage of total behavior.

Response	Introduction to females		Introduction to males	
	First 20 min	Last 20 min	First 20 min	Last 20 min
Does				
Contact aggression	5	2	39	18
Noncontact aggression	26	29	11	3
Submission	9	6	44	76
Sex	23	46	0	0
Other	37	17	6	3
Receives				
Contact aggression	2	0	49	32
Noncontact aggression	11	0	23	15
Submission	48	55	3	0
Sex	14	14	0	3
Other	25	31	25	50

tion. Samples were collected twice weekly during the 6 weeks of the female influence study, as well as 24 hours after initial introduction to the females. This collection schedule was not frequent enough to characterize precisely the peak response. In order to accomplish this, samples would have had to be drawn several times per day, which would have seriously disrupted the behavioral interactions of the group. However, every male responded during the 2 weeks with the females with a rise in plasma testosterone. Mean plasma testosterone showed a significant increase from 849 ng per 100 ml of plasma during the 2-week baseline (four samples per animal) to 1515 ng/100 ml when the males were with the females ($t = 4.71$, d.f. $= 3$, $P < .02$, t-test for correlated groups). Within a week after removal from the females, mean levels fell back toward baseline, to 1033 ng/100 ml. Among the four males, testosterone increases ranged from 109 to 247 percent of mean baseline values. This two- to threefold increase approximates the magnitude of response of the testis to administered gonadotropin in healthy human males (*3*).

Investigation of hormonal responses to aggressive encounters took advantage of the knowledge that established groups of rhesus macaques are intolerant to strange animals, especially males who are abruptly introduced to the group. The same four males previously introduced to the females were therefore introduced individually to a well-established group of 30 adult males. The response of the resident males was dramatic. Within minutes, they challenged and attacked the male that had just been introduced. In contrast to the pattern of social behavior with the females, among whom the introduced males received only 2 percent contact aggression in the first 20 minutes, males received an average of 49 percent contact aggression from the resident males (see Table 1). Moreover, the very high level of contact aggression received remained elevated throughout the hour, totaling 32 percent of all social interactions for the last 20 minutes of the first hour. Parallel to receiving frequent aggressive responses, submissive behavior by the introduced males increased from 44 to 76 percent during the first hour. Every male was removed within 2 hours after introduction. Experimenters interfered in prolonged fights to limit injuries, but two males did receive wounding serious enough to require suturing; the other two males were not seriously injured.

Plasma was drawn 24 hours and 3 to 5 days after this brief, but decisive exposure to defeat. All the males exhibited a marked fall in plasma testosterone by the end of the week, with values averaging an 80 percent drop from baseline levels. The main level for the group in the week following defeat was 328 ng per 100 ml of plasma, which was significantly lower than baseline levels ($t = 3.46$, d.f. $= 3$, $P < .05$). For two males, Ribot and Quid, samples were drawn 6 weeks and 9 weeks, respectively, after defeat, and testosterone levels were still markedly depressed.

To test the responsiveness of the pituitary-gonadal system, these two males were given access again to the group of females, 9 weeks and 15 weeks, respectively, after their exposure to defeat by the all-male group. Twenty-four hours after they were introduced to the females, testosterone showed significant increases, and within 4 days levels were equal to or greater than those observed originally with the females. Figure 1 summarizes the plasma testosterone responses of these two males during the 4-month period they were studied.

Plasma testosterone has been observed to rise in rabbits, bulls, and elephants, either following copulation with females or after being permitted visual access to receptive females (*4*). There are no parallel studies in primates. Urinary testosterone levels and beard growth have been reported anecdotally in human males in anticipation of future sexual activity (*5*). The rise in plasma testosterone observed in the four rhesus males following access to

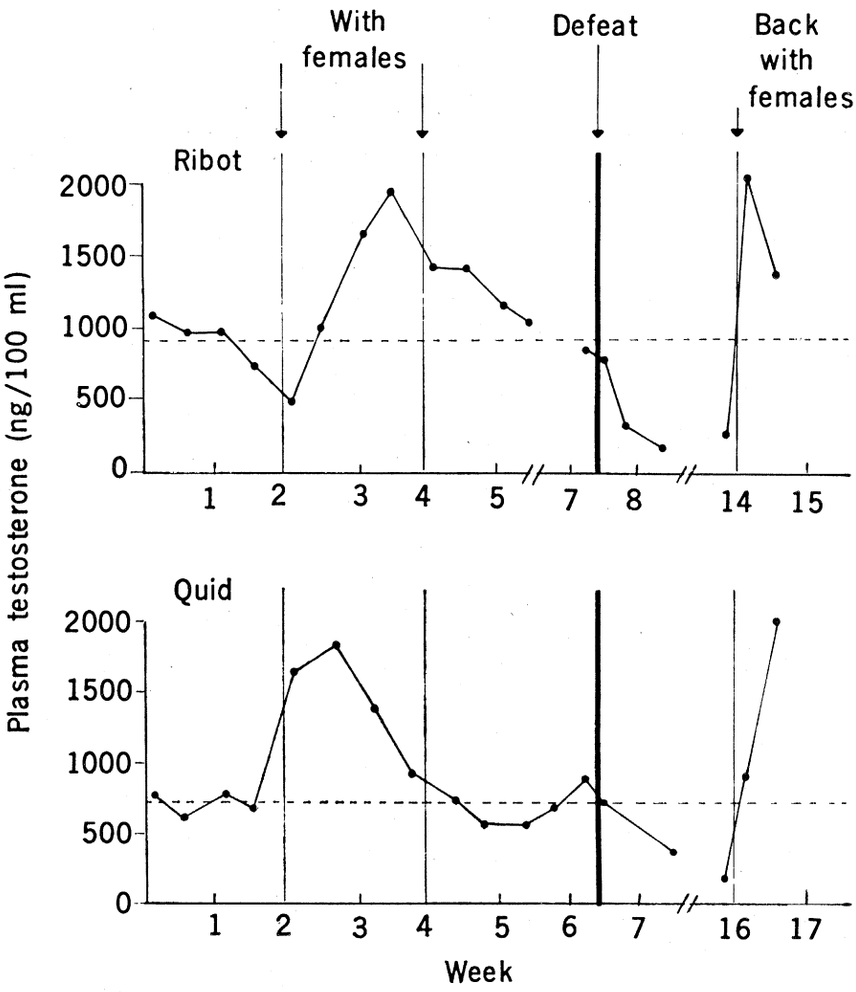

Fig. 1. Plot of the plasma testosterone responses for two males for approximately 4 months. Values on discontinuous weeks are not connected. After defeat, both males showed a drop below baseline levels, depicted as horizontal broken lines, which were determined from weeks 1 and 2 prior to access to the females. Within 2 to 4 days after reintroduction to the females, both animals showed a rise in plasma testosterone equivalent to what they had initially experienced.

the females is associated with two stimuli. Access to and copulation with the females was accompanied by becoming the alpha, or dominant, male in a new group. It is possible that the latter experience is a provocative stimulus to increased testosterone secretion, along with frequent sexual activity. Studies are needed to clarify this issue.

With more indirect techniques of assessing testosterone secretion, such as measurement of urinary metabolites, it has been reported that testosterone secretion appeared to fall following exposure to stressful situations (*6*). In the rat, plasma testosterone has been observed to fall following ether anesthesia or foot shock (*7*). In humans, plasma testosterone has been reported to fall following surgery (*8*), and recently testosterone levels were observed to be suppressed in young men during the early stressful phase of officer candidate training in the army (*9*).

The fall in testosterone levels in the four males following defeat could be secondary to the wounding they received, as well as related to the psychological effects of such an experience. While all four males showed marked decreases in plasma testosterone, only two animals were seriously wounded. However, it is still possible that physical injury could account for the fall in testosterone levels. Preliminary results of studies in progress indicate that testosterone also falls after males are subjected to defeat and fall in dominance rank without the occurrence of physical injury.

The males in the present study were placed back in individual cages after their defeat. When defeated animals remain in the group, they assume a very depressed dominance rank and restrict their social interaction with other animals for a prolonged period of time. These observations suggest that defeat and loss of dominance is a very significant and meaningful experience for the male rhesus, and may thus present the most relevant explanation for the fall in plasma testosterone observed.

These data support the interpretation that testosterone secretion can be influenced by social and environmental variables and is not fixed. It is also possible, however, that although the pituitary-gonadal system is subject to influence by environmental events, the subsequent alterations in plasma testosterone may significantly affect behavior. It could be argued that the fall in testosterone following defeat and loss of dominance rank functions as an adaptive response. As aggressive threats or challenges by a subordinate animal are severely punished by the dominant members of a group, high levels of testosterone stimulating such behavior could be viewed as inappropriate and maladaptive. In a parallel vein, increase in testosterone stimulated by access to females would function to support the increased frequency of sexual activity. Work is needed to clarify these issues.

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Narcotic Tolerance and Dependence and Serotonin Turnover

In a recent study of the effect of protein synthesis inhibitors on morphine tolerance, Loh *et al.* (*1*) reported that cerebral macromolecules play an important role in the development of narcotic tolerance and dependence. In a logical extension of this work involving a consideration of those reactions or enzymes associated with the putative neurohormones, Way and his co-workers (*2*) suggested that one of the proteins may be associated with serotonin (5-hydroxytryptamine) synthesis. This suggestion was based on the observation that serotonin turnover in the brain increases with the development of morphine tolerance. The method that Way and his co-workers used for the assessment of serotonin turnover was that of Tozer *et al.* (*3*), who stated that the increase of brain serotonin after monoamine oxidase inhibition could be used as a measure of serotonin turnover.

The findings of Way and his co-workers (*2*) have been confirmed by Maruyama *et al.* (*4*), who used the pargyline method of measuring serotonin turnover. However, Cheney *et al.* (*5*), using a "direct method" (*6*), have disputed the findings of Way and his co-workers and Maruyama *et al.* In our opinion, the data and calculations presented by Cheney *et al.* do not support their conclusion of a lack of relationship between morphine tolerance and brain serotonin turnover.

In their report, Cheney *et al.* used the steady-state kinetic approach and calculated the fractional rate constant (k_S) which in a steady-state system should reflect changes in monoamine turnover. The method involves the intravenous injection of a pulse dose of [^{3}H]tryptophan followed by measurement of changes in the specific activity of precursor and product.

From such data Cheney *et al.* calculated k_S for the sham-operated and for the morphine-tolerant mice. However, they arbitrarily selected only one time point pair (between 30 and 50 minutes after injection) to calculate k_S. They noted that the k_S for the sham-operated mice was nearly equal to the k_S for the morphine-tolerant mice and concluded that there was no difference in serotonin turnover between these two groups. We have since calculated, from a smoothed curve of the data they reported, the k_S for all 20-minute time intervals past 50 minutes. It is clearly shown in Table 1 that for each of the five time pairs the k_S is higher for the morphine-tolerant mice