effects of ethanol and barbiturates can be prevented, without halting the development of physical dependence, as exemplified by appearance of a withdrawal syndrome upon discontinuation of chronic drug ingestion.

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3. Blood obtained from the tail (50 μl) was added to 5 ml toluene containing 0.1 ml 1*M* phosphoric acid and 50 μl pentobarbital in chloroform (0.25 μg/μl, internal standard). For analysis of phenobarbital in brain, brain tissue was homogenized in 1 ml 1*M* phosphoric acid, and internal standard and toluene were added. After extraction, the toluene layer was carefully removed into Concentra Tubes (Laboratory Research Company). Prior to injection of sample into the gas chromatograph, 20 μl of 25 percent tetramethylammonium hydroxide (TMAH) in methanol (Southwestern Analytical Chemical Company) was added to the toluene extract, mixed thoroughly, and centrifuged. The TMAH solution collected in the reservoir of the Concentra Tubes; 1 μl of this solution was injected slowly (3 to 5 seconds) onto a 6-foot glass column containing 2 percent OV-17 on Gas Chrom Q (Beckman). Helium was used as the carrier gas, and the conditions for chromatography with a Packard Model 421 Gas Chromatograph with a flame ionization detector were injection port temperature, 350°C; oven, 140°C; detector, 240°C. Retention time for phenobarbital under gas flow conditions was 11 minutes. Blood obtained from mice consuming the control diet established blank values.
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Potency in Male Rhesus Monkeys: Effects of Continuously Receptive Females

Abstract. *Ejaculations decreased and mount latencies increased when intact males were paired regularly over a 3.5-year period (3180 tests) with ovariectomized females made constantly receptive by daily injections of estradiol. The deterioration in potency was abruptly and completely reversed by substituting a group of new but similarly treated females for the original ones.*

Although data are not complete and exceptions occur, the majority of primate genera that have been studied show breeding seasonality (*1*). The virtual lack of a sexual season in the human appears to place us in a somewhat special category. Man also differs from other higher primates because the influence of the female's menstrual cycle on the sexual activity of the pair appears to be reduced. The clear-cut sexual rhythms shown by certain Old World monkeys and apes (*2*) are more difficult to detect and quantify in the human (*3*). With the added psychosocial implications of the use of oral contraceptives, which tend to dampen the hormonal fluctuations natural to the woman's cycle, we have a situation in which the human is emancipated from most of the physiological and environmental factors that are responsible for sexual periodicity in lower mammals. In a species such as the rhesus monkey, the males show greater potency than men and are regularly able to ejaculate from one to four times in daily 1-hour tests, but in the wild, they are maximally active for only about 8 to 12 weeks each winter during the height of the relatively brief mating season. Sexual activity is also restricted in the female because a 165-day pregnancy normally supervenes, and sexual activity is virtually abolished during lactation. If pregnancy should fail to occur, there is usually a 3- to 4-month period of summer amenorrhea (*4*). Thus, both the male and female are seasonal; this is emphasized here to draw attention to a major difference between the sexual activity of our own species, in which sexual life is almost uninterrupted, and that of most other primates, for which rhythmicity and periodicity are the rule.

We report here on the decline in the potency of male rhesus monkeys when paired with female partners maintained in a continuously receptive state (to better resemble the human condition) over a 4-year period. We also report on the dramatic restoration of potency brought about by changing the female partners.

Four adult male (weighing 9.8 to 11.3 kg) and eight adult female (weighing 4.6 to 7.2 kg) rhesus monkeys were obtained through dealers directly from India and, after 4 to 10 months of quarantine, housed in individual cages in an animal room where the temperature was maintained throughout between 20.0° and 23.3°C. Artificial lighting was rigorously controlled to give a 14-hour day between 0615 and 2015 hours. Females were ovariectomized and throughout the experiment received daily 10 μg of estradiol benzoate in 0.2 ml of sesame oil injected subcutaneously (*5, 6*). Once a day, 5 days a week, from December 1972 to March 1975, each male was given 1-hour sexual behavior tests with one of four females. Females were used in rotation on consecutive days so that each female's test with the same male recurred every fifth test day. In this way, each male was paired with four different female partners (16 pairs) to provide variety and to control for the effects of individual partner preferences (*7*). Behavior testing was carried out in large observation cages with one-way mirrors as previously described (*6, 8*). At all other times each animal was housed in a single cage. In March 1975, the four original female partners ("old" females) were replaced by four similarly treated ones ("new" females) that had not previously been tested with these males. After 4 weeks of testing, the "new" females were replaced by the original "old" females, and testing continued with this latter group without interruption until March 1976. The behavioral indices given quantitative treatment here were (i) mean number of ejaculations per test and (ii) mean latent period (in minutes) to the first male mounting attempt per test. Blood samples (3 ml) were collected weekly at 0800 hours from the saphenous veins of untranquilized males previously adapted to the venipuncture procedure (*9*), and plasma testosterone was estimated by radioimmunoassay without chromatography (*10*).

Figure 1 shows changes in the mean number of ejaculations per test (top) and in the mean latency to the first male mounting attempt (bottom) in four successive years (1973, 1974, 1975A, 1976) during the months of January and February (to control for the effects of season and other long-term variables). By the fall of the second year of regular testing

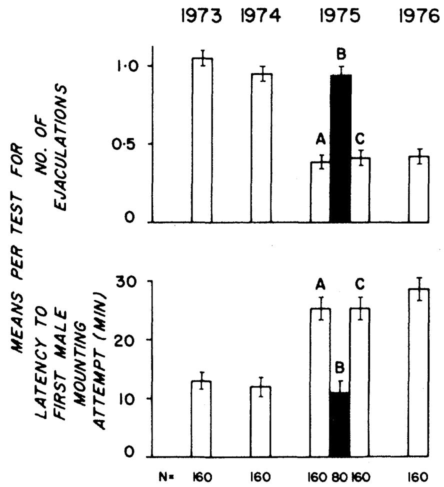

Fig. 1. Number of ejaculations and mounting attempt latencies of male rhesus monkeys tested regularly for several years with the same female partners. The data for 1973, 1974, 1975A, and 1976 are from January and February to control for seasonal effects. In 1975, the four original females were replaced by four new ones (1975B) and male potency abruptly increased. When the original females were reintroduced (1975C), there was an immediate deterioration in potency. Vertical bars give standard errors of means; N = number of tests.

with continuously receptive female partners, male sexual activity had markedly declined; by the start of 1975, ejaculations had dropped to 36.4 percent and latencies had lengthened by 99.5 percent (1975A). The abrupt introduction of four unfamiliar "new" females (1975B) completely reversed these effects. The stimulatory effect of "new" females on behavior was not transferred, and with the reintroduction of "old" females (1975C), male sexual activity returned to the levels seen previously (1975A). An unbalanced analysis of variance using repeated measures (*11*) showed that the changes in ejaculatory activity during 1975 were significant ($P < .001$).

Figure 2 shows the time course of behavior changes in the 8 weeks before, in the 4 weeks during, and in the 8 weeks after tests with "new" females; it also gives the changes in mean plasma testosterone concentrations in the males. The doubling of ejaculations and halving of latencies with "new" females occurred abruptly, as did the reversals of effects when "old" females were reintroduced. Indeed, males seemed to pick up almost exactly where they had left off when again confronted with their "old" female partners: there were no signs of a carryover effect from their experiences with "new" females. We do not know how long one would need to continue testing with "new" females before they, too, elicited the same responses as "old" ones. However, increased potency preceded any changes in plasma testosterone levels, and the rise during the fourth week of testing was more likely a consequence of the behavioral changes than a cause of them (*12*).

The marked decline in potency of male rhesus monkeys paired with constantly estrogenized females, receptive for long periods of time, has not to our knowledge been previously described in a primate species. The effect was not determined by gonadal androgens but appeared to depend on the nature of the bond between partners. Changing these bonds by substituting new partners for old ones immediately and fully restored the males' potency. The effect was the more remarkable because each male always had four female partners, a considerable variety of stimulation. The property shared by the "old" and "new" females was their constant receptivity and unvarying hormonal status. There were no significant differences between the "old" and "new" female groups in terms of hormone treatments, numbers of sexual invitations and refusals (*13*), or in the quality of their vaginal secretions, which were monitored for pheromone content by gas chromatography (*14*). The design of this experiment did not enable us to ascribe the mechanisms definitively to either the female or the male, although the latter seemed more likely. The phenomenon appears to be related to, but different from, the so-called Coolidge effect (*15*), well documented in rodents and farm animals (*16*). This short-term effect occurs when a sexually exhausted male rat shows some revival of interest in a second stimulus female presented during his refractory period, and a nonsexual stimulus (foot shock) may have the same result. In our study, sexual exhaustion did not play a significant role, for males responded with a 130 percent increase in potency in the first test with "new" females and maintained this activity for a period of 4 weeks.

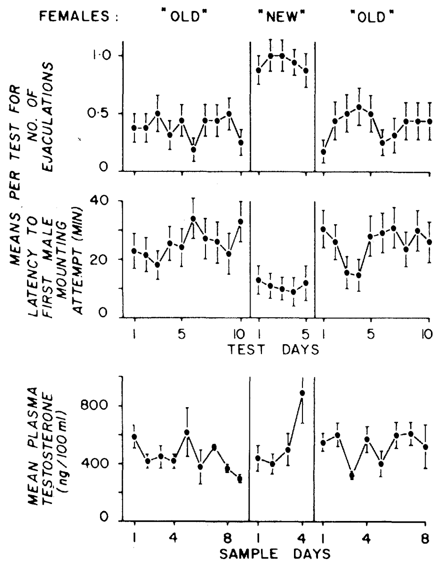

Fig. 2. Time course of behavioral changes in the 8 weeks preceding, the 4 weeks during, and the 8 weeks following tests with "new" females. With "new" females, ejaculations more than doubled and latencies halved. Changes in male plasma testosterone concentrations could not account for the changes in behavior. Each point in the two top sections is the mean of 16 tests, and each point in the bottom section is the mean of 4 plasma samples.

In the rhesus monkey under natural conditions, consort bonds are established and dissolved during the course of the menstrual cycle; as far as can be determined, the sexual potency of the males remains intact. Under our experimental conditions, when consort bonds were artificially protracted and the stimulus properties of the female were held rather constant, male potency declined (*17*). Do these findings have any implications for our own species? One can speculate that in societies with institutionalized monogamy, the uninterrupted sexual life of modern man—insulated as it is from exteroceptive seasonal factors—might provide conditions in which similar phenomena would be observed. Were this so, one would expect (i) a tendency to break and remake consort bonds (with new partners), (ii) the use of cultural means for periodically changing one's stimulus properties (clothing, adornment, coiffure, and odor), and (iii) an imposition of periodicity on sexual activity (menstrual and pregnancy taboos, Lent, safe periods, and so forth). Many of the prohibitions and customs surrounding sex in human societies are traditionally thought of as both protecting the sexes from each other and protecting the female from the constant sexual demands of the male. An alternative view is that they also function to maintain male potency. The rhesus data, although perhaps irrelevant for man, suggest the hypothesis that if the factors responsible for sexual rhythmicity and periodicity are absent, male potency is not fully maintained.

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5. Previous studies (6) have demonstrated that half of this daily dose was adequate to maintain the sexual receptivity and attractiveness of ovariectomized rhesus monkeys. "New" and "old" females were imported from India at approximately the same time, were ovariectomized for the same length of time (2 to 3 years), and received the same hormone treatment before testing. "New" females had been tested with a group of four different males for 12 months before their use in this experiment, and copulatory frequencies were in the same range. All females were fully mature according to somatic criteria, but their ages were unknown.
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15. This phenomenon takes its name from an incident that occurred when President and Mrs. Coolidge were touring a farm noted for the excellence of its breeding program. Mrs. Coolidge passed where a prize rooster was performing among its hens with sustained vigor, and remarked that the President would be interested in the bird's prowsess. When told, the President is said to have asked: "Was it always the same hen?"
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17. Unpublished data from our laboratory indicate that the sexual potency of male rhesus monkeys does not decline when they are tested over a 4- to 5-year period with different female partners in a variety of experimental situations.
18. We thank Dr. M. Kutner for statistical advice. Supported by National Institute of Mental Health grant MH19506 and by the Georgia Department of Human Resources.

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Bursting Neural Networks: A Reexamination

Abstract. *Many of the motor neurons in the lobster (*Panulirus interruptus*) stomatogastric ganglion exhibit plateau potentials; that is, prolonged regenerative depolarizations resulting from active membrane properties, that drive the neurons to fire impulses during bursts. Plateaus are latent in isolated ganglia but are unmasked by central input. These findings emphasize the role of cellular properties as compared to synaptic wiring in the production of cyclic motor patterns by ensembles of neurons.*

The bursting motor patterns underlying cyclic behaviors such as walking, chewing, and breathing have been attributed to two major types of mechanisms. (i) Bursting might arise as an emergent property of synaptic interactions among passive neurons having only simple capabilities such as repetitive firing of impulses. (ii) Alternatively, it might arise from the special active regenerative membrane properties of individual neurons, as in endogenously bursting neurons. The stomatogastric ganglion (STG) of lobsters can be used for studying rhythm generation. Its approximately 30 neurons can be individually identified; synaptic connections among them have been extensively described (Figs. 1B and 2A). The neurons produce two different rhythms underlying cyclic behaviors of the stomach during food digestion (*1*). The slow gastric rhythm has been considered as emerging from the network of synapses among 12 passive neurons (*2, 3*). For the faster pyloric rhythm, the 11 follower neurons have been considered to be passive and to be synaptically controlled by a separate group of three endogenous bursters (*1, 3, 4*). We have reexamined the properties of all the "passive" neurons, and have found that many have active regenerative membrane properties contributing to their bursting. Further, we have found that these special properties become evident when a neuron is under the influence of inputs from the central nervous system (CNS) (*5*).

We dissected the stomatogastric nervous system of the spiny lobster (*Panulirus interruptus*) and transferred it to a saline-filled dish (*6, 7*). A diagram of the preparation is shown in Fig. 1A; this preparation was used unless otherwise stated because, compared with the weak output of the isolated STG, both the gastric and pyloric rhythms remained quite active if the commissural ganglia from the CNS were left connected to the STG (*8*). In some experiments, the STG was isolated by cutting the "input" (stomatogastric) nerve (Fig. 1A), and the whole nerve was stimulated to drive command-fiber inputs to the STG (*9*). Identified neuron somata in the STG were impaled with double-barrel microelectrodes, or with two single electrodes, for conventional intracellular recording and current injection. It was essential to show that the evoked responses described here were due to the intrinsic properties of a neuron under study, rather than to synaptic network interactions. Given the known synaptic circuitry of the STG (see Figs. 1B and 2A), this was done by checking that responses were not associated with significant changes in the firing of any presynaptic neurons, monitored in extracellular nerve records. Also, presynaptic neurons were sometimes impaled and their firing directly controlled with intracellularly injected current to eliminate network interactions.

Our main finding is that many STG neurons have the capability of generating "plateau potentials": prolonged regenerative depolarizations resulting from intrinsic membrane properties and contributing to the production of bursts. Other examples of plateaus include the prolonged action potentials in heart muscle of vertebrates, and the spontaneous depolarizations in endogenously bursting neurons of crustaceans and mollusks (*10*). Such plateaus derive from a sustained negative-resistance characteristic of a cell's membrane. Several criteria were adapted from previous studies (*10*) to identify plateau-potential characteristics in STG neurons: (i) the occurrence of relatively large (for example, 5 to 20 mV) oscillations in membrane potential; (ii) the ability, when brief pulses of current are used (about 20 to 50 msec, 1 to 5 nA), to cause all-or-none transitions between a resting region of membrane potential and a more depolarized relatively stable (plateau) region of potential (*11*), at which a neuron typically fired impulses; (iii) the requirement for currents above a threshold intensity to cause transitions; and (iv) in certain cases, the production of bursts by a neuron when all the patterned synaptic input to it was abolished (*7, 12*).

Plateau characteristics are illustrated in Fig. 1 with the CP neuron (*13, 14*). During spontaneous gastric rhythms, the cell showed large oscillations of membrane potential with bursts of spikes occurring on the depolarized phases (Fig. 1C). Bursts were suppressed by a steady hyperpolarizing current, leaving smaller oscillations of membrane potential presumably due to synaptic input (Fig. 1D, left). A brief depolarizing current pulse then could trigger a response (burst) that outlasted and grew after the stimulus [that is, was regenerative; Fig. 1, D (right) and E]; a passive neuron would at most have fired only while the stimulus current was on. Once initiated, a response could be terminated by a brief hyperpolarizing pulse (Fig. 1F). Both the