

The consistent failure to find an effect of naloxone on experimental pain in humans suggests that endorphin release did not occur during these procedures. The failure in both experiments to find an effect of naloxone on tension-anxiety scores suggests that our previous positive finding may have been significant only by chance.

The naloxone doses administered in our studies were more than adequate to occupy the endorphin receptors. The 10-mg dose is 13 times higher than the largest dose used in the experiment of El-Sobky *et al.* (11), and also 25 times higher than the usual dose of naloxone used to arouse a comatose person suffering from an opiate overdose. Moreover, 0.2 mg of naloxone diminishes analgesia produced by electric brain stimulation (3), and a dose of 0.8 mg diminishes acupuncture analgesia (5). To elicit endorphin release, more painful and stressful stimuli may be necessary, such as the inescapable intermittent shocks used by Akil with rats (6) and the lengthy (2-minute) exposure of mice and rats to a hot plate as reported by Jacob (9), and replicated by us (10). In humans, this may require the study of pain and stress under more realistic conditions than obtain in the laboratory.

Note added in proof: A 1-hour delay was introduced following a naloxone (10 mg) or saline injection. Then a supplemental injection of naloxone (5 mg) or of saline was given, followed by the ischemic pain procedure exactly as described. Again naloxone had no significant effect on pain ratings or mood.

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Anosmia in Male Rhesus Monkeys Does Not Alter Copulatory Activity with Cycling Females

Abstract. Three adult male rhesus monkeys were tested daily with intact adult female partners over the course of four or five menstrual cycles. The males were made permanently anosmic by chemical ablation of the olfactory epithelium after the second or fourth cycle was completed. All males continued to display typical cycles of copulation with their partners after the anosmia procedures, with the shortest latencies to ejaculation occurring during the periovulatory phase of the partner's ovulatory cycle. Hence, female attractivity and cyclic copulatory performance of rhesus monkeys are not dependent upon olfactory signals.

When heterosexual pairs of rhesus monkeys are tested in the laboratory for sexual behavior throughout one or more complete menstrual cycles, males ejacu-

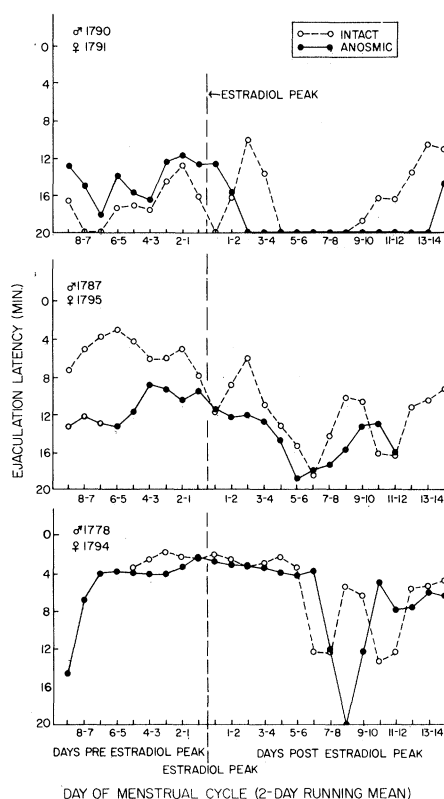


Fig. 1. Latency to first ejaculation during successive menstrual cycles of three rhesus pairs before and during peripheral anosmia of the males. Males 1790 and 1778 were made anosmic on the first menstrual day of their partners' cycle; male 1787, on the fifth day. Data are plotted relative to the estradiol peak (day 0) and are expressed as 2-day running means (the means for days 0 and 1, 1 and 2, 2 and 3, and so forth).

late most frequently and with the shortest latencies during the fertile, periovulatory phase of their partner's ovarian cycle (1). Under similar testing conditions, changes in sexual invitations or sexual refusals by the female have not been found to be so well correlated with changes in her hormonal state. Specifically, many females do not show obvious refusals of the male at any time in the cycle, and stimulation of invitational postures of the female by hormonal manipulations such as systemic or intracerebral implants of testosterone do not reliably increase copulatory probabilities (2). These observations have led some investigators to conclude that the clear behavioral cyclicity of the male when paired with an intact female is the result of his responding to nonbehavioral changes in the sexual attractiveness of the female, and that the quality of sexual attractiveness of the female rhesus monkey consists, at least in part, of olfactory cues emanating from the vagina (3). By such an interpretation, the male's cyclic sexual behavior is affected or produced by changes in the levels or characteristics of these cues. A critical test of the need for olfactory cues for the maintenance of cyclic sexual responding of male rhesus monkeys is to deprive the male of the ability to smell while paired with a cycling female. We report the results of such a study here, showing that copulatory performance and cyclicity in male sexual responses are maintained even though the male is anosmic.

Three vasectomized adult male and three intact adult female rhesus monkeys were obtained 9 months before the study directly from a semifree-ranging troop

maintained at the Carribean Regional Primate Research Center. Following quarantine procedures, the animals were housed in individual cages (males in a separate room from the females) and, over a 3-week period, were adapted to transport and observation cages and to the conditions of behavioral testing. Following 2 weeks of adaptation and compatibility tests, three heterosexual pairs were randomly formulated (no marked incompatibility of any male-female pair had been detected). Each pair was brought to a test room and allowed to interact for 20 minutes daily over the course of four to five successive menstrual cycles from February to June 1977. All tests were conducted from 9:30 to 11:30 a.m., 7 days per week, in a small observation cage (1.5 by 0.75 by 1.2 m) fitted with a one-way vision screen. The size of this cage prevents evaluation of several distance communication cues, since animals are brought into forced proximity, but it has been suggested that such a cage maximizes conditions under which olfactory communication might be detected (4). Behavioral data were collected by five observers operating in teams of two. An SSR event-recording keyboard (Semeiotic Systems Corp., Madison, Wisconsin) allowed the recording of incidence, duration, and sequence of target behaviors onto magnetic tape for subsequent computer analysis (5). Certain tests were also videotaped in order to establish interobserver reliability measures. Only data concerning the male's ejaculatory behavior are reported here.

The ablation procedure was performed early in the third or fifth complete menstrual cycle, cycle 3 day 1 (first day of menstruation of paired female) for male 1790, cycle 3 day 5 for male 1787, and cycle 5 day 1 for male 1778. Each male was anesthetized with ketamine (15 mg per kilogram of body weight), placed in an inverted position, and made permanently anosmic by applying sterile cotton pledgets (~1 cm long, 0.5 cm in diameter) saturated with 10 percent formalin bilaterally into direct contact with the olfactory epithelium for 10 to 12 minutes. The pledgets made contact with the epithelial surfaces covering the nasal septum, cribriform plate, and superior turbinates, which constitute the areas of olfactory sensory tissue in this species. Before placement, three to six drops of 1 percent Neo-Synephrine nose drops were applied to shrink the nasal tissues, and the pledgets were put in place with

Table 1. Mean percentage of tests with ejaculation and mean ejaculatory frequencies before and during anosmia. Data are given for two phases of the menstrual cycle, late follicular (days 3, 2, and 1 before the estradiol peak) and midluteal (days 6, 7, and 8 after the peak) and are for the same three pairs and same cycles shown in Fig. 1.

| Anosmia status | Tests with ejaculation (mean %) | Ejaculations per test (mean No.) |
|------------------------|---------------------------------|----------------------------------|
| <i>Late follicular</i> | | |
| Before | 100 | 1.6 |
| During | 100 | 1.7 |
| <i>Midluteal</i> | | |
| Before | 44 | 0.55 |
| During | 56 | 0.55 |

Hartman alligator forceps. The sudden and continued inability to perform an olfactory discrimination task that had been learned to criterion before the chemical ablation procedure confirmed that a completely anosmic condition had been achieved (6). Daily sexual testing continued without interruption for an additional one to two complete menstrual cycles. Blood samples were taken on selected days from each female and were assayed for estradiol using radioimmunoassay techniques (7) in order to determine the day of the preovulatory estradiol surge for each cycle studied.

Figure 1 displays the individual ejaculatory records of each of the three pairs of monkeys studied for the cycles immediately before and after chemical ablation of the olfactory epithelium of the males. Before ablation, each pair showed evidence of maximum or near maximum ejaculatory performance during the periovulatory phase of the cycle, and each pair showed a decrease in performance during luteal phases, typically followed by an improvement premenstrually. Each of these aspects of sexual responding remained after the males were made anosmic. Further, the data in Table 1 indicate that the percentage of tests with ejaculation as well as the frequency of ejaculation per test differed in late follicular compared to midluteal phases, and that anosmia had no influence on these differential outcomes. In the 7 days before the estradiol peak, the number of tests with ejaculation was the same—19 of 21 tests—for intact and anosmic cycles. Similarly, in the 7 days after the peak ejaculation occurred in 14 of 21 tests in each condition. Thus, the cyclic pattern of copulatory behavior displayed by all three males during anosmic sessions was extremely similar in

distribution and in temporal characteristics to their preablation performance. Two of the three males were studied for a second complete cycle following anosmia. Both males again displayed clear cyclicity. Also, we detected no obvious changes in the intensity, frequency, or duration of solicitation behaviors of the females following the induction of anosmia in the males, although complete analysis of the data for this question has not yet been undertaken.

While in no way inconsistent with the possibility that olfactory communication may play a role in the sexual behavior of this species, these data demonstrate that detection by the male of olfactory cues from the female is not a necessary condition either for the occurrence or for the cyclicity of copulatory behavior of the pair over the course of several ovulatory cycles.

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