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Inhibitory Centers in Sexual Behavior in the Male Rat

Abstract. *Small lesions placed near the diencephalic, mesencephalic junction, in either the lateral or medial mammillary region, resulted in an increase of copulatory behavior. This increase was expressed both by increased numbers of copulation plugs formed per 14-day interval and by increased percentage of days on which copulation occurred. Inhibitory structures thus form an essential part of the circuitry involved in mediation of sex behavior in the male.*

A number of reports indicate that deficiencies in mating behavior occur following destruction of localized regions of neurons within the diencephalon. There is general agreement that lesions in the preoptic or anterior hypothalamic area result in a decrease or abolition of overt sexual response in the male (*1, 2*). More posterior lesions involving the posterior hypothalamus and mammillary bodies have produced findings of loss of sex behavior (*2*) and findings of no change in sexual performance (*3*).

Reexamination of the problem of specific areas involved in overt sexual behavior was essential for two reasons. (i) The reported observations are in disagreement. (ii) Various studies in related "control systems" operating in the hypothalamus indicate that the results obtained could be a function of the metal material which was used in the electrode employed in making the lesion (*4*).

We observed the following effects presumably due to the destruction of discrete areas within the nervous system. Lesions in the mammillary region placed medially or laterally resulted in an increase in production of copulation plugs and in days on which copulation occurred (nine animals). Slightly smaller lesions in the same area (nine animals) resulted in an unchanged level of copulation following lesion. After lesions in the middle hypothalamus dorsal to the arcuate nucleus a gradual decline in copulatory level occurred. This decline in copulatory level paralleled a decline found in the control, unlesioned animals.

Rats are normally reared, from the time of weaning at 21 days of age, in groups segregated by sex. When a large mature male was caged with a single stimulus female for a period of 8 weeks, the peak of sexual activity usually occurred during the first 14-day interval. This was true when measured both as number of copulations per 14-day interval and the percentage of days on which copulation occurred. During the following 6-week period a gradual decline in total sexual activity was observed. This finding suggests that an adaptation occurs to the situation—that is, the constant presence of a stimulus female is no longer novel, so sex activity declines. Presumably if an experiment were extended over a sufficiently long time interval a steady state would eventually be established, which would represent the basic sex drive for a rat of a particular strain and age when caged with the same partner, who was in a constantly receptive state. Therefore it is important to realize that the control condition is not a steady state (Table 1*A*). A parallel decline in copulatory activity occurred following lesions in the dorsal area of the middle hypothalamus (Table 1*B*). The placement of lesions dorsal to the mammillary complex which extended into the habenula and overlying cortex also resulted in a similar decline in copulation (Table 1*C*). These observations are all in marked contrast to the mammillary lesions which resulted in a steady state or increasing levels of copulatory output (Table 1*D*). This strongly suggests that the dorsal medial hypothalamus is not important for the mediation or maintenance of copulatory behavior. Similarly, those structures dorsal to the mammillary area, including structures in and around the habenula, appear to be unessential for sexual behavior in the male; in contrast, the diencephalic mesencephalic juncture at the level of the mammillary bodies does contain structures which appear to exert an inhibitory control on the level of copulatory behavior. The overt sexual behavior expressed must therefore depend on the balance of activity between an integrative and activational (facilitory) system likely localized in the preoptic and anterior hypothalamic regions and a regulatory (inhibitory) system located in the region of the mammillary bodies.

Large males of the CFE strain (*5*) with a body weight of 370 to 410 g at the beginning of the experiment were used. The actual subjects were chosen by the criterion of having shown a minimum of 4 nights of mating during the original 14-day observation period. All animals were kept one pair per cage; thus the male had free access to a receptive female at all times. Receptivity of the female was assured by subcutaneous placement of two blobs

Table 1. Copulatory records for males, showing successive 14-day totals for copulation plugs and, in parentheses, percentages of nights on which copulation ocurred.

Control, 14 Days	Days 1–14	Days 15–28	Days 29–42	Days 43–57
	A. Control males (no lesion)			
	9(29)	5(29)	5(21)	7(21)
	11(36)	8(29)	10(29)	6(23)
	17(57)	17(50)	14(36)	10(38)
	7(36)	8(43)	6(29)	4(31)
	12(43)	13(43)	10(29)	12(54)
	13(64)	7(43)	5(14)	2(8)
	10(36)	7(21)	4(7)	2(8)
	17(57)	5(21)	2(14)	9(36)
	B. Males with lesions in middle hypothalamus			
10(36)	10(36)	5(21)	4(27)	
11(50)	9(29)	3(7)	4(18)	
15(71)	7(43)	8(29)	8(36)	
15(36)	6(21)	7(36)	8(36)	
10(29)	7(29)	4(21)	8(18)	
11(43)	15(57)	9(43)	8(18)	
15(57)	6(21)	5(21)	7(36)	
11(50)	7(43)	10(50)	5(36)	
6(29)	0(0)	3(7)	0(0)	
18(64)	21(93)	8(36)	6(36)	
	C. Males with lesions in habenula and overlying cortex			
11(50)	8(43)	3(14)	2(14)	
6(29)	3(14)	7(36)	15(50)	
16(50)	12(43)	16(43)	11(43)	
15(64)	8(43)	9(36)	0(0)	
12(43)	7(36)	6(29)	4(14)	
15(54)	7(29)	16(71)	10(57)	
11(46)	4(14)	0(0)	0(0)	
10(39)	13(36)	17(43)	13(57)	
16(46)	15(57)	10(21)	9(29)	
14(46)	15(57)	13(50)	5(21)	
	D. Males with mammillary lesions			
6(29)	3(21)	11(64)	16(64)	
14(36)	12(50)	11(50)	26(86)	
8(36)	19(79)	25(86)	25(93)	
11(36)	18(43)	12(50)	10(43)	
4(29)	12(43)	9(43)	12(36)	
7(29)	9(50)	10(43)	11(46)	
11(50)	14(43)	19(79)	18(64)	
13(67)	19(79)	12(43)	11(50)	
6(29)	15(57)	19(57)	17(77)	

of estradiol fused on stainless steel rods. One of these was placed in the pectoral region, the other under the scruff of the neck. This procedure, we find, produces a female whose receptivity remains constant over many months (*6*). The rats were maintained in cages with large-mesh flooring (12 mm) so all droppings would immediately fall through onto a paper-covered tray below. Every morning between 8:30 and 10:00 a.m. a record was made of the number of copulation plugs lying on the paper. These data were used to calculate the number of copulations and the percentage of days on which copulations occurred.

Following a 2-week control period lesions were made with platinum electrodes 0.36 mm in diameter (28 gauge), with the insulation cleared from about 0.5 mm at the tip. With the Grass S-4 stimulator a direct current of 1 ma (anodal) was applied for 15 seconds; the cathode was a large metal rod placed in the anus. The coordinates used were those of the de Groot (*7*) atlas, with the middle hypothalamic lesions made at A 6.0 and 5.6, midline and depth −3.0 mm. The mammillary lesions were made at A 4.2, midline and depth −4.0 mm; for the lateral lesions the same coordinates were used, except that they were 1.5 mm on either side of the midline. All lateral lesions were made bilaterally.

These findings clearly do not support the workers who found cessation of sexual activity following mammillary lesions. They are in agreement with those who found no change in sexual behavior following mammillary lesions. One report has appeared which indicated that fairly large lesions at the junction of the diencephalon and mesencephalon can result in changes in the behavior pattern making up a complete copulatory sequence (*8*). Following such lesions about 50 percent of the animals showed a decreased number of intromissions to ejaculation and a shortened latency period between an ejaculation and the beginning of the next copulatory sequence. Thus in a 30-minute test period the animals ejaculated a greater number of times than the controls. These changes were found to be stable during 2 to 6 months of testing. Similarly, for the female there is a report that lesions in the premammillary region resulted in five of six animals mating at diestrus (*9*).

In the two studies reported above iron-bearing electrodes were used; thus they might be open to interpretation from the standpoint that the results were dependent upon irritative foci set up by deposits of metal salts in the brain, especially in light of the fact that Everett and Radford got ovulation only when stimuli were passed through iron-bearing electrodes, and then only when a certain mass of nervous tissue had been affected by the iron deposits. Similar stimulation with platinum electrodes failed to produce ovulation (*4*).

Our study was made with platinum electrodes to obviate the possible problems inherent due to the possibilities of chronic stimulation resulting from metal deposits in the brain. Using the platinum electrode, we were able to produce striking changes in total sex behavior in the male as the result of placing small lesions in the mammillary bodies.

Therefore inhibitory structures important in regulation of the occurrence and frequency of sexual behavior must be assumed to exist in the mammillary body region in the male rat. In the male, lesions in the mammillary region lead to increased total copulatory performance, while in the female lesions in the mammillary region result in a release of overt sex behavior from the controlling influence of the hormonal milieu as expressed in the normal estrous cycle.

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6. Constant behavioral estrus can be maintained over long time intervals in the female rat via appropriate implants of a solid ball of estradiol fused to the end of 27-gauge hypodermic tubing. In some experiments a single estradiol implant was made via stereotaxic methods, the hormone being placed in the anterior hypothalamus. Subsequently we found two such implants placed subcutaneously were equally effective in maintaining the female in a constantly receptive state over a few months. Castration was not performed before placement of the estradiol implants.
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Neutron-Activation Analysis

Schroeder, Kraner, Evans, and Brydges [*Science* **151**, 815 (1966)] describe the use of lithium-drifted germanium detectors for neutron-activation analysis when destruction of the specimens must be avoided. I wish to suggest a rather obvious modification of the technique, not mentioned by the authors or elsewhere so far as I am aware.

The results reported pertain to irradiation by the whole neutron spectrum of the particular reactor used, in this case primarily a thermal neutron spectrum with a higher-energy tail. It is noted that the presence of Na may make observations of elements with similar half-life difficult, but that, in general, the data from the presence of elements with dissimilar half-lives can be enhanced or suppressed by choice of irradiation time. What is not mentioned is that this can also be done by spectral modification of the neutron flux. The modification consists in suppressing the number of neutrons in a given energy region of the spectrum—the region responsible for the activation. This can be done by surrounding the specimen by a suitable absorber of "Dagwood sandwich" of absorbers or by making a suitable geometry for the use of materials which selectively scatter neutrons away from the sample so that those impinging on it have the desired spectrum. The first method uses only the dependence of absorption cross section on neutron energy and the second uses the total cross section. The simplest arrangement is to use the element which it is desired to suppress. However, there are so many resonances among the many stable nuclides, and overlapping ones, that a large number of possibilities exists. Sometimes one may wish to employ a different primary spectrum by using a different reactor.

The suppression of Na is probably not the easiest case, though certainly some gain can be achieved by a scattering-out arrangement, for Na is a weak absorber. Undoubtedly, the bulk of activation occurs in the $1/v$ region for practically all nuclei, so one would wish strong filtering in this region with ^{10}B or ^{3}He in order to take advantage of the more selective spectral modification of the resonance region. Whenever the activation results from resonance capture, it should be possible to suppreess it almost wholly by filter-